

Medical Research Abstracts on Astaxanthin

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Note to the third edition, October 2021: For ease in finding the latest research, studies published over the last two and a half years have a summary on the top of the page in **BOLDED CAPITAL LETTERS**.

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Introduction

A wealth of research has been done on Astaxanthin showing far-ranging health benefits. As you'll soon see, the body of medical research on Astaxanthin has reached critical mass for many of its health benefits. Over the last several years, the volume of studies done by universities, governmental agencies and private researchers around the world has increased rapidly.

This document is designed to allow our Readers to easily explore this research which has been conveniently separated into the various categories of Astaxanthin's health benefits. There are ten areas of benefits for Astaxanthin which contain substantial human clinical research (a minimum of five human clinical trials in each area); these are listed in their own, individual chapters. They include far ranging benefits such as anti-aging, eye & brain health, cardiovascular health, anti-inflammatory benefits, skin health and applications for athletes. The next chapter, "Emerging Areas of *Mostly Pre-Clinical* Astaxanthin Research," contains a vast amount of additional research in areas that currently consist mostly of pre-clinical trials, with a few preliminary human clinical trials spread throughout. However, it's important to note that within this final chapter, there are some health benefits that have a very impressive amount of research, even though minimal or no human studies have been undertaken to date. For example, there have been dozens and dozens of rodent studies showing benefits for cancer prevention and tumor reduction. Yet, we feel that these studies should be isolated since we cannot relate this research directly to potential health benefits in humans.

The list begins with a review of Astaxanthin's antioxidant and anti-inflammatory benefits. Astaxanthin has been shown in many different head-to-head antioxidant experiments against other well-known antioxidants to be the world's strongest natural antioxidant, usually by at least a factor of 10 times stronger and up to 6000 times. Amazingly, many of these experiments were done against antioxidants in the same carotenoid family as Astaxanthin itself. Astaxanthin has also been shown to be a safe and natural, broad-spectrum anti-inflammatory, effective at controlling several different inflammatory markers. The reason that we have placed the antioxidant and anti-inflammatory chapters first is that these two benefits are the primary foundation from which all of Astaxanthin's other health benefits emanate.

This document is distributed by BGG World and its subsidiary, Algae Health Sciences (a leading producer of Natural Astaxanthin from *Haematococcus pluvialis* microalgae). Algae Health Sciences is proud to produce the world's purest Natural Astaxanthin with 97% levels of Pure Astaxanthin in our carotenoid fraction and without measurable levels of contaminants. BGG World also provides white papers and a comprehensive book on the various health benefits of Astaxanthin with detailed information in an easy-to-read format that both scientists as well as non-scientists usually find quite useful. For copies of these white papers, an electronic copy of our Astaxanthin book, or any other questions, please contact BGG World by e-mail at support@bggworld.com. (For a list of contact information for BGG World's offices in Switzerland, Japan and China, please visit us at www.bggworld.com/contact/)

Antioxidant

Astaxanthin supplementation improves oxidative stress markers in soccer players in randomized, double-blind, placebo-controlled human clinical study.

[Phytother Res.](#) 2013 Oct;27(10):1536-42. doi: 10.1002/ptr.4898. Epub 2012 Nov 28.

Effect of astaxanthin supplementation on paraoxonase 1 activities and oxidative stress status in young soccer players.

[Baralic I¹](#), [Djordjevic B](#), [Dikic N](#), [Kotur-Stevuljevic J](#), [Spasic S](#), [Jelic-Ivanovic Z](#), [Radivojevic N](#), [Andjelkovic M](#), [Pejic S](#).

Author information

Abstract

The purpose of the study was to examine the effects of astaxanthin (Asx) on paraoxonase (PON1) activities and oxidative stress status in soccer players. Forty soccer players were randomly assigned in a double-blind fashion to Asx and placebo (P) group. Blood samples were obtained before, 45 and 90 days after supplementation. PON1 activity was assessed by using two substrates: paraoxon and diazoxon. The oxidative stress biomarkers were also examined: total sulphhydryl group content (-SH groups), thiobarbituric acid-reactive substances (TBARS), advanced oxidation protein products and redox balance. The significant interaction effect of supplementation and training ($p < 0.05$) on PON1 activity toward paraoxon was observed. The PON1 activity toward diazoxon increased in Asx group after 90 days ($p < 0.01$), while there was no significant difference in P group. SH groups content rose from pre- to post-supplementation period only in Asx group (supplementation and training, $p < 0.05$; training, $p < 0.01$). TBARS levels decreased after 45 days and increased after 90 days of regular soccer training in both groups (training, $p < 0.001$). Redox balance decreased significantly in response to the regular training, regardless of treatment group (training, $p < 0.001$). Asx supplementation might increase total SH groups content and improve PON1 activity through protection of free thiol groups against oxidative modification.

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KEYWORDS:

astaxanthin; oxidative stress; paraoxonase 1 activity; soccer

PMID:

23192897

[PubMed - indexed for MEDLINE]

ASTAXANTHIN DECREASES LEVELS OF OXIDATIVE STRESS MARKER MALONDIALDEHYDE AND INFLAMMATORY CYTOKINE INTERLEUKIN-6 IN PATIENTS WITH TYPE-2 DIABETES IN RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED HUMAN CLINICAL TRIAL.

Int J Clin Pract. 2021 May;75(5):e14022.

doi: 10.1111/ijcp.14022. Epub 2021 Feb 2.

The antioxidant and anti-inflammatory effects of astaxanthin supplementation on the expression of miR-146a and miR-126 in patients with type 2 diabetes mellitus: A randomised, double-blind, placebo-controlled clinical trial

[Nafiseh Shokri-Mashhadi^{1,2}](#), [Maryam Tahmasebi^{3,4}](#), [Javad Mohammadi-Asl⁵](#), [Mehrnoosh Zakerkish⁶](#), [Majid Mohammadshahi²](#)

- PMID: 33445213 DOI: [10.1111/ijcp.14022](https://doi.org/10.1111/ijcp.14022)

Abstract

Background: The pathogenesis of type 2 diabetes mellitus (T2DM) is associated with chronic oxidative stress and inflammation. It is well known that the expression of some miRNAs such as miRNA-146a is upregulated in diabetic and hyperglycaemic patients, whereas circulating miRNA-126 is reduced. Therefore, we aimed to determine the effects of astaxanthin (AST) supplementation on the circulating malondialdehyde (MDA) and interleukin 6 (IL-6) levels, and the expression of miR-146a and miR-126 in patients with T2DM.

Methods: This randomised, double-blind, placebo-controlled clinical trial was conducted in 44 patients with T2DM randomly receiving 8 mg/d of oral AST (n = 22) or placebo (n = 22) for 8 weeks.

Results: We observed that AST supplementation could decrease plasma levels of MDA and IL-6 (P < .05) and decrease the expression level of miR-146a over time (fold change: -1/388) (P < .05).

Conclusion: AST supplementation might be beneficial for improving circulating MDA and IL-6 and the down-regulation of miR-146a. However, future investigations are suggested to confirm these results.

Astaxanthin increases oxygen scavenging activity and decreases peroxide production in human clinical trial.

[J Clin Biochem Nutr.](#) 2016 Jul;59(1):10-5. doi: 10.3164/jcbn.15-137. Epub 2016 May 21.

The effect of astaxanthin on vascular endothelial growth factor (VEGF) levels and peroxidation reactions in the aqueous humor.

[Hashimoto H¹](#), [Arai K²](#), [Hayashi S³](#), [Okamoto H⁴](#), [Takahashi J⁵](#), [Chikuda M²](#).

Author information

Abstract

We explored the effect of astaxanthin on vascular endothelial growth factor in the aqueous humor, by measuring vascular endothelial growth factor levels and oxidation-related parameters, including O₂ (•-) scavenging activity, H₂O₂ level, and total hydroperoxide level in the aqueous humor, obtained from 35 patients before and after astaxanthin administration. We evaluated the relationship between vascular endothelial growth factor and the oxidation-related parameters as well as the patient's diabetic status, age, and sex. Vascular endothelial growth factor levels did not change significantly but O₂ (•-) scavenging activity and total hydroperoxide level significantly ($p < 0.05$) increased and decreased, respectively. Both pre- and post- astaxanthin intake, vascular endothelial growth factor and total hydroperoxide levels were positively correlated (Pearson: $r = 0.42$, $p < 0.05$; $r = 0.55$, $p < 0.01$, respectively). Analysis of vascular endothelial growth factor levels and O₂ (•-) scavenging activities gave a negative correlation but only pre-astaxanthin intake ($r = -0.37$, $p < 0.05$). Differences in levels pre- and post-astaxanthin only showed association between vascular endothelial growth factor and total hydroperoxide ($r = 0.49$, $p < 0.01$) analyzed by multiple linear regression. Using multivariate analysis, pre-astaxanthin vascular endothelial growth factor level was associated with two factors of total hydroperoxide and O₂ (•-) scavenging activity ($r = 0.49$, $p < 0.05$), and post-astaxanthin vascular endothelial growth factor level with two factors of total hydroperoxide and sex ($r = 0.60$, $p < 0.01$). Astaxanthin intake may have affected vascular endothelial growth factor level through its antioxidant effects by increasing O₂ (•-) scavenging activity and suppressing peroxide production.

KEYWORDS: aqueous humor; astaxanthin; oxidation; superoxide; vascular endothelial growth factor

PMID: 27499573

PMCID: [PMC4933686](#)

DOI: [10.3164/jcbn.15-137](#)

[Free PMC Article](#)

Astaxanthin improves oxidative stress markers in healthy smokers in randomized placebo-controlled human clinical study and may be suitable as a supplement to prevent oxidative damage in smokers by suppressing lipid peroxidation and stimulating the activity of the antioxidant system.

[J Med Food](#). 2011 Nov;14(11):1469-75. doi: 10.1089/jmf.2011.1626. Epub 2011 Sep 1.

Protective effects of Haematococcus astaxanthin on oxidative stress in healthy smokers.

[Kim JH¹](#), [Chang MJ](#), [Choi HD](#), [Youn YK](#), [Kim JT](#), [Oh JM](#), [Shin WG](#).

Author information

Abstract

Free radicals induced by cigarette smoking have been strongly linked to increased oxidative stress in vivo, contributing to the pathobiology of various diseases. This study was performed to investigate the effects of Haematococcus astaxanthin (ASX), which has been known to be a potent antioxidant, on oxidative stress in smokers. Thirty-nine heavy smokers (≥ 20 cigarettes/day) and 39 non-smokers were enrolled in this study. Smokers were randomly divided into three dosage groups to receive ASX at doses of 5, 20, or 40 mg (n=13, each) once daily for 3 weeks. Oxidative stress biomarkers such as malondialdehyde, isoprostane, superoxide dismutase, and total antioxidant capacity, and ASX levels in plasma were measured at baseline and after 1, 2, and 3 weeks of treatment. Compared with baseline, the plasma malondialdehyde and isoprostane levels decreased, whereas superoxide dismutase level and total antioxidant capacity increased in all ASX intervention groups over the 3-week period. In particular, isoprostane levels showed a significant dose-dependent decrease after ASX intake. The results suggest that ASX supplementation might prevent oxidative damage in smokers by suppressing lipid peroxidation and stimulating the activity of the antioxidant system in smokers.

PMID:

21883001

[PubMed - indexed for MEDLINE]

ASTAXANTHIN IMPROVED EXERCISE TOLERANCE; REDUCED OXIDATIVE STRESS; AND IMPROVED CARDIAC CONTRACTILITY IN HEART FAILURE PATIENTS IN HUMAN CLINICAL STUDY.

Nutrients. 2020 Jun 26;12(6):1896.

doi: 10.3390/nu12061896.

Effects of 3-Month Astaxanthin Supplementation on Cardiac Function in Heart Failure Patients with Left Ventricular Systolic Dysfunction-A Pilot Study

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PMID: [32604721](#) PMCID: [PMC7353230](#) DOI: [10.3390/nu12061896](#)

Abstract

Astaxanthin has strong antioxidant properties. We conducted a prospective pilot study on heart failure (HF) patients with left ventricular (LV) systolic dysfunction to investigate improvements in cardiac function and exercise tolerance in relation to suppression of oxidative stress by 3-month astaxanthin supplementation. Oxidative stress markers-serum Diacron reactive oxygen metabolite (dROM), biological antioxidant potential (BAP), and urinary 8-hydroxy-2'-deoxyguanosine (8-OHdG) concentrations, LV ejection fraction (LVEF), and 6-min walk distance (6MWD) were assessed before and after 3-month astaxanthin supplementation. Finally, the data of 16 HF patients were analyzed. Following 3-month astaxanthin supplementation, dROM level decreased from 385.6 ± 82.6 U.CARR to 346.5 ± 56.9 U.CARR ($p = 0.041$) despite no changes in BAP and urinary 8-OHdG levels. LVEF increased from $34.1 \pm 8.6\%$ to $38.0 \pm 10.0\%$ ($p = 0.031$) and 6MWD increased from 393.4 ± 95.9 m to 432.8 ± 93.3 m ($p = 0.023$). Significant relationships were observed between percent changes in dROM level and those in LVEF. In this study, following 3-month astaxanthin supplementation, suppressed oxidative stress and improved cardiac contractility and exercise tolerance were observed in HF patients with LV systolic dysfunction. Correlation between suppression of oxidative stress and improvement of cardiac contractility suggests that suppression of oxidative stress by astaxanthin supplementation had therapeutic potential to improve cardiac functioning.

Astaxanthin shows potential benefits for blood lipid peroxidation in healthy men in double-blind, placebo-controlled randomized human clinical trial.

[Int J Vitam Nutr Res.](#) 2007 Jan;77(1):3-11.

Effects of astaxanthin supplementation on lipid peroxidation.

[Karppi J¹](#), [Rissanen TH](#), [Nyyssönen K](#), [Kaikkonen J](#), [Olsson AG](#), [Voutilainen S](#), [Salonen JT](#).

Author information

Abstract

Astaxanthin, the main carotenoid pigment in aquatic animals, has greater antioxidant activity in vitro (protecting against lipid peroxidation) and a more polar configuration than other carotenoids. We investigated the effect of three-month astaxanthin supplementation on lipid peroxidation in healthy non-smoking Finnish men, aged 19-33 years by using a randomized double-blind study design. Also absorption of astaxanthin from capsules into bloodstream and its safety were evaluated. The intervention group received two 4-mg astaxanthin (Astaxin) capsules daily, and the control group two identical-looking placebo capsules. Astaxanthin supplementation elevated plasma astaxanthin levels to 0.032 pmol/L ($p < 0.001$ for the change compared with the placebo group). We observed that levels of plasma 12- and 15-hydroxy fatty acids were reduced statistically significantly in the astaxanthin group ($p = 0.048$ and $p = 0.047$ respectively) during supplementation, but not in the placebo group and the change of 15-hydroxy fatty acid was almost significantly greater ($p = 0.056$) in the astaxanthin group, as compared with the placebo group. The present study suggests that intestinal absorption of astaxanthin delivered as capsules is adequate, and well tolerated. Supplementation with astaxanthin may decrease in vivo oxidation of fatty acids in healthy men.

PMID:

17685090

[PubMed - indexed for MEDLINE]

Astaxanthin decreases blood pressure and improves oxidative stress in human clinical trial.

Anti-Aging Med

Anti-Aging Med 6(4), 15-21, 2009

Japanese Society of Anti-Aging Medicine

Efficacy and safety of eight-week treatment with astaxanthin in individuals screened for increased oxidative stress burden

- [Iwabayashi Masaaki](#), [Fujioka Noriko](#), [Nomoto Keitaro](#), [Miyazaki Ryo](#), [Takahashi Hozumi](#), [Hibino Sawako](#), [Takahashi Yoko](#), [Nishikawa Koji](#), [Nishida Mitsunori](#), [Yonei Yoshikazu](#),
- Abstract

Objective: An open-label noncontrolled study was conducted in subjects with increased oxidative stress burden to evaluate the mental and physical effects of antioxidant astaxanthin. Methods: Of 35 healthy postmenopausal women, 21 with high oxidative stress (diacron-reactive oxygen metabolites; d-ROM) were selected, and 20 (55.7±4.8 years old, BMI 22.1±3.9) were included in the study, after excluding 1 dropout. In subjects orally treated with astaxanthin (Fuji Chemical Industry) at a daily dose of 12 mg for eight weeks, Anti-Aging QOL Common Questionnaire, somatometry, hematological examination/urinalysis, oxidative stress test, and vascular function tests (cardio ankle vascular index, CAVI; ankle brachial pressure index, ABI; fingertip acceleration pulse wave; flow-mediated dilation FMD) were performed before and four and eight weeks after the start of the study. Results: After eight-week treatment with astaxanthin, significant improvement was observed in 5 of 34 physical symptoms listed in the common questionnaire, including "tired eyes", "stiff shoulders", "constipation", "gray hair", and "cold skin", and in 3 of 21 mental symptoms, including "daily life is not enjoyable", "difficulty in falling asleep", and "a sense of tension". In addition, systolic (118.0±16.4 mmHg at baseline, -4.6%, p=0.021) and diastolic blood pressure (74.1±11.7 mmHg at baseline, -6.9%, p<0.001) significantly decreased. In the vascular function test, CAVI, fingertip acceleration pulse wave, and FMD did not change, but ABI significantly increased from 1.06±0.10 at baseline to 1.10±0.06 at Week 8 (+3.7%, p=0.030). In the oxidative stress test, d-ROM did not change, but BAP significantly increased (+4.6%, p=0.030). In biochemical examination, AST (-19.2%, p=0.044), LDH (-6.4%, p=0.006), and HbA1c (-3.2%, p<0.001) significantly improved. Although IGF-I and insulin did not change, DHEA-s (-15.1%, p<0.001), cortisol (-22.8%, p=0.002), and adiponectin (-14.1%, p=0.003) decreased. No serious adverse event occurred during or after the study. Conclusion: Results show that astaxanthin may enhance antioxidant capacity (increase BAP), reduce lower limb vascular resistance (increase ABI), decrease blood pressure, and improve physical symptoms in women with high oxidative stress.

Astaxanthin added to dark chocolate decreases oxidative stress in aging volunteers in randomized, placebo-controlled human clinical study.

[J Nutr Health Aging.](#) 2018;22(9):1092-1098. doi: 10.1007/s12603-018-1063-z.

Markers of Hypoxia and Oxidative Stress in Aging Volunteers Ingesting Licosomal Formulation of Dark Chocolate Containing Astaxanthin.

[Petyaev IM¹](#), [Klochkov VA](#), [Chalyk NE](#), [Pristensky DV](#), [Chernyshova MP](#), [Kyle NH](#), [Bashmakov YK](#).

Author information

Abstract

OBJECTIVE: To determine if ingestion of licosome-formulated dark chocolate (DC) containing astaxanthin (ASTX) improves bioavailability of ASTX and affects markers of hypoxia and oxidative stress in aging individuals.

DESIGN: Randomized, blinded, four-arm, prospective study.

SETTINGS: Lycotec Ltd, Cambridge, United Kingdom and Institute of Cardiology, Saratov, Russian Federation.

PARTICIPANTS: 32 healthy individuals aged 60-70 years with confirmed signs of oxidative stress (increased serum levels of oxidized LDL and malonic dialdehyde) randomized into four study groups (8 volunteers each).

INTERVENTION: Volunteers of first group were given orally 10 gr of dark chocolate (DC). Individuals from the second group received 7 mg of astaxanthin (ASTX). Third group of volunteers was supplemented with 10 gr of DC and 7 mg of ASTX ingested simultaneously as two separate formulations. Last group of the individuals was given 10 gr of a licosomal formulation of DC containing 7 mg of co-crystalized ASTX (L-DC-ASTX), a newly developed highly bioavailable nutraceutical composition of DC containing 2 groups of antioxidants (cocoa flavanols and ASTX). All formulations were given orally, once daily for a month.

MEASUREMENTS: Serum ASTX was measured by high-performance liquid chromatography. Nitric oxide, malonic dialdehyde and oxidized LDL were quantified spectrophotometrically. Oxygenation parameters were evaluated by near-infrared spectroscopy.

RESULTS: One month ingestion of singular formulation of ASTX lead to a 20 fold buildup in serum ASTX level whereas the 4 week ingestion of L-DC-ASTX formulation was accompanied by more prominent accumulation of ASTX in serum (a 40 fold increase over the basal values) at the same daily dose of ASTX. Both antioxidants taken separately decreased serum levels of oxidized LDL and malonic dialdehyde. However effect of L-DC-ASTX formulation was more prominent. ASTX ingested alone caused a borderline increase ($p=0.054$) in serum nitric oxide (NO) levels, whereas

DC ingestion lead to small but statistically significant increase in serum NO concentration. Higher values of NO level were seen after co-ingestion of DC and ASTX, especially in case of L-DC-ASTX formulation suggesting additive/synergistic effects of DC and ASTX on nitric oxide production.

These changes were in agreement with the increase in plasma oxygen transport and tissue oxygen saturation seen in the volunteers supplemented with L-DC-ASTX formulation.

CONCLUSION: The nutraceutical formulation of DC and ASTX with an enhanced bioavailability of ASTX can be efficiently used for the correction of oxidative status in aging individuals.

KEYWORDS:

Dark chocolate; astaxanthin; nitric oxide; oxidized LDL

PMID: 30379308

DOI: [10.1007/s12603-018-1063-z](https://doi.org/10.1007/s12603-018-1063-z)

ASTAXANTHIN-CONTAINING FORMULA INCREASES RESTING OXYGEN CONSUMPTION; DECREASES OXIDATION MARKER AFTER EXERCISE; AND INCREASES MAXIMAL VOLUNTARY CONTRACTION, LEADING TO CONCLUSION THAT THE FORMULA SUPPORTS RESISTANCE TRAINING-INDUCED STRENGTH AND METABOLIC APPLICATIONS IN HUMAN CLINICAL TRIAL.

Antioxidants (Basel). 2021 Jan 14;10(1):113.
doi: 10.3390/antiox10010113.

Astaxanthin-, β -Carotene-, and Resveratrol-Rich Foods Support Resistance Training-Induced Adaptation

[Aki Kawamura](#)^{1,2}, [Wataru Aoi](#)¹, [Ryo Abe](#)^{1,3}, [Yukiko Kobayashi](#)¹, [Masashi Kuwahata](#)¹, [Akane Higashi](#)¹

PMID: 33466842 PMCID: [PMC7830030](#) DOI: [10.3390/antiox10010113](#) **Free PMC article**

Abstract

Resistance training adaptively increases the muscle strength associated with protein anabolism. Previously, we showed that the combined intake of astaxanthin, β -carotene, and resveratrol can accelerate protein anabolism in the skeletal muscle of mice. The purpose of this study was to investigate the effect of anabolic nutrient-rich foods on muscle adaptation induced by resistance training. Twenty-six healthy men were divided into control and intervention groups. All participants underwent a resistance training program twice a week for 10 weeks. Astaxanthin-, β -carotene-, and resveratrol-rich foods were provided to the intervention group. Body composition, nutrient intake, maximal voluntary contraction of leg extension, oxygen consumption, and serum carbonylated protein level were measured before and after training. The skeletal muscle mass was higher after training than before training in both groups ($p < 0.05$). Maximal voluntary contraction was increased after training in the intervention group ($p < 0.05$), but not significantly increased in the control group. Resting oxygen consumption was higher after training in the intervention group only ($p < 0.05$). As an oxidative stress marker, serum carbonylated protein level tended to be lower immediately after exercise than before exercise in the intervention group only ($p = 0.056$). Intake of astaxanthin-, β -carotene-, and resveratrol-rich foods supported resistance training-induced strength and metabolic adaptations.

Astaxanthin shows positive effects on sperm parameters and fertility and reduces reactive oxygen species in double-blind, placebo-controlled randomized human clinical trial.

[Asian J Androl.](#) 2005 Sep;7(3):257-62.

Combined conventional/antioxidant "Astaxanthin" treatment for male infertility: a double blind, randomized trial.

[Comhaire FH¹](#), [El Garem Y](#), [Mahmoud A](#), [Eertmans F](#), [Schoonjans F](#).

Author information

Abstract

AIM:

To evaluate the treatment of male infertility with a strong natural antioxidant, in addition to conventional treatment.

METHODS:

Using a double blind, randomized trial design, 30 men with infertility of > or =2 months and female partners with no demonstrable cause of infertility received conventional treatment according to the guidelines of the World Health Organization (WHO), and either a strong antioxidant Astaxanthin 16 mg/day (AstaCarox, AstaReal AB, Gustavsberg, Sweden) or placebo for 3 months. The effects of treatment on semen parameters, reactive oxygen species (ROS), zona-free hamster oocyte test, serum hormones including testosterone, luteinizing hormone (LH), follicle stimulating hormone (FSH) and Inhibin B, and spontaneous or intrauterine insemination (IUI)-induced pregnancies were evaluated.

RESULTS:

ROS and Inhibin B decreased significantly and sperm linear velocity increased in the Astaxanthin group (n = 11), but not in the placebo group (n = 19). The results of the zona-free hamster oocyte test tended to improve in the Astaxanthin group in contrast with the placebo group, though not reaching statistical significance. The total and per cycle pregnancy rates among the placebo cases (10.5 % and 3.6 %) were lower compared with 54.5 % and 23.1 % respectively in the Astaxanthin group (P = 0.028; P = 0.036).

CONCLUSION:

Although the present study suggests a positive effect of Astaxanthin on sperm parameters and fertility, the results need to be confirmed in a larger trial before recommending Astaxanthin for the complementary treatment of infertile men.

PMID:

16110353

[PubMed - indexed for MEDLINE]

Free full text

Astaxanthin dose-dependently prolongs the oxidation lag time in-vitro and inhibits low-density lipoprotein oxidation in a human clinical trial leading to the conclusion that it may contribute to the prevention of atherosclerosis.

[J Atheroscler Thromb.](#) 2000;7(4):216-22.

Inhibition of low-density lipoprotein oxidation by astaxanthin.

[Iwamoto T](#)¹, [Hosoda K](#), [Hirano R](#), [Kurata H](#), [Matsumoto A](#), [Miki W](#), [Kamiyama M](#), [Itakura H](#), [Yamamoto S](#), [Kondo K](#).

[Author information](#)

Abstract

Marine animals produce astaxanthin which is a carotenoid and antioxidant. In this study we determined the in vitro and ex vivo effects of astaxanthin on LDL oxidation. The oxidation of LDL was measured in a 1 ml reaction system consisting of increasing concentrations of astaxanthin (12.5, 25.0, 50.0 microg/ml), 400 microM V-70 (2, 2'-azobis(4-methoxy-2, 4-dimethylvaleronitrile)), and LDL (70 microg/ml protein). Astaxanthin dose, dependently significantly prolonged the oxidation lag time (31.5, 45.4, 65.0 min) compared with the control (19.9 min). For the ex vivo study 24 volunteers (mean age 28.2 [SD 7.8] years) consumed astaxanthin at doses of 1.8, 3.6, 14.4 and 21.6 mg per day for 14 days. No other changes were made in the diet. Fasting venous blood samples were taken at days 0, +14. LDL lag time was longer (5.0, 26.2, 42.3 and 30.7% respectively) compared with day 0 after consuming astaxanthin at doses of 1.8, 3.6, 14.4 and 21.6 mg for 14 days compared with day 0, but there was no difference in oxidation of LDL between day 0 (lag time 59.9+/-7.2 min) and day 14 (57.2+/-6.0 min) in the control group. Our results provide evidence that consumption of marine animals producing astaxanthin inhibits LDL oxidation and possibly therefore contributes to the prevention of atherosclerosis.

PMID:

11521685

[PubMed - indexed for MEDLINE]

Astaxanthin improves LDL cholesterol levels, ApoB and oxidative stress biomarkers in overweight subjects in double-blind, placebo-controlled randomized human clinical study.

[Plant Foods Hum Nutr.](#) 2011 Nov;66(4):363-9. doi: 10.1007/s11130-011-0258-9.

Positive effects of astaxanthin on lipid profiles and oxidative stress in overweight subjects.

[Choi HD¹](#), [Youn YK](#), [Shin WG](#).

Author information

Abstract

Astaxanthin, a carotenoid, has antioxidant activity as well as many positive effects, such as anticancer and anti-inflammatory effects. We performed a randomized, double-blind, placebo-controlled study to investigate the effects of astaxanthin on lipid profiles and oxidative stress in overweight and obese adults in Korea. In total, 27 subjects with body mass index >25.0 kg/m² were enrolled and randomly assigned into two groups administered astaxanthin or placebo capsules for 12 weeks. Total cholesterol, triglycerides, high density lipoprotein (HDL) cholesterol, low density lipoprotein (LDL) cholesterol, apolipoprotein A1 (ApoA1), and apolipoprotein B (ApoB) were measured before and after intervention. Malondialdehyde (MDA), isoprostane (ISP), superoxide dismutase (SOD), and total antioxidant capacity (TAC), as oxidative stress biomarkers, were measured at baseline and at 4, 8, and 12 weeks after intervention. LDL cholesterol and ApoB were significantly lower after treatment with astaxanthin, compared with the start of administration, whereas none of the lipid profiles was changed in the placebo group. At the baseline, all four biomarkers were not significantly different between the two groups. Compared with the placebo group, MDA and ISP were significantly lower, but TAC was significantly higher in the astaxanthin group at 12 weeks. These results suggest that supplementary astaxanthin has positive effects by improving the LDL cholesterol, ApoB, and oxidative stress biomarkers.

PMID:

21964877

[PubMed - indexed for MEDLINE]

Astaxanthin could prevent exercise-induced free radical production and depletion of non-enzymatic antioxidant defense in elite soccer players as evidenced in double-blind, placebo-controlled randomized human clinical study.

[J Sports Med Phys Fitness](#). 2012 Aug;52(4):382-92.

Effect of astaxanthin supplementation on muscle damage and oxidative stress markers in elite young soccer players.

[Djordjevic B¹](#), [Baralic I](#), [Kotur-Stevuljevic J](#), [Stefanovic A](#), [Ivanisevic J](#), [Radivojevic N](#), [Andielkovic M](#), [Dikic N](#).

Author information

Abstract

AIM:

The purpose of the current study was to examine the effect of Astaxanthin (Asx) supplementation on muscle enzymes as indirect markers of muscle damage, oxidative stress markers and antioxidant response in elite young soccer players.

METHODS:

Thirty-two male elite soccer players were randomly assigned in a double-blind fashion to Asx and placebo (P) group. After the 90 days of supplementation, the athletes performed a 2 hour acute exercise bout. Blood samples were obtained before and after 90 days of supplementation and after the exercise at the end of observational period for analysis of thiobarbituric acid-reacting substances (TBARS), advanced oxidation protein products (AOPP), superoxide anion ($O_2^{\bullet-}$), total antioxidative status (TAS), sulphhydryl groups (SH), superoxide-dismutase (SOD), serum creatine kinase (CK) and aspartate aminotransferase (AST).

RESULTS:

TBARS and AOPP levels did not change throughout the study. Regular training significantly increased $O_2^{\bullet-}$ levels (main training effect, $P<0.01$). $O_2^{\bullet-}$ concentrations increased after the soccer exercise (main exercise effect, $P<0.01$), but these changes reached statistical significance only in the P group (exercise x supplementation effect, $P<0.05$). TAS levels decreased significantly post-exercise only in P group ($P<0.01$). Both Asx and P groups experienced increase in total SH groups content (by 21% and 9%, respectively) and supplementation effect was marginally significant ($P=0.08$). Basal SOD activity significantly decreased both in P and in Asx group by the end of the study (main training effect, $P<0.01$). All participants showed a significant decrease in basal CK and AST activities after 90 days (main training effect, $P<0.01$ and $P<0.001$, respectively). CK and AST activities in serum significantly increased as result of soccer exercise (main exercise effect, $P<0.001$ and $P<0.01$, respectively). Postexercise CK and AST levels were significantly lower in Asx group compared to P group ($P<0.05$)

CONCLUSION:

The results of the present study suggest that soccer training and soccer exercise are associated with excessive production of free radicals and oxidative stress, which might diminish antioxidant system efficiency. Supplementation with Asx could prevent exercise induced free radical production and depletion of non-enzymatic antioxidant defense in young soccer players.

PMID: 22828460 [PubMed - indexed for MEDLINE]

Astaxanthin improves oxidative stress biomarkers in overweight adults in randomized human clinical study.

[Phytother Res.](#) 2011 Dec;25(12):1813-8. doi: 10.1002/ptr.3494. Epub 2011 Apr 8.

Effects of astaxanthin on oxidative stress in overweight and obese adults.

[Choi HD¹](#), [Kim JH](#), [Chang MJ](#), [Kyu-Youn Y](#), [Shin WG](#).

Author information

Abstract

Oxidative stress is caused by an imbalance between the antioxidant and the reactive oxygen species, which results in damage to cells or tissues. Recent studies have reported that oxidative stress is involved in obesity, in addition to many other human diseases and aging. A prospective, randomized, double-blind study was performed to investigate the effect of astaxanthin (ASX), which is known to be a potent antioxidant, on oxidative stress in overweight and obese adults in Korea. Twenty-three adults with BMI > 25.0 kg/m² enrolled in this study and were randomly assigned to two dose groups: ASX 5 mg and 20 mg once daily for 3 weeks. Malondialdehyde (MDA), isoprostane (ISP), superoxide dismutase (SOD) and total antioxidant capacity (TAC), as oxidative stress biomarkers, were measured at baseline and 1, 2 and 3 weeks after ASX administration. Compared with baseline, the MDA (by 34.6% and 35.2%) and ISP (by 64.9% and 64.7%) levels were significantly lowered, whereas SOD (by 193% and 194%) and TAC (by 121% and 125%) levels were significantly increased in two dose groups after the 3 week intervention.

This study revealed that supplemental ASX for 3 weeks improved oxidative stress biomarkers by suppressing lipid peroxidation and stimulating the activity of the antioxidant defense system.

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PMID:

21480416

[PubMed - indexed for MEDLINE]

Astaxanthin shows therapeutic potential for salivary secretion in human clinical trial and reduces the level of an oxidative stress marker in the subjects' saliva.

[J Clin Biochem Nutr.](#) 2010 Sep;47(2):130-7. Epub 2010 Jun 22.

Evaluation of therapeutic effects of astaxanthin on impairments in salivary secretion.

[Yamada T](#), [Ryo K](#), [Tai Y](#), [Tamaki Y](#), [Inoue H](#), [Mishima K](#), [Tsubota K](#), [Saito I](#).

Source

Department of Pathology, Tsurumi University School of Dental Medicine, 2-1-3, Tsurumi, Tsurumi-ku, Yokohama 230-8501, Japan.

Abstract

The involvement of reactive oxygen species (ROS) in the pathophysiology of Sjögren's syndrome (SS), an autoimmune disorder, and irradiation-induced impairments in salivary secretion has been reported. Meanwhile, the strong antioxidant astaxanthin (Ast) has been suggested to have therapeutic effects on various diseases. In the present study, we examined the ROS scavenging capacity of Ast using a human salivary gland epithelial cell line (HSY) and investigated the effects of Ast on salivary secretion in a mouse model of irradiation-induced salivary gland dysfunction. Furthermore, we performed a clinical study of Ast in six SS patients and six normal individuals, quantifying the volume of saliva secretion and the level of oxidative stress markers in the saliva. Ast partially suppressed hydrogen peroxide-induced ROS in HSY cells. The mouse model demonstrated that the pre-administration of Ast resulted in the suppression of irradiation-induced hyposalivation. Furthermore, the administration of Ast appeared to increase salivary output in both the SS and normal groups. The level of oxidative stress marker, hexanoyl-lysine, in the saliva was reduced after Ast intake. These results suggest that Ast might act as an ROS scavenger, providing benefits to SS patients with impaired salivary secretion.

PMID: 20838568 [PubMed]

PMCID: PMC2935153

ASTAXANTHIN FORMULA MODULATES TRAINING-INDUCED AEROBIC METABOLISM OF CARBS AND FAT DURING REST AND EXERCISE IN HEALTHY YOUNG MEN IN HUMAN CLINICAL TRIAL.

J Clin Biochem Nutr. 2019 Jan;64(1):79-85.

doi: 10.3164/jcbn.18-40. Epub 2018 Aug 8.

Effect of dietary antioxidant-rich foods combined with aerobic training on energy metabolism in healthy young men

[Maki Takami](#)¹, [Wataru Aoi](#)¹, [Hitomi Terajima](#)¹, [Yuko Tanimura](#)², [Sayori Wada](#)¹, [Akane Higashi](#)¹

PMID: 30705516 PMCID: [PMC6348409](#) DOI: [10.3164/jcbn.18-40](#) [Free PMC article](#)

Abstract

Although supplementation with several antioxidants has been suggested to improve aerobic metabolism during exercise, whether dietary foods containing such antioxidants can exert the metabolic modulation is unclear. This study aimed to investigate the effect of intake of the specific antioxidant-rich foods coupled with exercise training on energy metabolism. Twenty young healthy, untrained men were assigned to antioxidant and control groups: participants in the antioxidant group were encouraged to consume foods containing catechin, astaxanthin, quercetin, glutathione, and anthocyanin. All participants performed cycle training at 60% maximum oxygen consumption for 30 min, 3 days per week for 4 weeks. Maximum work load was significantly increased by training in both groups, while oxygen consumption during exercise was significantly increased in the antioxidant group only. There were positive correlations between maximum work load and fat/carbohydrate oxidations in the antioxidant group. Carbohydrate oxidation during rest was significantly higher in the post-training than that in the pre-training only in the antioxidant group. More decreased levels of serum insulin and HOMA-IR after training were observed in the antioxidant group than in the control group. This study suggests that specific antioxidant-rich foods could modulate training-induced aerobic metabolism of carbohydrate and fat during rest and exercise.

ASTAXANTHIN SHOWS POTENTIAL TO WORK AS EYE ANTIOXIDANT DURING CATARACT SURGERY IN FEMALES IN HUMAN CLINICAL STUDY.

J Clin Biochem Nutr. 2019 Jul;65(1):47-51.

doi: 10.3164/jcfn.18-110. Epub 2019 Apr 18.

Effects of astaxanthin on VEGF level and antioxidation in human aqueous humor: difference by sex

[Hirotaka Hashimoto](#)¹, [Kiyomi Arai](#)², [Jiro Takahashi](#)³, [Makoto Chikuda](#)²

- PMID: **31379413**
- PMCID: [PMC6667389](#)
- DOI: [10.3164/jcfn.18-110](#)

Free PMC article

Abstract

In our previous report, we showed the effect of astaxanthin intake on VEGF level in the aqueous humor and the relationship between VEGF level and reactive oxygen species-related parameters and other relevant factors. VEGF level is associated with total hydroperoxide level, and a multivariate analysis identified sex as a secondary factor affecting these relationships. Here, we analyzed the effects of astaxanthin on the relationship between VEGF level and reactive oxygen species-related parameters by sex. Patients (16 males and 19 females, aged 71.3 and 70.6, respectively) underwent bilateral cataract surgery on one side before and the other side after astaxanthin treatment (6 mg/day for 2 weeks). Levels of VEGF, hydrogen peroxide, and total hydroperoxide, and O₂^{-•} scavenging activity, were measured in the aqueous humor. In females only, VEGF level was negatively correlated with O₂^{-•} scavenging activity before the astaxanthin intake ($r = -0.6$, $p < 0.01$) and positively correlated with total hydroperoxide level before and after the astaxanthin intake ($r = 0.7$ and 0.8 , respectively, $p < 0.01$). In conclusion, astaxanthin appears to affect O₂^{-•} scavenging activity in the aqueous humor in females, and is likely to be involved in the control of VEGF levels in the anterior eye.

ESTERIFIED ASTAXANTHIN (E.G. FOUND IN ALGAE) IS SUPERIOR TO NON-ESTERIFIED ASTAXANTHIN (E.G. SYNTHETIC ASTAXANTHIN OR THAT DERIVED FROM YEAST) IN PROTECTING AGAINST NEURONAL CELL DEATH AND PREVENTING BEHAVIORAL DEFICITS IN MOUSE MODEL OF PARKINSON'S.

Food Funct. 2020 Sep 23;11(9):8038-8050.
doi: 10.1039/d0fo01176b.

Docosahexaenoic acid-acylated astaxanthin ester exhibits superior performance over non-esterified astaxanthin in preventing behavioral deficits coupled with apoptosis in MPTP-induced mice with Parkinson's disease

[Cheng-Cheng Wang](#)¹, [Hao-Hao Shi](#)¹, [Jie Xu](#)¹, [Teruyoshi Yanagita](#)², [Chang-Hu Xue](#)³, [Tian-Tian Zhang](#)¹, [Yu-Ming Wang](#)³

PMID: 32845953 DOI: [10.1039/d0fo01176b](https://doi.org/10.1039/d0fo01176b)

Abstract

Non-esterified astaxanthin (AST) has been reported to exhibit protective effects from Parkinson's disease (PD). Notably, DHA-acylated astaxanthin ester (DHA-AST) is widely distributed in the seafood. However, whether DHA-AST has an effect on PD, and the differences between DHA-AST, non-esterified AST and the combination of non-esterified AST (AST) with DHA (DHA + AST) is unclear. In the present study, mice with PD, induced by 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP), were employed to investigate the effects of DHA-AST, AST and DHA + AST on Parkinson's disease. The rotarod test results showed that DHA-AST significantly suppressed the PD development in MPTP-induced mice, and was better than the effects of AST and DHA + AST. Further mechanistic studies indicated that all three astaxanthin supplements could inhibit oxidative stress in the brain. It was noted that DHA-AST had the best ability to suppress the apoptosis of dopaminergic neurons via the mitochondria-mediated pathway and JNK and P38 MAPK pathway in the brain among the three treated groups. DHA-AST was superior to AST in preventing behavioral deficits coupled with apoptosis rather than oxidative stress, and might provide a valuable reference for the prevention and treatment of neurodegenerative diseases.

Natural Astaxanthin's intracellular antioxidant activity is approximately 90X stronger than Synthetic Astaxanthin's.

[Mar Drugs](#). 2015 May 7;13(5):2857-74. doi: 10.3390/md13052857.

Astaxanthin from Haematococcus pluvialis Prevents Oxidative Stress on Human Endothelial Cells without Toxicity.

[Régnier P](#)¹, [Bastias J](#)², [Rodriguez-Ruiz V](#)³, [Caballero-Casero N](#)⁴, [Caballo C](#)⁵, [Sicilia D](#)⁶, [Fuentes A](#)⁷, [Maire M](#)⁸, [Crepin M](#)⁹, [Letourneur D](#)¹⁰, [Guequen V](#)¹¹, [Rubio S](#)¹², [Pavon-Djavid G](#)¹³.

Author information

Abstract

Astaxanthin, a powerful antioxidant, is a good candidate for the prevention of intracellular oxidative stress. The aim of the study was to compare the antioxidant activity of astaxanthin present in two natural extracts from *Haematococcus pluvialis*, a microalgae strain, with that of synthetic astaxanthin. Natural extracts were obtained either by solvent or supercritical extraction methods. UV, HPLC-DAD and (HPLC-(atmospheric pressure chemical ionization (APCI+)/ion trap-MS) characterizations of both natural extracts showed similar compositions of carotenoids, but different percentages in free astaxanthin and its ester derivatives. The Trolox equivalent antioxidant capacity (TEAC) assay showed that natural extracts containing esters displayed stronger antioxidant activities than free astaxanthin. Their antioxidant capacities to inhibit intracellular oxidative stress were then evaluated on HUVEC cells. The intracellular antioxidant activity in natural extracts was approximately 90-times higher than synthetic astaxanthin (5 µM). No modification, neither in the morphology nor in the viability, of vascular human cells was observed by in vitro biocompatibility study up to 10 µM astaxanthin concentrations. Therefore, these results revealed the therapeutic potential of the natural extracts in vascular human cell protection against oxidative stress without toxicity, which could be exploited in prevention and/or treatment of cardiovascular diseases.

PMID: 25962124

PMCID: [PMC4446609](#)

DOI: [10.3390/md13052857](#)

[PubMed - indexed for MEDLINE]

[Free PMC Article](#)

Astaxanthin shown to be 75X to 6000X stronger than other common natural antioxidants in singlet oxygen quenching activities.

Carotenoid Science, Vol.11, 2007, 16-20

Quenching Activities of Common Hydrophilic and Lipophilic Antioxidants against Singlet Oxygen Using Chemiluminescence Detection System

Yasuhiro Nishida*, Eiji Yamashita and Wataru Miki
Institute for Food Science Research, Japan

The singlet oxygen quenching activities among common hydrophilic and lipophilic antioxidants such as polyphenols, tocopherols, carotenoids, ascorbic acid, coenzyme Q10 and α -lipoic acid were recorded under the same test condition: the chemiluminescence detection system for direct 1O_2 counting using the thermodissociable endoperoxides of 1,4-dimethylnaphthalene as 1O_2 generator in DMF : $CDCl_3$ (9 : 1). Carotenoids exhibited larger total quenching rate constants than other antioxidants, with astaxanthin showing the strongest activity. α -Tocopherol and α -lipoic acid showed considerable activities, whereas the activities of ascorbic acid, CoQ10 and polyphenols were only slight; these included capsaicin, probucol, edaravon, BHT and Trolox. This system has the potential of being a powerful tool to evaluate the quenching activity against singlet oxygen for various hydrophilic and lipophilic compounds.

Summary of Above Abstract.

**From Nishida, Yamashita, Miki, Carotenoid Science, Vol. 11, 2007, 16-20
(in Japanese)**

Astaxanthin has exceptional antioxidant activity to combat singlet oxygen when compared to other antioxidants. In particular, Astaxanthin can be used to defend against singlet oxygen damage for eye and skin health, which are especially susceptible to UV damage and aging effects.

Singlet oxygen is an active oxygen species generated in human skin by exposure to ultraviolet radiation (UV) that causes skin damage and eye damage. In this study, Astaxanthin extracted from *Haematococcus* microalgae powerfully quenched singlet oxygen. Results show that the quenching effect of Astaxanthin is 800 times greater than coenzyme Q10. Astaxanthin was also about 75 times greater than alpha lipoic acid, about 550 times greater than green tea catechins and about 6000 times greater than Vitamin C.

Astaxanthin 550 times stronger than Vitamin E and 11 times stronger than Beta-Carotene in singlet oxygen quenching.

Carotenoids as Singlet Oxygen Quenchers in Marine Organisms

Shimidzu, Goto, Miki, 1996. Fisheries Science 62(1), 134-137

To understand the roles of carotenoids as singlet oxygen quenchers in marine organisms, quenching activities of eight major carotenoids, astaxanthin, canthaxanthin, β -carotene, zeaxanthin, lutein, tunaxanthin, fucoxanthin and halocynthiaxanthin were examined according to the method using a thermodissociable endoperoxide of 1,4-dimethylnaphthalene as a singlet oxygen generator. The second-order rate constant for the singlet oxygen quenching activity by each carotenoid was determined, suggesting that an increasing number of conjugated double bonds in carotenoid was proportional to greater quenching activity. The quenching activity of each carotenoid was found to be approximately 40 to 600 times greater than that of α -tocopherol. The potency of these carotenoids suggests that they may play a role in protecting marine organisms from active oxygen species.

Summary: Results indicated that Astaxanthin was significantly stronger than all other antioxidants tested as singlet oxygen quenchers. Among the results Astaxanthin was shown to be 550X stronger than Vitamin E; 11X stronger than Beta-Carotene; 2.75X stronger than Lutein.

Astaxanthin is 14 to 65 times stronger than other common antioxidants in free radical scavenging and Natural Astaxanthin is 20 times stronger than Synthetic Astaxanthin in free radical scavenging.

Nutrafoods (2013)
DOI 10.1007/s13749-013-0051-5

Synthetic astaxanthin is significantly inferior to algal-based astaxanthin as an antioxidant and may not be suitable as a human nutraceutical supplement

Bob Capelli, Debasis Bagchi, Gerald R. Cysewski

Received 7 January / Accepted 3 December 2013

© Springer Healthcare – CEC Editore 2013

Abstract

Synthetic astaxanthin (S-AX) was tested against natural astaxanthin from *Haematococcus pluvialis* microalgae (N-AX) for antioxidant activity. *In vitro* studies conducted at Creighton University and Brunswick Laboratories showed N-AX to be over 50 times stronger than S-AX in singlet oxygen quenching and approximately 20 times stronger in free radical elimination. N-AX has been widely used over the last 15 years as a human nutraceutical supplement after extensive safety data and several health benefits were established. S-AX, which is synthesised from petrochemicals, has been used as a feed ingredient, primarily to pigment the flesh of salmonids. S-AX has never been demonstrated to be safe for use as a human nutraceutical supplement and has not been tested for health benefits in humans. Due to safety concerns with the use of synthetic forms of other carotenoids such as canthaxanthin and beta-carotene in humans, the authors recommend against the use of S-AX as a human nutraceutical supplement until extensive, long-term safety parameters have been established and human clinical trials have been conducted showing potential health benefits. Additionally, differences in various other properties between S-AX and N-AX such as stereochemistry, esterification and the presence of supporting naturally occurring carotenoids in N-AX are discussed, all of which elicit further questions as to the safety and potential health benefits of S-AX. Ultimately, should S-AX prove safe for direct human consumption, dosage levels roughly 20–30 times greater than N-AX should be used as a result of the extreme difference in antioxidant activity between the two forms.

Natural Astaxanthin 90 times stronger than Synthetic Astaxanthin in intracellular antioxidant activity.

[Mar Drugs](#). 2015 May 7;13(5):2857-74. doi: 10.3390/md13052857.

Astaxanthin from *Haematococcus pluvialis* Prevents Oxidative Stress on Human Endothelial Cells without Toxicity.

[Régnier P](#)¹, [Bastias J](#)², [Rodriguez-Ruiz V](#)³, [Caballero-Casero N](#)⁴, [Caballo C](#)⁵, [Sicilia D](#)⁶, [Fuentes A](#)⁷, [Maire M](#)⁸, [Crepin M](#)⁹, [Letourneur D](#)¹⁰, [Guequen V](#)¹¹, [Rubio S](#)¹², [Pavon-Djavid G](#)¹³.

Author information

Abstract

Astaxanthin, a powerful antioxidant, is a good candidate for the prevention of intracellular oxidative stress. The aim of the study was to compare the antioxidant activity of astaxanthin present in two natural extracts from *Haematococcus pluvialis*, a microalgae strain, with that of synthetic astaxanthin. Natural extracts were obtained either by solvent or supercritical extraction methods. UV, HPLC-DAD and (HPLC-(atmospheric pressure chemical ionization (APCI)+)/ion trap-MS) characterizations of both natural extracts showed similar compositions of carotenoids, but different percentages in free astaxanthin and its ester derivatives. The Trolox equivalent antioxidant capacity (TEAC) assay showed that natural extracts containing esters displayed stronger antioxidant activities than free astaxanthin. Their antioxidant capacities to inhibit intracellular oxidative stress were then evaluated on HUVEC cells. The intracellular antioxidant activity in natural extracts was approximately 90-times higher than synthetic astaxanthin (5 μM). No modification, neither in the morphology nor in the viability, of vascular human cells was observed by in vitro biocompatibility study up to 10 μM astaxanthin concentrations. Therefore, these results revealed the therapeutic potential of the natural extracts in vascular human cell protection against oxidative stress without toxicity, which could be exploited in prevention and/or treatment of cardiovascular diseases.

PMID: [25962124](#)

PMCID: [PMC4446609](#)

DOI: [10.3390/md13052857](#)

[PubMed - indexed for MEDLINE]

[Free PMC Article](#)

Natural Astaxanthin superior to Synthetic in prolonging the life of investigational worms by reducing reactive oxygen species more effectively.

[J Food Sci.](#) 2016 Sep;81(9):H2280-7. doi: 10.1111/1750-3841.13417. Epub 2016 Aug 16.

Mechanism of Different Stereoisomeric Astaxanthin in Resistance to Oxidative Stress in *Caenorhabditis elegans*.

[Liu X¹](#), [Luo Q²](#), [Cao Y²](#), [Goulette T³](#), [Liu X³](#), [Xiao H⁴](#).

Author information

Abstract

As a potent antioxidant in human diet, astaxanthin (AST) may play important roles in alleviating oxidative stress-driven adverse physiological effects. This study examined the effects of different stereoisomers of AST in protecting *Caenorhabditis elegans* from chemically induced oxidative stress. Three stereoisomers of AST investigated herein included 3S,3'S (S) AST, 3R,3'R (R) AST, and a statistical mixture (S: meso: R = 1:2:1) (M) AST. Under paraquat-induced oxidative conditions, all three types of AST significantly enhanced survival rate of *C. elegans*. The accumulation levels of ROS in the worms were reduced by 40.12%, 30.05%, and 22.04% by S, R, and M AST, respectively ($P < 0.05$). Compared with R and M AST, S significantly enhanced the expression levels of SOD-3. The results of RNA-Seq analysis demonstrated that AST protected *C. elegans* from oxidative damage potentially by modulating genes involved in the insulin/insulin-like growth factor (IGF) signaling (IIS) pathway and the oxidoreductase system. It is noteworthy that different stereoisomers of AST showed different effects on the expression levels of various genes related with oxidative stress. This study revealed important information on the *in vivo* antioxidative effects of AST stereoisomers, which might provide useful information for better utilization of AST.

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KEYWORDS:

Caenorhabditis elegans; RNA-seq; astaxanthin; oxidative stress; stereoisomeric

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27527357

DOI:

[10.1111/1750-3841.13417](https://doi.org/10.1111/1750-3841.13417)

[PubMed - in process]

ASTAXANTHIN EXHIBITS ANTIOXIDANT POTENTIAL IN FISH LIVERS.

Antioxidants (Basel). 2019 Dec 6;8(12):626.

doi: 10.3390/antiox8120626.

Influence of Dietary Astaxanthin on the Hepatic Oxidative Stress Response Caused by Episodic Hyperoxia in Rainbow Trout

[Carmen Tatiana Kalinowski¹](#), [Laurence Larroquet²](#), [Vincent Véron²](#), [Lidia Robaina¹](#), [María Soledad Izquierdo¹](#), [Stéphane Panserat²](#), [Sachi Kaushik¹](#), [Stéphanie Fontagné-Dicharry²](#)

PMID: 31817693 PMCID: [PMC6943655](#) DOI: [10.3390/antiox8120626](#) [Free PMC article](#)

Abstract

A 13-week feeding trial was carried out with juvenile rainbow trout to test two diets: a control diet without astaxanthin (AX) supplementation (CTRL diet), and a diet supplemented with 100 mg/kg of synthetic AX (ASTA diet). During the last week of the feeding trial, fish were exposed to episodic hyperoxia challenge for 8 consecutive hours per day. Episodic hyperoxia induced physiological stress responses characterized by a significant increase in plasma cortisol and hepatic glycogen and a decrease in plasma glucose levels. The decrease of plasma glucose and the increase of hepatic glycogen content due to episodic hyperoxia were emphasized with the ASTA diet. Hyperoxia led to an increase in thiobarbituric acid-reactive substances in the muscle, diminished by dietary AX supplementation in both liver and muscle. Muscle and liver AX were increased and decreased respectively after 7-day episodic hyperoxia, leading to an increase in flesh redness. This augment of muscle AX could not be attributed to AX mobilization, since plasma AX was not affected by hyperoxia. Moreover, hyperoxia decreased most of antioxidant enzyme activities in liver, whereas dietary AX supplementation specifically increased glutathione reductase activity. A higher mRNA level of hepatic glutathione reductase, thioredoxin reductase, and glutamate-cysteine ligase in trout fed the ASTA diet suggests the role of AX in glutathione and thioredoxin recycling and in de novo glutathione synthesis. Indeed, dietary AX supplementation improved the ratio between reduced and oxidized glutathione (GSH/GSSG) in liver. In addition, the ASTA diet up-regulated glucokinase and glucose-6-phosphate dehydrogenase mRNA level in the liver, signaling that dietary AX supplementation may also stimulate the oxidative phase of the pentose phosphate pathway that produces NADPH, which provides reducing power that counteracts oxidative stress. The present results provide a broader understanding of the mechanisms by which dietary AX is involved in the reduction of oxidative status.

ASTAXANTHIN IMPROVES ANTIOXIDANT STATUS AND REGULATES LIPID METABOLISM IN CHICKENS.

Poult Sci. 2020 Nov;99(11):5874-5882.

doi: 10.1016/j.psj.2020.08.029. Epub 2020 Aug 31.

Effects of dietary supplementation of natural astaxanthin from *Haematococcus pluvialis* on antioxidant capacity, lipid metabolism, and accumulation in the egg yolk of laying hens

[Shan Gao¹](#), [Runhua Li¹](#), [Nuo Heng¹](#), [Yu Chen²](#), [Liang Wang²](#), [Zheng Li³](#), [Yong Guo¹](#), [Xihui Sheng¹](#), [Xiangguo Wang¹](#), [Kai Xing¹](#), [Hemin Ni¹](#), [Xiaolong Qi⁴](#)

PMID: [33142505](#) PMCID: [PMC7647864](#) DOI: [10.1016/j.psj.2020.08.029](#) [Free PMC article](#)

Abstract

The present study evaluated the effects of natural astaxanthin (ASTA) from *Haematococcus pluvialis* on the antioxidant capacity, lipid metabolism, and ASTA accumulation in the egg yolk of laying hens. Hy-Line Brown layers (n = 288, 50 wk old) were randomly assigned to 1 of 4 dietary treatment groups. Each group had 6 replicates of 12 hens each. All birds were given a corn-soybean meal-based diet containing 0, 25, 50, or 100 mg/kg ASTA for 6 wk. The results showed that the total antioxidant capacity, superoxide dismutase level, and glutathione peroxidase level in the plasma, livers, and egg yolks were significantly increased in the ASTA groups compared with those of the control group (P < 0.05), whereas the content of malondialdehyde linearly decreased (P < 0.05). The plasma levels of high-density and very-low-density lipoprotein cholesterol in the ASTA groups were significantly higher than those in the control group (P < 0.05). In addition, ASTA supplementation decreased low-density lipoprotein cholesterol and triglyceride plasma levels (P < 0.05). However, there were no significant differences in the other lipid metabolism parameters among the ASTA-supplemented groups relative to the control group except for an increase in high-density lipoprotein cholesterol in the liver. Compared with the control, dietary ASTA supplementation significantly increased the enrichment of ASTA in egg yolks at the end of week 2, 4, and 6 (P < 0.05). The mRNA expression of scavenger receptor class B type 1 (SCARB1) and very-low-density lipoprotein receptor (VLDLR) in the ASTA groups was markedly higher (P < 0.05) than that in the control group in the liver and ovaries, respectively. In conclusion, these results suggest that dietary ASTA enhances the antioxidant capacity and regulates lipid metabolism in laying hens. ASTA enrichment in egg yolks may be closely related to the upregulation of SCARB1 and VLDLR gene expression.

Astaxanthin from *H. pluvialis* microalgae is superior to Synthetic Astaxanthin as an antioxidant and Natural Astaxanthin shows stronger protective properties in the livers of rats.

[J Food Sci Technol](#). 2015 Oct;52(10):6703-10. doi: 10.1007/s13197-015-1775-6. Epub 2015 Mar 5.

Evaluation of hepatoprotective and antioxidant activity of astaxanthin and astaxanthin esters from microalga-*Haematococcus pluvialis*.

[Rao AR](#)¹, [Sarada R](#)², [Shylaja MD](#)³, [Ravishankar GA](#)⁴.

Author information

Abstract

Effect of isolated astaxanthin (ASX) and astaxanthin esters (ASXEs) from green microalga-*Haematococcus pluvialis* on hepatotoxicity and antioxidant activity against carbon tetrachloride (CCl₄) induced toxicity in rats was compared with synthetic astaxanthin (SASX). ASX, ASXEs, and SASX, all dissolved in olive oil, fed to rats with 100 and 250 µg/kg b.w for 14 days. They were evaluated for their hepatoprotective and antioxidant activity by measuring appropriate enzymes. Among the treated groups, the SGPT, SGOT and ALP levels were decreased by 2, 2.4, and 1.5 fold in ASXEs treated group at 250 µg/Kg b.w. when compared to toxin group. Further, antioxidant enzymes catalase, glutathione, superoxide dismutase and lipid peroxidase levels were estimated in treated groups, their levels were reduced by 30-50 % in the toxin group, however these levels restored by 136.95 and 238.48 % in ASXEs treated group at 250 µg/kg. The lipid peroxidation was restored by 5.2 and 2.8 fold in ASXEs and ASX treated groups at 250 µg/kg. The total protein, albumin and bilirubin contents were decreased in toxin group, whereas normalized in ASXEs treated group. These results indicate that ASX and ASXEs have better hepatoprotection and antioxidant activity, therefore can be used in pharmaceutical and nutraceutical applications and also extended to use as food colorant.

KEYWORDS:

ASX; ASXEs; Antioxidants; CCl₄; *H. pluvialis*; Hepatoprotection; SGPT, SGOT, ALP

PMID:

26396419

[PubMed]

PMCID:

PMC4573148

[Available on 2016-10-01]

Astaxanthin decreases lipid peroxidation in bovine embryos.

[Reprod Domest Anim.](#) 2015 Oct;50(5):793-9. doi: 10.1111/rda.12589. Epub 2015 Aug 17.

Astaxanthin Normalizes Epigenetic Modifications of Bovine Somatic Cell Cloned Embryos and Decreases the Generation of Lipid Peroxidation.

[Li R¹](#), [Wu H¹](#), [Zhuo WW¹](#), [Mao QF¹](#), [Lan H¹](#), [Zhang Y¹](#), [Hua S¹](#).

Author information

Abstract

Astaxanthin is an extremely common antioxidant scavenging reactive oxygen species (ROS) and blocking lipid peroxidation. This study was conducted to investigate the effects of astaxanthin supplementation on oocyte maturation, and development of bovine somatic cell nuclear transfer (SCNT) embryos. Cumulus-oocyte complexes were cultured in maturation medium with astaxanthin (0, 0.5, 1.0, or 1.5 mg/l), respectively. We found that 0.5 mg/l astaxanthin supplementation significantly increased the proportion of oocyte maturation. Oocytes cultured in 0.5 mg/l astaxanthin supplementation were used to construct SCNT embryos and further cultured with 0, 0.5, 1.0 or 1.5 mg/l astaxanthin. The results showed that the supplementation of 0.5 mg/l astaxanthin significantly improved the proportions of cleavage and blastulation, as well as the total cell number in blastocysts compared with the control group, yet this influence was not concentration dependent. Chromosomal analyses revealed that more blastomeres showed a normal chromosomal complement in 0.5 mg/l astaxanthin treatment group, which was similar to that in IVF embryos. The methylation levels located on the exon 1 of the imprinted gene H19 and IGF2, pluripotent gene OCT4 were normalized, and global DNA methylation, H3K9 and H4K12 acetylation were also improved significantly, which was comparable to that in vitro fertilization (IVF) embryos. Moreover, we also found that astaxanthin supplementation significantly decreased the level of lipid peroxidation. Our findings showed that the supplementation of 0.5 mg/l astaxanthin to oocyte maturation medium and embryo culture medium improved oocyte maturation, SCNT embryo development, increased chromosomal stability and normalized the epigenetic modifications, as well as inhibited overproduction of lipid peroxidation.

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PMID:

26280670

[PubMed - in process]

Astaxanthin reduces oxidative damage to DNA.

**Comparison of Astaxanthin's Singlet Oxygen Quenching Activity with
Common Fat and Water Soluble Antioxidants**

United States Patent Application

20060217445

Kind Code

A1

Chew; Boon P. ; et al.

September 28, 2006

Natural astaxanthin extract reduces DNA oxidation

Abstract

Provided herein are methods for reducing oxidative DNA damage in a subject, by administering to the subject astaxanthin, for instance a natural, astaxanthin-enriched extract from *Haematococcus pluvialis*. It is shown that doses as low as 2 mg/day, given orally to a human subject for a period of four weeks, is sufficient to reduced measurable endogenous oxidative DNA damage by about 40%.

Astaxanthin prevents lipid and protein oxidation and increases the activity of antioxidant enzymes in human cells.

[Phytother Res.](#) 2009 Jun 22. [Epub ahead of print]

Cytoprotective role of astaxanthin against glycated protein/iron chelate-induced toxicity in human umbilical vein endothelial cells.

[Nishigaki I](#), [Rajendran P](#), [Venugopal R](#), [Ekambaram G](#), [Sakthisekaran D](#), [Nishigaki Y](#).

NPO International Laboratory of Biochemistry, 1-166 Uchide, Nakagawa-ku Nagoya 454-0926, Japan.

Astaxanthin (ASX), a red carotenoid pigment with no pro-vitamin A activity, is a biological antioxidant that occurs naturally in a wide variety of plants, algae and seafoods. This study investigated whether ASX could inhibit glycated protein/iron chelate-induced toxicity in human umbilical-vein endothelial cells (HUVEC) by interfering with ROS generation in these cells. Glycated fetal bovine serum (GFBS) was prepared by incubating fetal bovine serum (FBS) with high-concentration glucose. Stimulation of cultured HUVECs with 50 mm 1 mL of GFBS significantly enhanced lipid peroxidation and decreased antioxidant enzyme activities and levels of phase II enzymes. However, preincubation of the cultures with ASX resulted in a marked decrease in the level of lipid peroxide (LPO) and an increase in the levels of antioxidant enzymes in an ASX concentration-dependent manner. These results demonstrate that ASX could inhibit LPO formation and enhance the antioxidant enzyme status in GFBS/iron chelate-exposed endothelial cells by suppressing ROS generation, thereby limiting the effects of the AGE-RAGE interaction. The results indicate that ASX could have a beneficial role against glycated protein/iron chelate-induced toxicity by preventing lipid and protein oxidation and increasing the activity of antioxidant enzymes.

PMID: 19548280 [PubMed - as supplied by publisher]

Astaxanthin improves liver oxidative stress in diabetic rats.

[Pharmacol Rep.](#) 2015 Apr;67(2):310-6. doi: 10.1016/j.pharep.2014.09.012. Epub 2014 Oct 7.

Ability of natural astaxanthin from shrimp by-products to attenuate liver oxidative stress in diabetic rats.

[Sila A¹](#), [Kamoun Z²](#), [Ghliissi Z³](#), [Makni M²](#), [Nasri M⁴](#), [Sahnoun Z³](#), [Nedjar-Arroume N⁵](#), [Bougatef A⁶](#).

Author information

Abstract

BACKGROUND:

Reactive oxygen species play a crucial role in the pathogenesis of diabetes and its complications. The present study was undertaken, in vivo, to examine the protective effect of astaxanthin extracted from the shell waste of deep-water pink shrimp (*Parapenaeus longirostris*) against oxidative stress of alloxanic adult male rats.

RESULTS:

Alloxan treatment revealed a significant elevation in plasma glycemia and lipid parameters such as total lipid, total cholesterol and triglycerides compared to the control group (C). In addition, liver malonaldehyde levels (MDA), an index of lipid peroxidation, significantly increased compared to control group. The activities of antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx) and glutathione reductase (GR) and reduced glutathione (GSH) levels decreased significantly compared to control group. Moreover, diabetic rats presented a significant increase in the activities of aspartate transaminase (AST) alanine transaminase (ALT) and alkaline phosphatase (ALP) in plasma, indicating considerable hepatocellular injury. Astaxanthin treatment restores these parameters near to control values. Histological studies on the liver tissue of alloxan and astaxanthin treated rats confirmed the protective effects of astaxanthin.

CONCLUSIONS:

The results revealed that astaxanthin may be helpful in preventing diabetic complications in adult rats by reversing hepatotoxicity. It can be one of the ingredients in a number of healthy products.

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KEYWORDS:

Astaxanthin; Diabetes; Liver; Oxidative stress; Rats

PMID:

25712656

[PubMed - in process]

Astaxanthin shows anti-aging effects in fruit flies under oxidative stress.

[J Agric Food Chem](#). 2013 Aug 14;61(32):7800-4. doi: 10.1021/jf402224w. Epub 2013 Aug 6.

Antiaging effects of astaxanthin-rich alga *Haematococcus pluvialis* on fruit flies under oxidative stress.

[Huangfu J](#)¹, [Liu J](#), [Sun Z](#), [Wang M](#), [Jiang Y](#), [Chen ZY](#), [Chen F](#).

Author information

Abstract

The microalga *Haematococcus pluvialis* (HP) is the best natural producer of astaxanthin (AX), which is a potent antioxidant with broad health benefits. The present study investigated the antiaging potential of HP biomass using the fruit fly *Drosophila melanogaster* as the animal model. The results showed that in wild-type flies the treatment of HP induced the early mortality at a concentration of 20 mg/mL, which was associated with the decreased enzymatic activities of CuZn-superoxide dismutase (SOD1) and Mn-superoxide dismutase (SOD2) as well as the down-regulation of SOD1, SOD2, and catalase (CAT) at the transcriptional level. In SOD(n108) mutant flies, the supplementation of HP (10 or 20 mg/mL) significantly extended their lifespan and ameliorated the age-related decline in locomotor function. Further studies suggested that HP may play a role as a complement to the defective endogenous antioxidant system to exert such lifespan elongation effects. These results, taken together, strongly support the antiaging properties of HP and its therapeutic rather than preventive potential against aging-related diseases.

PMID:

23879808

[PubMed - indexed for MEDLINE]

Astaxanthin and Vitamin C shown in-vitro that they may be helpful to improve the immune function of patients with exacerbated production of reactive oxygen species.

[Int Immunopharmacol.](#) 2012 Dec;14(4):690-7. doi: 10.1016/j.intimp.2012.10.003. Epub 2012 Oct 17.

Changes in lymphocyte oxidant/antioxidant parameters after carbonyl and antioxidant exposure.

[Bolin AP](#)¹, [Guerra BA](#), [Nascimento SJ](#), [Otton R](#).

Author information

Abstract

During normal B- and T-cell life, processes including activation, proliferation, signaling pathways and apoptosis are markedly dependent on ROS generation. However, these cells can also suffer the effect of oxidant overproduction. Thus, the purpose of the present study was to examine the possible pro-oxidant effects of MGO/high glucose and antioxidant effects of astaxanthin associated with vitamin C on some oxidative and antioxidant parameters of human lymphocytes in vitro. Lymphocytes from healthy subjects were treated with 20mM of glucose and 30 μ M MGO followed or not by the addition of the antioxidants astaxanthin (2 μ M) and vitamin C (100 μ M) for up to 24h. We examined superoxide dismutase (SOD), catalase, glutathione peroxidase, glutathione reductase, and glucose-6-phosphate dehydrogenase (G6PDH) activities, GSH/GSSG ratio and total thiol and carbonyl content. Oxidative parameters included superoxide anion, hydrogen peroxide and nitric oxide production. The association of astaxanthin and vitamin C proved to be a powerful antioxidant in human lymphocytes as showed by the marked reduction in superoxide anion, and hydrogen peroxide production as well as increased GSH content, GSH/GSSG ratio, GPx and GR activities. The antioxidant association showed to be more potent than their individual application. High glucose and methylglyoxal did not promote oxidative stress in human lymphocytes, since neither the oxidative parameters nor the antioxidant defense system was altered. According to these results, new therapies with the association of astaxanthin and vitamin C may be helpful to improve the immune function of patients with exacerbated production of ROS.

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PMID:

23085288

[PubMed - indexed for MEDLINE]

Free full text

Astaxanthin may prevent age-related decrease in saliva secretion and decreases oxidative stress in aging mice.

[J Clin Biochem Nutr.](#) 2016 Sep;59(2):79-85. Epub 2016 Jul 16.

Astaxanthin affects oxidative stress and hyposalivation in aging mice.

[Kuraji M](#)¹, [Matsuno T](#)¹, [Sato T](#)¹.

Author information

Abstract

Oral dryness, a serious problem for the aging Japanese society, is induced by aging-related hyposalivation and causes dysphagia, dysgeusia, inadaptation of dentures, and growth of oral *Candida albicans*. Oxidative stress clearly plays a role in decreasing saliva secretion and treatment with antioxidants such as astaxanthin supplements may be beneficial. Therefore, we evaluated the effects of astaxanthin on the oral saliva secretory function of aging mice. The saliva flow increased in astaxanthin-treated mice 72 weeks after administration while that of the control decreased by half. The plasma d-ROMs values of the control but not astaxanthin-treated group measured before and 72 weeks after treatment increased. The diacron-reactive oxygen metabolites (d-ROMs) value of astaxanthin-treated mice 72 weeks after treatment was significantly lower than that of the control group was. The plasma biological antioxidative potential (BAP) values of the control but not astaxanthin-treated mice before and 72 weeks after treatment decreased. Moreover, the BAP value of the astaxanthin-treated group 72 weeks after treatment was significantly higher than that of the control was. Furthermore, the submandibular glands of astaxanthin-treated mice had fewer inflammatory cells than the control did. Specifically, immunofluorescence revealed a significantly large aquaporin-5 positive cells in astaxanthin-treated mice. Our results suggest that astaxanthin treatment may prevent age-related decreased saliva secretion.

KEYWORDS:

aquaporin-5; astaxanthin; hyposalivation; inflammation; oral dryness

PMID: 27698533

PMCID: [PMC5018570](#)

DOI: [10.3164/jcbn.15-150](#) PubMed - in process]

Free PMC Article

Astaxanthin from algae superior to Astaxanthin from mutated Phaffia yeast or Synthetic Astaxanthin from petrochemicals in increasing endurance and protecting tissues from oxidative damage in mice.

[J Clin Biochem Nutr.](#) 2018 Mar;62(2):161-166. doi: 10.3164/jcbn.17-89. Epub 2017 Dec 27.

Comparison of the effect of non-esterified and esterified astaxanthins on endurance performance in mice.

[Aoi W](#)¹, [Maoka T](#)², [Abe R](#)¹, [Fujishita M](#)³, [Tominaga K](#)³.

Author information

Abstract

Astaxanthin, a natural antioxidant, exists in non-esterified and esterified forms. Although it is known that astaxanthin can improve exercise endurance and cause metabolic improvement in skeletal muscle, the effects of the two different forms are unclear. We investigated the effects of the different forms of astaxanthin on endurance in mice. Eight-week-old ICR mice were divided into four groups: control; astaxanthin extracted from *Haematococcus pluvialis* in an esterified form; astaxanthin extracted from *Phaffia rhodozyma* in a non-esterified form; and astaxanthin synthesized chemically in a non-esterified form. After 5 weeks of treatment, each group was divided into sedentary and exercise groups. In the group fed astaxanthin from *Haematococcus*, the running time to exhaustion was longest, and the plasma and tissue concentrations of astaxanthin were significantly higher than those in the other groups. Astaxanthin from *Haematococcus* increased 5'-adenosine monophosphate-activated protein kinase levels in the skeletal muscle. Although the mice in the *Haematococcus* group ran for longer, hexanoyl lysine adduct levels in the skeletal muscle mitochondria were similar in the control and *Haematococcus* groups. Our results suggested that esterified astaxanthin promoted energy production and protected tissues from oxidative damage during exercise owing to its favorable absorption properties, leading to a longer running time.

KEYWORDS:

astaxanthin; energy metabolism; esterified form and non-esterified form; oxidative damage; running exercise

PMID: 29610556

PMCID: [PMC5874239](#)

DOI: [10.3164/jcbn.17-89](#)

[Free PMC Article](#)

Astaxanthin reduces cognitive impairment in rat model by decreasing inflammation, oxidation and cell death.

[Mol Neurobiol.](#) 2018 Jul;55(7):5727-5740. doi: 10.1007/s12035-017-0797-7. Epub 2017 Oct 16.

Astaxanthin Ameliorates Doxorubicin-Induced Cognitive Impairment (Chemobrain) in Experimental Rat Model: Impact on Oxidative, Inflammatory, and Apoptotic Machineries.

[El-Agamy SE¹](#), [Abdel-Aziz AK¹](#), [Wahdan S¹](#), [Esmat A¹](#), [Azab SS²](#).

Author information

Abstract

Chemobrain refers to a common sequelae experienced by 15-80% of cancer patients exposed to chemotherapeutics. The antineoplastic agent doxorubicin (DOX) has been implicated in a strenuous neurotoxicity manifested as decline in cognitive functions, most probably via cytokine-induced oxidative and nitrosative damage to brain tissues. Astaxanthin (AST), a naturally occurring carotenoid, is reputable for its outstanding antioxidant, anti-inflammatory, and antiapoptotic activities. Therefore, the aim of the current study was to investigate the potential neuroprotective and memory-enhancing effects of AST against DOX-induced behavioral and neurobiological abnormalities. Briefly, AST treatment (25 mg/kg) significantly protected against DOX-induced memory impairment. Furthermore, AST restored hippocampal histopathological architecture, halted DOX-induced oxidative and inflammatory insults, mitigated the increase in acetylcholinesterase activity, and consistently downregulated the overactive apoptotic machineries. In conclusion, these findings suggest that AST offers neuroprotection against DOX-induced cognitive impairment which could be explained at least partly by its antioxidant, anti-inflammatory, and antiapoptotic effects.

KEYWORDS:

Apoptosis; Astaxanthin; Chemobrain; Doxorubicin; Neuroinflammation; Oxidative stress

PMID: 29039023

DOI: [10.1007/s12035-017-0797-7](https://doi.org/10.1007/s12035-017-0797-7)

Astaxanthin improves cardiac dysfunction and oxidative status in rats.

[Naunyn-Schmiedeberg's Arch Pharmacol.](#) 2018 Nov 30. doi: 10.1007/s00210-018-1595-0. [Epub ahead of print]

Astaxanthin ameliorates cardiomyocyte apoptosis after coronary microembolization by inhibiting oxidative stress via Nrf2/HO-1 pathway in rats.

[Xue Y¹](#), [Sun C¹](#), [Hao Q¹](#), [Cheng J²](#).

Author information

Abstract

Coronary microembolization (CME) caused by physical obstruction in coronary microcirculation induces myocardial apoptosis and cardiac dysfunction, and it was reported that the inactivation of the Nrf2/HO-1 signaling was involved in this process. Astaxanthin (AST) is a reddish pigment that belongs to keto-carotenoids. It is also a potent antioxidant and has been reported to activate Nrf2/HO-1 signaling in vein endothelial cells. However, it is still unknown whether AST is able to activate Nrf2/HO-1 signaling pathway to protect cardiac functions from CME in vivo. To address this question, rats were orally administrated with AST or AST plus Zinc protoporphyrin IX (ZnPP, a HO-1 inhibitor), followed by CME modeling operation. Then, cardiac function was evaluated by echocardiographic measurement. Myocardial infarction was measured by HBFP staining, and apoptosis was assessed by TUNEL staining. The protein levels and mRNA expressions of Bax and Bcl-2 were measured by Western blot and qRT-PCR, respectively. ELISA was performed to measure the activity of enzymes related to oxidative stress. AST pretreatment dramatically attenuated CME-induced cardiac dysfunction, myocardial infarction, and cardiomyocyte apoptosis. Mechanistically, AST suppressed CME-induced oxidative stress by re-activating Nrf2/HO-1 signaling. HO-1 inhibitor ZnPP completely eliminated the benefits of AST in CEM, supporting the critical role of Nrf2/HO-1 signaling in mediating the cardioprotective function of AST in CME. Conclusion: AST suppresses oxidative stress via activating Nrf2/HO-1 pathway and thus prevents CME-induced cardiomyocyte apoptosis and ameliorates cardiac dysfunction in rats.

KEYWORDS:

Astaxanthin; Cardiomyocyte apoptosis; Coronary microembolization; Nrf2/HO-1 signaling; Oxidative stress

PMID: 30506291

DOI: [10.1007/s00210-018-1595-0](https://doi.org/10.1007/s00210-018-1595-0)

Astaxanthin increases lifespan, decreases cell death and decreases oxidative stress in *Saccharomyces cerevisiae* (a yeast that is a model for cell death and aging).

[FEMS Yeast Res.](#) 2019 Jan 1;19(1). doi: 10.1093/femsyr/foy113.

Astaxanthin enhances the longevity of *Saccharomyces cerevisiae* by decreasing oxidative stress and apoptosis.

[Sj S¹](#), [Veerabhadrapa B¹](#), [Subramanian S¹](#), [Dyavaiah M¹](#).

Author information

Abstract

The budding yeast, *Saccharomyces cerevisiae*, is an efficient model for studying oxidative stress, programmed cell death and aging. The present study was carried out to investigate antioxidant, the anti-apoptotic and anti-aging activity of a natural compound, astaxanthin, in *S. cerevisiae* model. The survivability of yeast antioxidant-deficient strains (*sod1Δ*, *sod2Δ*, *cta1Δ*, *ctt1Δ* and *tsa1Δ*) increased by 20%-40% when cells were pre-treated with astaxanthin, compared to hydrogen peroxide alone, as demonstrated in spot and colony forming unit assays. Reduced reactive oxygen species (ROS) levels, increased glutathione, decreased lipid peroxidation and induced superoxide dismutase activity in astaxanthin-treated cells indicate that astaxanthin protected the cells from oxidative-stress-induced cell death. In addition, astaxanthin protected anti-apoptotic-deficient strains (*pep4Δ* and *fis1Δ*) against acetic acid and hydrogen peroxide-induced cell death that suggests anti-apoptotic property of astaxanthin, and it was further confirmed by acridine orange/ethidium bromide, annexin V and 4',6-diamidino-2-phenylindole staining. The yeast chronological lifespan assay results showed that astaxanthin extends the lifespan of antioxidant-deficient strains by scavenging ROS, and anti-apoptotic-deficient mutants by protecting from apoptotic cell death compared to their respective untreated cells and wild type. Our results suggest that astaxanthin enhances the longevity of yeast *S. cerevisiae* by reducing oxidative stress and apoptosis.

PMID: 30312390

DOI: [10.1093/femsyr/foy113](https://doi.org/10.1093/femsyr/foy113)

Astaxanthin shows anti-inflammatory and antioxidant effects in-vitro and in mice and multiple anti-inflammatory mechanisms were found.

[J Nutr Biochem](#). 2018 Dec;62:202-209. doi: 10.1016/j.jnutbio.2018.09.005. Epub 2018 Sep 19.

Astaxanthin exerts anti-inflammatory and antioxidant effects in macrophages in NRF2-dependent and independent manners.

[Farruggia C](#)¹, [Kim MB](#)¹, [Bae M](#)¹, [Lee Y](#)¹, [Pham TX](#)¹, [Yang Y](#)¹, [Han MJ](#)², [Park YK](#)¹, [Lee JY](#)³.

Author information

Abstract

Although anti-inflammatory effects of astaxanthin (ASTX) have been suggested, the underlying mechanisms have not been fully understood. Particularly, the modulatory action of ASTX in the interplay between nuclear factor E2-related factor 2 (NRF2) and nuclear factor κ B (NF κ B) to exert its anti-inflammatory effect in macrophages is unknown. The effect of ASTX on mRNA and protein expression of pro-inflammatory and antioxidant genes and/or cellular reactive oxygen species (ROS) accumulation were determined in RAW 264.7 macrophages, bone marrow-derived macrophages (BMDM) from wild-type (WT) and Nrf2-deficient mice, and/or splenocytes and peritoneal macrophages of obese mice fed ASTX. The effect of ASTX on M1 and M2 macrophage polarization was evaluated in BMDM. ASTX significantly decreased LPS-induced mRNA expression of interleukin 6 (Il-6) and Il-1 β by inhibiting nuclear translocation of NF κ B p65; and attenuated LPS-induced ROS with an increase in NRF2 nuclear translocation, concomitantly decreasing NADPH oxidase 2 expression in RAW 264.7 macrophages. In BMDM of WT and Nrf2-deficient mice, ASTX decreased basal and LPS-induced ROS accumulation. The induction of Il-6 mRNA by LPS was repressed by ASTX in both types of BMDM while Il-1 β mRNA was decreased only in WT BMDM. Furthermore, ASTX consumption lowered LPS sensitivity of splenocytes in obese mice. ASTX decreased M1 polarization of BMDM while increasing M2 polarization. ASTX exerts its anti-inflammatory effect by inhibiting nuclear translocation of NF κ B p65 and by preventing ROS accumulation in NRF2-dependent and -independent mechanisms. Thus, ASTX is an agent with anti-inflammatory and antioxidant properties that may be used for the prevention of inflammatory conditions.

KEYWORDS:

Anti-inflammatory; Antioxidant; Astaxanthin; Macrophages; NF κ B; NRF2

PMID: 30308382

DOI: [10.1016/j.jnutbio.2018.09.005](https://doi.org/10.1016/j.jnutbio.2018.09.005)

Astaxanthin reduces alcohol-induced liver injury by reducing inflammation and oxidation in rodents.

[Sci Rep.](#) 2018 Sep 20;8(1):14090. doi: 10.1038/s41598-018-32497-w.

Astaxanthin alleviated ethanol-induced liver injury by inhibition of oxidative stress and inflammatory responses via blocking of STAT3 activity.

[Han JH¹](#), [Ju JH¹](#), [Lee YS¹](#), [Park JH¹](#), [Yeo IJ¹](#), [Park MH¹](#), [Roh YS¹](#), [Han SB¹](#), [Hong JT²](#).

Author information

Abstract

Astaxanthin (AXT) is classified as a xanthophyll carotenoid compound which have broader functions including potent antioxidant, anti-inflammatory and neuroprotective properties. Considerable researches have demonstrated that AXT shows preventive and therapeutic properties against for Diabetes, Osteoarthritis and Rheumatoid Arthritis. However, the protective effect of AXT on liver disease has not yet been reported. In this study, we investigated effects of AXT on ethanol-induced liver injury in chronic plus binge alcohol feeding model. The hepatic steatosis and inflammation induced by ethanol administration were alleviated by AXT. Serum levels of aspartate transaminase and alanine transaminase were decreased in the livers of AXT administrated group. The ethanol-induced expression of cytochrome P450 2E1 (CYP2E1), pro-inflammatory proteins, cytokines, chemokines and reactive oxygen species (ROS) levels were also reduced in the livers of AXT administrated group. Moreover, ethanol-induced infiltration of neutrophils was decreased in the livers of AXT administrated group. Docking model and pull-down assay showed that AXT directly binds to the DNA binding site of STAT3. Moreover, AXT decreased STAT3 phosphorylation in the liver of AXT administration group. Therefore, these results suggest that AXT could prevent ethanol-induced hepatic injury via inhibition of oxidant and inflammatory responses via blocking of STAT3 activity.

PMID: 30237578

DOI: [10.1038/s41598-018-32497-w](https://doi.org/10.1038/s41598-018-32497-w)

Free full text

Astaxanthin protects brain function and reduces inflammation and oxidative stress in rats.

[Front Pharmacol.](#) 2018 Jul 10;9:748. doi: 10.3389/fphar.2018.00748. eCollection 2018.

The Protective Effect of Astaxanthin on Cognitive Function via Inhibition of Oxidative Stress and Inflammation in the Brains of Chronic T2DM Rats.

[Feng Y¹](#), [Chu A²](#), [Luo Q³](#), [Wu M¹](#), [Shi X¹](#), [Chen Y³](#).

Author information

Abstract

Currently, there are no effective treatments for diabetes-related cognitive dysfunction. Astaxanthin (AST), the most powerful antioxidant in nature, exhibits diverse biological functions. In this study, we tried to explore whether AST would ameliorate cognitive dysfunction in chronic type 2 diabetes mellitus (T2DM) rats. The T2DM rat model was induced via intraperitoneal injection of streptozotocin. Forty Wistar rats were divided into a normal control group, an acute T2DM group, a chronic T2DM group, and an AST group (treated with AST at a dose of 25 mg/kg three times a week). The Morris water maze test showed that the percentage of time spent in the target quadrant of the AST group was identical to that of the chronic T2DM group, while the escape latency of the AST group was decreased in comparison to that of the chronic T2DM group. Histology of the hippocampus revealed that AST ameliorated the impairment in the neurons of diabetic rats. Western blot showed that AST could upregulate nuclear factor erythroid 2-related factor 2 (Nrf2) and heme oxygenase 1 (HO-1) expression and inhibit nuclear transcription factor kappa B (NF- κ B) p65 activation in the hippocampus. We found that AST increased the level of superoxide dismutase (SOD) and decreased the level of malondialdehyde (MDA) in the hippocampus. In addition, the levels of interleukin 1 beta (IL-1 β) and interleukin 6 (IL-6) were reduced in the AST group compared with those in the chronic T2DM group. The findings of this research imply that AST might inhibit oxidative stress and inflammatory responses by activating the Nrf2-ARE signaling pathway.

KEYWORDS:

Nrf2; astaxanthin; cytokines; inflammatory response; oxidative stress; type 2 diabetes mellitus

PMID: 30042685

PMCID: [PMC6048598](#)

DOI: [10.3389/fphar.2018.00748](#)

Free PMC Article

Astaxanthin protects sperm plasma membrane from free radicals and lipid peroxidation in pigs.

[Biomed Res Int](#). 2018 Apr 19;2018:6784591. doi: 10.1155/2018/6784591. eCollection 2018.

Effects of Astaxanthin on Miniature Pig Sperm Cryopreservation.

[Lee E¹](#), [Kim D¹](#).

[Author information](#)

Abstract

The purpose of this study is to evaluate the effects of astaxanthin added to freezing buffer on semen parameters, total sperm oxidation stress after postthawing of boar sperm, and lipid peroxidation (LPO) which is caused by reactive oxygen species (ROS) in sperm membrane. Varying concentrations of astaxanthin (0, 10, 50, 100, and 500 μM) were used in the freezing buffer during cryopreservation to protect the DNA of thawed miniature pig sperm. Semen parameter was measured using computer-assisted sperm analysis (CASA) for sperm motility, and then ROS rate and oxidative stress of boar sperm were determined using fluorescence-activated cell sorting (FACS). Sperm motility was higher ($p < 0.05$) in the astaxanthin group than in the control group. Sperm motility and the number of progressive motile sperm were higher ($p < 0.05$) in the astaxanthin 500 μM group than in the control group. In ROS evaluation, the astaxanthin group had lower intracellular O_2 and H_2O_2 in viable sperm. Yo-Pro-I/HE and PI/H2DCFDA staining as revealed using flow cytometry was lower in astaxanthin groups than in the other groups. As a result, we found that astaxanthin could protect the sperm plasma membrane from free radicals and LPO during boar sperm postthawing.

PMID: 29850549

PMCID: [PMC5933026](#)

DOI: [10.1155/2018/6784591](#)

[Indexed for MEDLINE]

[Free PMC Article](#)

Astaxanthin reduces spinal cord lesions, prevents cell death and inhibits lipid peroxidation in rats.

[Zhongguo Xiu Fu Chong Jian Wai Ke Za Zhi](#). 2018 May 1;32(5):548-553. doi: 10.7507/1002-1892.201712127.

[Effect of astaxanthin on the apoptosis after spinal cord injury in rats].

[Article in Chinese; Abstract available in Chinese from the publisher]

[Ren X¹](#), [Ding W²](#), [Yang X³](#).

Author information

Abstract

in [English](#), [Chinese](#)

OBJECTIVE:

To study the effects of astaxanthin on the apoptosis after spinal cord injury in rats.

METHODS:

One hundred and forty-four healthy adult Sprague Dawley rats were divided into experimental group, control group, and sham group according to the random number table ($n=48$). In the control group and the experimental group, the modified Allen's method was used to make the spinal cord injury model; in the sham group, only the lamina was cut without damaging the spinal cord. At immediate after operation, the rats in the experimental group were given intragastric administration of astaxanthin (75 mg/kg) twice a day; and the rats in the control group and the sham group were given equal amount of olive oil by gavage twice a day. BBB score was used to assess the motor function at 1 day and 1, 2, 3, and 4 weeks after operation. The malondialdehyde (MDA) content was determined by the thiobarbituric acid method at 24 hours after operation; and the activity of superoxide dismutase (SOD) was determined by the xanthine oxidase method. Apoptosis index (AI) was determined by TUNEL method at 6, 24, and 48 hours after operation. At 48 hours after operation, the water content of spinal cord was measured by dry-wet weight method, the lesion ratio of spinal cord was calculated, the ultrastructure of the spinal cord was observed by transmission electron microscopy, and ultrastructure scoring was performed using the Kaptanoglu score method.

RESULTS:

The BBB score in the control group and the experimental group was significantly lower than that in the sham group at each postoperative time point ($P<0.05$); and the BBB score in the experimental group were significantly higher than that in the control group at 1-4 weeks postoperatively ($P<0.05$). The MDA content in the control group and the experimental group was significantly higher than that in the sham group at 24 hours after operation, and in the experimental group was significantly lower than in the control group ($P<0.05$). The SOD activity in the control group and the experimental group was significantly lower than that in the sham group, and in the experimental group was significantly

higher than in the control group ($P<0.05$). At each time point postoperatively, the AI in the control group and the experimental group was significantly higher than that in the sham group, and in the experimental group was significantly lower than in the control group ($P<0.05$). At 48 hours after operation, the water content of spinal cord, the lesion ratio of spinal cord, and the ultrastructure score in the control group and the experimental group were significantly higher than those in the sham group, and in the experimental group were significantly lower than in the control group ($P<0.05$).

CONCLUSION:

Astaxanthin can inhibit the lipid peroxidation, reduce the apoptosis, reduce the spinal cord edema, reduce the spinal cord lesion, reduce the histopathological damage after spinal cord injury, and improve the motor function of rats with spinal cord injury, and protect the spinal cord tissue, showing an obvious neuroprotective effect.

KEYWORDS:

Astaxanthin; apoptosis; rat; spinal cord injury

PMID: 29806341

DOI: [10.7507/1002-1892.201712127](https://doi.org/10.7507/1002-1892.201712127)

[Indexed for MEDLINE]

Astaxanthin increases testosterone levels and testis weight and improves oxidative status in rats fed a high fructose diet.

[Andrologia](#). 2018 May 9:e13042. doi: 10.1111/and.13042. [Epub ahead of print]

Effects of astaxanthin on biochemical and histopathological parameters related to oxidative stress on testes of rats on high fructose regime.

[Dokumacioglu E¹](#), [Iskender H¹](#), [Yenice G²](#), [Kapakin KAT³](#), [Sevim C⁴](#), [Hayirli A²](#), [Sara S⁵](#), [Comakli S³](#).

Author information

Abstract

Astaxanthin (ASX) is a xanthophyll family of hydroxycarotenoids which contains several double bonds. It is produced by *Haemococcus pluvialis*, a microalgae and possesses antioxidant and anti-inflammatory properties. The aim of this study was to test whether ASX could protect against oxidative damage in the testicular tissues of rats receiving high fructose. The rats (n = 24) were randomly divided into two main groups: control and fructose (30%, via drinking water) and then each main group either not supplemented or supplemented with ASX (1 mg kg⁻¹ day⁻¹, within 0.2 ml olive oil) via oral gavage. Data were subjected to two-way ANOVA. High fructose consumption tended to increase testis weight and serum testosterone concentration and decreased testicular tissue glutathione-S-transferase (GST) and superoxide dismutase (SOD) levels, but did not affect testicular tissue malondialdehyde (MDA) concentration. Astaxanthin administration increased testosterone, GST and SOD levels and testis weight and decreased MDA concentration. However, ASX administration did not reverse alterations in antioxidant parameters caused by high fructose consumption. Inducible nitric oxide synthase (iNOS) tended to increase in sertoli cell, spermatid and spermatogonia, but not in spermatocytes and leydig cell in response to high fructose consumption. Astaxanthin administration tended to reverse elevation in iNOS in testis cells. In conclusion, ASX could help alleviate oxidative damage caused by high fructose consumption.

KEYWORDS:

astaxanthin; fructose; oxidative stress; testes

PMID: 29744903

DOI: [10.1111/and.13042](https://doi.org/10.1111/and.13042)

Astaxanthin fed to chickens improves their antioxidant defense and meat quality.

[J Agric Food Chem](#). 2018 Jun 6;66(22):5521-5530. doi: 10.1021/acs.jafc.8b00860. Epub 2018 May 23.

Dose-Dependent Enrichments and Improved Redox Status in Tissues of Broiler Chicks under Heat Stress by Dietary Supplemental Microalgal Astaxanthin.

[Sun T¹](#), [Yin R¹](#), [Magnuson AD¹](#), [Tolba SA¹](#), [Liu G¹](#), [Lei XG¹](#).

Author information

Abstract

Astaxanthin (AST) is a well-known carotenoid with a high antioxidant capacity. This study was designed to evaluate the nutritional and metabolic effects of microalgal AST added to the diets of broiler chicks under heat stress. A total of 240 Cornish male chicks (1 day old) were divided into six cages per treatment (eight chicks per cage) and fed a corn-soybean meal diet supplemented with AST from *Haematococcus pluvialis* at 0, 10, 20, 40, and 80 mg/kg for 6 weeks. Heat stress was employed during weeks 4-6. The supplementation led to dose-dependent enrichments ($P < 0.05$) of AST and total carotenoids in the plasma, the liver, and the breast and thigh muscles. There were similar enhancements ($P < 0.05$) of oxygen-radical-absorbance capacities, but there were decreases or mixed responses ($P < 0.05$) of glutathione concentrations and glutathione peroxidase activities in the tissues. In conclusion, supplemental dietary microalgal AST was bioavailable to the chicks and enriched in their tissues independent of heat stress, leading to coordinated changes in their endogenous antioxidant defense and meat quality.

KEYWORDS:

antioxidant; astaxanthin; chick; fatty acid; microalgae

PMID: 29733582

DOI: [10.1021/acs.jafc.8b00860](https://doi.org/10.1021/acs.jafc.8b00860)

ASTAXANTHIN IS A STRONG ANTIOXIDANT WITHOUT PRO-OXIDANT EFFECTS.

Food Chem. 2018 Dec 1;268:542-549.

doi: 10.1016/j.foodchem.2018.06.063. Epub 2018 Jun 14.

Thermodynamics of radical scavenging of symmetric carotenoids and their charged species

[Peter Poliak](#)¹, [Peter Škorňa](#)², [Erik Klein](#)³, [Vladimír Lukeš](#)³

- PMID: 30064795
- DOI: [10.1016/j.foodchem.2018.06.063](https://doi.org/10.1016/j.foodchem.2018.06.063)

Abstract

For nine symmetric natural carotenoids, a comprehensive thermodynamics study of processes associated with their radical scavenging activity is proposed. We have investigated the hydrogen atom transfer (HAT) from the parent carotenoid, mono-radical species, radical cations and radical anions. Electron transfer and proton transfer reactions were also studied. Terminal units and carbon atoms in their vicinity were identified as thermodynamically favoured reaction sites of the HAT mechanism. Rhodoxanthin, canthaxanthin and astaxanthin, as strong antioxidants, without any pro-oxidative effect, were found to have bond dissociation enthalpies (BDE) higher than 300 kJ mol⁻¹ and the most negative electron affinities. The electron transfer to a carotenoid is exothermic, while other studied reactions are endothermic. In solvent, the electron transfer reactions may be preferred instead of hydrogen atom transfer.

Astaxanthin shows antioxidative properties in-vitro.

[Mar Drugs](#). 2018 Apr 12;16(4). pii: E126. doi: 10.3390/md16040126.

Astaxanthin Restrains Nitrate-Oxidative Peroxidation in Mitochondrial-Mimetic Liposomes: A Pre-Apoptosis Model.

[Mano CM](#)^{1,2,3}, [Guaratini T](#)^{4,5}, [Cardozo KHM](#)^{6,7}, [Colepicolo P](#)⁸, [Bechara EJH](#)^{9,10}, [Barros MP](#)^{11,12}.

Author information

Abstract

Astaxanthin (ASTA) is a ketocarotenoid found in many marine organisms and that affords many benefits to human health. ASTA is particularly effective against radical-mediated lipid peroxidation, and recent findings hypothesize a "mitochondrial-targeted" action of ASTA in cells. Therefore, we examined the protective effects of ASTA against lipid peroxidation in zwitterionic phosphatidylcholine liposomes (PCLs) and anionic phosphatidylcholine: phosphatidylglycerol liposomes (PCPGLs), at different pHs (6.2 to 8.0), which were challenged by oxidizing/nitrating conditions that mimic the regular and preapoptotic redox environment of active mitochondria. Pre-apoptotic conditions were created by oxidized/nitr(osyl)ated cytochrome c and resulted in the highest levels of lipoperoxidation in both PCL and PCPGLs (pH 7.4). ASTA was less protective at acidic conditions, especially in anionic PCPGLs. Our data demonstrated the ability of ASTA to hamper oxidative and nitrate events that lead to cytochrome c-peroxidase apoptosis and lipid peroxidation, although its efficiency changes with pH and lipid composition of membranes.

KEYWORDS:

antioxidant; apoptosis; carotenoid; lipid peroxidation; liposome; membrane; mitochondria; oxidative stress

PMID: 29649159

PMCID: [PMC5923413](#)

DOI: [10.3390/md16040126](#)

[Indexed for MEDLINE]

[Free PMC Article](#)

Astaxanthin improves behavioral disorder and oxidative stress in mouse model of autism.

[Behav Brain Res.](#) 2015 Jun 1;286:112-21. doi: 10.1016/j.bbr.2015.02.041. Epub 2015 Feb 28.

Astaxanthin improves behavioral disorder and oxidative stress in prenatal valproic acid-induced mice model of autism.

[Al-Amin MM¹](#), [Rahman MM¹](#), [Khan FR¹](#), [Zaman F¹](#), [Mahmud Reza H²](#).

Author information

Abstract

Prenatal exposure to valproic acid on gestational day 12.5 may lead to the impaired behavior in the offspring, which is similar to the human autistic symptoms. To the contrary, astaxanthin shows neuroprotective effect by its antioxidant mechanism. We aimed to (i) develop mice model of autism and (ii) investigate the effect of astaxanthin on such model animals. Valproic acid (600 mg/kg) was administered intraperitoneally to the pregnant mice on gestational day 12.5. Prenatal valproic acid-exposed mice were divided into 2 groups on postnatal day 25 and astaxanthin (2mg/kg) was given to the experimental group (VPA_AST, n=10) while saline was given to the control group (VPA, n=10) for 4 weeks. Behavioral test including social interaction, open field and hot-plate were conducted on postnatal day 25 and oxidative stress markers such as lipid peroxidation, advanced protein oxidation product, nitric oxide, glutathione, and activity of superoxide dismutase and catalase were estimated on postnatal day 26 to confirm mice model of autism and on postnatal day 56 to assess the effect of astaxanthin. On postnatal day 25, prenatal valproic acid-exposed mice exhibited (i) delayed eye opening (ii) longer latency to respond painful stimuli, (iii) poor sociability and social novelty and (iv) high level of anxiety. In addition, an increased level of oxidative stress was found by determining different oxidative stress markers. Treatment with astaxanthin significantly ($p < 0.05$) improved the behavioral disorder and reduced the oxidative stress in brain and liver. In conclusion, prenatal exposure to valproic acid in pregnant mice leads to the development of autism-like features. Astaxanthin improves the impaired behavior in animal model of autism presumably by its antioxidant activity.

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KEYWORDS:

Astaxanthin; Autism; Oxidative stress; Valproic acid

PMID:

25732953

[PubMed - in process]

Astaxanthin protects mice from ischemia/reperfusion in the kidneys which is attributed to its antioxidant activity.

[J Transl Med.](#) 2015 Jan 27;13:28. doi: 10.1186/s12967-015-0388-1.

Protective effects of astaxanthin against ischemia/reperfusion induced renal injury in mice.

[Qiu X](#)^{1,2,3}, [Fu K](#)^{4,5}, [Zhao X](#)^{6,7}, [Zhang Y](#)⁸, [Yuan Y](#)⁹, [Zhang S](#)¹⁰, [Gu X](#)¹¹, [Guo H](#)¹².

Author information

Abstract

Astaxanthin (ATX) is a powerful antioxidant that occurs naturally in a wide variety of living organisms. Previous studies have shown that ATX has effects of eliminating oxygen free radicals and can protect organs from ischemia/reperfusion (IR) induced injury. The present study was designed to further investigate the protective effects of ATX on oxidative stress induced toxicity in tubular epithelial cells and on IR induced renal injury in mice. ATX, at a concentration of 250 nM, attenuated 100 μ M H₂O₂-induced viability decrease of tubular epithelial cells. In vivo, ATX preserved renal function 12 h or 24 h post IR. Pretreatment of ATX via oral gavage for 14 consecutive days prior to IR dramatically prevented IR induced histological damage 24 h post IR. Histological results showed that the pathohistological score, number of apoptotic cells, and the expression of α -smooth muscle actin were significantly decreased by pretreatment of ATX. In addition, oxidative stress and inflammation in kidney samples were significantly reduced by ATX 24 h post IR. Taken together, the current study suggests that pretreatment of ATX is effective in preserving renal function and histology via antioxidant activity.

PMID:

25623758

[PubMed - in process]

PMCID:

PMC4323259

[Free PMC Article](#)

Astaxanthin has a neuroprotective effect in rat ganglion cells subjected to oxidative stress and other insults.

[Mol Vis.](#) 2014 Dec 31;20:1796-805. eCollection 2014.

Neuroprotective effect of astaxanthin against rat retinal ganglion cell death under various stresses that induce apoptosis and necrosis.

[Yamaqishi R](#)¹, [Aihara M](#)².

Author information

Abstract

PURPOSE:

Astaxanthin is a type of carotenoid known to have strong antioxidant effects. The purpose of this study was to investigate whether astaxanthin confers a neuroprotective effect against glutamate stress, oxidative stress, and hypoxia-induced apoptotic or necrotic cell death in primary cultures of rat retinal ganglion cells (RGCs).

METHODS:

Purified rat RGCs were exposed to three kinds of stressors induced by 25 μ M glutamate for 72 h, B27 medium without an antioxidant for 4 h, and a reduced oxygen level of 5% for 12 h. Each assay was repeated 12 times, with or without 1 nM, 10 nM, and 100 nM astaxanthin. The number of live RGCs was then counted using a cell viability assay. RGC viability in each condition was evaluated and compared with controls. In addition, we measured apoptosis and DNA damage.

RESULTS:

We found that under glutamate stress, RGC viability was reduced to 58%. Cultures with 1 nM, 10 nM, and 100 nM astaxanthin showed an increase in RGC viability of 63%, 74%, and 84%, respectively. Under oxidative stress, RGC viability was reduced to 40%, and astaxanthin administration resulted in increased viability of 43%, 50%, and 67%, respectively. Under hypoxia, RGC viability was reduced to 66%, and astaxanthin administration resulted in a significant increase in viability to 67%, 77%, and 93%, respectively. These results indicate that 100 nM astaxanthin leads to a statistically significant increase in RGC viability under the three kinds of stressors tested, compared to controls (Dunnett's test, $p < 0.05$). The apoptotic activity of RGCs under glutamate stress increased to 32%, but was reduced to 15% with 100 nM astaxanthin administration. Glutamate stress led to a 58% increase in DNA damage, which was reduced to 43% when cultured with 100 nM astaxanthin. Thus, 100 nM astaxanthin showed a statistically significant reduction in apoptosis and DNA damage in RGCs (Wilcoxon rank-sum test, $p < 0.05$).

CONCLUSIONS:

Our results suggest that astaxanthin has a neuroprotective effect against RGC death induced by glutamate stress, oxidative stress, and hypoxia, which induce apoptotic and necrotic cell death.

PMID:

25593507 [PubMed - in process] PMID: PMC4287717

[Free PMC Article](#)

Astaxanthin alleviates early brain injury in rats which may be due to inducing antioxidant activity and detoxifying enzymes.

[Mar Drugs](#). 2014 Dec 18;12(12):6125-41. doi: 10.3390/md12126125.

Astaxanthin activates nuclear factor erythroid-related factor 2 and the antioxidant responsive element (Nrf2-ARE) pathway in the brain after subarachnoid hemorrhage in rats and attenuates early brain injury.

[Wu Q](#)¹, [Zhang XS](#)², [Wang HD](#)³, [Zhang X](#)⁴, [Yu Q](#)⁵, [Li W](#)⁶, [Zhou ML](#)⁷, [Wang XL](#)⁸.

Author information

Abstract

Astaxanthin (ATX) has been proven to ameliorate early brain injury (EBI) after experimental subarachnoid hemorrhage (SAH) by modulating cerebral oxidative stress. This study was performed to assess the effect of ATX on the Nrf2-ARE pathway and to explore the underlying molecular mechanisms of antioxidant properties of ATX in EBI after SAH. A total of 96 male SD rats were randomly divided into four groups. Autologous blood was injected into the prechiasmatic cistern of the rat to induce an experimental SAH model. Rats in each group were sacrificed at 24 h after SAH. Expressions of Nrf2 and heme oxygenase-1 (HO-1) were measured by Western blot and immunohistochemistry analysis. The mRNA levels of HO-1, NAD (P) H: quinone oxidoreductase 1 (NQO-1), and glutathione S-transferase- α 1 (GST- α 1) were determined by real-time polymerase chain reaction (PCR). It was observed that administration of ATX post-SAH could up-regulate the cortical expression of these agents, mediated in the Nrf2-ARE pathway at both pretranscriptional and posttranscriptional levels. Meanwhile, oxidative damage was reduced. Furthermore, ATX treatment significantly attenuated brain edema, blood-brain barrier (BBB) disruption, cellular apoptosis, and neurological dysfunction in SAH models. This study demonstrated that ATX treatment alleviated EBI in SAH model, possibly through activating the Nrf2-ARE pathway by inducing antioxidant and detoxifying enzymes.

Astaxanthin inhibits colonic lesions in mice in obesity-related colorectal carcinogenesis model by reducing oxidative stress and reducing chronic inflammation.

[BMC Gastroenterol.](#) 2014 Dec 17;14:212. doi: 10.1186/s12876-014-0212-z.

Inhibitory effects of astaxanthin on azoxymethane-induced colonic preneoplastic lesions in C57/BL/KsJ-db/db mice.

[Kochi T](#)¹, [Shimizu M](#)², [Sumi T](#)³, [Kubota M](#)⁴, [Shirakami Y](#)⁵, [Tanaka T](#)⁶, [Moriwaki H](#)⁷.

Author information

Abstract

BACKGROUND:

Obesity and related metabolic abnormalities, including excess oxidative stress and chronic inflammation, are associated with colorectal carcinogenesis. Astaxanthin, a xanthophyll carotenoid found in aquatic animals, is known to possess antioxidant, anti-inflammatory, and antineoplastic properties. The present study examined the effects of astaxanthin on the development of azoxymethane (AOM)-induced colonic premalignant lesions in C57BL/KsJ-db/db (db/db) obese mice.

METHOD:

Male db/db mice were administered 4 weekly subcutaneous injections of AOM (15 mg/kg body weight) from 5 weeks of age and subsequently, from 1 week after the last injection of AOM, were fed a diet containing 200 ppm astaxanthin throughout the experiment (8 weeks).

RESULT:

The development of colonic premalignant lesions, i.e., aberrant crypt foci and β -catenin accumulated crypts, was significantly inhibited in mice treated with astaxanthin than in mice fed the basal diet. Astaxanthin administration markedly reduced urinary levels of 8-OHdG and serum levels of d-ROMs, which are oxidative stress markers, while increasing the expression of mRNA for the antioxidant enzymes GPx1, SOD1, and CAT in the colonic mucosa of AOM-treated db/db mice. The expression levels of IL-1 β , IL-6, F4/80, CCL2, and CXCL2 mRNA in the colonic mucosa of AOM-treated mice were significantly decreased by astaxanthin. Dietary feeding with astaxanthin also resulted in a reduction in the numbers of NF- κ B- and PCNA-positive cells that were increased by AOM exposure, in the colonic epithelium.

CONCLUSION:

These findings suggest that astaxanthin inhibits the development of colonic premalignant lesions in an obesity-related colorectal carcinogenesis model by reducing oxidative stress, attenuating chronic inflammation, and inhibiting NF- κ B activation and cell proliferation in the colonic mucosa. Astaxanthin, therefore, may be a potential candidate as a chemoprevention agent against colorectal carcinogenesis in obese individuals.

PMID: 25515685

[PubMed - indexed for MEDLINE]

PMCID: PMC4273491

[Free PMC Article](#)

Astaxanthin increases endurance and limits oxidative stress in mice during exercise.

[Nutrients](#). 2014 Dec 12;6(12):5819-38. doi: 10.3390/nu6125819.

Astaxanthin supplementation delays physical exhaustion and prevents redox imbalances in plasma and soleus muscles of Wistar rats.

[Polotow TG](#)¹, [Vardaris CV](#)², [Mihaliuc AR](#)³, [Gonçalves MS](#)⁴, [Pereira B](#)⁵, [Ganini D](#)⁶, [Barros MP](#)⁷.

Author information

Abstract

Astaxanthin (ASTA) is a pinkish-orange carotenoid commonly found in marine organisms, especially salmon. ASTA is a powerful antioxidant and suggested to provide benefits for human health, including the inhibition of LDL oxidation, UV-photoprotection, and prophylaxis of bacterial stomach ulcers. Exercise is associated to overproduction of free radicals in muscles and plasma, with pivotal participation of iron ions and glutathione (GSH). Thus, ASTA was studied here as an auxiliary supplement to improve antioxidant defenses in soleus muscles and plasma against oxidative damage induced by exhaustive exercise. Long-term 1 mg ASTA/kg body weight (BW) supplementation in Wistar rats (for 45 days) significantly delayed time to exhaustion by 29% in a swimming test. ASTA supplementation increased scavenging/iron-chelating capacities (TEAC/FRAP) and limited exercise-induced iron overload and its related pro-oxidant effects in plasma of exercising animals. On the other hand, ASTA induced significant mitochondrial Mn-dependent superoxide dismutase and cytosolic glutathione peroxidase antioxidant responses in soleus muscles that, in turn, increased GSH content during exercise, limited oxidative stress, and delayed exhaustion. We also provided significant discussion about a putative "mitochondrial-targeted" action of ASTA based on previous publications and on the positive results found in the highly mitochondrial populated (oxidative-type) soleus muscles here.

PMID:

25514562

[PubMed - in process]

PMCID:

PMC4277001

[Free PMC Article](#)

Astaxanthin effective in free radical scavenging and protects against nitrite stress in shrimp.

[J Agric Food Chem](#). 2014 Dec 24;62(51):12326-31. doi: 10.1021/jf503754q. Epub 2014 Dec 10.

Effect of dietary astaxanthin on free radical scavenging capacity and nitrite stress tolerance of postlarvae shrimp, *Pleoticus muelleri*.

[Díaz AC](#)¹, [Velurtas SM](#), [Espino ML](#), [Fenucci JL](#).

Author information

Abstract

The aim of this study was to investigate the effect of astaxanthin feed supplementation and environmental nitrite stress in postlarvae of *Pleoticus muelleri* (15 ± 0.004 mg initial weight) under culture conditions. Diets containing three levels of astaxanthin, 0 mg kg⁻¹ of diet (C0), 100 mg kg⁻¹ of diet (C(100)), and 300 mg kg⁻¹ of diet (C(300)), were used. Postlarvae fed with each diet were exposed to different concentrations of nitrite (NO(2)Na) (0-200 mg L⁻¹). The 96 h median lethal concentration (LC50) values of nitrite N were 76.3, 89.7, and 157 mg L⁻¹ for shrimps fed to C0, C(100), and C(300). The scavenging properties were evaluated against the stable 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical by electron resonance spectroscopy (EPR). For all feed treatments, the extracts exhibited strong DPPH scavenging activity; however, shrimp fed with C(100) and C(300) showed the greatest activity to quench DPPH (62 and 59%, respectively) with respect to C0 (43%). It can be concluded that astaxanthin acts as a protector of nitrite stress in *P. muelleri*.

KEYWORDS:

Pleoticus muelleri; astaxanthin; histopathology; nitrite; scavenging capacity

PMID:

25427235

[PubMed - indexed for MEDLINE]

Astaxanthin increases hepatic antioxidant gene expression in diet-induced obese mice.

[Br J Nutr.](#) 2014 Dec 14;112(11):1797-804. doi: 10.1017/S0007114514002554. Epub 2014 Oct 20.

Astaxanthin lowers plasma TAG concentrations and increases hepatic antioxidant gene expression in diet-induced obesity mice.

[Yang Y¹](#), [Pham TX¹](#), [Wegner CJ¹](#), [Kim B¹](#), [Ku CS¹](#), [Park YK¹](#), [Lee JY¹](#).

Author information

Abstract

Non-alcoholic fatty liver disease (NAFLD) is significantly associated with hyperlipidaemia and oxidative stress. We have previously reported that astaxanthin (ASTX), a xanthophyll carotenoid, lowers plasma total cholesterol and TAG concentrations in apoE knockout mice. To investigate whether ASTX supplementation can prevent the development of NAFLD in obesity, male C57BL/6J mice (n 8 per group) were fed a high-fat diet (35%, w/w) supplemented with 0, 0.003, 0.01 or 0.03% of ASTX (w/w) for 12 weeks. The 0.03% ASTX-supplemented group, but not the other groups, exhibited a significant decrease in plasma TAG concentrations, suggesting that ASTX at a 0.03% supplementation dosage exerts a hypotriacylglycerolaemic effect. Although there was an increase in the mRNA expression of fatty acid synthase and diglyceride acyltransferase 2, the mRNA levels of acyl-CoA oxidase 1, a critical enzyme in peroxisomal fatty acid β -oxidation, exhibited an increase in the 0.03% ASTX-supplemented group. There was a decrease in plasma alanine transaminase (ALT) and aspartate transaminase (AST) concentrations in the 0.03% ASTX-supplemented group. There was a significant increase in the hepatic mRNA expression of nuclear factor erythroid 2-related factor 2 and its downstream genes, which are critical for endogenous antioxidant mechanism, in the 0.03% ASTX-supplemented group. Furthermore, there was a significant decrease in the mRNA abundance of IL-6 in the primary splenocytes isolated from the 0.03% ASTX-supplemented group upon lipopolysaccharide (LPS) stimulation when compared with that in the splenocytes isolated from the control group. In conclusion, ASTX supplementation lowered the plasma concentrations of TAG, ALT and AST, increased the hepatic expression of endogenous antioxidant genes, and rendered splenocytes less sensitive to LPS stimulation. Therefore, ASTX may prevent obesity-associated metabolic disturbances and inflammation.

PMID:

25328157

[PubMed - indexed for MEDLINE]

Astaxanthin inhibits apoptosis in-vivo and in-vitro due to its antioxidant activity and may be of therapeutic value in lung fibrosis treatment.

[J Cell Mol Med.](#) 2014 Nov;18(11):2198-212. doi: 10.1111/jcmm.12347. Epub 2014 Sep 12.

Astaxanthin inhibits apoptosis in alveolar epithelial cells type II in vivo and in vitro through the ROS-dependent mitochondrial signalling pathway.

[Song X¹](#), [Wang B](#), [Lin S](#), [Jing L](#), [Mao C](#), [Xu P](#), [Lv C](#), [Liu W](#), [Zuo J](#).

Author information

Abstract

Oxidative stress is an important molecular mechanism underlying lung fibrosis. The mitochondrion is a major organelle for oxidative stress in cells. Therefore, blocking the mitochondrial signalling pathway may be the best therapeutic manoeuvre to ameliorate lung fibrosis. Astaxanthin (AST) is an excellent antioxidant, but no study has addressed the pathway of AST against pulmonary oxidative stress and free radicals by the mitochondrion-mediated signalling pathway. In this study, we investigated the antioxidative effects of AST against H₂O₂ - or bleomycin (BLM)-induced mitochondrial dysfunction and reactive oxygen species (ROS) production in alveolar epithelial cells type II (AECs-II) in vivo and in vitro. Our data show that AST blocks H₂O₂ - or BLM-induced ROS generation and dose-dependent apoptosis in AECs-II, as characterized by changes in cell and mitochondria morphology, translocation of apoptotic proteins, inhibition of cytochrome c (Cyt c) release, and the activation of caspase-9, caspase-3, Nrf-2 and other cytoprotective genes. These data suggest that AST inhibits apoptosis in AECs-II cells through the ROS-dependent mitochondrial signalling pathway and may be of potential therapeutic value in lung fibrosis treatment.

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KEYWORDS:

ROS; astaxanthin; lung fibrosis; mitochondrial signalling pathway; oxidative stress

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25215580

[PubMed - indexed for MEDLINE]

PMCID:

PMC4224554

Free PMC Article

Astaxanthin improves age-associated changes of vocal folds in rats which may be due to its ability to prevent reactive oxygen species-induced diseases.

[Laryngoscope](#). 2014 Oct;124(10):E411-7. doi: 10.1002/lary.24733. Epub 2014 May 27.

Effect of AST on age-associated changes of vocal folds in a rat model.

[Mizuta M¹](#), [Hirano S](#), [Hiwatashi N](#), [Kobayashi T](#), [Tateya I](#), [Kanemaru S](#), [Nakamura T](#), [Ito J](#).

Author information

Abstract

OBJECTIVES/HYPOTHESIS:

Reactive oxygen species (ROS) are associated with aging. Astaxanthin (AST) is a strong antioxidant and has been reported to prevent various ROS-induced diseases. In the current study, we investigated the effect of AST on age-associated histological and mRNA changes of vocal folds.

STUDY DESIGN:

Prospective animal experiment with control.

METHODS:

Six-month-old Sprague-Dawley rats were fed on a normal powder diet with 0.01% (w/w) AST (aged AST-treated group) or without AST (aged sham-treated group). After 12 months of feeding, the larynges were harvested for histology, immunohistochemical detection of 4-hydroxy-2-nonenal (4-HNE), and quantitative real-time polymerase chain reaction for basic fibroblast growth factor (bFGF) and hepatocyte growth factor (HGF). Thirteen-week-old rats were used as a young control group (young group).

RESULTS:

The expression of 4-HNE, an oxidative stress marker, significantly increased in the two aged groups compared with the young group. Histological examination showed that the deposition of hyaluronic acid in the lamina propria (LP) was significantly reduced in the aged sham-treated group compared with the young group, but no significant difference was observed between the aged AST-treated group and the young group. There were no significant differences in the mRNA expression of bFGF and HGF between the aged AST-treated group and the young group, although the expression of these genes was significantly reduced in the aged sham-treated group as compared with the young group.

CONCLUSIONS:

These results suggest that AST has the potential to attenuate age-associated changes of vocal folds.

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KEYWORDS:

AST; age-associated changes; reactive oxygen species; vocal folds

PMID:

24764173

[PubMed - indexed for MEDLINE]

Astaxanthin protects against light-induced retinal damage in mice via the mechanism of its antioxidant effect.

[J Pharmacol Sci.](#) 2013;123(3):209-18. Epub 2013 Oct 22.

Protective effects of a dietary carotenoid, astaxanthin, against light-induced retinal damage.

[Otsuka T¹](#), [Shimazawa M](#), [Nakanishi T](#), [Ohno Y](#), [Inoue Y](#), [Tsuruma K](#), [Ishibashi T](#), [Hara H](#).

Author information

Abstract

Dietary carotenoids exhibit various biological activities, including antioxidative activity. In particular, astaxanthin, a type of carotenoid, is well known as a powerful antioxidant. We investigated whether astaxanthin would protect against light-induced retinal damage. In an in vivo study, ddY male mice were exposed to white light at 8,000 lux for 3 h to induce retinal damage. Five days after light exposure, retinal damage was evaluated by measuring electroretinogram (ERG) amplitude and outer nuclear layer (ONL) thickness. Furthermore, expression of apoptotic cells, 8-hydroxy-deoxyguanosine (8-OHdG), was measured. In an in vitro study, retinal damage was induced by white light exposure at 2,500 lux for 24 h, and propidium iodide (PI)-positive cells was measured and intracellular reactive oxygen species (ROS) activity was examined. Astaxanthin at 100 mg/kg inhibited the retinal dysfunction in terms of ERG and ONL loss and reduced the expression of apoptotic and 8-OHdG-positive cells induced by light exposure. Furthermore, astaxanthin protected against increases of PI-positive cells and intracellular reactive oxygen species (ROS) activity in 661W cells. These findings suggest that astaxanthin has protective effects against light-induced retinal damage via the mechanism of its antioxidative effect.

PMID:

24152963

[PubMed - indexed for MEDLINE]

Free full text

Astaxanthin shows anti-inflammatory, anti-coagulatory and antioxidant effects in diabetic rats.

[J Food Sci.](#) 2012 Feb;77(2):H76-80. doi: 10.1111/j.1750-3841.2011.02558.x. Epub 2012 Feb 6.

Anticoagulatory and antiinflammatory effects of astaxanthin in diabetic rats.

[Chan KC¹](#), [Pen PJ](#), [Yin MC](#).

Author information

Abstract

Astaxanthin at 0.01 or 0.05% of the diet was supplied to diabetic rats for 12 wk. Astaxanthin intake significantly increased its deposit in plasma, and retained glutathione content, reduced the production of reactive oxygen species, interleukin-6, tumor necrosis factor- α , and monocyte chemoattractant protein-1 in blood and kidney of diabetic rats ($P < 0.05$). Astaxanthin treatments also significantly decreased plasma levels of C-reactive protein and von Willebrand factor in diabetic rats ($P < 0.05$). Astaxanthin intake at 0.05% significantly diminished plasminogen activator inhibitor-1 and factor VII activities, enhanced antithrombin-III and protein C activities in circulation ($P < 0.05$). These results support that astaxanthin could attenuate diabetes associated coagulatory, oxidative, and inflammatory stress.

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PMID:

22309505

[PubMed - indexed for MEDLINE]

Astaxanthin inhibits thrombosis in cerebral vessels of stroke-prone, hypertensive rats which may be attributed to decreased inactivation of nitric oxide by reactive oxygen species.

[Nutr Res.](#) 2011 Oct;31(10):784-9. doi: 10.1016/j.nutres.2011.09.010.

Astaxanthin inhibits thrombosis in cerebral vessels of stroke-prone spontaneously hypertensive rats.

[Sasaki Y¹](#), [Kobara N](#), [Higashino S](#), [Giddings JC](#), [Yamamoto J](#).

Author information

Abstract

It is known that vitamin E and some carotenoids have antioxidant activities that alleviate endothelial dysfunction and play a protective role against cardiovascular disease. The current study was designed to examine the hypothesis that astaxanthin, a red pigment carotenoid found in salmonid and crustacean aquaculture, protects stroke-prone spontaneously hypertensive rats (SHRSP) from vascular oxidative damage, hypertension, and cerebral thrombosis. Male 6-week-old SHRSP were classified into 4 groups: a control group, 2 astaxanthin groups, and a vitamin E group. The treated animals were given either astaxanthin or vitamin E for 3 weeks. Body weights in each group were not significantly different from control group during the treatment period, but the usual increase in systolic blood pressure in SHRSP observed with age was significantly suppressed by treatment. Thrombogenesis, assessed using a helium-neon (He-Ne) laser technique in pial blood vessels, together with antioxidant activity, assessed by measuring urinary 8-OHdG levels, were significantly moderated. Urinary nitric oxide (NO) metabolites were increased after treatment. These results supported our hypothesis and strongly suggested that the antithrombotic and antihypertensive effects of astaxanthin or vitamin E may be related to an increase in bioavailable NO, possibly mediated by decreased inactivation of NO by reactive oxygen species.

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PMID:

22074803

[PubMed - indexed for MEDLINE]

Astaxanthin may have protective effects against oxidative damage and DNA damage induced by gamma rays.

[Wei Sheng Yan Jiu](#). 2011 Sep;40(5):551-4.

[Protective effects of astaxanthin against oxidative damage induced by 60Co gamma-ray irradiation].

[Article in Chinese]

[Zhao W](#)¹, [Jing X](#), [Chen C](#), [Cui J](#), [Yang M](#), [Zhang Z](#).

Author information

Abstract

OBJECTIVE:

To investigate the protection effect of haematococcus pluvialis (containing astaxanthin) against the impairment of anti-oxidative system and DNA damage in mice induced by 60Co gamma-rays.

METHODS:

Fifty mice were randomly divided into five groups, i.e. three haematococcus pluvialis groups (41.7, 83.3 and 166.7 mg/kg in vegetable oil, respectively), control group and model group (vegetable oil only). All mice except control group were irradiated by 8 Gy 60Co gamma-rays 30 days later, and executed in the 4th day after irradiation. Liver cells were collected for the analysis of the integrity of DNA by comet assay, as well as MDA contents, SOD and GSH-Px activities in liver by commercial kits. Peripheral granulocyte and bone marrow nucleated cells were counted by hematocyte counter.

RESULTS:

MDA contents of model group were higher than those of control group ($P < 0.01$), and SOD, GSH-Px activities of model group were lower than those of control group ($P < 0.01$). Compared with the model group, MDA contents were decreased ($P < 0.01$), and SOD and GSH-Px activities were increased ($P < 0.01$) in all haematococcus pluvialis groups, especially in the high haematococcus pluvialis group, and the more haematococcus pluvialis in the diet of mice, the lower rate of comet tail and OTM value were shown ($P < 0.01$). Furthermore, the counts of peripheral granulocyte and bone marrow nucleated cells of model group were lower than those of the control group, while the counts of peripheral granulocyte and bone marrow nucleated cells of medium and high haematococcus pluvialis groups were increased significantly when compared with the model group ($P < 0.01$).

CONCLUSION:

Astaxanthin might have some protective effect against oxidative impairment and DNA damage induced by 60Co gamma-rays in mice.

PMID:

22043699

[PubMed - indexed for MEDLINE]

Astaxanthin more effective than other carotenoids as a neuroprotectant in rats due to its reactive oxygen species scavenging activities.

[Kaohsiung J Med Sci](#). 2013 Aug;29(8):412-21. doi: 10.1016/j.kjms.2012.12.002. Epub 2013 Feb 8.

Reactive oxygen species scavenging activities in a chemiluminescence model and neuroprotection in rat pheochromocytoma cells by astaxanthin, beta-carotene, and canthaxanthin.

[Chang CS](#)¹, [Chang CL](#), [Lai GH](#).

Author information

Abstract

The objective of this study was to determine chemiluminescence (CL) antioxidant activities and neuroprotective effects of astaxanthin, beta-carotene (β -carotene), and canthaxanthin on undifferentiated rat pheochromocytoma (PC12) cells. We performed three CL antioxidant assays, and the three carotenoids showed varying degrees of antioxidant activity, with astaxanthin exhibiting the highest antioxidant activity than the other two samples. Results of a pyrogallol-luminol assay revealed β -carotene to have higher antioxidant activity than canthaxanthin, whereas cupric sulfate-Phen-Vc-hydrogen peroxide (H_2O_2) assay showed canthaxanthin to have higher antioxidant activity than β -carotene. Luminol- H_2O_2 assay showed the antioxidant activity series as canthaxanthin > β -carotene at 62.5-1000 μ g/mL and β -carotene > canthaxanthin at 1000-4000 μ g/mL. Astaxanthin exhibited partial neuroprotective activity against H_2O_2 and the strongest neuroprotective activity against amyloid beta-peptide(25-35) [$A\beta$ (25-35)]-induced undifferentiated PC12 cell deaths at 0.5-5.0 μ M. Canthaxanthin showed partial neuroprotective activity in $A\beta$ (25-35)-induced undifferentiated PC12 cell deaths at 1.0-5.0 μ M. Astaxanthin protected undifferentiated PC12 cells from the damaging effects of H_2O_2 and $A\beta$ (25-35) by the following ways: (1) scavenging superoxide anion radicals, hydroxyl radicals, and H_2O_2 ; (2) securing cell viability; (3) suppressing the production of reactive oxygen species; and (4) eliminating calcium ion influx. Our results conclusively show that astaxanthin has the merit as a potential neuron protectant.

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KEYWORDS:

Astaxanthin; Canthaxanthin; Chemiluminescence antioxidant activity; Neuroprotective effect; β -carotene

Astaxanthin has a protective effect against fetal alcohol spectrum disorder in mice which may be due to its effect on oxidative stress and TLR4 signaling associated inflammatory reaction.

[Neuropharmacology](#). 2014 Sep;84:13-8. doi: 10.1016/j.neuropharm.2014.04.013. Epub 2014 Apr 26.

The protective effect of astaxanthin on fetal alcohol spectrum disorder in mice.

[Zheng D](#)¹, [Li Y](#)², [He L](#)², [Tang Y](#)², [Li X](#)², [Shen Q](#)², [Yin D](#)³, [Peng Y](#)⁴.

Author information

Abstract

Astaxanthin is a strong antioxidant with the ability of reducing the markers of inflammation. To explore the protective effect of astaxanthin on maternal ethanol induced embryonic deficiency, and to investigate the underlying mechanisms, we detected the morphology, expression of neural marker genes, oxidative stress indexes, and inflammatory factors in mice model of fetal alcohol spectrum disorder with or without astaxanthin pretreatment. Our results showed that astaxanthin blocked maternal ethanol induced retardation of embryonic growth, and the down-regulation of neural marker genes, Otx1 and Sox2. Moreover, astaxanthin also reversed the increases of malondialdehyde (MDA), hydrogen peroxide (H₂O₂), and the decrease of glutathione peroxidase (GPx) in fetal alcohol spectrum disorder. In addition, maternal ethanol induced up-regulation of toll-like receptor 4 (TLR4), and the down-streaming myeloid differentiation factor 88 (MyD88), NF- κ B, TNF- α , and IL-1 β in embryos, and this was inhibited by astaxanthin pretreatment. These results demonstrated a protective effect of astaxanthin on fetal alcohol spectrum disorder, and suggested that oxidative stress and TLR4 signaling associated inflammatory reaction are involved in this process.

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KEYWORDS:

Astaxanthin; Embryo; Ethanol

Astaxanthin protects multiple organs in rats due to its antioxidant and anti-inflammatory properties.

[J Surg Res.](#) 2015 May 15;195(2):559-67. doi: 10.1016/j.jss.2015.02.026. Epub 2015 Feb 18.

Protective effect of astaxanthin against multiple organ injury in a rat model of sepsis.

[Zhou L¹](#), [Gao M²](#), [Xiao Z³](#), [Zhang J¹](#), [Li X¹](#), [Wang A⁴](#).

Author information

Abstract

BACKGROUND:

Astaxanthin, a xanthophyll carotenoid, holds exceptional promise as an antioxidant, anti-inflammatory, and anticancer agent. No evidence has been published whether it has protective effects on sepsis. The study aimed to investigate the potential effects of astaxanthin on sepsis and multiple organ dysfunctions.

MATERIALS AND METHODS:

Sepsis was induced by cecal ligation and puncture (CLP) in Sprague-Dawley rats. Animals subjected to CLP and sham-operated control rats were given vehicle or astaxanthin 100 mg/kg/d by oral gavage for 7 d before the operation. The rats were killed at the indicated time points, and the specimen was collected. Cytokines and multiorgan injury-associated enzymatic and oxidative stress indicators were investigated. Multiorgan tissues were assessed histologically, the peritoneal bacterial load and the 72-h survival was observed too.

RESULTS:

Sepsis resulted in a significant increase in serum tumor necrosis factor- α , interleukin-1 β , and interleukin-6 levels showing systemic inflammatory response; it also caused a remarkable decrease in the superoxide dismutase activity and a significant increase in the malondialdehyde content showing oxidative damage; sepsis caused a great increase in organ injury-associated indicators, including blood urea nitrogen, creatinine, lactate dehydrogenase, creatine kinase isoenzyme-MB isotype, alanine aminotransferase, and aspartate aminotransferase, which was confirmed by histologic examination. And there was a dramatical increase of colony-forming units in the peritoneal cavity in septic rats. Astaxanthin reversed these inflammatory and oxidant response, alleviated the organ injury, reduced the peritoneal bacterial load, and improved the survival of septic rats induced by CLP.

CONCLUSIONS:

Astaxanthin exerts impressively protective effects on CLP-induced multiple organ injury. It might be used as a potential treatment for clinical sepsis.

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KEYWORDS:

Astaxanthin; Cecal ligation and puncture; Multiple organ dysfunction syndrome; Sepsis

PMID:

25770740

[PubMed - indexed for MEDLINE]

Astaxanthin is an efficient antioxidant against peroxidative activity.

[Biochim Biophys Acta](#). 2001 Jun 6;1512(2):251-8.

Efficient radical trapping at the surface and inside the phospholipid membrane is responsible for highly potent antiperoxidative activity of the carotenoid astaxanthin.

[Goto S](#), [Kogure K](#), [Abe K](#), [Kimata Y](#), [Kitahama K](#), [Yamashita E](#), [Terada H](#).

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Kogure@ph.tokushima-u.ac.jp

The effects of the carotenoids beta-carotene and astaxanthin on the peroxidation of liposomes induced by ADP and Fe(2+) were examined. Both compounds inhibited production of lipid peroxides, astaxanthin being about 2-fold more effective than beta-carotene. The difference in the modes of destruction of the conjugated polyene chain between beta-carotene and astaxanthin suggested that the conjugated polyene moiety and terminal ring moieties of the more potent astaxanthin trapped radicals in the membrane and both at the membrane surface and in the membrane, respectively, whereas only the conjugated polyene chain of beta-carotene was responsible for radical trapping near the membrane surface and in the interior of the membrane. The efficient antioxidant activity of astaxanthin is suggested to be due to the unique structure of the terminal ring moiety.

Publication Types:

PMID: 11406102 [PubMed - indexed for MEDLINE]

Astaxanthin effective against oxidative stress and DNA damage in mice.

[Chem Biol Interact.](#) 2009 Aug 14;180(3):398-406. Epub 2009 Apr 2.

Intervention of astaxanthin against cyclophosphamide-induced oxidative stress and DNA damage: a study in mice.

[Tripathi DN](#), [Jena GB](#).

Department of Pharmacology and Toxicology, National Institute of Pharmaceutical Education and Research, Sector-67, S.A.S. Nagar, Punjab 160062, India.

Astaxanthin, a natural and nutritional red carotenoid pigment, is used as a dietary supplement. The intention of the present study was to investigate the beneficial effects of dietary pigment astaxanthin, against cyclophosphamide-induced oxidative stress and DNA damage. The end points of evaluation of the study included: (a) malondialdehyde, glutathione and superoxide dismutase concentration in liver to detect oxidative stress; (b) normal and modified alkaline comet assays (the latter includes lesion-specific enzymes formamidopyrimidine-DNA glycosylase and endonuclease-III) to detect normal and oxidative stress-induced DNA damage by cyclophosphamide in the mouse bone marrow and the peripheral blood lymphocytes. In addition, micronucleus assay and chromosomal aberration test capable of detecting the DNA damage were also carried out in peripheral blood and bone marrow of mice. Cyclophosphamide (100 mg/kg intra-peritoneal) treatment led to significant increase in liver malondialdehyde and decreased the antioxidant enzymes glutathione and superoxide dismutase. Further, cyclophosphamide also significantly increased the DNA damage as observed from normal and modified comet assays as well as micronucleus and chromosomal aberration assay. Pre-treatment with astaxanthin (12.5, 25 and 50 mg/kg/day for 5 days per oral) resulted in the restoration of oxidative stress markers such as malondialdehyde, glutathione and superoxide dismutase in liver. The amelioration of oxidative stress with astaxanthin pre-treatment correlated well with the decreased DNA damage as evident from normal and modified alkaline comet assays of bone marrow cells and peripheral blood lymphocytes. Further astaxanthin pre-treatment also reduced the frequency of chromosomal breakage and micronucleus formation in the mouse bone marrow cells and peripheral blood reticulocytes. It is thus concluded that pre-treatment with astaxanthin attenuates cyclophosphamide-induced oxidative stress and subsequent DNA damage in mice and it can be used as a chemoprotective agent against the toxicity of anticancer drug cyclophosphamide.

[Research Support, Non-U.S. Gov't](#)

PMID: 19539803 [PubMed - in process]

Astaxanthin is the most potent antioxidant amongst carotenoids tested.

[J Agric Food Chem.](#) 2000 Apr;48(4):1150-4.

Antioxidant activities of astaxanthin and related carotenoids.

[Naguib YM.](#)

Phytochem Technologies, Chelmsford, MA 01824, USA.

The antioxidant activities of astaxanthin and related carotenoids have been measured by employing a newly developed fluorometric assay. This assay is based on 4,4-difluoro-3,5-bis(4-phenyl-1,3-butadienyl)-4-bora-3a,4a-diaza-s-indacene (BODIPY 665/676) as an indicator; 2,2'-azobis-2,4-dimethylvaleronitrile (AMVN) as a peroxy radical generator; and 6-hydroxy-2,5,7,8-tetramethylchroman-2-carboxylic acid (Trolox) as a calibrator in an organic and liposomal media. By employing this assay, three categories of carotenoids were examined: namely, the hydrocarbon carotenoids lycopene, alpha-carotene, and beta-carotene; the hydroxy carotenoid lutein; and the alpha-hydroxy-ketocarotenoid astaxanthin. The relative peroxy radical scavenging activities of Trolox, astaxanthin, alpha-tocopherol, lycopene, beta-carotene, lutein, and alpha-carotene in octane/butyronitrile (9:1, v/v) were determined to be 1.0, 1.0, 1.3, 0.5, 0.4, 0.3, and 0.2, respectively. In dioleoylphosphatidyl choline (DOPC) liposomal suspension in Tri-HCl buffer (pH 7.4 at 40 degrees C), the relative reactivities of astaxanthin, beta-carotene, alpha-tocopherol, and lutein were found to be 1.00, 0.9, 0.6, and 0.6, respectively. When BODIPY 665/676 was replaced by 4,4-difluoro-5-(4-phenyl-1,3-butadienyl)-4-bora-3a,4a-diaza-s-indacene-3-undecanoic acid (BODIPY 581/591 C(11)) as an indicator, astaxanthin showed the highest antioxidant activity toward peroxy radicals. The relative reactivities of Trolox, astaxanthin, alpha-tocopherol, alpha-carotene, lutein, beta-carotene, and lycopene were determined to be 1.0, 1.3, 0.9, 0.5, 0.4, 0.2, and 0.4, respectively.

PMID: 10775364 [PubMed - indexed for MEDLINE]

Astaxanthin increases liver antioxidative activity and reduces the concentration of lipid peroxidase in hamsters.

[PLoS One](#). 2015 Aug 11;10(8):e0134733. doi: 10.1371/journal.pone.0134733. eCollection 2015.

In Vivo Effects of Free Form Astaxanthin Powder on Anti-Oxidation and Lipid Metabolism with High-Cholesterol Diet.

[Chen YY](#)¹, [Lee PC](#)², [Wu YL](#)³, [Liu LY](#)².

Author information

Abstract

Astaxanthin extracted from *Pomacea canaliculata* eggs was made into free-form astaxanthin powder (FFAP) and its effects on lipid metabolism, liver function, antioxidants activities and astaxanthin absorption rate were investigated. 45 hamsters were split into 5 groups and fed with normal diet, high-cholesterol control (0.2% cholesterol), 1.6FFAP (control+1.6% FFAP), 3.2FFAP (control+3.2% FFAP) and 8.0FFAP (control+8.0% FFAP), respectively, for 6 weeks. FFAP diets significantly decreased the liver total cholesterol, triglyceride levels and increased liver fatty acids (C20:5n3; C22:6n3) compositions. It decreased plasma alanine aminotransferase and aspartate aminotransferase. In terms of anti-oxidative activities, we found 8.0 FFAP diet significantly decreased plasma and liver malonaldehyde ($4.96 \pm 1.96 \mu\text{g TEP eq./mL}$ and $1.56 \pm 0.38 \mu\text{g TEP eq./g liver}$) and liver 8-isoprostane levels ($41.48 \pm 13.69 \mu\text{g 8-ISOP/g liver}$). On the other hand, it significantly increased liver catalase activity ($149.10 \pm 10.76 \mu\text{mol/min/g liver}$), Vitamin C ($2082.97 \pm 142.23 \mu\text{g/g liver}$), Vitamin E ($411.32 \pm 81.67 \mu\text{g/g liver}$) contents, and glutathione levels ($2.13 \pm 0.42 \text{ mg GSH eq./g liver}$). Furthermore, 80% of astaxanthin absorption rates in all FFAP diet groups suggest FFAP is an effective form in astaxanthin absorption. Finally, astaxanthin was found to re-distribute to the liver and eyes in a dose dependent manner. Taken together, our results suggested that the appropriate addition of FFAP into high cholesterol diets increases liver anti-oxidative activity and reduces the concentration of lipid peroxidase and therefore, it may be beneficial as a material in developing healthy food.

PMID:

26262684

[PubMed - in process]

PMCID:

PMC4532504

[Free PMC Article](#)

Astaxanthin protects the mitochondria against oxidative stress.

[J Nutr Biochem](#). 2009 May 6. [Epub ahead of print]

Astaxanthin protects mitochondrial redox state and functional integrity against oxidative stress.

[Wolf AM](#), [Asoh S](#), [Hiranuma H](#), [Ohsawa I](#), [Iio K](#), [Satou A](#), [Ishikura M](#), [Ohta S](#).

Department of Biochemistry and Cell Biology, Institute of Development and Aging Sciences, Nippon Medical School, Nakahara-ku, Kawasaki, Kanagawa 211-8533, Japan.

Mitochondria combine the production of energy with an efficient chain of reduction-oxidation (redox) reactions but also with the unavoidable production of reactive oxygen species. Oxidative stress leading to mitochondrial dysfunction is a critical factor in many diseases, such as cancer and neurodegenerative and lifestyle-related diseases. Effective antioxidants thus offer great therapeutic and preventive promise. Investigating the efficacy of antioxidants, we found that a carotenoid, astaxanthin (AX), decreased physiologically occurring oxidative stress and protected cultured cells against strong oxidative stress induced with a respiratory inhibitor. Moreover, AX improved maintenance of a high mitochondrial membrane potential and stimulated respiration. Investigating how AX stimulates and interacts with mitochondria, a redox-sensitive fluorescent protein (roGFP1) was stably expressed in the cytosol and mitochondrial matrix to measure the redox state in the respective compartments. AX at nanomolar concentrations was effective in maintaining mitochondria in a reduced state. Additionally, AX improved the ability of mitochondria to remain in a reduced state under oxidative challenge. Taken together, these results suggest that AX is effective in improving mitochondrial function through retaining mitochondria in the reduced state.

PMID: 19423317 [PubMed - as supplied by publisher]

Astaxanthin prevents or decreases oxidative damage by hydrogen peroxide

[Zhongguo Gu Shang](#). 2008 Mar;21(3):187-9.

[Effects of Astaxanthin on the damage of osteoblast induced by H₂O₂]

[Article in Chinese]

[Pei LP](#), [Dong FH](#), [Hui BD](#).

Institute of Orthopaedics and Traumatology, China Academy of Chinese Medical Science, Beijing 100700, China.

OBJECTIVE: To investigate the effect of Astaxanthin on enhancing the function of anti-oxidative damage in osteoblast. **METHODS:** MC3T3-E1 osteoblasts were randomly divided into five groups, including control group, model group, Astaxanthin group [low-dose (1×10^{-7}) mol/L), middle-dose (1×10^{-6}) mol/L), high-dose (1×10^{-5}) mol/L)], in which the activity of cells, activity of superoxide dismutase (SOD), the content of reactive oxygen species (ROS), lipid oxygen (LPO) and membrane fluidity were tested and compared. **RESULTS:** Compared with Astaxanthin groups, the activity of cells, SOD activity and membrane fluidity in the model group were significantly decreased ($P < 0.01$). However, the contents of ROS and LPO were significantly raised ($P < 0.01$). **CONCLUSION:** H₂O₂ can cause oxidative damage of MC3T3-E1 osteoblasts, but Astaxanthin can prevent or decrease its influence.

PMID: 19105434 [PubMed - indexed for MEDLINE]

Astaxanthin attenuates apoptosis of retinal ganglion cells in mice by inhibition of oxidative stress and may be developed as an antioxidant drug to treat diabetic retinopathy.

[Mar Drugs](#). 2013 Mar 21;11(3):960-74. doi: 10.3390/md11030960.

Astaxanthin attenuates the apoptosis of retinal ganglion cells in db/db mice by inhibition of oxidative stress.

[Dong LY¹](#), [Jin J](#), [Lu G](#), [Kang XL](#).

Author information

Abstract

Diabetic retinopathy is a common diabetic eye disease caused by changes in retinal ganglion cells (RGCs). It is an ocular manifestation of systemic disease, which affects up to 80% of all patients who have had diabetes for 10 years or more. The genetically diabetic db/db mouse, as a model of type-2 diabetes, shows diabetic retinopathy induced by apoptosis of RGCs. Astaxanthin is a carotenoid with powerful antioxidant properties that exists naturally in various plants, algae and seafood. Here, astaxanthin was shown to reduce the apoptosis of RGCs and improve the levels of oxidative stress markers, including superoxide anion, malondialdehyde (MDA, a marker of lipid peroxidation), 8-hydroxy-2-deoxyguanosine (8-OHdG, indicator of oxidative DNA damage) and MnSOD (manganese superoxide dismutase) activity in the retinal tissue of db/db mouse. In addition, astaxanthin attenuated hydrogen peroxide(H₂O₂)-induced apoptosis in the transformed rat retinal ganglion cell line RGC-5. Therefore, astaxanthin may be developed as an antioxidant drug to treat diabetic retinopathy.

PMID:

23519150

[PubMed - indexed for MEDLINE]

PMCID:

PMC3705382

Free PMC Article

Astaxanthin protects the kidneys of rats against functional impairment caused by oxidative stress.

[Food Chem Toxicol.](#) 2008 Jan;46(1):212-9. Epub 2007 Aug 14.

Effect of astaxanthin on kidney function impairment and oxidative stress induced by mercuric chloride in rats.

[Augusti PR](#), [Conterato GM](#), [Somacal S](#), [Sobieski R](#), [Spohr PR](#), [Torres JV](#), [Charão MF](#), [Moro AM](#), [Rocha MP](#), [Garcia SC](#), [Emanuelli T](#).

Post-graduate Program on Toxicological Biochemistry, Center of Natural and Exact Sciences, Federal University of Santa Maria, 97105-900 Santa Maria, RS, Brazil.

Reactive oxygen species are implicated as mediators of tissue damage in the acute renal failure induced by inorganic mercury. Astaxanthin (ASX), a carotenoid with potent antioxidant properties, exists naturally in various plants, algae, and seafoods. This paper evaluated the ability of ASX to prevent HgCl₂ nephrotoxicity. Rats were injected with HgCl₂ (0 or 5 mg/kg b.w., sc) 6h after ASX had been administered (0, 10, 25, or 50mg/kg, by gavage) and were killed 12h after HgCl₂ exposure. Although ASX prevented the increase of lipid and protein oxidation and attenuated histopathological changes caused by HgCl₂ in kidney, it did not prevent creatinine increase in plasma and delta-aminolevulinic acid dehydratase inhibition induced by HgCl₂. Glutathione peroxidase and catalase activities were enhanced, while superoxide dismutase activity was depressed in HgCl₂-treated rats when compared to control and these effects were prevented by ASX. Our results indicate that ASX could have a beneficial role against HgCl₂ toxicity by preventing lipid and protein oxidation, changes in the activity of antioxidant enzymes and histopathological changes.

Publication Types:

PMID: 17881112 [PubMed - indexed for MEDLINE]

Astaxanthin shows a strong antioxidant effect while other carotenoids such as lycopene and beta-carotene can have a pro-oxidant effect due to different membrane interaction mechanisms.

[Biochim Biophys Acta](#). 2007 Jan;1768(1):167-74. Epub 2006 Sep 22.

Differential effects of carotenoids on lipid peroxidation due to membrane interactions: X-ray diffraction analysis.

[McNulty HP](#), [Byun J](#), [Lockwood SF](#), [Jacob RF](#), [Mason RP](#).

Elucida Research, 100 Cummings Center, Suite 135L, P.O. Box 7100, Beverly, MA 01915-0091, USA. hmcnulty@elucidaresearch.com

The biological benefits of certain carotenoids may be due to their potent antioxidant properties attributed to specific physico-chemical interactions with membranes. To test this hypothesis, we measured the effects of various carotenoids on rates of lipid peroxidation and correlated these findings with their membrane interactions, as determined by small angle X-ray diffraction approaches. The effects of the homochiral carotenoids (astaxanthin, zeaxanthin, lutein, beta-carotene, lycopene) on lipid hydroperoxide (LOOH) generation were evaluated in membranes enriched with polyunsaturated fatty acids. Apolar carotenoids, such as lycopene and beta-carotene, disordered the membrane bilayer and showed a potent pro-oxidant effect (>85% increase in LOOH levels) while astaxanthin preserved membrane structure and exhibited significant antioxidant activity (40% decrease in LOOH levels). These findings indicate distinct effects of carotenoids on lipid peroxidation due to membrane structure changes. These contrasting effects of carotenoids on lipid peroxidation may explain differences in their biological activity.

PMID: 17070769 [PubMed - indexed for MEDLINE]

Astaxanthin is a very effective antioxidant for ameliorating insulin resistance by protecting cells against oxidative stress generated by various stimuli.

[Endocrinology](#). 2013 Aug;154(8):2600-12. doi: 10.1210/en.2012-2198. Epub 2013 May 28.

Impact of divergent effects of astaxanthin on insulin signaling in L6 cells.

[Ishiki M](#)¹, [Nishida Y](#), [Ishibashi H](#), [Wada T](#), [Fujisaka S](#), [Takikawa A](#), [Urakaze M](#), [Sasaoka T](#), [Usui I](#), [Tobe K](#).

Author information

Abstract

Because oxidative stress promotes insulin resistance in obesity and type 2 diabetes, it is crucial to find effective antioxidant for the purpose of decreasing this threat. In this study, we explored the effect of astaxanthin, a carotenoid antioxidant, on insulin signaling and investigated whether astaxanthin improves cytokine- and free fatty acid-induced insulin resistance in vitro. We examined the effect of astaxanthin on insulin-stimulated glucose transporter 4 (GLUT4) translocation, glucose uptake, and insulin signaling in cultured rat L6 muscle cells using plasma membrane lawn assay, 2-deoxyglucose uptake, and Western blot analysis. Next, we examined the effect of astaxanthin on TNF α - and palmitate-induced insulin resistance. The amount of reactive oxygen species generated by TNF α or palmitate with or without astaxanthin was evaluated by dichlorofluorescein staining. We also compared the effect of astaxanthin on insulin signaling with that of other antioxidants, α -lipoic acid and α -tocopherol. We observed astaxanthin enhanced insulin-stimulated GLUT4 translocation and glucose uptake, which was associated with an increase in insulin receptor substrate-1 tyrosine and Akt phosphorylation and a decrease in c-Jun N-terminal kinase (JNK) and insulin receptor substrate-1 serine 307 phosphorylation. Furthermore, astaxanthin restored TNF α - and palmitate-induced decreases in insulin-stimulated GLUT4 translocation or glucose uptake with a concomitant decrease in reactive oxygen species generation. α -Lipoic acid enhanced Akt phosphorylation and decreased ERK and JNK phosphorylation, whereas α -tocopherol enhanced ERK and JNK phosphorylation but had little effect on Akt phosphorylation. Collectively these findings indicate astaxanthin is a very effective antioxidant for ameliorating insulin resistance by protecting cells from oxidative stress generated by various stimuli including TNF α and palmitate.

PMID:

23715867

[PubMed - indexed for MEDLINE]

Astaxanthin protects against hydrogen peroxide-induced oxidative stress in mouse cells.

[Mar Drugs](#). 2015 Mar 16;13(3):1375-88. doi: 10.3390/md13031375.

Astaxanthin protects steroidogenesis from hydrogen peroxide-induced oxidative stress in mouse Leydig cells.

[Wang JY](#)¹, [Lee YJ](#)², [Chou MC](#)³, [Chang R](#)⁴, [Chiu CH](#)⁵, [Liang YJ](#)⁶, [Wu LS](#)⁷.

Author information

Abstract

Androgens, especially testosterone produced in Leydig cells, play an essential role in development of the male reproductive phenotype and fertility. However, testicular oxidative stress may cause a decline in testosterone production. Many antioxidants have been used as reactive oxygen species (ROS) scavengers to eliminate oxidative stress to protect steroidogenesis. Astaxanthin (AST), a natural extract from algae and plants ubiquitous in the marine environment, has been shown to have antioxidant activity in many previous studies. In this study, we treated primary mouse Leydig cells or MA-10 cells with hydrogen peroxide (H₂O₂) to cause oxidative stress. Testosterone and progesterone production was suppressed and the expression of the mature (30 kDa) form of StAR protein was down-regulated in MA-10 cells by H₂O₂ and cAMP co-treatment. However, progesterone production and expression of mature StAR protein were restored in MA-10 cells by a one-hour pretreatment with AST. AST also reduced ROS levels in cells so that they were lower than the levels in untreated controls. These results provide additional evidence of the potential health benefits of AST as a potential food additive to ease oxidative stress.

PMID:

25786065

[PubMed - in process]

PMCID:

PMC4377989

[Free PMC Article](#)

Astaxanthin improves oxidative stress and mitochondrial-related apoptosis in rats' kidneys.

[Mar Drugs](#). 2015 Apr 13;13(4):2105-23. doi: 10.3390/md13042105.

Astaxanthin attenuates early acute kidney injury following severe burns in rats by ameliorating oxidative stress and mitochondrial-related apoptosis.

[Guo SX](#)¹, [Zhou HL](#)², [Huang CL](#)³, [You CG](#)⁴, [Fang Q](#)⁵, [Wu P](#)⁶, [Wang XG](#)⁷, [Han CM](#)⁸.

Author information

Abstract

Early acute kidney injury (AKI) is a devastating complication in critical burn patients, and it is associated with severe morbidity and mortality. The mechanism of AKI is multifactorial. Astaxanthin (ATX) is a natural compound that is widely distributed in marine organisms; it is a strong antioxidant and exhibits other biological effects that have been well studied in various traumatic injuries and diseases. Hence, we attempted to explore the potential protection of ATX against early post burn AKI and its possible mechanisms of action. The classic severe burn rat model was utilized for the histological and biochemical assessments of the therapeutic value and mechanisms of action of ATX. Upon ATX treatment, renal tubular injury and the levels of serum creatinine and neutrophil gelatinase-associated lipocalin were improved. Furthermore, relief of oxidative stress and tubular apoptosis in rat kidneys post burn was also observed. Additionally, ATX administration increased Akt and Bad phosphorylation and further down-regulated the expression of other downstream pro-apoptotic proteins (cytochrome c and caspase-3/9); these effects were reversed by the PI3K inhibitor LY294002. Moreover, the protective effect of ATX presents a dose-dependent enhancement. The data above suggested that ATX protects against early AKI following severe burns in rats, which was attributed to its ability to ameliorate oxidative stress and inhibit apoptosis by modulating the mitochondrial-apoptotic pathway, regarded as the Akt/Bad/Caspases signalling cascade.

PMID:

25871290

[PubMed - in process]

PMCID:

PMC4413202

[Free PMC Article](#)

Astaxanthin inhibits oxidative damage in iron-liposomes.

[Biochem Biophys Res Commun](#). 2001 Oct 19;288(1):225-32.

Astaxanthin and peridinin inhibit oxidative damage in Fe(2+)-loaded liposomes: scavenging oxyradicals or changing membrane permeability?

[Barros MP](#), [Pinto E](#), [Colepicolo P](#), [Pedersén M](#).

Department of Botany, Stockholm University, SE-10691 Stockholm, Sweden.
mpbarros@botan.su.se

Astaxanthin and peridinin, two typical carotenoids of marine microalgae, and lycopene were incorporated in phosphatidylcholine multilamellar liposomes and tested as inhibitors of lipid oxidation. Contrarily to peridinin results, astaxanthin strongly reduced lipid damage when the lipoperoxidation promoters-H₂O₂, tert-butyl hydroperoxide (t-ButOOH) or ascorbate-and Fe(2+):EDTA were added simultaneously to the liposomes. In order to check if the antioxidant activity of carotenoids was also related to their effect on membrane permeability, the peroxidation processes were initiated by adding the promoters to Fe(2+)-loaded liposomes (encapsulated in the inner aqueous solution). Despite that the rigidifying effect of carotenoids in membranes was not directly measured here, peridinin probably has decreased membrane permeability to initiators (t-ButOOH > ascorbate > H₂O₂) since its incorporation limited oxidative damage on iron-liposomes. On the other hand, the antioxidant activity of astaxanthin in iron-containing vesicles might be derived from its known rigidifying effect and the inherent scavenging ability.

Publication Types:

PMID: 11594777 [PubMed - indexed for MEDLINE]

Astaxanthin is the most difficult dietary carotenoid to become oxidized by its radical cation.

[Arch Biochem Biophys.](#) 2001 Jan 1;385(1):13-9.

The interaction of dietary carotenoids with radical species.

Mortensen A, Skibsted LH, Truscott TG.

Department of Dairy and Food Science, Royal Veterinary and Agricultural University, Frederiksberg, Denmark.

Dietary carotenoids react with a wide range of radicals such as CCl_3O_2^* , RSO_2^* , NO_2^* , and various arylperoxyl radicals via electron transfer producing the radical cation of the carotenoid. Less strongly oxidizing radicals, such as alkylperoxyl radicals, can lead to hydrogen atom transfer generating the neutral carotene radical. Other processes can also arise such as adduct formation with sulphur-centered radicals. The oxidation potentials have been established, showing that, in Triton X-100 micelles, lycopene is the easiest carotenoid to oxidize to its radical cation and astaxanthin is the most difficult. The interaction of carotenoids and carotenoid radicals with other antioxidants is of importance with respect to anti- and possibly pro-oxidative reactions of carotenoids. In polar environments the vitamin E (alpha-tocopherol) radical cation is deprotonated ($\text{TOH}^{*+} \rightarrow \text{TO}^* + \text{H}^+$) and TO^* does not react with carotenoids, whereas in nonpolar environments such as hexane, TOH^{*+} is converted to TOH by hydrocarbon carotenoids. However, the nature of the reaction between the tocopherol and various carotenoids shows a marked variation depending on the specific tocopherol homologue. The radical cations of the carotenoids all react with vitamin C so as to "repair" the carotenoid.

Publication Types:

- [Research Support, Non-U.S. Gov't](#)
- [Review](#)

PMID: 11361009 [PubMed - indexed for MEDLINE]

ASTAXANTHIN EFFICIENT AT PREVENTING CYTOTOXICITY DUE TO OXIDATIVE STRESS IN YEAST.

3 Biotech. 2019 Mar;9(3):88.

doi: 10.1007/s13205-019-1634-7. Epub 2019 Feb 15.

Astaxanthin supplementation reduces dichlorvos-induced cytotoxicity in *Saccharomyces cerevisiae*

[S J Sudharshan](#)¹, [Subasri Subramaniyan](#)¹, [Greeshma Satheeshan](#)¹, [Madhu Dyavaiah](#)¹

Affiliations expand

- PMID: **30800599**
- PMCID: [PMC6385069](#)
- DOI: [10.1007/s13205-019-1634-7](#)

Free PMC article

Abstract

This study evaluates the protective effect of astaxanthin against dichlorvos cytotoxicity in yeast *Saccharomyces cerevisiae*. Dichlorvos induce a dose-dependent cytotoxicity in yeast cells, which is mediated by oxidative stress. Our experimental results showed pre-treatment with astaxanthin enhances cell viability by 20-30% in yeast cells exposed to dichlorvos. A decrease in DCF fluorescence intensity and lipid peroxidation, increased SOD activity, and glutathione levels in astaxanthin-treated cells indicate that astaxanthin protected the cells against dichlorvos-induced oxidative stress. Reduced chromatin condensation and nuclear fragmentation in astaxanthin pre-treated cells also indicate that astaxanthin rescued the cells from dichlorvos-induced apoptosis. Our overall results suggest that dichlorvos induces oxidative stress-mediated cytotoxicity in yeast cells, and that was rescued by astaxanthin pre-treatment.

ASTAXANTHIN IMPROVES ANTIOXIDANT ENZYME ACTIVITY AND FREE RADICAL SCAVENGING IN CHICKENS.

Poult Sci. 2021 May;100(5):101045.

doi: 10.1016/j.psj.2021.101045. Epub 2021 Feb 15.

Dietary supplementation with natural astaxanthin from *Haematococcus pluvialis* improves antioxidant enzyme activity, free radical scavenging ability, and gene expression of antioxidant enzymes in laying hens

[Nuo Heng](#)¹, [Shan Gao](#)¹, [Yu Chen](#)², [Liang Wang](#)², [Zheng Li](#)³, [Yong Guo](#)¹, [Xihui Sheng](#)¹, [Xiangguo Wang](#)¹, [Kai Xing](#)¹, [Longfei Xiao](#)¹, [Hemin Ni](#)¹, [Xiaolong Qi](#)⁴

- PMID: 33752070 PMCID: [PMC8005829](#) DOI: [10.1016/j.psj.2021.101045](#) [Free PMC article](#)

Abstract

The objective of this study was to evaluate the effects of natural astaxanthin (ASTA) from *Haematococcus pluvialis* on production performance, egg quality, antioxidant enzyme activity, free radical scavenging ability, and gene expression of antioxidant enzymes in laying hens. Nongda No. 3 laying hens (n = 450) were randomly allocated to 1 of 5 dietary treatments. Each treatment had 6 replicates of 15 hens each. All birds were assigned to a corn-soybean meal-based diet containing 0, 20, 40, 80, or 160 mg/kg ASTA for 4 wk. With increasing dietary ASTA, no significant effects were observed on egg weight, feed consumption, feed efficiency, laying rate, Haugh unit, or eggshell strength. Yolk color darkened linearly with increasing dose of ASTA ($P < 0.05$). Glutathione peroxidase activity was improved in the kidney with dietary ASTA at levels of 40 mg/kg. Total superoxide dismutase (SOD) was significantly increased in the liver, kidney, and plasma with dietary ASTA supplementation at 40 mg/kg. With increasing dietary ASTA, the scavenging abilities of hydroxyl radicals and superoxide anions were linearly increased ($P < 0.05$), and the malondialdehyde content decreased linearly ($P < 0.05$). Compared with the control group, mRNA expression of Cu-Zn SOD (SOD1), Mn SOD (SOD2), and nuclear factor E2-related factor 2 (NRF2) in the liver and kidney was significantly increased in the 40 mg/kg ASTA group ($P < 0.05$). The level of GPX4 mRNA in the liver and kidney was significantly increased with ASTA supplementation at 40 and 80 mg/kg ($P < 0.05$). The results demonstrate that dietary ASTA improves free radical scavenging ability and antioxidant enzyme activity, which may be related in part to the upregulated mRNA expression of genes encoding antioxidant enzymes and NRF2.

Astaxanthin shows antioxidant functions in Atlantic salmon.

[J Nutr.](#) 2000 Jul;130(7):1800-8.

Depletion of alpha-tocopherol and astaxanthin in Atlantic salmon (*Salmo salar*) affects autoxidative defense and fatty acid metabolism.

[Bell JG](#), [McEvoy J](#), [Tocher DR](#), [Sargent JR](#).

Institute of Aquaculture, University of Stirling, Stirling FK9 4LA, Scotland, U.K.

Duplicate groups of Atlantic salmon post-smolts were fed four purified diets supplemented with both vitamin E and the carotenoid astaxanthin (Ax) (+E, +Ax), or supplemented with either vitamin E or Ax (-E, +Ax and +E, -Ax) or deficient in both vitamin E and Ax (-E, -Ax) for 22 wk. There were no effects of diet on growth rate, but an extensive lipoid liver degenerative lesion was observed in 15% of fish fed diets deficient in vitamin E. Tissue vitamin E concentrations varied in accordance with dietary vitamin E in liver, muscle, heart, plasma, brain and eye; levels were reduced to approximately 3% in liver but only to 40% in eye of fish fed diets deficient in vitamin E compared with those fed diets supplemented with vitamin E. An interactive sparing of Ax supplementation on tissue vitamin E concentration was observed, but only in brain. Dietary deficiency of both vitamin E and Ax significantly increased the recovery of desaturated and elongated products of both [1-(14)C] 18:3(n-3) and [1-(14)C] 20:5(n-3) in isolated hepatocytes, suggesting that conversion of fatty acids to their long-chain highly unsaturated products can be stimulated by a deficiency of lipid-soluble antioxidants. The antioxidant synergism of vitamin E and Ax was supported by their ability to reduce malondialdehyde formation in an in vitro stimulation of microsomal lipid peroxidation and to reduce plasma levels of 8-isoprostane. The results of this study suggest that both vitamin E and the carotenoid Ax have antioxidant functions in Atlantic salmon.

Publication Types:

PMID: 10867054 [PubMed - indexed for MEDLINE]

Astaxanthin shows stronger protective activity than canthaxanthin against peroxidation.

[Biochim Biophys Acta](#). 2000 Jan 15;1463(1):179-87.

**Exogenously incorporated ketocarotenoids in large unilamellar vesicles.
Protective activity against peroxidation.**

[Rengel D](#), [Díez-Navajas A](#), [Serna-Rico A](#), [Veiga P](#), [Muga A](#), [Milicua JC](#).

Department of Biochemistry and Molecular Biology, University of the Basque Country, P.O. Box 644, 48080, Bilbao, Spain.

The ability of astaxanthin and canthaxanthin as chain-breaking antioxidants was studied in Cu(2+)-initiated peroxidation of phosphatidylcholine large unilamellar vesicles (LUVs). Both carotenoids increased the lag period that precedes the maximum rate of lipid peroxidation, though astaxanthin showed stronger activity. For these experiments, different amounts of xanthophylls were exogenously added to previously made LUVs, non-incorporated pigment being afterwards removed. Differential scanning calorimetry assays with L-beta,gamma-dimyristoyl-alpha-phosphatidylcholine LUVs demonstrated that xanthophylls incorporated as described interact with the lipid matrix becoming interspersed among the phospholipid molecules.

Publication Types:

PMID: 10631307 [PubMed - indexed for MEDLINE]

Astaxanthin alleviates brain aging in rats by attenuating oxidative stress.

[Food Funct.](#) 2014 Jan;5(1):158-66. doi: 10.1039/c3fo60400d.

Astaxanthin alleviates brain aging in rats by attenuating oxidative stress and increasing BDNF levels.

[Wu W¹](#), [Wang X](#), [Xiang Q](#), [Meng X](#), [Peng Y](#), [Du N](#), [Liu Z](#), [Sun Q](#), [Wang C](#), [Liu X](#).

Author information

Abstract

Astaxanthin (AST) is a carotenoid pigment which possesses potent antioxidative, anti-inflammatory, and neuroprotective properties. The aim of this study was to investigate whether administration of AST had protective effects on D-galactose-induced brain aging in rats, and further examined its protective mechanisms. The results showed that AST treatment significantly restored the activities of glutathione peroxidase (GSH-PX) and superoxide dismutase (SOD), and increased glutathione (GSH) contents and total antioxidant capacity (T-AOC), but decreased malondialdehyde (MDA), protein carbonylation and 8-hydroxy-2'-deoxyguanosine (8-OHdG) levels in the brains of aging rats. Furthermore, AST increased the ratio of Bcl-2/Bax, but decreased the expression of Cyclooxygenase-2 (COX-2) in the brains of aging rats. Additionally, AST ameliorated histopathological changes in the hippocampus and restored brain derived neurotrophic factor (BDNF) levels in both the brains and hippocampus of aging rats. These results suggested that AST could alleviate brain aging, which may be due to attenuating oxidative stress, ameliorating hippocampus damage, and upregulating BDNF expression.

PMID:

24326685

[PubMed - indexed for MEDLINE]

Astaxanthin is more stable than zeaxanthin, canthaxanthin and beta-carotene during lipid peroxidation.

[Z Lebensm Unters Forsch.](#) 1993 May;196(5):423-9.

Carotenoid scavenging of radicals. Effect of carotenoid structure and oxygen partial pressure on antioxidative activity.

[Jørgensen K.](#) [Skibsted LH.](#)

RVAU Centre for Food Research, Royal Veterinary and Agricultural University, Frederiksberg, Denmark.

Carotenoid scavenging of free radicals has been investigated in peroxidizing methyl esters of unsaturated fatty acids using (i) metmyoglobin as a water-based free-radical initiator in a heterogeneous lipid/water system, and (ii) azo-bis-isobutyronitrile as a free-radical initiator in a homogeneous chloroform solution. For the heterogeneous system, using a combination of electrochemical oxygen depletion measurements, spectrophotometric determination of lipid hydroperoxides and carotenoid degradation, it was demonstrated that each of the four carotenoids astaxanthin, beta-carotene, canthaxanthin, and zeaxanthin protects the methyl esters against oxidation. The antioxidative effect increases with increasing carotenoid concentration, increases with decreasing oxygen partial pressure ($0.010 < pO_2 < 0.50$ atm), and shows little dependence on the structure of the carotenoid. For a homogeneous solution, the effect of the structure of the carotenoid was further investigated, and it was shown that the stability of the four carotenoids in the oxidizing system are different, with the order of decreasing stability being: astaxanthin > canthaxanthin > beta-carotene > zeaxanthin. Each of the four carotenoids can suppress lipid oxidation and the degree of suppression of peroxidation of methyl linoleate corresponds to the difference in stability.

PMID: 8511974 [PubMed - indexed for MEDLINE]

Astaxanthin increases survival and provides antioxidant protection in citrus red mites.

[Environ Entomol.](#) 2017 Oct 1;46(5):1143-1150. doi: 10.1093/ee/nvx121.

Antioxidant Protection by Astaxanthin in the Citrus Red Mite (Acari: Tetranychidae).

[Atarashi M](#)¹, [Manabe Y](#)², [Kishimoto H](#)³, [Sugawara T](#)², [Osakabe M](#)¹.

Author information

Abstract

Solar ultraviolet-B (UVB) radiation and radiant heat have lethal effects on plant-dwelling mites, including spider mites, and their natural enemies, such as phytoseiid mites, leading them to reside on lower leaf surfaces. Panonychus spider mites are outcompeted by Tetranychus spider mites and thus exploit upper leaf surfaces, where they are exposed to both UVB radiation and radiant heat. Panonychus spider mites are thought to produce astaxanthin constitutionally. In this study, we compared carotenoid components, antioxidant capacity, lipid peroxidation, survival, and egg production in wild-type (WTS) and albino-type strains (ATS) of Panonychus citri (McGregor). Four carotenoids (neoxanthin, violaxanthin, lutein, and carotene) and their isomers and esters were identified in both strains, but astaxanthin and its esters were present only in WTS. The singlet oxygen scavenging capacity of lipid-soluble ingredients was greater in WTS than in ATS, whereas the oxygen radical absorbance capacities of hydrophilic ingredients were equivalent between them. Lipid peroxide accumulation was clearly higher in ATS than in WTS under both UVB irradiation (25 °C) and high temperature (35 °C) conditions. The findings are consistent with an antioxidant protective function of astaxanthin in this mite. Survival periods at 38 °C were longer in WTS than in ATS, although no difference was shown at 35 °C or under UVB irradiation. Therefore, astaxanthin accumulation was shown to be a major mechanism for survival under radiant heat, although other mechanisms, such as photoreactivation, might play a major role in survival under UVB radiation.

KEYWORDS:

Carotenoid; Lipid peroxidation; Oxygen Radical Absorbance Capacity; Singlet Oxygen Scavenging Capacity; Tetranychidae

PMID: 28981670

DOI: [10.1093/ee/nvx121](https://doi.org/10.1093/ee/nvx121)

[Indexed for MEDLINE]

Astaxanthin enhances immunity, improves resistance to environmental stress, increases growth rates and supports the antioxidant defense system in pufferfish.

[Fish Physiol Biochem.](#) 2018 Feb;44(1):209-218. doi: 10.1007/s10695-017-0425-5. Epub 2017 Sep 21.

Effect of dietary astaxanthin on the growth performance, non-specific immunity, and antioxidant capacity of pufferfish (*Takifugu obscurus*) under high temperature stress.

[Cheng CH](#)^{1,2}, [Guo ZX](#)^{3,4}, [Ye CX](#)^{2,5}, [Wang AL](#)^{6,7}.

Author information

Abstract

The present study was conducted to investigate the effects of astaxanthin on growth performance, biochemical parameters, ROS production, and immune-related gene expressions of the pufferfish (*Takifugu obscurus*) under high temperature stress. The experimental basal diets supplemented with astaxanthin at the rates of 0 (control), 20, 40, 80, 160, and 320 mg kg⁻¹ were fed to fish for 8 weeks. The results showed that the fish fed diet with 80, 160, and 320 mg kg⁻¹ astaxanthin significantly improved weight gain and specific growth rate. Furthermore, fish fed the moderate dietary astaxanthin increased plasma alkaline phosphatase activities, and decrease plasma aspartate aminotransferase and alanine aminotransferase activities. After the feeding trial, the fish were exposed to high temperature stress for 48 h. The results shown that astaxanthin could suppress ROS production induced by high temperature stress. Meanwhile, compared with the control group, the astaxanthin groups increased SOD, CAT, and HSP70 mRNA levels under high temperature stress. These results showed that the basal diet supplemented with 80-320 mg kg⁻¹ astaxanthin could enhance growth, nonspecific immune responses, and antioxidant defense system and improve resistance against high temperature stress in pufferfish.

KEYWORDS:

Astaxanthin; Growth performance; High temperature stress; Immune response; *Takifugu obscurus*

PMID: 28936571

DOI: [10.1007/s10695-017-0425-5](https://doi.org/10.1007/s10695-017-0425-5)

[Indexed for MEDLINE]

Astaxanthin displays anti-inflammatory and antioxidant effects in-vitro.

PLoS One. 2017 Sep 19;12(9):e0184332. doi: 10.1371/journal.pone.0184332. eCollection 2017.

Scavenging of reactive oxygen species by astaxanthin inhibits epithelial-mesenchymal transition in high glucose-stimulated mesothelial cells.

Hara K¹, Hamada C¹, Wakabayashi K¹, Kanda R^{1,2}, Kaneko K¹, Horikoshi S¹, Tomino Y^{1,2}, Suzuki Y¹.

Author information

Abstract

BACKGROUND: High glucose concentrations influence the functional and structural development of the peritoneal membrane. We previously reported that the oral administration of astaxanthin (AST) suppressed peritoneal fibrosis (PF) as well as inhibited oxidative stress, inflammation, and epithelial-mesenchymal transition (EMT) of peritoneal mesothelial cells (PMCs) in a chlorhexidine-induced PF rat model. This suggests that oxidative stress induction of EMT is a key event during peritoneal damage. The present study evaluated the therapeutic effect of AST in suppressing EMT, in response to glucose-induced oxidative stress.

METHODS: Temperature-sensitive mesothelial cells (TSMCs) were cultured in the presence or absence of AST and then treated with 140 mM glucose for 3 or 12 hours. Expression levels of TNF- α , TGF- β , and VEGF were determined at the mRNA and protein levels, and nuclear factor kappa B (NF- κ B) activity was evaluated. We measured NO₂⁻/NO₃⁻ concentrations in cellular supernatants and determined 8-hydroxy-2'-deoxyguanosine (8-OHdG) levels in mitochondrial and nuclear DNA. The expressions of E-cadherin and alpha-smooth muscle actin (α -SMA) were evaluated by double immunofluorescence and protein levels.

RESULTS: High glucose concentrations induced overproduction of reactive oxidative species (ROS), increasing 8-OHdG mitochondrial DNA and cytokine levels. The NF- κ B pathway was activated in response to high glucose concentrations, whereas de novo α -SMA expression was observed with decreased E-cadherin expression. AST treatment attenuated ROS production, inflammatory cytokine production, NF- κ B activation, and EMT.

CONCLUSION: The findings of the present study indicate that AST may have an anti-EMT effect due to anti-oxidative and anti-inflammatory activities by scavenging glucose-induced ROS from mitochondria in PMCs. AST may be an efficacious treatment for PF.

PMID: 28926603 PMCID: [PMC5604950](https://pubmed.ncbi.nlm.nih.gov/PMC5604950/) DOI: [10.1371/journal.pone.0184332](https://doi.org/10.1371/journal.pone.0184332) [Indexed for MEDLINE]

[Free PMC Article](#)

Astaxanthin reduces acute lung injury by ameliorating the inflammatory and oxidative response in mice.

[Biomed Pharmacother.](#) 2017 Nov;95:974-982. doi: 10.1016/j.biopha.2017.09.012. Epub 2017 Sep 11.

Astaxanthin alleviated acute lung injury by inhibiting oxidative/nitrative stress and the inflammatory response in mice.

Bi J¹, Cui R², Li Z¹, Liu C³, Zhang J⁴.

Author information

Abstract

The purpose of the present study was to assess the effect of astaxanthin (ASX) treatment on the acute lung injury (ALI) induced by cecal ligation and puncture (CLP) in mice. Mice were randomly allocated into the following groups: (1) the saline control group, in which mice were given saline before sham operation; (2) the ASX control group, in which mice received ASX before sham operation; (3) the ALI group, in which mice were given saline before CLP operation; and (4) the ALI+ASX group, in which mice received ASX before CLP operation. ASX was dissolved in olive oil and administrated by oral gavage for 14days consecutively before the CLP or sham operation. In experiment 1, Kaplan-Meier survival analysis was conducted for 72h after CLP. In experiment 2, blood, bronchoalveolar lavage fluid (BALF) and lung tissues were collected at 24h after the CLP or sham operation to determine the severity of lung injury. The results showed that ASX treatment could significantly decrease the CLP-induced mortality rate in mice. Meanwhile, ASX treatment significantly attenuated CLP-induced lung histopathological injury, inflammatory infiltration, total protein and albumin concentration, and total cell and neutrophil counts in the BALF. Furthermore, ASX treatment alleviated oxidative/nitrative stress, inflammation levels and pulmonary apoptosis in lung tissues. In addition, ASX treatment markedly down-regulated the expression of inducible nitric oxide synthase (i-NOS), nitrotyrosine (NT) and nuclear factor-kappa B (NF-Kb) P65 in the lung tissues compared with that in the ALI group. Astaxanthin treatment had markedly protective effect against ALI in mice, and the potential mechanism is associated with its ability to inhibit the inflammatory response, oxidative/nitrative stress, and pulmonary apoptosis, as well as down-regulate NF-kB P65 expression.

KEYWORDS:

Acute lung injury; Astaxanthin; Inflammatory response; NF-kB P65; Oxidative stress; Pulmonary apoptosis

PMID: 28915539

DOI: [10.1016/j.biopha.2017.09.012](https://doi.org/10.1016/j.biopha.2017.09.012)

[Indexed for MEDLINE]

Astaxanthin is a potent antioxidant in a membrane model, much more so than beta-carotene.

[Arch Biochem Biophys.](#) 1992 Sep;297(2):291-5.

Astaxanthin and canthaxanthin are potent antioxidants in a membrane model.

[Palozza P](#), [Krinsky NI](#).

Department of Biochemistry, Tufts University School of Medicine, Boston, Massachusetts 02111-1837.

When the conjugated keto-carotenoids, either astaxanthin or canthaxanthin, are added to rat liver microsomes undergoing radical-initiated lipid peroxidation under air, they are as effective as alpha-tocopherol in inhibiting this process. This contrasts with the effect of beta-carotene, which is a much less potent antioxidant when added in this system, without the addition of other antioxidants.

Publication Types:

PMID: 1497349 [PubMed - indexed for MEDLINE]

Astaxanthin and other xanthophyll carotenoids show antioxidant activity on phospholipid peroxidation.

[Biochim Biophys Acta](#). 1992 Jun 22;1126(2):178-84.

Antioxidant activity of xanthophylls on peroxy radical-mediated phospholipid peroxidation.

[Lim BP](#), [Nagao A](#), [Terao J](#), [Tanaka K](#), [Suzuki T](#), [Takama K](#).

National Food Research Institute, Ministry of Agriculture, Forestry and Fisheries, Ibaraki, Japan.

The ability of xanthophylls (canthaxanthin, zeaxanthin, and astaxanthin) as chain-breaking antioxidants was investigated in peroxy radical-mediated peroxidation of phosphatidylcholine (PC) liposomes under atmospheric conditions using lipid-soluble and water-soluble radical generators. These xanthophylls retarded the chain propagation reaction of phosphatidylcholine hydroperoxides (PC-OOH) formation, although their activities to trap chain-carrying peroxy radical were much less than that of alpha-tocopherol. In chick plasma studies, it was observed that endogenous xanthophylls participated in the antioxidant defenses against the attack of aqueous peroxy radical. It was concluded that xanthophylls possess the ability to act as chain-breaking antioxidants in the peroxidation of membraneous phospholipids. Dietary xanthophylls may, therefore, be helpful in resisting membraneous phospholipids against oxidative damage in vivo.

PMID: 1627620 [PubMed - indexed for MEDLINE]

Astaxanthin protects against early brain injury and combats oxidative stress in rats.

[J Neurosurg.](#) 2014 Jul;121(1):42-54. doi: 10.3171/2014.2.JNS13730. Epub 2014 Apr 11.

Amelioration of oxidative stress and protection against early brain injury by astaxanthin after experimental subarachnoid hemorrhage.

[Zhang XS¹](#), [Zhang X](#), [Zhou ML](#), [Zhou XM](#), [Li N](#), [Li W](#), [Cong ZX](#), [Sun Q](#), [Zhuang Z](#), [Wang CX](#), [Shi JX](#).

Author information

Abstract

OBJECT.: Aneurysmal subarachnoid hemorrhage (SAH) causes devastating rates of mortality and morbidity. Accumulating studies indicate that early brain injury (EBI) greatly contributes to poor outcomes after SAH and that oxidative stress plays an important role in the development of EBI following SAH. Astaxanthin (ATX), one of the most common carotenoids, has a powerful antioxidative property. However, the potential role of ATX in protecting against EBI after SAH remains obscure. The goal of this study was to assess whether ATX can attenuate SAH-induced brain edema, blood-brain barrier permeability, neural cell death, and neurological deficits, and to elucidate whether the mechanisms of ATX against EBI are related to its powerful antioxidant property.

METHODS:

Two experimental SAH models were established, including a prechiasmatic cistern SAH model in rats and a one-hemorrhage SAH model in rabbits. Both intracerebroventricular injection and oral administration of ATX were evaluated in this experiment. Posttreatment assessments included neurological scores, body weight loss, brain edema, Evans blue extravasation, Western blot analysis, histopathological study, and biochemical estimation.

RESULTS:

It was observed that an ATX intracerebroventricular injection 30 minutes post-SAH could significantly attenuate EBI (including brain edema, blood-brain barrier disruption, neural cell apoptosis, and neurological dysfunction) after SAH in rats. Meanwhile, delayed treatment with ATX 3 hours post-SAH by oral administration was also neuroprotective in both rats and rabbits. In addition, the authors found that ATX treatment could prevent oxidative damage and upregulate the endogenous antioxidant levels in the rat cerebral cortex following SAH.

CONCLUSIONS:

These results suggest that ATX administration could alleviate EBI after SAH, potentially through its powerful antioxidant property. The authors conclude that ATX might be a promising therapeutic agent for EBI following SAH.

KEYWORDS:

ATX = astaxanthin; BBB = blood-brain barrier; DAB = 3,3'-diaminobenzidine; EB = Evans blue; EBI = early brain injury; GAPDH = glyceraldehyde-3-phosphate dehydrogenase; GSH = glutathione; H₂O₂ = hydrogen peroxide; MDA = malondialdehyde; PBS = phosphate-buffered saline; SAH = subarachnoid hemorrhage; SOD = superoxide dismutase; TBS-T = Tris-buffered saline with Tween 20; astaxanthin; early brain injury; oxidative stress; rabbit; rat; subarachnoid hemorrhage; vascular disorders

PMID: 24724856 [PubMed - indexed for MEDLINE]

Astaxanthin has a protective effect in the kidneys of rats and the mechanism of action for this effect may be antioxidant protection against oxidative injury and reduction of arsenic accumulation.

[Nutr Res Pract](#). 2014 Feb;8(1):46-53. doi: 10.4162/nrp.2014.8.1.46. Epub 2014 Jan 29.

Nephroprotective effect of astaxanthin against trivalent inorganic arsenic-induced renal injury in wistar rats.

[Wang X¹](#), [Zhao H¹](#), [Shao Y¹](#), [Wang P¹](#), [Wei Y¹](#), [Zhang W¹](#), [Jiang J¹](#), [Chen Y¹](#), [Zhang Z¹](#).

Author information

Abstract

Inorganic arsenic (iAs) is a toxic metalloid found ubiquitously in the environment. In humans, exposure to iAs can result in toxicity and cause toxicological manifestations. Arsenic trioxide (As₂O₃) has been used in the treatment for acute promyelocytic leukemia. The kidney is the critical target organ of trivalent inorganic As (iAs(III)) toxicity. We examine if oral administration of astaxanthin (AST) has protective effects on nephrotoxicity and oxidative stress induced by As₂O₃ exposure (via intraperitoneal injection) in rats. Markers of renal function, histopathological changes, Na(+)-K(+) ATPase, sulfhydryl, oxidative stress, and As accumulation in kidneys were evaluated as indicators of As₂O₃ exposure. AST showed a significant protective effect against As₂O₃-induced nephrotoxicity. These results suggest that the mechanisms of action, by which AST reduces nephrotoxicity, may include antioxidant protection against oxidative injury and reduction of As accumulation. These findings might be of therapeutic benefit in humans or animals suffering from exposure to iAs(III) from natural sources or cancer therapy.

KEYWORDS:

Astaxanthin; arsenic accumulation; nephrotoxicity; oxidative stress; trivalent inorganic arsenic

PMID:

24611105

[PubMed]

PMCID:

PMC3944156

Free PMC Article

Astaxanthin restores the antioxidant network activity of superoxide dismutase and catalase in-vitro.

[PLoS One](#). 2014 Feb 10;9(2):e88359. doi: 10.1371/journal.pone.0088359. eCollection 2014.

Astaxanthin treatment confers protection against oxidative stress in U937 cells stimulated with lipopolysaccharide reducing O₂⁻ production.

[Franceschelli S¹](#), [Pesce M¹](#), [Ferrone A¹](#), [De Lutiis MA¹](#), [Patruno A¹](#), [Grilli A²](#), [Felaco M¹](#), [Speranza L¹](#).

Author information

Abstract

Recently, astaxanthin (ASTA) studies have focused on several biological functions such as radical scavenging, singlet oxygen quenching, anti-carcinogenesis, anti-diabetic, anti-obesity, anti-inflammatory, anti-melanogenesis, and immune enhancement activities. In this study, we investigated the potential role protective of ASTA, an antioxidant marine carotenoid, in restoring physiological conditions in U937 cells stimulated with LPS (10 µg/ml). Our results show that pre-treatment with ASTA (10 µM) for 1 h attenuates the LPS-induced toxicity and ROS production. The beneficial effect of ASTA is associated with a reduction intracellular O₂⁻ production by restoring the antioxidant network activity of superoxide dismutase (SOD) and catalase (CAT), which influence HO-1 expression and activity by inhibiting nuclear translocation of Nrf2. We accordingly hypothesize that ASTA has therapeutic properties protecting U937 cells from LPS-induced inflammatory and oxidative stress.

PMID:

24520374

[PubMed - indexed for MEDLINE]

PMCID:

PMC3919765

Free PMC Article

Astaxanthin improvement in spatial memory impairment in mice attributed to its reduction of oxidative stress.

[Eur J Pharmacol.](#) 2016 Apr 15;777:60-9. doi: 10.1016/j.ejphar.2016.02.062. Epub 2016 Feb 27.

Astaxanthin ameliorates aluminum chloride-induced spatial memory impairment and neuronal oxidative stress in mice.

[Al-Amin MM¹](#), [Reza HM²](#), [Saadi HM²](#), [Mahmud W²](#), [Ibrahim AA²](#), [Alam MM²](#), [Kabir N²](#), [Saifullah AR²](#), [Tropa ST²](#), [Quddus AH³](#).

Author information

Abstract

Aluminum chloride induces neurodegenerative disease in animal model. Evidence suggests that aluminum intake results in the activation of glial cells and generation of reactive oxygen species. By contrast, astaxanthin is an antioxidant having potential neuroprotective activity. In this study, we investigate the effect of astaxanthin on aluminum chloride-exposed behavioral brain function and neuronal oxidative stress (OS). Male Swiss albino mice (4 months old) were divided into 4 groups: (i) control (distilled water), (ii) aluminum chloride, (iii) astaxanthin+aluminum chloride, and (iv) astaxanthin. Two behavioral tests; radial arm maze and open field test were conducted, and OS markers were assayed from the brain and liver tissues following 42 days of treatment. Aluminum exposed group showed a significant reduction in spatial memory performance and anxiety-like behavior. Moreover, aluminum group exhibited a marked deterioration of oxidative markers; lipid peroxidation (MDA), nitric oxide (NO), glutathione (GSH) and advanced oxidation of protein products (AOPP) in the brain. To the contrary, co-administration of astaxanthin and aluminum has shown improved spatial memory, locomotor activity, and OS. These results indicate that astaxanthin improves aluminum-induced impaired memory performances presumably by the reduction of OS in the distinct brain regions. We suggest a future study to determine the underlying mechanism of astaxanthin in improving aluminum-exposed behavioral deficits.

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KEYWORDS:

Behavior; Glutathione; Memory; Nitric oxide; Superoxide dismutase

PMID: 26927754

DOI: [10.1016/j.ejphar.2016.02.062](https://doi.org/10.1016/j.ejphar.2016.02.062)

[PubMed - indexed for MEDLINE]

Astaxanthin protects vascular endothelial cells by reducing reactive oxygen species.

[Life Sci.](#) 2016 Apr 1;150:24-31. doi: 10.1016/j.lfs.2016.02.087. Epub 2016 Feb 27.

Astaxanthin alleviates oxidative stress insults-related derangements in human vascular endothelial cells exposed to glucose fluctuations.

[Abdelzاهر LA](#)¹, [Imaizumi T](#)¹, [Suzuki T](#)¹, [Tomita K](#)¹, [Takashina M](#)¹, [Hattori Y](#)².

Author information

Abstract

Glycemic fluctuations may play a critical role in the pathogenesis of diabetic complications, such as cardiovascular disease. We investigated whether the oxycarotenoid astaxanthin can reduce the detrimental effects of fluctuating glucose on vascular endothelial cells. Human umbilical venous endothelial cells were incubated for 3 days in media containing 5.5mM glucose, 22 mM glucose, or 5.5mM glucose alternating with 22 mM glucose in the absence or presence of astaxanthin or N-acetyl-L-cysteine (NAC). Constant high glucose increased reactive oxygen species (ROS) generation, but such an effect was more pronounced in fluctuating glucose. This was associated with up-regulated p22(phox) expression and down-regulated peroxisome proliferator activated receptor- γ coactivator (PGC-1 α) expression. Astaxanthin inhibited ROS generation, p22(phox) up-regulation, and PGC-1 α down-regulation by the stimuli of glucose fluctuation. Fluctuating glucose, but not constant high glucose, significantly decreased the endothelial nitric oxide synthase (eNOS) phosphorylation level at Ser-1177 without affecting total eNOS expression, which was prevented by astaxanthin as well as by the anti-oxidant NAC. Transferase-mediated dUTP nick end labeling (TUNEL) showed increased cell apoptosis in fluctuating glucose. Glucose fluctuation also resulted in up-regulating gene expression of pro-inflammatory mediators, interleukin-6 and intercellular adhesion molecule-1. These adverse changes were subdued by astaxanthin. The phosphorylation levels of c-Jun N-terminal kinase (JNK) and p38 were significantly increased by glucose fluctuations, and astaxanthin significantly inhibited the increase in JNK and p38 phosphorylation. Taken together, our results suggest that astaxanthin can protect vascular endothelial cells against glucose fluctuation by reducing ROS generation.

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KEYWORDS:

Apoptosis; Astaxanthin; Endothelial cells; Endothelial nitric oxide synthase; Glucose fluctuation; Reactive oxygen species

PMID: 26924495 DOI: [10.1016/j.lfs.2016.02.087](https://doi.org/10.1016/j.lfs.2016.02.087) [PubMed - indexed for MEDLINE]

Astaxanthin is effective at vocal fold wound healing in rats by regulating oxidative stress.

[Laryngoscope](#). 2014 Jan;124(1):E1-7. doi: 10.1002/lary.24197. Epub 2013 Oct 15.

Effect of astaxanthin on vocal fold wound healing.

[Mizuta M¹](#), [Hirano S](#), [Hiwatashi N](#), [Tateya I](#), [Kanemaru S](#), [Nakamura T](#), [Ito J](#).

Author information

Abstract

OBJECTIVES/HYPOTHESIS:

Our previous study demonstrated that a large amount of reactive oxygen species (ROS) is produced during the early phase of vocal fold wound healing. In the current study, we investigated the effect of astaxanthin, which is a strong antioxidant, on the regulation of oxidative stress and scarring during vocal fold wound healing.

STUDY DESIGN:

Prospective animal experiment with control.

METHODS:

Sprague-Dawley rats were dosed with astaxanthin (Ast-treated group, 100 mg/kg/day) or olive oil (sham-treated group) by oral gavage daily from preinjury day 1 to postinjury day 4. After vocal folds were injured under the endoscope, larynges were harvested for histological and immunohistochemical examinations on postinjury days 1, 3, 5, and 56, and quantitative real time polymerase chain reaction (PCR) on postinjury days 1 and 3.

RESULTS:

The expression of 4-hydroxy-2-nonenal, which is an oxidative stress marker, was reduced significantly in the lamina propria of the Ast-treated group as compared to the sham-treated group. Histological examination showed significantly less tissue contraction with favorable deposition of hyaluronic acid in the lamina propria of the Ast-treated group compared to the sham-treated group. Real time PCR revealed significantly upregulated mRNA expression of basic fibroblast growth factor on postinjury day 1 and procollagen type I in the Ast-treated group compared to the sham-treated group.

CONCLUSIONS:

These findings suggest that astaxanthin has the potential to prevent vocal fold scarring by regulating oxidative stress during the early phase of vocal fold wound healing.

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KEYWORDS:

Astaxanthin; reactive oxygen species; vocal fold; wound healing

PMID:

23686840

[PubMed - indexed for MEDLINE]

Astaxanthin functions as a potent antioxidant in-vitro and in-vivo by inhibition of oxidative injury of biological membranes.

[Physiol Chem Phys Med NMR](#). 1990;22(1):27-38.

Inhibition of oxidative injury of biological membranes by astaxanthin.

[Kurashige M](#), [Okimasu E](#), [Inoue M](#), [Utsumi K](#).

Department of Medical Biology, Kochi Medical School, Japan.

The value of astaxanthin, a carotenoid pigment, in the treatment of oxidative injury is assessed. Astaxanthin protects the mitochondria of vitamin E-deficient rats from damage by Fe²⁺-catalyzed lipid peroxidation both in vivo and in vitro. The inhibitory effect of astaxanthin on mitochondrial lipid peroxidation is stronger than that of alpha-tocopherol. Thin layer chromatographic analysis shows that the change in phospholipid components of erythrocytes from vitamin E-deficient rats induced by Fe²⁺ and Fe³⁺-xanthine/xanthine oxidase system was significantly suppressed by astaxanthin. Carrageenan-induced inflammation of the paw is also significantly inhibited by administration of astaxanthin. These data indicate that astaxanthin functions as a potent antioxidant both in vivo and in vitro.

PMID: 2084711 [PubMed - indexed for MEDLINE]

Astaxanthin is a more effective antioxidant than beta-carotene by stabilizing trapped radicals.

[Lipids](#). 1989 Jul;24(7):659-61.

Antioxidant activity of beta-carotene-related carotenoids in solution.

[Terao J.](#)

Research Institute for Food Science, Kyoto University, Uji, Kyoto 611, Japan.

The effect of the antioxidant activity of beta-carotene and related carotenoids on the free radical-oxidation of methyl linoleate in solution was examined by measuring the production of methyl linoleate hydroperoxides. Canthaxanthin and astaxanthin which possess oxo groups at the 4 and 4'-positions in the beta-ionone ring retarded the hydroperoxide formation more efficiently than beta-carotene and zeaxanthin which possess no oxo groups. The rates of autocatalytic oxidation of canthaxanthin and astaxanthin were also slower than those of beta-carotene and zeaxanthin. These results suggest that canthaxanthin and astaxanthin are more effective antioxidants than beta-carotene by stabilizing the trapped radicals.

Publication Types:

PMID: 2779372 [PubMed - indexed for MEDLINE]

Astaxanthin's health benefits including antioxidant activity are reviewed.

Critical Reviews in Food Science and Nutrition, 46:185–196 (2006)

Astaxanthin: A Review of its Chemistry and Applications

I. HIGUERA-CIAPARA, L. F ´ELIX-VALENZUELA, and F. M. GOYCOOLEA

Centro de Investigaci´on en Alimentaci´on y Desarrollo, A.C., P.O. Box 1735.
Hermosillo, Sonora. M´exico. 83000

Astaxanthin is a carotenoid widely used in salmonid and crustacean aquaculture to provide the pink color characteristic of that species. This application has been well documented for over two decades and is currently the major market driver for the pigment. Additionally, astaxanthin also plays a key role as an intermediary in reproductive processes. Synthetic astaxanthin dominates the world market but recent interest in natural sources of the pigment has increased substantially. Common sources of natural astaxanthin are the green algae *Haematococcus pluvialis*, the red yeast, *Phaffia rhodozyma*, as well as crustacean byproducts. Astaxanthin possesses an unusual antioxidant activity which has caused a surge in the nutraceutical market for the encapsulated product. Also, health benefits such as cardiovascular disease prevention, immune system boosting, bioactivity against *Helicobacter pylori*, and cataract prevention, have been associated with astaxanthin consumption. Research on the health benefits of astaxanthin is very recent and has mostly been performed in vitro or at the pre-clinical level with humans. This paper reviews the current available evidence regarding astaxanthin chemistry and its potential beneficial effects in humans.

Astaxanthin improves muscle fibrosis by suppressing oxidative stress.

[J Physiol Sci.](#) 2016 Oct 6. [Epub ahead of print]

Astaxanthin supplementation attenuates immobilization-induced skeletal muscle fibrosis via suppression of oxidative stress.

[Maezawa T](#)¹, [Tanaka M](#)^{1,2}, [Kanazashi M](#)³, [Maeshige N](#)¹, [Kondo H](#)⁴, [Ishihara A](#)⁵, [Fujino H](#)⁶.

Author information

Abstract

Immobilization induces skeletal muscle fibrosis characterized by increasing collagen synthesis in the perimysium and endomysium. Transforming growth factor- β 1 (TGF- β 1) is associated with this lesion via promoting differentiation of fibroblasts into myofibroblasts. In addition, reactive oxygen species (ROS) are shown to mediate TGF- β 1-induced fibrosis in tissues. These reports suggest the importance of ROS reduction for attenuating skeletal muscle fibrosis. Astaxanthin, a powerful antioxidant, has been shown to reduce ROS production in disused muscle. Therefore, we investigated the effects of astaxanthin supplementation on muscle fibrosis under immobilization. In the present study, immobilization increased the collagen fiber area, the expression levels of TGF- β 1, α -smooth muscle actin, and superoxide dismutase-1 protein and ROS production. However, these changes induced by immobilization were attenuated by astaxanthin supplementation. These results indicate the effectiveness of astaxanthin supplementation on skeletal muscle fibrosis induced by ankle joint immobilization.

KEYWORDS:

Astaxanthin; Immobilization; Reactive oxygen species; Skeletal muscle fibrosis; Transforming growth factor- β 1

PMID:

27714500

DOI:

[10.1007/s12576-016-0492-x](https://doi.org/10.1007/s12576-016-0492-x)

ASTAXANTHIN INHIBITS ALCOHOL-INDUCED INFLAMMATION AND OXIDATIVE STRESS IN MOUSE CELLS.

Biochim Biophys Acta Mol Cell Biol Lipids. 2021 Jan;1866(1):158838.
doi: 10.1016/j.bbalip.2020.158838. Epub 2020 Oct 13.

Inhibition of alcohol-induced inflammation and oxidative stress by astaxanthin is mediated by its opposite actions in the regulation of sirtuin 1 and histone deacetylase 4 in macrophages

[Hyunju Kang](#)¹, [Young-Ki Park](#)¹, [Ji-Young Lee](#)²

MID: 33065288 DOI: [10.1016/j.bbalip.2020.158838](https://doi.org/10.1016/j.bbalip.2020.158838)

Abstract

We previously demonstrated that astaxanthin (ASTX), a xanthophyll carotenoid, repressed ethanol-induced inflammation and oxidative stress in macrophages. We explored the role of sirtuin 1 (SIRT1) and histone deacetylase 4 (HDAC4) in the inhibitory effect of ASTX on inflammation and oxidative stress in macrophages exposed to ethanol. Ethanol decreased mRNA and protein of SIRT1 while increasing those of HDAC4, which was attenuated by ASTX in RAW 264.7 macrophages and mouse bone marrow-derived macrophages (BMDMs). Inhibition of SIRT1 expression or activity augmented ethanol-induced Hdac4 expression, but SIRT1 activation elicited the opposite effect. Consistently, Hdac4 knockdown increased Sirt1 expression with decreases in ethanol-induced inflammatory gene expression, but its overexpression resulted in the opposite effects. Furthermore, BMDMs from mice with macrophage specific-deletion of Hdac4 (Hdac4^{MKO}) showed significant decreases in ethanol-induced inflammatory genes and ROS accumulation but an increase in Sirt1 expression. Macrophage specific deletion of Hdac4 or ASTX abolished the changes in genes for mitochondrial biogenesis and glycolysis by ethanol. Ethanol increased mitochondrial respiration, ATP production, and proton leak, but decreased maximal respiration and spare respiratory capacity, all of which were abolished by ASTX in RAW 264.7 macrophages. The ethanol-induced alterations in mitochondrial respiration were abrogated in Hdac4^{MKO} BMDMs. In conclusion, the anti-inflammatory and antioxidant properties of ASTX in ethanol-treated macrophages may be mediated, at least partly, by its opposite effect on SIRT1 and HDAC4 to empower SIRT1 to counteract ethanol-induced activation of HDAC4.

ASTAXANTHIN REDUCES OXIDATIVE STRESS INDUCED BY PERFLUOROCTANOIC ACID IN YEAST CELLS.

Toxicol Res (Camb). 2019 Nov 18;8(6):1009-1015.

doi: 10.1039/c9tx00215d. eCollection 2019 Nov 1.

Astaxanthin reduces perfluorooctanoic acid cytotoxicity in *Saccharomyces cerevisiae*

[S J Sudharshan](#)¹, [Raghavendra Tirupathi](#)², [Madhu Dyavaiah](#)¹

- PMID: **32922741**
- PMCID: [PMC7478099](#)
- DOI: [10.1039/c9tx00215d](#)

Free PMC article

Abstract

Perfluorooctanoic acid (PFA) has been identified as an environmental contaminant of high concern for human health. In this study, we demonstrated that PFA induces a dose (0 to 1.5 mM) dependent cytotoxicity in *S. cerevisiae* cells which can be rescued by astaxanthin. The percent sensitivity induced by PFA and the cell protection offered by astaxanthin (30 μ M) were demonstrated by CFU counts and spots. The increase in intracellular ROS, superoxide dismutase (SOD), glutathione and lipid peroxidation levels in PFA treated cells suggested that increased oxidative stress resulted in yeast cell death. In contrast, decreased ROS level, increased SOD activity, reduced glutathione and decreased lipid peroxidation by astaxanthin supplementation suggest that the cells are protected from the PFA induced oxidative stress mediated cytotoxicity. Reduced chromatin condensation and nuclear fragmentation in astaxanthin pre-treated cells indicate that astaxanthin rescued the cells from PFA induced apoptosis. Our overall results suggest that PFA induces oxidative stress-mediated cytotoxicity in yeast cells, which were rescued by astaxanthin treatment.

Astaxanthin shows superior antioxidant properties than three other carotenoids.

Lebensm Unters Forsch (1993) 196: 423-429

Carotenoid Scavenging of Radicals

Effect of carotenoid structure and oxygen partial pressure on antioxidative activity

Kevin Jorgensen and Leif H. Skibsted

Carotenoid scavenging of free radicals has been investigated in peroxidating methyl esters of unsaturated fatty acids using (i) metmyoglobin as a water-based free-radical initiator in a heterogeneous lipid/water system, and (ii) azo-*bis*-isobutyronitrile as a free-radical initiator homogeneous chloroform solution. For the heterogeneous system, using a combination of electrochemical oxygen depletion measurements, spectrophotometric determination of lipid hydroperoxides and carotenoid degradation, it was demonstrated that each of the four carotenoids astaxanthin, β -carotene, canthaxanthin, and zeaxanthin protects the methyl esters against oxidation. The antioxidant effect increases with increasing carotenoid concentration increases with decreasing oxygen partial pressure ($0.010 < 0.50$ atm), and shows little dependence on the structure of the carotenoid. For a homogeneous solution, the effect of the structure of the carotenoid was further investigated, and it was shown that the stability of the four carotenoids in the oxidizing system are different, with the order of decreasing stability being: astaxanthin > canthaxanthin > β -carotene > zeaxanthin. Each of the four carotenoids can suppress lipid oxidation and the degree of suppression of peroxidation of methyl linoleate corresponds to the difference in stability.

Astaxanthin is approximately 10 times stronger than other carotenoids and 100 times stronger than Vitamin E as an antioxidant in scavenging free radicals.

Pure & Appl. Chem., Vol. 63, No. 1, pp. 141-146, 1991.

Printed in Great Britain.

1991 IUPAC

Biological functions and activities of animal carotenoids

Wataru Miki

Astaxanthin, one of the dominant carotenoids in marine animals, showed both a strong quenching effect against singlet oxygen, and a strong scavenging effect against free radicals. These effects are considered to be defense mechanisms in the animals for attacking these active oxygen species. The activities of astaxanthin are approximately 10 times stronger than those of other carotenoids that were tested, namely zeaxanthin, lutein, tunaxanthin, canthaxanthin and β -carotene, and 100 times greater than those of a tocopherol. Astaxanthin also showed strong activity as an inhibitor of lipid peroxidation mediated by these active forms of oxygen. From these results, astaxanthin has the properties of a "SUPER VITAMIN E".

Astaxanthin protects against oxidative stress and lens protein degradation in pigs.

[J Agric Food Chem.](#) 2006 Mar 22;54(6):2418-23.

Astaxanthin protects against oxidative stress and calcium-induced porcine lens protein degradation.

[Wu TH](#), [Liao JH](#), [Hou WC](#), [Huang FY](#), [Maher TJ](#), [Hu CC](#).

Department of Clinical Pharmacy, School of Pharmacy, Taipei Medical University, Taipei 110, Taiwan. thwu@tmu.edu.tw

Astaxanthin (ASTX), a carotenoid with potent antioxidant properties, exists naturally in various plants, algae, and seafoods. In this study, we investigated the *in vitro* ability of ASTX to protect porcine lens crystallins from oxidative damage by iron-mediated hydroxyl radicals or by calcium ion-activated protease (calpain), in addition to the possible underlying biochemical mechanisms. ASTX (1 mM) was capable of protecting lens crystallins from being oxidized, as measured by changes in tryptophan fluorescence, in the presence of a Fenton reaction solution containing 0.2 mM Fe²⁺ and 2 mM H₂O₂. Sodium dodecyl sulfate-polyacrylamide gel electrophoresis analysis demonstrated that beta(high)-crystallin was the most vulnerable protein under these conditions of free radical exposure. The proteolysis of lens crystallins induced by calcium ion-activated calpain was also inhibited by ASTX (0.03-1 mM) as determined by daily measurement of the light-scattering intensity at 405 nm for five consecutive days. ASTX at 1 mM was as potent as a concentration of 0.1 mM calpain inhibitor E64 in protecting the oxidative damage/hydrolysis of porcine crystallins. At a concentration of 1 mM, ASTX provided better protection than the endogenous antioxidant glutathione in terms of suppressing calcium-induced turbidity of lens proteins. Thin-layer chromatography analysis indicated that ASTX interacted with calcium ions to form complexes, which we believe interfere with the hydrolysis of lens crystallins by calcium-activated calpain. This *in vitro* study shows that ASTX is capable of protecting porcine lens proteins from oxidative insults and degradation by calcium-induced calpain.

PMID: 16536628 [PubMed - indexed for MEDLIN]

Astaxanthin's improvement in behavioral deficits attributed to its antioxidant properties.

[BMC Neurosci.](#) 2016 Feb 8;17:11. doi: 10.1186/s12868-016-0245-z.

Astaxanthin ameliorates prenatal LPS-exposed behavioral deficits and oxidative stress in adult offspring.

[Al-Amin MM](#)^{1,2}, [Sultana R](#)³, [Sultana S](#)⁴, [Rahman MM](#)⁵, [Reza HM](#)⁶.

Author information

Abstract

BACKGROUND:

Prenatal maternal lipopolysaccharide (LPS) exposure leads to behavioral deficits such as depression, anxiety, and schizophrenia in the adult lives. LPS-exposure resulted in the production of cytokines and oxidative damage. On the contrary, astaxanthin is a carotenoid compound, showed neuroprotective properties via its antioxidant capacity. This study examines the effect of astaxanthin on the prenatal maternal LPS-induced postnatal behavioral deficit in mice.

RESULTS:

We found that prenatal LPS-exposed mice showed extensive immobile phase in the tail suspension test, higher frequent head dipping in the hole-board test and greater hypolocomotion in the open field test. All these values were statistically significant ($p < 0.05$). In addition, a marked elevation of the level of lipid peroxidation, advanced protein oxidation product, nitric oxide, while a pronounced depletion of antioxidant enzymes (superoxide dismutase, catalase and glutathione) were observed in the adult offspring mice that were prenatally exposed to LPS. To the contrary, 6-weeks long treatment with astaxanthin significantly improved all behavioral deficits ($p < 0.05$) and diminished prenatal LPS-induced oxidative stress markers in the brain and liver.

CONCLUSIONS:

Taken together, these results suggest that prenatal maternal LPS-exposure leads to behavioral deficits in the adults, while astaxanthin ameliorates the behavioral deficits presumably via its antioxidant property.

PMID: 26856812

PMCID: [PMC4746928](#)

DOI: [10.1186/s12868-016-0245-z](#) [PubMed - indexed for MEDLINE]

[Free PMC Article](#)

Astaxanthin reduces diabetic-associated cognitive decline in rats by reducing oxidative stress.

[Mol Med Rep](#). 2016 Jan;13(1):973-9. doi: 10.3892/mmr.2015.4615. Epub 2015 Nov 25.

Astaxanthin reduces type 2 diabetic-associated cognitive decline in rats via activation of PI3K/Akt and attenuation of oxidative stress.

[Li X](#)¹, [Qi Z](#)², [Zhao L](#)³, [Yu Z](#)⁴.

Author information

Abstract

Astaxanthin (AST) is an oxygenated derivative of carotenoid, which possesses a strong antioxidant activity. AST can effectively remove active oxygen from the body, and is thus considered to have an important role in disease prevention and treatment. The present study aimed to determine the effects of AST on type 2 diabetic-associated cognitive decline (DACD) in rats. Rats were intraperitoneally injected with streptozotocin (STZ), in order to establish a model of diabetes mellitus (DM). A total of 40 rats were randomly divided into five groups: The control group, the DM group, the AST (50 mg/kg) group, the AST (100 mg/kg) group, and the AST+LY294002 group (AST, 50 mg/kg and LY, 0.25 µg/100 g). Following a 14-day treatment with AST, the body weight, blood glucose levels and cognitive function were determined. In addition, the protein expression levels of phosphatidylinositol 3-kinase (PI3K)/Akt, glutathione peroxidase and superoxide dismutase activity, glutathione and malondialdehyde content, and inducible nitric oxide synthase (iNOS), caspase-3 and caspase-9 activity were detected in the rats with DM. AST clearly augmented body weight and reduced blood glucose levels in rats with DM. Furthermore, treatment with AST significantly improved the cognitive function of rats with DM. Treatment with AST activated the PI3K/Akt pathway, and suppressed oxidative stress in the DM rats. In the cerebral cortex and hippocampus of the rats with DM, the activities of iNOS, caspase-3 and caspase-9 were markedly reduced. Furthermore, treatment with the Akt inhibitor LY294002 reduced the effectiveness of AST on DACD in rats. In conclusion, AST may reduce type 2 DACD in rats via activation of PI3K/Akt and attenuation of oxidative stress.

PMID: 26648531

DOI: [10.3892/mmr.2015.4615](https://doi.org/10.3892/mmr.2015.4615) PubMed - indexed for MEDLINE]

Astaxanthin has an antioxidant effect against nitric oxide-induced oxidative stress and may ameliorate developmental competence of bovine embryos.

[Reprod Domest Anim.](#) 2009 Nov 18. [Epub ahead of print]

Antioxidative Effects of Astaxanthin against Nitric Oxide-Induced Oxidative Stress on Cell Viability and Gene Expression in Bovine Oviduct Epithelial Cell and the Developmental Competence of Bovine IVM/IVF Embryos.

[Jang HY](#), [Ji SJ](#), [Kim YH](#), [Lee HY](#), [Shin JS](#), [Cheong HT](#), [Kim JT](#), [Park IC](#), [Kong HS](#), [Park CK](#), [Yang BK](#).

College of Animal Life Science, Kangwon National University, Chuncheon, Korea.

Abstract

Contents The aim of the present study was to elucidate the fundamental mechanism of bovine oviduct epithelial cell (BOEC) co-culture on developmental capacity of bovine in vitro oocyte maturation/in vitro fertilization (IVM/IVF) embryos. We examined the effects of astaxanthin against nitric oxide-induced oxidative stress on cell viability by MTT assay, lipid peroxidation (LPO) by using thiobarbituric acid (TBA) reaction for malondialdehyde (MDA) and the expression of antioxidant genes (CuZnSOD, MnSOD and Catalase) or apoptosis genes (Bcl-2, Caspase-3 and Bax) by RT-PCR in BOEC. We also evaluated the developmental rates of bovine IVM/IVF embryos co-cultured with BOEC pre-treated with astaxanthin (500 μm) in the presence or absence of sodium nitroprusside (SNP, 1000 μm) for 24 h. Cell viability in BOEC treated with SNP (50-2000 μm) lowered, while astaxanthin addition (50-500 μm) increased it in a dose-dependent manner. Cell viability in astaxanthin plus SNP (1000 μm) gradually recovered according to the increase in astaxanthin additions (100-500 μm). The LPO in astaxanthin group (50-500 μM) gradually decreased in a dose dependent manner and among SNP or astaxanthin plus SNP group, SNP alone and astaxanthin (50 μM) plus SNP shown a significant increase than other groups ($p < 0.05$). Expression of apoptosis or antioxidant genes was detected by RT-PCR. Bcl-2 and antioxidant genes were detected in astaxanthin or astaxanthin plus SNP group, and Caspase-3 and Bax genes were only found in SNP group. When bovine IVM/IVF embryos were cultured for 6-7 days under co-culture system such as BOEC treated with astaxanthin in the presence or absence of SNP, the developmental ability to blastocysts in 500 μm astaxanthin group was the highest of all groups. These results suggest that astaxanthin has a antioxidative effect on cell viability and LPO of BOEC, and development of bovine IVM/IVF embryos due to the induction of antioxidant genes and suppression of apoptosis genes.

PMID: 19930137 [PubMed - as supplied by publisher]

Astaxanthin protects against oxidative stress in-vitro and should be strongly considered as a potential neuroprotectant and adjuvant for patients with Parkinson's disease.

[BMC Neurosci.](#) 2012 Dec 29;13:156. doi: 10.1186/1471-2202-13-156.

Astaxanthin protects against MPP(+)-induced oxidative stress in PC12 cells via the HO-1/NOX2 axis.

[Ye Q¹](#), [Huang B](#), [Zhang X](#), [Zhu Y](#), [Chen X](#).

Author information

Abstract

BACKGROUND:

Although the etiology of PD remains unclear, increasing evidence has shown that oxidative stress plays an important role in its pathogenesis and that of other neurodegenerative disorders. NOX2, a cytochrome subunit of NOX, transports electrons across the plasma membrane to generate ROS, leading to physiological and pathological processes. Heme oxygenase-1 (HO-1) can be rapidly induced by oxidative stress and other noxious stimuli in the brain or other tissues. Astaxanthin (ATX), a carotenoid with antioxidant properties, is 100-1000 times more effective than vitamin E. The present study investigated the neuroprotective effects of ATX on MPP(+)-induced oxidative stress in PC12 cells.

RESULTS:

MPP(+) significantly decreased MTT levels in a concentration-dependent manner. Hemin, SnPPIX and ATX didn't exhibit any cytotoxic effects on PC12 cells. Pretreatment with ATX (5, 10, 20 μ M), caused intracellular ROS production in the MPP(+) group to decrease by 13.06%, 22.13%, and 27.86%, respectively. MPP(+) increased NOX2, NRF2 and HO-1 protein expression compared with control ($p < 0.05$). Co-treatment with hemin or ATX suppressed NOX2 expression ($p < 0.01$), and greatly increased NRF2 and HO-1 expression ($p < 0.01$). MPP(+) treatment up-regulated both NOX2 ($p < 0.01$) and HO-1 ($p < 0.01$) mRNA levels. Co-treatment with hemin or ATX significantly increased HO-1 mRNA levels ($p < 0.01$), and decreased NOX2 mRNA levels ($p < 0.01$). MPP(+) increased NOX2 and HO-1 expression with considerable fluorescence extending out from the perinuclear region toward the periphery; this was attenuated by DPI. Co-treatment with hemin or ATX significantly up-regulated HO-1 expression and decreased NOX2 expression with considerable fluorescence intensity (stronger than the control and MPP(+) groups).

CONCLUSIONS:

ATX suppresses MPP(+)-induced oxidative stress in PC12 cells via the HO-1/NOX2 axis. ATX should be strongly considered as a potential neuroprotectant and adjuvant therapy for patients with Parkinson's disease.

PMID: 23272707 [PubMed - indexed for MEDLINE] PMID: PMC3541259

[Free PMC Article](#)

Astaxanthin prevents oxidative stress in human endothelial cells without toxicity.

[Mar Drugs](#). 2015 May 7;13(5):2857-74. doi: 10.3390/md13052857.

Astaxanthin from *Haematococcus pluvialis* Prevents Oxidative Stress on Human Endothelial Cells without Toxicity.

[Régnier P](#)¹, [Bastias J](#)², [Rodriguez-Ruiz V](#)³, [Caballero-Casero N](#)⁴, [Caballo C](#)⁵, [Sicilia D](#)⁶, [Fuentes A](#)⁷, [Maire M](#)⁸, [Crepin M](#)⁹, [Letourneur D](#)¹⁰, [Guequen V](#)¹¹, [Rubio S](#)¹², [Pavon-Djavid G](#)¹³.

Author information

Abstract

Astaxanthin, a powerful antioxidant, is a good candidate for the prevention of intracellular oxidative stress. The aim of the study was to compare the antioxidant activity of astaxanthin present in two natural extracts from *Haematococcus pluvialis*, a microalgae strain, with that of synthetic astaxanthin. Natural extracts were obtained either by solvent or supercritical extraction methods. UV, HPLC-DAD and (HPLC-(atmospheric pressure chemical ionization (APCI)+)/ion trap-MS) characterizations of both natural extracts showed similar compositions of carotenoids, but different percentages in free astaxanthin and its ester derivatives. The Trolox equivalent antioxidant capacity (TEAC) assay showed that natural extracts containing esters displayed stronger antioxidant activities than free astaxanthin.

Their antioxidant capacities to inhibit intracellular oxidative stress were then evaluated on HUVEC cells. The intracellular antioxidant activity in natural extracts was approximately 90-times higher than synthetic astaxanthin (5 μ M). No modification, neither in the morphology nor in the viability, of vascular human cells was observed by in vitro biocompatibility study up to 10 μ M astaxanthin concentrations. Therefore, these results revealed the therapeutic potential of the natural extracts in vascular human cell protection against oxidative stress without toxicity, which could be exploited in prevention and/or treatment of cardiovascular diseases.

PMID:

25962124

[PubMed - in process]

PMCID:

PMC4446609

[Free PMC Article](#)

Astaxanthin works as an antioxidant in the brains of young mice at a higher activity level than in the brains of old mice.

[Metab Brain Dis.](#) 2015 Oct;30(5):1237-46. doi: 10.1007/s11011-015-9699-4. Epub 2015 Jun 27.

The antioxidant effect of astaxanthin is higher in young mice than aged: a region specific study on brain.

[Al-Amin MM¹](#), [Akhter S](#), [Hasan AT](#), [Alam T](#), [Nageeb Hasan SM](#), [Saifullah AR](#), [Shohel M](#).

Author information

Abstract

Astaxanthin is a potential antioxidant which shows neuroprotective property. We aimed to investigate the age-dependent and region-specific antioxidant effects of astaxanthin in mice brain. Animals were divided into 4 groups; treatment young (3 months, n = 6) (AY), treatment old (16 months, n = 6) (AO), placebo young (3 months, n = 6) (PY) and placebo old (16 months, n = 6) (PO) groups. Treatment group was given astaxanthin (2 mg/kg/day, body weight), and placebo group was given 100 µl of 0.9 % normal saline orally to the healthy Swiss albino mice for 4 weeks. The level of non-enzymatic oxidative markers namely malondialdehyde (MDA); nitric oxide (NO); advanced protein oxidation product (APOP); glutathione (GSH) and the activity of enzymatic antioxidants i.e.; catalase (CAT) and superoxide dismutase (SOD) were determined from the isolated brain regions. Treatment with astaxanthin significantly ($p < 0.05$) reduces the level of MDA, APOP, NO in the cortex, striatum, hypothalamus, hippocampus and cerebellum in both age groups. Astaxanthin markedly ($p < 0.05$) enhances the activity of CAT and SOD enzymes while improves the level of GSH in the brain. Overall, improvement of oxidative markers was significantly greater in the young group than the aged animal. In conclusion, we report that the activity of astaxanthin is age-dependent, higher in young in compared to the aged brain.

PMID:

26116165

[PubMed - in process]

Astaxanthin prevents oxidative injury in human cells in-vitro.

[Cell Biol Toxicol.](#) 2010 Oct;26(5):457-67. Epub 2010 Mar 14.

Astaxanthin prevents in vitro auto-oxidative injury in human lymphocytes.

[Bolin AP](#), [Macedo RC](#), [Marin DP](#), [Barros MP](#), [Otton R](#).

Cellular Physiology Laboratory, Postgraduate Program-Health Science, CBS, Cruzeiro do Sul University, Tatuapé, São Paulo, Brazil.

Abstract

Upon mitogen sensitization, lymphocytes undergo proliferation by oxyradical-based mechanisms. Through continuous resting-restimulation cycles, lymphocytes accumulate auto-induced oxidative lesions which lead to cell dysfunction and limit their viability. Astaxanthin (ASTA) is a nutritional carotenoid that shows notable antioxidant properties. This study aims to evaluate whether the in vitro ASTA treatment can limit oxyradical production and auto-oxidative injury in human lymphocytes. Activated lymphocytes treated with 5 microM ASTA showed immediate lower rates of $O(2)(^{*-})/H(2)O(2)$ production whilst NO^* and intracellular $Ca(2+)$ levels were concomitantly enhanced (≤ 4 h). In long-term treatments (>24 h), the cytotoxicity test for ASTA showed a sigmoidal dose-response curve ($LC50 = 11.67 \pm 0.42$ microM), whereas higher activities of superoxide dismutase and catalase in 5 microM ASTA-treated lymphocytes were associated to significant lower indexes of oxidative injury. On the other hand, lower proliferative scores of ASTA lymphocytes might be a result of diminished intracellular levels of pivotal redox signaling molecules, such as $H(2)O(2)$. Further studies are necessary to establish the ASTA-dose compensation point between minimizing oxidative damages and allowing efficient redox-mediated immune functions, such as proliferation, adhesion, and oxidative burst.

PMID: 20229275 [PubMed - in process]

Astaxanthin prevents oxidative damage in lipids and proteins in human neutrophils.

[Eur J Nutr.](#) 2010 Apr 2. [Epub ahead of print]

Astaxanthin addition improves human neutrophils function: in vitro study.

[Macedo RC](#), [Bolin AP](#), [Marin DP](#), [Otton R](#).

Postgraduate Program, Health Science, CBS, Cruzeiro do Sul University, Avenida Regente Feijó, 1295. Tatuapé, São Paulo, SP, CEP 03342-000, Brazil.

Abstract

PURPOSE: The aim of the present study was to evaluate the in vitro effect of carotenoid astaxanthin (ASTA) on the phagocytic and microbicidal capacities, cytokine release, and reactive oxygen species production in human neutrophils.

METHODS: The following parameters were evaluated: cytotoxic effect of ASTA on human neutrophils viability, phagocytic and microbicidal capacities of neutrophils by using *Candida albicans* assay, intracellular calcium mobilization (Fura 2-AM fluorescent probe), superoxide anion (lucigenin and DHE probes), hydrogen peroxide (H₂O₂), phenol red), and nitric oxide (NO.) (Griess reagent) production, activities of antioxidant enzymes (total/Mn-SOD, CAT, GPx, and GR), oxidative damages in biomolecules (TBARS assay and carbonyl groups), and cytokine (IL-6 and TNF-alpha) release.

RESULTS: Astaxanthin significantly improves neutrophil phagocytic and microbicidal capacity, and increases the intracellular calcium concentration and NO. production. Both functional parameters were accompanied by a decrease in superoxide anion and hydrogen peroxide and IL-6 and TNF-alpha production. Oxidative damages in lipids and proteins were significantly decreased after ASTA-treatment.

CONCLUSIONS: Taken together our results are supportive to a beneficial effect of astaxanthin-treatment on human neutrophils function as demonstrated by increased phagocytic and fungicide capacity as well as by the reduced superoxide anion and hydrogen peroxide production, however, without affecting neutrophils capacity to kill *C. albicans*. This process appears to be mediated by calcium released from intracellular storages as well as nitric oxide production.

PMID: 20361333 [PubMed - as supplied by publisher]

Astaxanthin prevents lipid and protein oxidation and increases the activity of antioxidant enzymes.

[Phytother Res.](#) 2010 Jan;24(1):54-9.

Cytoprotective role of astaxanthin against glycated protein/iron chelate-induced toxicity in human umbilical vein endothelial cells.

[Nishigaki I](#), [Rajendran P](#), [Venugopal R](#), [Ekambaram G](#), [Sakthisekaran D](#), [Nishigaki Y](#).

NPO International Laboratory of Biochemistry, 1-166 Uchide, Nakagawa-ku Nagoya 454-0926, Japan. nishigaki@se.starcat.ne.jp

Abstract

Astaxanthin (ASX), a red carotenoid pigment with no pro-vitamin A activity, is a biological antioxidant that occurs naturally in a wide variety of plants, algae and seafoods. This study investigated whether ASX could inhibit glycated protein/iron chelate-induced toxicity in human umbilical-vein endothelial cells (HUVEC) by interfering with ROS generation in these cells. Glycated fetal bovine serum (GFBS) was prepared by incubating fetal bovine serum (FBS) with high-concentration glucose. Stimulation of cultured HUVECs with 50 mm 1 mL of GFBS significantly enhanced lipid peroxidation and decreased antioxidant enzyme activities and levels of phase II enzymes. However, preincubation of the cultures with ASX resulted in a marked decrease in the level of lipid peroxide (LPO) and an increase in the levels of antioxidant enzymes in an ASX concentration-dependent manner. These results demonstrate that ASX could inhibit LPO formation and enhance the antioxidant enzyme status in GFBS/iron chelate-exposed endothelial cells by suppressing ROS generation, thereby limiting the effects of the AGE-RAGE interaction. The results indicate that ASX could have a beneficial role against glycated protein/iron chelate-induced toxicity by preventing lipid and protein oxidation and increasing the activity of antioxidant enzymes.

PMID: 19548280 [PubMed - indexed for MEDLINE]

Astaxanthin and omega-3 fatty acids individually and in combination protect against oxidative stress.

[Food Chem Toxicol.](#) 2013 Dec;62:869-75. doi: 10.1016/j.fct.2013.10.023. Epub 2013 Oct 21.

Astaxanthin and omega-3 fatty acids individually and in combination protect against oxidative stress via the Nrf2-ARE pathway.

[Saw CL¹](#), [Yang AY](#), [Guo Y](#), [Kong AN](#).

Author information

Abstract

Oxidative stress is a major driver of many diseases, including cancer. The induction of Nrf2-ARE-mediated antioxidant enzymes provides a cellular defense against oxidative stress. Astaxanthin (AST), a red dietary carotenoid, possesses potent antioxidant activity, and inhibits oxidative damages. Polyunsaturated fatty acids (PUFAs), docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), are important nutritional essentials and potent antioxidants found in fish oil. In the present study, we investigated whether AST in combination with low concentrations of DHA or EPA has a synergistic antioxidant effect in a HepG2-C8-ARE-luciferase cell line system. Using free radical scavenging DPPH assay, AST was more potent DPPH radical scavenger than DHA and EPA. MTS assay revealed that AST was non-toxic up to 100 μ M compared with more toxic DHA and EPA. The three compounds alone and in combination elevated cellular GSH levels, increased the total antioxidant activity, induced mRNA expression of Nrf2 and Nrf2 downstream target genes NQO1, HO-1, and GSTM2. Lower concentrations of AST show synergistic effects when combined with DHA or EPA. In summary, our study shows synergistic antioxidant effects of AST and PUFAs at low concentrations. The Nrf2/ARE pathway plays an important role in the antioxidative effects induced by AST, DHA, and EPA.

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Astaxanthin is stronger as an antioxidant than lutein and beta-carotene and rats deficient in retinol can convert Astaxanthin into retinol.

[Can J Physiol Pharmacol](#). 2010 Oct;88(10):977-85.

Retinol-deficient rats can convert a pharmacological dose of astaxanthin to retinol: antioxidant potential of astaxanthin, lutein, and β -carotene.

[Sangeetha RK](#), [Baskaran V](#).

Source

Department of Biochemistry and Nutrition, Central Food Technological Research Institute, CSIR, Mysore, Karnataka, India.

Abstract

Retinol (ROH) and provitamin-A carotenoids are recommended to treat ROH deficiency. Xanthophyll carotenoids, being potent antioxidants, can modulate health disorders. We hypothesize that nonprovitamin-A carotenoids may yield ROH and suppress lipid peroxidation under ROH deficiency. This study aimed to (i) study the possible bioconversion of astaxanthin and lutein to ROH similar to β -carotene and (ii) determine the antioxidant potential of these carotenoids with reference to Na(+)/K(+)-ATPase, antioxidant molecules, and lipid peroxidation (Lpx) induced by ROH deficiency in rats. ROH deficiency was induced in rats (n = 5 per group) by feeding a diet devoid of ROH. Retinol-deficient (RD) rats were gavaged with astaxanthin, lutein, β -carotene, or peanut oil alone (RD group) for 7 days. Results show that the RD group had lowered plasma ROH levels (0.3 μ mol/L), whereas ROH rose in astaxanthin and β -carotene groups (4.9 and 5.7 μ mol/L, respectively), which was supported by enhanced (69% and 70%) intestinal β -carotene 15,15'-monooxygenase activity. Astaxanthin, lutein, and β -carotene lowered Lpx by 45%, 41%, and 40% (plasma), respectively, and 59%, 64%, and 60% (liver), respectively, compared with the RD group. Lowered Na(+)/K(+)-ATPase and enhanced superoxide dismutase, catalase, and glutathione-S-transferase activities support the lowered Lpx. To conclude, this report confirms that astaxanthin is converted into β -carotene and ROH in ROH-deficient rats, and the antioxidant potential of carotenoids was in the order astaxanthin > lutein > β -carotene.

PMID: 20962897 [PubMed - indexed for MEDLINE]

Astaxanthin's antioxidative properties lead to prevention of cytotoxicity from cobalt.

[BMC Pharmacol Toxicol](#). 2017 Jul 24;18(1):58. doi: 10.1186/s40360-017-0166-1.

Astaxanthin mitigates cobalt cytotoxicity in the MG-63 cells by modulating the oxidative stress.

[Li D](#)¹, [Tong W](#)², [Liu D](#)², [Zou Y](#)², [Zhang C](#)², [Xu W](#)³.

Author information

Abstract

BACKGROUND: With the re-popularity of metal-on-metal (MoM) bearing in recent years, the cobalt toxicity has been a cause for concern in the total hip replacement surgery by both physicians and patients.

METHODS: MG-63 cell line was cultured in vitro and incubated with cobalt (II) chloride (CoCl₂) and/or with astaxanthin (ASX) for 24 h. MTT assay was conducted to evaluate the cell viability after cobalt exposure and ASX treatment. Fluorescence-activated cell sorting (FACS) analysis was performed to examine the reactive oxygen species (ROS) level. Quantitative real-time polymerase chain reaction (PCR) was adopted to determine the mRNA levels of related targets. And western blot analysis was used to examine the protein expressions. One-way ANOVA with posttest Newman-Keuls multiple comparisons was adopted to analysis all the obtained data.

RESULTS: In the current study, ASX exhibited significant protective effect against the Co(II)-induced cytotoxicity in MG-63 cell line. We also found that ASX protected the cells against Co-induced apoptosis by regulating the expression of Bcl-2 family proteins. Besides, heme oxygenase 1 (HO-1) could be activated by Co exposure; ASX treatment significantly inhibited HO-1 activation, suppressing the oxidative stress induced by Co exposure. Moreover, c-Jun N-terminal Kinase (JNK) phosphorylation was shown to participate in the signaling pathway of the protective effect of ASX. However, knockdown of JNK expression by siRNA transfection or JNK inhibitor SP600125 treatment did not affect the protective effect of ASX against cobalt cytotoxicity in MG-63 cells.

CONCLUSIONS: ASX mitigated cobalt cytotoxicity in the MG-63 cells by modulating the oxidative stress. And ASX could be a promising therapy against cobalt toxicity in the hip articulation surgery.

KEYWORDS: Astaxanthin; Cobalt cytotoxicity; MG-63 cells; Oxidative stress

PMID: 28738843

PMCID: [PMC5525213](#)

DOI: [10.1186/s40360-017-0166-1](#)

[Indexed for MEDLINE]

[Free PMC Article](#)

Astaxanthin prevents oxidative stress in cells more effectively than N-acetyl cysteine.

[Mar Drugs](#). 2017 Jun 20;15(6). pii: E185. doi: 10.3390/md15060185.

The Novel Mechanisms Concerning the Inhibitions of Palmitate-Induced Proinflammatory Factor Releases and Endogenous Cellular Stress with Astaxanthin on MIN6 β -Cells.

[Kitahara A](#)¹, [Takahashi K](#)², [Morita N](#)³, [Murashima T](#)⁴, [Onuma H](#)⁵, [Sumitani Y](#)⁶, [Tanaka T](#)⁷, [Kondo T](#)⁸, [Hosaka T](#)⁹, [Ishida H](#)¹⁰.

Author information

Abstract

Astaxanthin, an antioxidant agent, can protect pancreatic β -cells of db/db mice from glucotoxicity and resolve chronic inflammation in adipose tissue. Nonetheless, the effects of astaxanthin on free-fatty-acid-induced inflammation and cellular stress in β -cells remain to be demonstrated. Meanwhile, palmitate enhances the secretion of pro-inflammatory adipokines monocyte chemoattractant protein-1 (MCP-1) and VEGF₁₂₀ (vascular endothelial growth factor). We therefore investigated the influence of astaxanthin on palmitate-stimulated MCP-1 and VEGF₁₂₀ secretion in mouse insulinoma (MIN6) pancreatic β -cells. Furthermore, whether astaxanthin prevents cellular stress in MIN6 cells was also assessed. Pre-treatment with astaxanthin or with *N*-acetyl-cysteine (NAC) which is an antioxidant drug, significantly attenuated the palmitate-induced MCP-1 release through downregulation of phosphorylated c-Jun NH₂-terminal protein kinase (JNK) pathways, and suppressed VEGF₁₂₀ through the PI3K/Akt pathways relative to the cells stimulated with palmitate alone. In addition, palmitate significantly upregulated homologous protein (CHOP) and anti-glucose-regulated protein (GRP78), which are endoplasmic reticulum (ER) stress markers, in MIN6 cells. On the other hand, astaxanthin attenuated the increased CHOP content, but further up-regulated palmitate-stimulated GRP78 protein expression. By contrast, NAC had no effects on either CHOP or GRP78 enhancement induced by palmitate in MIN6 cells. In conclusion, astaxanthin diminishes the palmitate-stimulated increase in MCP-1 secretion via the downregulation of JNK pathways in MIN6 cells, and affects VEGF₁₂₀ secretion through PI3K/Akt pathways. Moreover, astaxanthin can prevent not only oxidative stress caused endogenously by palmitate but also ER stress, which NAC fails to attenuate, via upregulation of GRP78, an ER chaperon.

KEYWORDS:

astaxanthin; palmitate; pancreatic β -cell

PMID: 28632169 PMID: [PMC5484135](#) DOI: [10.3390/md15060185](#) [Indexed for MEDLINE] [Free PMC Article](#)

Astaxanthin prevents oxidative stress in heart and kidneys of aged rats after inducement of heart attack.

[J Diet Suppl.](#) 2018 Jan 2;15(1):42-54. doi: 10.1080/19390211.2017.1321078. Epub 2017 May 10.

Astaxanthin Prevented Oxidative Stress in Heart and Kidneys of Isoproterenol-Administered Aged Rats.

[Alam MN¹](#), [Hossain MM¹](#), [Rahman MM¹](#), [Subhan N¹](#), [Mamun MAA¹](#), [Ulla A¹](#), [Reza HM¹](#), [Alam MA¹](#).

Author information

Abstract

The objective of this study was to investigate the effect of astaxanthin on isoproterenol (ISO)-induced myocardial infarction and cardiac hypertrophy in rats. To evaluate the effect of astaxanthin on ISO-induced cardiac dysfunction, 18 aged Long Evans male rats were evenly divided into three groups. Group I (Control group) was given only the laboratory-ground food and normal water. Group II (ISO group) was administered ISO at a dose of 50 mg/kg subcutaneously (SC) twice a week for two weeks. Group III (Astaxanthin + ISO group) was treated with astaxanthin (25 mg/kg) orally every day and ISO 50 mg/kg SC twice a week for two weeks. ISO administration in rats increased the heart and left ventricular wet weights and increased inflammatory cell infiltration and fibrosis. Moreover, ISO administration increased the lipid peroxidation and decreased antioxidant enzyme activities in heart tissues. Astaxanthin treatment prevented the increased wet weight of heart and decreased inflammatory cell infiltration and fibrosis. The protective effect of astaxanthin was associated with reduction of free radicals by improving antioxidant enzyme function, as well as normalization and/or suppression of elevated oxidative stress markers, such as malondialdehyde (MDA), nitric oxide (NO), and advanced protein oxidation product (APOP) in ISO-administered rats. Furthermore, astaxanthin decreased the elevated activities of aspartate transaminase (AST), alanine transaminase (ALT), and creatinin kinase muscle/brain (CK-MB) in ISO-administered rats. In conclusion, astaxanthin may protect cardiac tissues in ISO-administered rats through suppression of oxidative stress and enhancement of antioxidant enzyme functions.

KEYWORDS:

antioxidant enzymes; astaxanthin; free radicals; heart, fibrosis; oxidative stress

PMID: 28489954 DOI: [10.1080/19390211.2017.1321078](https://doi.org/10.1080/19390211.2017.1321078)

[Indexed for MEDLINE]

Astaxanthin provides neuroprotection by suppressing reactive oxygen species in rats after stroke is induced.

[Brain Res Bull.](#) 2017 Apr;130:211-220. doi: 10.1016/j.brainresbull.2017.01.024. Epub 2017 Feb 1.

Preventive treatment of astaxanthin provides neuroprotection through suppression of reactive oxygen species and activation of antioxidant defense pathway after stroke in rats.

[Pan L](#)¹, [Zhou Y](#)², [Li XF](#)³, [Wan QJ](#)⁴, [Yu LH](#)⁵.

Author information

Abstract

Astaxanthin, a natural antioxidant carotenoid, has been shown to reduce cerebral ischemic injury in rodents. However, there have not been any studies specifically addressing whether preventive administration of astaxanthin can protect against cerebral ischemia. The purpose of this study was to examine whether pretreatment of astaxanthin can protect against ischemic injuries in the adult rats. The rats were pre-administered intragastrically with astaxanthin for seven days (once a day), and middle cerebral artery occlusion was performed at 1h after the final administration. It was found that astaxanthin prevented neurological deficits and reduced cerebral infarction volume. To evaluate the mechanisms underlying this protection, brain tissues were assayed for free radical damage, antioxidant gene expression, cell apoptosis and regeneration. The results showed that the mechanisms involved suppression of reactive oxygen species, activation of antioxidant defense pathway, and inhibition of apoptosis as well as promotion of neural regeneration. Astaxanthin did not alter body weights and the protective effect was found to be dose-dependent. Collectively, our data suggest that pretreatment of astaxanthin can protect against ischemia-related damages in brain tissue through multiple mechanisms, hinting that astaxanthin may have significant protective effects for patients vulnerable or prone to ischemic events.

KEYWORDS:

Astaxanthin; Cerebral ischemia; Mechanisms; Protective effects; Rats

PMID: 28161193

DOI: [10.1016/j.brainresbull.2017.01.024](https://doi.org/10.1016/j.brainresbull.2017.01.024)

[Indexed for MEDLINE]

Astaxanthin protects stem cells from irradiation by inhibiting oxidative stress and cell death.

[Stem Cell Res Ther.](#) 2017 Jan 23;8(1):7. doi: 10.1186/s13287-016-0464-3.

Astaxanthin attenuates total body irradiation-induced hematopoietic system injury in mice via inhibition of oxidative stress and apoptosis.

[Xue XL](#)¹, [Han XD](#)¹, [Li Y](#)¹, [Chu XF](#)¹, [Miao WM](#)², [Zhang JL](#)³, [Fan SJ](#)⁴.

Author information

Abstract

BACKGROUND: The hematopoietic system is especially sensitive to total body irradiation (TBI), and myelosuppression is one of the major effects of TBI. Astaxanthin (ATX) is a powerful natural anti-oxidant with low toxicity. In this study, the effect of ATX on hematopoietic system injury after TBI was investigated.

METHODS: Flow cytometry was used to detect the proportion of hematopoietic progenitor cells (HPCs) and hematopoietic stem cells (HSCs), the level of intracellular reactive oxygen species (ROS), expression of cytochrome C, cell apoptosis, and NRF2-related proteins. Immunofluorescence staining was used to detect Nrf2 translocation. Western blot analysis was used to evaluate the expression of apoptotic-related proteins. Enzymatic activities assay kits were used to analyze SOD2, CAT, and GPX1 activities.

RESULTS: Compared with the TBI group, ATX can improve radiation-induced skewed differentiation of peripheral blood cells and accelerate hematopoietic self-renewal and regeneration. The radio-protective effect of ATX is probably attributable to the scavenging of ROS and the reduction of cell apoptosis. These changes were associated with increased activation of Nrf2 and downstream anti-oxidative proteins, and regulation of apoptotic-related proteins.

CONCLUSIONS: This study suggests that ATX could be used as a potent therapeutic agent to protect the hematopoietic system against TBI-induced bone marrow suppression.

KEYWORDS: Astaxanthin; Cell apoptosis; Hematopoietic stem cells; Ionizing radiation; Reactive oxygen species

PMID: 28115023

PMCID: [PMC5260077](#)

DOI: [10.1186/s13287-016-0464-3](#)

[Indexed for MEDLINE]

[Free PMC Article](#)

Astaxanthin improves muscle fibrosis caused by immobilization by reducing oxidative stress.

[J Physiol Sci](#). 2017 Sep;67(5):603-611. doi: 10.1007/s12576-016-0492-x. Epub 2016 Oct 6.

Astaxanthin supplementation attenuates immobilization-induced skeletal muscle fibrosis via suppression of oxidative stress.

[Maezawa T](#)¹, [Tanaka M](#)^{1,2}, [Kanazashi M](#)³, [Maeshige N](#)¹, [Kondo H](#)⁴, [Ishihara A](#)⁵, [Fujino H](#)⁶.

Author information

Abstract

Immobilization induces skeletal muscle fibrosis characterized by increasing collagen synthesis in the perimysium and endomysium. Transforming growth factor- β 1 (TGF- β 1) is associated with this lesion via promoting differentiation of fibroblasts into myofibroblasts. In addition, reactive oxygen species (ROS) are shown to mediate TGF- β 1-induced fibrosis in tissues. These reports suggest the importance of ROS reduction for attenuating skeletal muscle fibrosis. Astaxanthin, a powerful antioxidant, has been shown to reduce ROS production in disused muscle. Therefore, we investigated the effects of astaxanthin supplementation on muscle fibrosis under immobilization. In the present study, immobilization increased the collagen fiber area, the expression levels of TGF- β 1, α -smooth muscle actin, and superoxide dismutase-1 protein and ROS production. However, these changes induced by immobilization were attenuated by astaxanthin supplementation. These results indicate the effectiveness of astaxanthin supplementation on skeletal muscle fibrosis induced by ankle joint immobilization.

KEYWORDS:

Astaxanthin; Immobilization; Reactive oxygen species; Skeletal muscle fibrosis; Transforming growth factor- β 1

PMID: 27714500

DOI: [10.1007/s12576-016-0492-x](https://doi.org/10.1007/s12576-016-0492-x)

[Indexed for MEDLINE]

ASTAXANTHIN DISPLAYS ANTIOXIDANT EFFECT SUPERIOR TO VITAMIN C IN CELL STUDY.

J Agric Food Chem. 2019 Dec 11;67(49):13568-13576.

doi: 10.1021/acs.jafc.9b04587. Epub 2019 Nov 27.

Studies on Protection of Astaxanthin from Oxidative Damage Induced by H₂O₂ in RAW 264.7 Cells Based on ¹H NMR Metabolomics

[Suhuan Mei](#)¹, [Xiao Song](#)¹, [Yali Wang](#)¹, [Jun Wang](#)², [Shufang Su](#)², [Jianhua Zhu](#)², [Yue Geng](#)¹

- PMID: 31709793
- DOI: [10.1021/acs.jafc.9b04587](https://doi.org/10.1021/acs.jafc.9b04587)

Abstract

Astaxanthin (AST) is a fat-soluble and non-vitamin A source of carotenoid that can quench reactive oxygen species and it has strong antioxidant and anti-inflammatory abilities. Herein, we have used H₂O₂ to establish a model of oxidative damage to RAW 264.7 cells and cells treated with vitamin C as the positive control group. The changes in metabolome were examined using ¹H NMR and the results demonstrated that H₂O₂ treatment and various metabolic pathways such as amino acid, glucose, and glycerolipid metabolism were downregulated, which in turn affected citric acid cycle and energy status. AST could reverse downregulation of some of these metabolic pathways to a certain extent, and reduce cellular oxidative stress and death. The AST group differed from the vitamin C group in regulating d-glutamine, d-glutamic acid, pyruvate, and glycerolipid metabolism. The experimental results help to further understand the antioxidant effects of AST.

ASTAXANTHIN IS FAR MORE EFFECTIVE THAN GLUTATHIONE IN REDUCING OXIDATIVE STRESS IN-VITRO.

Bioprocess Biosyst Eng. 2020 Oct;43(10):1813-1821.
doi: 10.1007/s00449-020-02372-y. Epub 2020 May 12.

Enhancement of ϵ -poly-L-lysine production in *Streptomyces griseofuscus* by addition of exogenous astaxanthin

[Shu Li](#)¹, [Jinyi Ji](#)², [Shengjie Hu](#)², [Guanjun Chen](#)²

- PMID: 32399749
- DOI: [10.1007/s00449-020-02372-y](https://doi.org/10.1007/s00449-020-02372-y)

Abstract

Addition of exogenous astaxanthin for improving ϵ -poly-L-lysine (ϵ -PL) production in *Streptomyces griseofuscus* was investigated in this study. By this unique strategy, the ϵ -PL production in shaker-flask fermentation was 2.48 g/L, which was 67.5% higher than the control at the addition dosage of 1.0 g/L, owing to the oxidation resistance of astaxanthin. In fed-batch fermentation, the ϵ -PL production reached 36.1 g/L, a 36.3% increase compared to the control. Intracellular response for oxidation in *S. griseofuscus* such as ROS generation and lipid peroxidation was reduced by astaxanthin addition. Illumina RNA deep sequencing (RNA-seq) technology further revealed that *S. griseofuscus* with astaxanthin addition showed down-regulated transcriptions of genes involved in oxidative stress. This research proved that the beneficial effect of astaxanthin addition was far better than glutathione (GSH) owing to the stronger antioxidant capacity, and provided a novel approach to regulate ϵ -PL synthesis.

ASTAXANTHIN PREVENTS OXIDATION FROM HYDROGEN PEROXIDE IN-VITRO.

Syst Biol Reprod Med. 2021 Feb;67(1):79-88.

doi: 10.1080/19396368.2020.1824031. Epub 2020 Oct 25.

Astaxanthin inhibiting oxidative stress damage of placental trophoblast cells in vitro

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- PMID: 33103484
- DOI: [10.1080/19396368.2020.1824031](https://doi.org/10.1080/19396368.2020.1824031)

Abstract

Oxidative stress from the trophoblasts is one of the possible pathological mechanisms of Preeclampsia (PE). This study aimed at exploring the potential effects of astaxanthin (ATX) on oxidative stress damaged placental trophoblast cell line HTR-8/SVneo. Oxidative stress-induced damaged through H₂O₂ treatment was checked by MTS CellTiter 96® cell viability, 2',7'-dichlorofluorescein diacetate (DCFH-DA) induced fluorescence, the level of the intracellular malondialdehyde (MDA), and the detection of glutathione peroxidase (GSH-Px), superoxide dismutase (SOD) and catalase (CAT). Different concentrations of ATX were applied, and then the proliferation rate, apoptotic percentage, cell cycle distribution, invasion test and relative biological function of the rescued cells were followed. We provide evidence that ATX had an anti-oxidative effect against oxidative stress induced by H₂O₂ on the trophoblast cell line and had beneficial role in promoting cell proliferation, inhibiting cell apoptosis, and inducing cell invasion.

Abbreviations: UV: ultraviolet; DCFH-DA: 2',7'-dichlorofluorescein diacetate; EVT: extravillous trophoblast; MMPs: matrix metalloproteinases; IUGR: intrauterine growth restriction.

Astaxanthin protects against high blood pressure during pregnancy by reducing inflammation and oxidative stress in rats.

[Mol Med Rep](#). 2016 Sep;14(3):2697-704. doi: 10.3892/mmr.2016.5569. Epub 2016 Jul 28.

Astaxanthin blocks preeclampsia progression by suppressing oxidative stress and inflammation.

[Xuan RR¹](#), [Niu TT²](#), [Chen HM²](#).

Author information

Abstract

To investigate the antioxidative effect of astaxanthin on Nω-nitro-L-arginine methyl ester (L-NAME)-induced preeclamptic rats. Cell survival, the level of reactive oxygen species (ROS) and the changes in mitochondrial membrane potential (MMP) were examined in astaxanthin and H₂O₂-treated human umbilical vein endothelial cells (HUVECs). The preeclamptic Sprague-Dawley (SD) rat model was established by injection of L-NAME and treatment with astaxanthin. The activities of malondialdehyde (MDA), superoxide dismutase (SOD) and nitric oxide synthase (NOS) in serum were analyzed. Pathological changes were examined by hematoxylin and eosin (H&E) staining. The expression of nuclear factor (NF)-κB, Rho-associated protein kinase II (ROCK II), heme oxygenase-1 (HO-1) and caspase 3 in preeclamptic placentas were examined by immunohistochemistry. Astaxanthin significantly reduced H₂O₂-induced HUVEC cell death, decreased ROS and increased MMP. Astaxanthin significantly reduced blood pressure and the content of MDA, but significantly increased the activity of SOD in preeclamptic rats. The urinary protein and the level of NO and NOS were also decreased. H&E staining revealed that the thickness of the basilar membrane was increased, while the content of trophoblast cells and spiral arteries were reduced following astaxanthin treatment. Immunohistochemistry results showed that the expression of NF-κB, ROCK II and caspase 3 in preeclamptic placentas was significantly decreased after astaxanthin treatment, while HO-1 expression was increased. In conclusion, astaxanthin inhibited H₂O₂-induced oxidative stress in HUVECs. Astaxanthin treatment significantly improved L-NAME-induced preeclamptic symptoms and reduced the oxidative stress and inflammatory damages in preeclamptic placentas. Astaxanthin treatment may effectively prevent and treat preeclampsia.

PMID: 27484589

DOI: [10.3892/mmr.2016.5569](https://doi.org/10.3892/mmr.2016.5569)

[Indexed for MEDLINE]

Astaxanthin has neuroprotective effects and reduces inflammation and oxidative stress in diabetic rats.

[PLoS One](#). 2016 Jan 14;11(1):e0146438. doi: 10.1371/journal.pone.0146438. eCollection 2016.

Astaxanthin Inhibits Expression of Retinal Oxidative Stress and Inflammatory Mediators in Streptozotocin-Induced Diabetic Rats.

[Yeh PT](#)^{1,2}, [Huang HW](#)³, [Yang CM](#)^{1,4}, [Yang WS](#)^{5,6}, [Yang CH](#)^{1,4}.

Abstract

PURPOSE: We evaluated whether orally administered astaxanthin (AST) protects against oxidative damage in the ocular tissues of streptozotocin (STZ)-induced diabetic rats.

METHODS AND RESULTS: Fifty 6-week-old female Wistar rats were randomly assigned to receive an injection of STZ to induce diabetes (n = 40) or to remain uninduced (n = 10). The diabetic rats were randomly selected into four groups and they were separately administered normal saline, 0.6 mg/kg AST, 3 mg/kg AST, or 0.5 mg/kg lutein daily for eight weeks. Retinal functions of each group were evaluated by electroretinography. The expression of oxidative stress and inflammatory mediators in the ocular tissues was then assessed by immunohistochemistry, western blot analysis, ELISA, RT-PCR, and electrophoretic mobility shift assay (EMSA). Retinal functions were preserved by AST and lutein in different levels. Ocular tissues from AST- and lutein-treated rats had significantly reduced levels of oxidative stress mediators (8-hydroxy-2'-deoxyguanosine, nitrotyrosine, and acrolein) and inflammatory mediators (intercellular adhesion molecule-1, monocyte chemoattractant protein-1, and fractalkine), increased levels of antioxidant enzymes (heme oxygenase-1 and peroxiredoxin), and reduced activity of the transcription factor nuclear factor-kappaB (NF-κB).

CONCLUSION: The xanthophyll carotenoids AST and lutein have neuroprotective effects and reduce ocular oxidative stress, and inflammation in the STZ diabetic rat model, which may be mediated by downregulation of NF-κB activity.

PMID: 26765843

PMCID: [PMC4713224](#)

DOI: [10.1371/journal.pone.0146438](#)

[Indexed for MEDLINE]

[Free PMC Article](#)

Astaxanthin is more effective as an antioxidant with higher electron transfer activity than other carotenoids.

Fast regeneration of carotenoids from radical cations by isoflavonoid dianions: importance of the carotenoid keto group for electron transfer.

[Han RM](#), [Chen CH](#), [Tian YX](#), [Zhang JP](#), [Skibsted LH](#).

J. Phys. Chem. A, **2010**, *114* (1), pp 126–132

DOI: 10.1021/jp907349x

Publication Date (Web): December 3, 2009

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Abstract

Electron transfer to radical cations of beta-carotene, zeaxanthin, canthaxanthin, and astaxanthin from each of the three acid/base forms of the diphenolic isoflavonoid daidzein and its C-glycoside puerarin, as studied by laser flash photolysis in homogeneous methanol/chloroform (1/9) solution, was found to depend on carotenoid structures and more significantly on the deprotonation degree of the isoflavonoids. None of the carotenoid radical cations reacted with the neutral forms of the isoflavonoids while the monoanionic and dianionic forms of the isoflavonoids regenerated the oxidized carotenoid. Electron transfer to the beta-carotene radical cation from the puerarin dianion followed second order kinetics with the rate constant at 25 degrees C $k(2) = 5.5 \times 10(9) \text{ M}(-1) \text{ s}(-1)$, zeaxanthin $8.5 \times 10(9) \text{ M}(-1) \text{ s}(-1)$, canthaxanthin $6.5 \times 10(10) \text{ M}(-1) \text{ s}(-1)$, and astaxanthin $11.1 \times 10(10) \text{ M}(-1) \text{ s}(-1)$ approaching the diffusion limit and establishing a linear free energy relationship between rate constants and driving force. Comparable results found for the daidzein dianion indicate that the steric hindrance from the glucoside is not important suggesting the more reducing but less acidic 4'-OH/4'-O(-) as electron donors. On the basis of the rate constants obtained from kinetic analyses, the keto group of carotenoids is concluded to facilitate electron transfer. The driving force was estimated from oxidation potentials, as determined by cyclic-voltametry for puerarin and daidzein in aqueous solutions at varying pH conditions, which led to the standard reduction potentials $E^{\circ} = 1.13$ and 1.10 V versus NHE corresponding to the uncharged puerarin and daidzein. For $\text{pH} > \text{pK}(a2)$, the apparent potentials of both puerarin and daidzein became constants and were $E^{\circ} = 0.69$ and 0.65 V , respectively. Electron transfer from isoflavonoids to the carotenoid radical cation, as formed during oxidative stress, is faster for astaxanthin than for the other carotenoids, which may relate to astaxanthins more effective antioxidative properties and in agreement with the highest electron accepting index of astaxanthin.

PMID: 19957978 [PubMed - indexed for MEDLINE]

Astaxanthin in combination with fish oil shows promise as a strategy to prevent oxidative stress induced by polyunsaturated fatty acids and Astaxanthin may also potentiate the immune-enhancing effect of fish oil.

[Eur J Nutr.](#) 2011 Oct 5. [Epub ahead of print]

Combined fish oil and astaxanthin supplementation modulates rat lymphocyte function.

[Otton R](#), [Marin DP](#), [Bolin AP](#), [de Cássia Santos Macedo R](#), [Campoio TR](#), [Fineto C Jr](#), [Guerra BA](#), [Leite JR](#), [Barros MP](#), [Mattei R](#).

Source

Postgraduate Program, Health Sciences, CBS, Cruzeiro do Sul University, Av. Regente Feijó, 1295, Sao Paulo, SP, 03342000, Brazil, rosemary.otton@cruzeirosul.edu.br.

Abstract

PURPOSE: Higher intakes of n-3 polyunsaturated fatty acids that are abundant in marine fishes have been long described as a "good nutritional intervention" with increasing clinical benefits to cardiovascular health, inflammation, mental, and neurodegenerative diseases. The present study was designed to investigate the effect of daily fish oil (FO-10 mg EPA/kg body weight (BW) and 7 mg DHA/kg BW) intake by oral gavage associated with the antioxidant astaxanthin (ASTA-1 mg/kg BW) on the redox metabolism and the functional properties of lymphocytes from rat lymph nodes.

METHODS: This study was conducted by measurements of lymphocyte proliferation capacity, ROS production [superoxide (O₂^{•-}) and hydrogen peroxide (H₂O₂)], nitric oxide (NO[•]) generation, intracellular calcium release, oxidative damage to lipids and proteins, activities of major antioxidant enzymes, GSH/GSSG content, and cytokines release.

RESULTS: After 45 days of FO + ASTA supplementation, the proliferation capacity of activated T- and B-lymphocytes was significantly diminished followed by lower levels of O₂^{•-}, H₂O₂ and NO[•] production, and increased activities of total/SOD, GR and GPx, and calcium release in cytosol. ASTA was able to prevent oxidative modification in cell structures through the suppression of the oxidative stress condition imposed by FO. L-selectin was increased by FO, and IL-1 β was decreased only by ASTA supplementation.

CONCLUSION: We can propose that association of ASTA with FO could be a good strategy to prevent oxidative stress induced by polyunsaturated fatty acids and also to potentiate immunomodulatory effects of FO.

PMID: 21972007 [PubMed - as supplied by publisher]

Astaxanthin mixed with tocotrienols in liposomes provides synergistic free radical scavenging.

[J Clin Biochem Nutr.](#) 2016 Sep;59(2):100-106. Epub 2016 Sep 1.

Synergistic antioxidative effect of astaxanthin and tocotrienol by co-encapsulated in liposomes.

[Kamezaki C¹](#), [Nakashima A¹](#), [Yamada A¹](#), [Uenishi S¹](#), [Ishibashi H¹](#), [Shibuya N²](#), [Hama S¹](#), [Hosoi S¹](#), [Yamashita E³](#), [Kogure K⁴](#).

Author information

Abstract

Astaxanthin and vitamin E are both effective antioxidants that are frequently used in cosmetics, as food additives, and in to prevent oxidative damage. A combination of astaxanthin and vitamin E would be expected to show an additive antioxidant effect. In this study, liposomes co-encapsulating astaxanthin and the vitamin E derivatives α -tocopherol (α -T) or tocotrienols (T3) were prepared, and the antioxidative activity of these liposomes toward singlet oxygen and hydroxyl radical was evaluated *in vitro*. Liposomes co-encapsulating astaxanthin and α -T showed no additive antioxidant effect, while the actual scavenging activity of liposomes co-encapsulating astaxanthin and T3 was higher than the calculated additive activity. To clarify why this synergistic effect occurs, the most stable structure of astaxanthin in the presence of α -T or α -T3 was calculated. Only α -T3 was predicted to form hydrogen bonding with astaxanthin, and the astaxanthin polyene chain would partially interact with the α -T3 triene chain, which could explain why there was a synergistic effect between astaxanthin and T3 but not α -T. In conclusion, co-encapsulation of astaxanthin and T3 induces synergistic scavenging activity by intermolecular interactions between the two antioxidants.

KEYWORDS:

astaxanthin; intermolecular interaction; synergistic activity; tocotrienol; vitamin E

PMID: 27698536

PMCID: [PMC5018571](#)

DOI: [10.3164/jcbn.15-153](#)

[Free PMC Article](#)

Astaxanthin can partially prevent oxidative stress in human lymphocytes induced by a fatty acid mixture.

[Toxicol In Vitro](#). 2011 Oct;25(7):1448-56. Epub 2011 Apr 27.

Oxidative stress in human lymphocytes treated with fatty acid mixture: role of carotenoid astaxanthin.

[Campoio TR](#), [Oliveira FA](#), [Otton R](#).

Source

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Abstract

Fatty acids (FA) have been shown to alter leukocyte function, and depending on concentration and type, they can modulate both inflammatory and immune responses. Astaxanthin (ASTA) is a carotenoid that shows notable antioxidant properties. In the present study we propose to evaluate the oxidative stress in human lymphocytes induced by a FA mixture and the possible protective role of ASTA. The present study showed that the FA mixture at 0.3mM caused a marked increase in the production of superoxide anion, hydrogen peroxide and nitric oxide, which was accompanied by an increase in total-SOD activity, in TBARS levels and a reduction of catalase activity and content of GSH and free thiol groups. The FA mixture also promoted an increase in intracellular Ca(2+) mobilization and in the proliferative capacity of B-lymphocytes. The addition of ASTA (2 µM) partially decreased the ROS production and TBARS levels and increased the levels of free thiol groups. ASTA decreased the proliferative capacity of cells treated with FA but not by reducing intracellular calcium concentration. Based on these results we can conclude that ASTA can partially prevent oxidative stress in human lymphocytes induced by a fatty acid mixture, probably by blenching/quenching free radical production.

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PMID: 21549829 [PubMed - in process]

Astaxanthin improves cholesterol and lipid metabolism as well as antioxidant defense mechanisms in mice.

[J Nutr.](#) 2011 Sep;141(9):1611-7. Epub 2011 Jul 6.

Astaxanthin-rich extract from the green alga *Haematococcus pluvialis* lowers plasma lipid concentrations and enhances antioxidant defense in apolipoprotein E knockout mice.

[Yang Y](#), [Seo JM](#), [Nguyen A](#), [Pham TX](#), [Park HJ](#), [Park Y](#), [Kim B](#), [Bruno RS](#), [Lee J](#).

Source

Department of Nutritional Sciences, University of Connecticut, Storrs, CT, USA.

Abstract

Dyslipidemia and oxidative stress contribute to atherogenesis. Astaxanthin (ASTX) is a red-colored carotenoid well known for its high antioxidant capacity. However, its effects on lipid metabolism and antioxidant defense mechanisms have received only limited investigation. We fed male apoE knockout (apoE)(-/-) mice, a mouse model for atherosclerosis, a high-fat (15%)/high-cholesterol (0.2%) diet alone (control) or supplemented with ASTX-rich *Hematococcus pluvialis* extract (0.03% ASTX by weight) for 4 wk. ASTX-fed apoE(-/-) mice had significantly lower plasma total cholesterol and TG concentrations than controls, but body weight and plasma alanine aminotransferase and aspartate aminotransferase did not differ between the groups. qRT-PCR analysis demonstrated significantly greater mRNA levels of LDL receptor (LDLR), 3-hydroxy-3-methylglutaryl CoA reductase, and sterol regulatory element binding protein 2 (SREBP-2) and greater mature SREBP-2 protein in the livers of ASTX-fed mice, indicating that increased LDLR expression may be responsible for the hypocholesterolemic effect of ASTX. Hepatic lipogenic gene expression was not altered, but carnitine palmitoyl transferase 1, acetyl-CoA carboxylase β , and acyl-CoA oxidase mRNA abundance were significantly increased by ASTX supplementation, suggesting the TG-lowering effect of ASTX may be due to increased fatty acid β -oxidation in the liver. Expression of the nuclear factor E2 related factor 2-responsive endogenous antioxidant gene also was induced with concomitantly lower glutathione disulfide levels in the livers of ASTX-fed apoE(-/-) mice compared to controls. In conclusion, these results suggest that supplementation of ASTX-rich *H. pluvialis* extract improves cholesterol and lipid metabolism as well as antioxidant defense mechanisms, all of which could help mitigate the progression of atherosclerosis.

PMID:21734060 [PubMed - in process]

Astaxanthin can enhance the antioxidant system and some biochemical parameters in trout.

[Fish Physiol Biochem.](#) 2011 Jun 22. [Epub ahead of print]

Effects of *Haematococcus pluvialis* supplementation on antioxidant system and metabolism in rainbow trout (*Oncorhynchus mykiss*).

[Sheikhzadeh N](#), [Tayefi-Nasrabadi H](#), [Khani Oushani A](#), [Najafi Enferadi MH](#).

Source

Department of Food Hygiene and Aquatic Animals, Faculty of Veterinary Medicine, University of Tabriz, Tabriz, Iran, nsheikh@tabrizu.ac.ir.

Abstract

Effects of commercial source for astaxanthin (*Haematococcus pluvialis*) (H.p) on antioxidant power, specific marker enzymes, and some metabolites were examined in rainbow trout (*Oncorhynchus mykiss*). Fish were fed on diets containing 1, 3, and 10 g microalga kg(-1) feed for 30 days. Serum total antioxidant activity and lipid peroxidation product, indicated by malondialdehyde (MDA), significantly enhanced with different doses of administration, indicating the elevated antioxidant status in all treatment groups. In group fed with high dose of alga, significantly elevated aspartate aminotransferase activity (AST) was noted, indicating damage of normal liver function in this group. Alkaline phosphatase (ALP) and alanine aminotransferase (ALT) were not affected in all groups. Although serum total protein remained unaffected, serum glucose level was decreased significantly in lower doses of administration. Furthermore, triglyceride and cholesterol levels showed significant decrease in 3 g kg(-1) microalga group by modulation of lipid metabolism in this group. On the other hand, in highest dose, significant increase in lipids was observed, indicating the slight dysfunction in lipid metabolism in this treatment group. The present study suggests that *Haematococcus pluvialis* especially in dose of 3 g kg(-1) feed administration may effectively enhance the antioxidant system and some biochemical parameters in rainbow trout.

PMID: 21695482 [PubMed - as supplied by publisher]

Astaxanthin inhibits sodium azide-induced cytotoxicity, probably through its ability to quench reactive oxygen species.

[Yao Xue Xue Bao](#). 2011 May;46(5):521-6.

[Astaxanthin inhibits sodium azide-induced cytotoxicity in hepatocyte L-02 cells probably by H⁺ transferring function].

[Article in Chinese]

[Ma J](#), [Chen HM](#), [Yan XJ](#), [Wang F](#), [Xu WF](#).

Source

Key Laboratory of Applied Marine Biotechnology, Ningbo University, Ningbo 315211, China.

Abstract

This study is to investigate the protective effect of astaxanthin against injured hepatocyte L-02 cells induced by sodium azide (NaN₃) and reveal the possible mechanisms. Hepatocyte L-02 cells were exposed to 100 mmol.L⁻¹ NaN₃ with various concentrations of astaxanthin pre-incubated, then the cell viability was measured by MTT method; The level of reactive oxygen species (ROS) was determined by DCFH-DA method; The changes of mitochondrial membrane potential (MMP) and apoptosis ratio were detected by JC-1 method and Annexin V-FITC/PI double stain method, respectively. Results showed that after cells were exposed to 100 mmol.L⁻¹ NaN₃ for 3 hours, the cell viability significantly decreased; ROS level and the percentage of late phase apoptosis increased obviously; MMP was also declined. When cells were pretreated with astaxanthin, the cell damage and late phase apoptosis ratio reduced and MMP was maintained. However, the level of ROS showed insignificant decrease (P>0.05). The beneficial concentration of astaxanthin in improving cell viability and MMP was not in a dose dependent manner and the most effective of which was 0.10 nmol.L⁻¹ (P<0.01). In order to reveal its possible non-antioxidant mechanism, mitochondrial membrane was imitated and H⁺ transferring function of astaxanthin was also detected by bilayer lipid membrane (BLM) method. Results showed that 2.0% astaxanthin could transfer H⁺ efficiently. These suggested the mechanisms of astaxanthin in protection of hepatocyte L-02 cells not via its ROS quenching capability but via its H⁺ transferring function, which improved the mitochondrial function and had the sequence biology effects.

PMID: 21800538 [PubMed - in process]

The biosynthesis of Astaxanthin's algae cells as a response to stress is reviewed.

[Photosynth Res.](#) 2010 Nov;106(1-2):155-77. Epub 2010 Aug 13.

Secondary ketocarotenoid astaxanthin biosynthesis in algae: a multifunctional response to stress.

[Lemoine Y](#), [Schoefs B](#).

Source

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Abstract

Under stressful environments, many green algae such as *Haematococcus pluvialis* accumulate secondary ketocarotenoids such as canthaxanthin and astaxanthin. The carotenogenesis, responsible for natural phenomena such as red snows, generally accompanies larger metabolic changes as well as morphological modifications, i.e., the conversion of the green flagellated macrozooids into large red cysts. Astaxanthin accumulation constitutes a convenient way to store energy and carbon, which will be used for further synthesis under less stressful conditions. Besides this, the presence of high amount of astaxanthin enhances the cell resistance to oxidative stress generated by unfavorable environmental conditions including excess light, UV-B irradiation, and nutrition stress and, therefore, confers a higher survival capacity to the cells. This better resistance results from the quenching of oxygen atoms for the synthesis itself as well as from the antioxidant properties of the astaxanthin molecules. Therefore, astaxanthin synthesis corresponds to a multifunctional response to stress. In this contribution, the various biochemical, genetic, and molecular data related to the biosynthesis of ketocarotenoids by *Haematococcus pluvialis* and other taxa are reviewed and compared. A tentative regulatory model of the biochemical network driving astaxanthin production is proposed.

PMID: 20706789 [PubMed - indexed for MEDLINE]

Astaxanthin prevents oxidative stress damage and DNA damage and early formation of liver cancer in rats.

[Mutat Res.](#) 2010 Feb;696(1):69-80. Epub 2009 Dec 28.

Astaxanthin intervention ameliorates cyclophosphamide-induced oxidative stress, DNA damage and early hepatocarcinogenesis in rat: role of Nrf2, p53, p38 and phase-II enzymes.

[Tripathi DN](#), [Jena GB](#).

Source

Department of Pharmacology and Toxicology, National Institute of Pharmaceutical Education and Research (NIPER), Sector-67, S.A.S. Nagar, Mohali, Punjab-160062, India.
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Abstract

Cyclophosphamide, an alkylating agent, disturbs the oxidant and antioxidant balance that is associated with several unwanted toxic effects and induction of secondary cancers. Astaxanthin is a powerful antioxidant and possess several beneficial effects against various human diseases and physiological disorders. The present study was aimed to investigate the effects of astaxanthin against cyclophosphamide-induced oxidative stress, DNA damage, cell death and induction of GST-P foci in rat liver. Further attempt has been made to study the influence of astaxanthin on antioxidant response element (ARE) and the transcription factor Nrf2 (nuclear factor E(2)-related factor 2) in the induction of phase-II enzymes NAD(P)H: quinine oxidoreductase-1(NQO-1) and Hemoxygenase-1 (HO-1). Both pre- and post-treatment with astaxanthin (25mg/kg) decreased cyclophosphamide-induced oxidative stress and DNA damage in the liver as evident from the restoration in malondialdehyde and glutathione level as well as modified comet assay parameters. Significant decrease in the number as well as area of GST-P foci in rat hepatocytes was observed with astaxanthin post-treatment. Treatment with astaxanthin significantly decreased the expression of p53 and p38 as compared to cyclophosphamide treated group. It was further observed that the level of Nrf2 and phase-II enzymes, i.e. NQO-1 and HO-1 were increased with astaxanthin treatment. The present study confirms that astaxanthin is a potent antioxidant and attenuates oxidative stress, DNA damage, cell death as well as induction of early hepatocarcinogenesis in rat induced by cyclophosphamide. Our results provide the evidence that one of the mechanism of chemoprotection offered by astaxanthin is mediated through Nrf2-ARE pathway.

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PMID: 20038455 [PubMed - indexed for MEDLINE]

Astaxanthin protects against liver cell damage after ischemia in rats; the mechanism of action is attributed to Astaxanthin's antioxidant protection against oxidative injury.

[Toxicology](#). 2010 Jan 12;267(1-3):147-53. Epub 2009 Nov 10.

Effect of astaxanthin on hepatocellular injury following ischemia/reperfusion.

[Curek GD](#), [Cort A](#), [Yucel G](#), [Demir N](#), [Ozturk S](#), [Elpek GO](#), [Savas B](#), [Aslan M](#).

Source

Department of Biochemistry, Akdeniz University Medical School, Antalya 07070, Turkey.

Abstract

This study investigated the effect of astaxanthin (ASX; 3,3-dihydroxybeta, beta-carotene-4,4-dione), a water-dispersible synthetic carotenoid, on liver ischemia-reperfusion (IR) injury. Astaxanthin (5 mg/kg/day) or olive oil was administered to rats via intragastric intubation for 14 consecutive days before the induction of hepatic IR. On the 15th day, blood vessels supplying the median and left lateral hepatic lobes were occluded with an arterial clamp for 60 min, followed by 60 min reperfusion. At the end of the experimental period, blood samples were obtained from the right ventricle to determine plasma alanine aminotransferase (ALT) and xanthine oxidase (XO) activities and animals were sacrificed to obtain samples of nonischemic and postischemic liver tissue. The effects of ASX on IR injury were evaluated by assessing hepatic ultrastructure via transmission electron microscopy and by histopathological scoring. Hepatic conversion of xanthine dehydrogenase (XDH) to XO, total GSH and protein carbonyl levels were also measured as markers of oxidative stress. Expression of NOS2 was determined by immunohistochemistry and Western blot analysis while nitrate/nitrite levels were measured via spectral analysis. Total histopathological scoring of cellular damage was significantly decreased in hepatic IR injury following ASX treatment. Electron microscopy of postischemic tissue demonstrated parenchymal cell damage, swelling of mitochondria, disarrangement of rough endoplasmic reticulum which was also partially reduced by ASX treatment. Astaxanthine treatment significantly decreased hepatic conversion of XDH to XO and tissue protein carbonyl levels following IR injury. The current results suggest that the mechanisms of action by which ASX reduces IR damage may include antioxidant protection against oxidative injury.

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PMID: 19900500 [PubMed - indexed for MEDLINE]

Astaxanthin prevents hydrogen peroxide-induced oxidative damage.

[Zhongguo Gu Shang](#). 2008 Mar;21(3):187-9.

[Effects of Astaxanthin on the damage of osteoblast induced by H₂O₂].

[Article in Chinese]

[Pei LP](#), [Dong FH](#), [Hui BD](#).

Source

Institute of Orthopaedics and Traumatology, China Academy of Chinese Medical Science, Beijing 100700, China.

Abstract

OBJECTIVE: To investigate the effect of Astaxanthin on enhancing the function of anti-oxidative damage in osteoblast.

METHODS: MC3T3-E1 osteoblasts were randomly divided into five groups, including control group, model group, Astaxanthin group [low-dose (1×10^{-7} mol/L), middle-dose (1×10^{-6} mol/L), high-dose (1×10^{-5} mol/L)], in which the activity of cells, activity of superoxide dismutase (SOD), the content of reactive oxygen species (ROS), lipid oxygen (LPO) and membrane fluidity were tested and compared.

RESULTS: Compared with Astaxanthin groups, the activity of cells, SOD activity and membrane fluidity in the model group were significantly decreased ($P < 0.01$). However, the contents of ROS and LPO were significantly raised ($P < 0.01$).

CONCLUSION: H₂O₂ can cause oxidative damage of MC3T3-E1 osteoblasts, but Astaxanthin can prevent or decrease its influence.

PMID: 19105434 [PubMed - indexed for MEDLINE]

Astaxanthin combined with tocotrienols provides antioxidant effects in liposomes.

[J Clin Biochem Nutr.](#) 2016 Sep;59(2):100-106. Epub 2016 Sep 1.

Synergistic antioxidative effect of astaxanthin and tocotrienol by co-encapsulated in liposomes.

[Kamezaki C](#)¹, [Nakashima A](#)¹, [Yamada A](#)¹, [Uenishi S](#)¹, [Ishibashi H](#)¹, [Shibuya N](#)², [Hama S](#)¹, [Hosoi S](#)¹, [Yamashita E](#)³, [Kogure K](#)⁴.

Author information

Abstract

Astaxanthin and vitamin E are both effective antioxidants that are frequently used in cosmetics, as food additives, and in to prevent oxidative damage. A combination of astaxanthin and vitamin E would be expected to show an additive antioxidant effect. In this study, liposomes co-encapsulating astaxanthin and the vitamin E derivatives α -tocopherol (α -T) or tocotrienols (T3) were prepared, and the antioxidative activity of these liposomes toward singlet oxygen and hydroxyl radical was evaluated *in vitro*. Liposomes co-encapsulating astaxanthin and α -T showed no additive antioxidant effect, while the actual scavenging activity of liposomes co-encapsulating astaxanthin and T3 was higher than the calculated additive activity. To clarify why this synergistic effect occurs, the most stable structure of astaxanthin in the presence of α -T or α -T3 was calculated. Only α -T3 was predicted to form hydrogen bonding with astaxanthin, and the astaxanthin polyene chain would partially interact with the α -T3 triene chain, which could explain why there was a synergistic effect between astaxanthin and T3 but not α -T. In conclusion, co-encapsulation of astaxanthin and T3 induces synergistic scavenging activity by intermolecular interactions between the two antioxidants.

KEYWORDS:

astaxanthin; intermolecular interaction; synergistic activity; tocotrienol; vitamin E

PMID: 27698536

PMCID: [PMC5018571](#)

DOI: [10.3164/jcbn.15-153](#) [PubMed - in process]

Free PMC Article

Astaxanthin shows potential on oxidative stress markers in a mouse peritoneal inflammation model.

[Life Sci.](#) 2006 Jun 6;79(2):162-74. Epub 2006 Feb 8.

The effects of oral Cardax (disodium disuccinate astaxanthin) on multiple independent oxidative stress markers in a mouse peritoneal inflammation model: influence on 5-lipoxygenase in vitro and in vivo.

[Lockwood SF](#), [Penn MS](#), [Hazen SL](#), [Bikádi Z](#), [Zsila F](#).

Source

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Abstract

Disodium disuccinate astaxanthin (rac'-dAST; Cardax) is a water-dispersible C40 carotenoid derivative under development for oral and parenteral administration for cardioprotection of the at-risk ischemic cardiovascular patient. In experimental infarction models in animals (rats, rabbits, and dogs), significant myocardial salvage has been obtained, up to 100% at the appropriate dose in dogs. The documented mechanism of action in vitro includes direct scavenging of biologically produced superoxide anion; in vivo in rabbits, modulation of the complement activity of serum has also been shown. A direct correlation between administration of the test compound in animals and reductions of multiple, independent markers of oxidative stress in serum was recently obtained in a rat experimental infarction model. For the current study, it was hypothesized that oral Cardax administration would inhibit oxidative damage of multiple relevant biological targets in a representative, well-characterized murine peritoneal inflammation model. A previously developed mass spectrometry-based (LC/ESI/MS/MS) approach was used to interrogate multiple distinct pathways of oxidation in a black mouse (C57/BL6) model system. In vivo markers of oxidant stress from peritoneal lavage samples (supernatants) were evaluated in mice on day eight (8) after treatment with either Cardax or vehicle (lipophilic emulsion without drug) orally by gavage at 500 mg/kg once per day for seven (7) days at five (5) time points: (1) baseline prior to treatment (t=0); (2) 16 h following intraperitoneal (i.p.) injection with thioglycollate to elicit a neutrophilic infiltrate; (3) 4 h following i.p. injection of yeast cell wall (zymosan; t=16 h/4 h thioglycollate+zymosan); (4) 72 h following i.p. injection with thioglycollate to elicit monocyte/macrophage infiltration; and (5) 72 h/4 h thioglycollate+zymosan. A statistically significant sparing effect on the arachidonic acid (AA) and linoleic acid (LA) substrates was observed at time points two and five. When normalized to the concentration of the oxidative substrates, statistically significant reductions of 8-isoprostane-F(2alpha) (8-iso-F(2alpha)) at time point three (maximal neutrophil recruitment/activation), and 5-HETE, 5-oxo-EET, 11-HETE, 9-HODE, and PGF(2alpha) at time point five (maximal monocyte/macrophage recruitment/activation) were observed. Subsequently, the direct interaction of the optically inactive stereoisomer of Cardax (meso-dAST) with human 5-lipoxygenase (5-LOX) was evaluated in vitro with circular dichroism (CD) and electronic absorption (UV/Vis) spectroscopy, and subsequent molecular docking calculations were made using mammalian 15-LOX as a surrogate (for which XRC data has been reported). The results suggested that the meso-compound was capable of interaction with, and binding to, the solvent-exposed surface of the enzyme. These preliminary studies provide the foundation for more detailed evaluation of the therapeutic effects of this compound on the 5-LOX enzyme, important in chronic diseases such as atherosclerosis, asthma, and prostate cancer in humans.

PMID:

16466747

[PubMed - indexed for MEDLINE]

Astaxanthin reviewed for its effects on oxidative stress-induced mitochondrial dysfunction.

[Nutrients](#). 2018 Aug 21;10(9). pii: E1137. doi: 10.3390/nu10091137.

Inhibitory Effect of Astaxanthin on Oxidative Stress-Induced Mitochondrial Dysfunction-A Mini-Review.

[Kim SH](#)¹, [Kim H](#)².

[Author information](#)

Abstract

Oxidative stress is a major contributor to the pathogenesis of various human diseases as well as to the aging process. Mitochondria, as the center of cellular metabolism and major regulators of redox balance, play a critical role in disease development and progression. Mitochondrial dysfunction involving structural and metabolic impairment is prominent in oxidative stress-related diseases. Increased oxidative stress can damage mitochondria, and subsequent mitochondrial dysfunction generates excesses of mitochondrial reactive oxygen species that cause cellular damage. Mitochondrial dysfunction also activates the mitochondrial apoptotic pathway, resulting in cellular death. Astaxanthin, a red-colored xanthophyll carotenoid, exerts an anti-oxidative and anti-inflammatory effect on various cell lines. In this manner astaxanthin maintains mitochondrial integrity under various pathological conditions. In this review, the inhibitory effects of astaxanthin on oxidative stress-induced mitochondrial dysfunction and related disease development are discussed.

KEYWORDS:

astaxanthin; disease prevention; mitochondrial dysfunction; oxidative stress

PMID: 30134611

PMCID: [PMC6165470](#)

DOI: [10.3390/nu10091137](#)

[Indexed for MEDLINE]

[Free PMC Article](#)

Anti-Inflammatory: Joint, Tendon and Muscle Health and CRP Reduction

Studies Demonstrating Astaxanthin's Multiple Anti-Inflammatory Mechanisms of Action

Astaxanthin's Anti-Inflammatory mechanisms found to be broad-spectrum.

[Mol Cells](#). 2003 Aug 31;16(1):97-105.

Astaxanthin inhibits nitric oxide production and inflammatory gene expression by suppressing I(kappa)B kinase-dependent NF-kappaB activation.

[Lee SJ](#), [Bai SK](#), [Lee KS](#), [Namkoong S](#), [Na HJ](#), [Ha KS](#), [Han JA](#), [Yim SV](#), [Chang K](#), [Kwon YG](#), [Lee SK](#), [Kim YM](#).

Vascular System Research Center and Department of Molecular and Cellular Biochemistry, Kangwon National University Biology, Chunchon 200-701, Korea.

Astaxanthin, a carotenoid without vitamin A activity, has shown anti-oxidant and anti-inflammatory activities; however, its molecular action and mechanism have not been elucidated. We examined in vitro and in vivo regulatory function of astaxanthin on production of nitric oxide (NO) and prostaglandin E2 (PGE2) as well as expression of inducible NO synthase (iNOS), cyclooxygenase-2, tumor necrosis factor-alpha (TNF-alpha), and interleukin-1beta (IL-1beta). Astaxanthin inhibited the expression or formation production of these proinflammatory mediators and cytokines in both lipopolysaccharide (LPS)-stimulated RAW264.7 cells and primary macrophages. Astaxanthin also suppressed the serum levels of NO, PGE2, TNF-alpha, and IL-1beta in LPS-administrated mice, and inhibited NF-kappaB activation as well as iNOS promoter activity in RAW264.7 cells stimulated with LPS. This compound directly inhibited the intracellular accumulation of reactive oxygen species in LPS-stimulated RAW264.7 cells as well as H2O2-induced NF-kappaB activation and iNOS expression. Moreover, astaxanthin blocked nuclear translocation of NF-kappaB p65 subunit and I(kappa)B(alpha) degradation, which correlated with its inhibitory effect on I(kappa)B kinase (IKK) activity. These results suggest that astaxanthin, probably due to its antioxidant activity, inhibits the production of inflammatory mediators by blocking NF-kappaB activation and as a consequent suppression of IKK activity and I(kappa)B-alpha degradation.

Publication Types: [Research Support, Non-U.S. Gov't](#) PMID: 14503852 [PubMed - indexed for MEDLINE]

Astaxanthin inhibits a variety of pro-inflammatory cytokines in cells.

[Eur J Nutr.](#) 2010 Mar;49(2):119-26. Epub 2009 Sep 26.

Astaxanthin suppresses scavenger receptor expression and matrix metalloproteinase activity in macrophages.

[Kishimoto Y](#), [Tani M](#), [Uto-Kondo H](#), [Iizuka M](#), [Saita E](#), [Sone H](#), [Kurata H](#), [Kondo K](#).

Source

Institute of Environmental Science for Human Life, Ochanomizu University, Tokyo, Japan.

Abstract

BACKGROUND: *Astaxanthin is a red carotenoid pigment which has significant potential for antioxidant activity. The macrophages in atherosclerotic lesions, known as activated macrophages, express scavenger receptors responsible for the clearance of pathogenic lipoproteins. In addition, the expression and secretion of proteolytic enzymes, matrix metalloproteinases (MMPs), and pro-inflammatory cytokines are remarkably promoted in activated macrophages.*

AIM OF THE STUDY: *In this study, we investigated the effects of astaxanthin on the expression of scavenger receptors, MMPs, and pro-inflammatory cytokines in macrophages.*

METHODS: *THP-1 macrophages were incubated with 5-10 microM astaxanthin for 24 h. The expression levels of scavenger receptors, MMPs, and pro-inflammatory cytokines were determined by Western blot analysis or real-time RT-PCR. The MMP-9 and -2 activities were examined by gelatin zymography and total MMP activity was measured by fluorometry.*

RESULTS: *We found that astaxanthin remarkably decreased the class A scavenger receptor and CD36 expression in the protein and mRNA levels. Astaxanthin also reduced MMP-1, -2, -3, -9, -12, and -14 activity and expression. The mRNA expression of tumor necrosis factor-alpha, interleukin-1beta, interleukin-6, inducible nitric oxide synthase, and cyclooxygenase-2 were significantly suppressed by astaxanthin. Furthermore, astaxanthin inhibited the phosphorylation of nuclear factor-kappaB.*

CONCLUSIONS: *These results indicate that astaxanthin has inhibitory effects on macrophage activation, such as scavenger receptors up-regulation, MMPs activation, and pro-inflammatory cytokines secretion.*

PMID: 19784539 [PubMed - indexed for MEDLINE]

Astaxanthin found to be a multi-faceted anti-inflammatory with various mechanisms of action.

[Invest Ophthalmol Vis Sci](#). 2003 Jun;44(6):2694-701.

Effects of astaxanthin on lipopolysaccharide-induced inflammation in vitro and in vivo.

[Ohgami K](#), [Shiratori K](#), [Kotake S](#), [Nishida T](#), [Mizuki N](#), [Yazawa K](#), [Ohno S](#).

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PURPOSE: Astaxanthin (AST) is a carotenoid that is found in marine animals and vegetables. Several previous studies have demonstrated that AST exhibits a wide variety of biological activities including antioxidant, antitumor, and anti-Helicobacter pylori effects. In this study, attention was focused on the antioxidant effect of AST. The object of the present study was to investigate the efficacy of AST in endotoxin-induced uveitis (EIU) in rats. In addition, the effect of AST on endotoxin-induced nitric oxide (NO), prostaglandin E2 (PGE2), and tumor necrosis factor (TNF)-alpha production in a mouse macrophage cell line (RAW 264.7) was studied in vitro. **METHODS:** EIU was induced in male Lewis rats by a footpad injection of lipopolysaccharide (LPS). AST or prednisolone was administered intravenously at 30 minutes before, at the same time as, or at 30 minutes after LPS treatment. The number of infiltrating cells and protein concentration in the aqueous humor collected at 24 hours after LPS treatment was determined. RAW 264.7 cells were pretreated with various concentrations of AST for 24 hours and subsequently stimulated with 10 microg/mL of LPS for 24 hours. The levels of PGE2, TNF-alpha, and NO production were determined in vivo and in vitro. **RESULTS:** AST suppressed the development of EIU in a dose-dependent fashion. The anti-inflammatory effect of 100 mg/kg AST was as strong as that of 10 mg/kg prednisolone. AST also decreased production of NO, activity of inducible nitric oxide synthase (NOS), and production of PGE2 and TNF-alpha in RAW264.7 cells in vitro in a dose-dependent manner. **CONCLUSIONS:** This study suggests that AST has a dose-dependent ocular anti-inflammatory effect, by the suppression of NO, PGE2, and TNF-alpha production, through directly blocking NOS enzyme activity.

Publication Types:

- [Comparative Study](#)
- [Research Support, Non-U.S. Gov't](#)

PMID: 12766075 [PubMed - indexed for MEDLINE]

Astaxanthin inhibits the production of inflammatory markers by blocking nitric oxide and Cox-2.

[J Microbiol Biotechnol](#). 2008 Dec;18(12):1990-6.

Effects of astaxanthin on the production of NO and the expression of COX-2 and iNOS in LPS-stimulated BV2 microglial cells.

[Choi SK](#), [Park YS](#), [Choi DK](#), [Chang HI](#).

Department of Biotechnology, School of Life Sciences and Biotechnology, Korea University, Seoul 136-701, Korea.

Astaxanthin has shown antioxidant, antitumor, and antiinflammatory activities; however, its molecular action and mechanism in the nervous system have yet to be elucidated. We examined the in vitro effects of astaxanthin on the production of nitric oxide (NO), as well as the expression of inducible NO synthase (iNOS) and cyclooxygenase-2 (COX-2) in lipopolysaccharide (LPS)-stimulated BV2 microglial cells. Astaxanthin inhibited the expression or formation of nitric oxide (NO), iNOS and COX-2 in lipopolysaccharide (LPS)-stimulated BV-2 microglial cells. Astaxanthin also suppressed the protein levels of iNOS and COX-2 in LPS-stimulated BV2 microglial cells. These results suggest that astaxanthin, probably due to its antioxidant activity, inhibits the production of inflammatory mediators by blocking iNOS and COX-2 activation or by the suppression of iNOS and COX-2 degradation.

PMID: 19131704 [PubMed - in process]

Astaxanthin shows anti-inflammatory and antioxidant effects in-vitro and in mice and multiple anti-inflammatory mechanisms were found.

[J Nutr Biochem](#). 2018 Dec;62:202-209. doi: 10.1016/j.jnutbio.2018.09.005. Epub 2018 Sep 19.

Astaxanthin exerts anti-inflammatory and antioxidant effects in macrophages in NRF2-dependent and independent manners.

[Farruggia C](#)¹, [Kim MB](#)¹, [Bae M](#)¹, [Lee Y](#)¹, [Pham TX](#)¹, [Yang Y](#)¹, [Han MJ](#)², [Park YK](#)¹, [Lee JY](#)³.

Author information

Abstract

Although anti-inflammatory effects of astaxanthin (ASTX) have been suggested, the underlying mechanisms have not been fully understood. Particularly, the modulatory action of ASTX in the interplay between nuclear factor E2-related factor 2 (NRF2) and nuclear factor κ B (NF κ B) to exert its anti-inflammatory effect in macrophages is unknown. The effect of ASTX on mRNA and protein expression of pro-inflammatory and antioxidant genes and/or cellular reactive oxygen species (ROS) accumulation were determined in RAW 264.7 macrophages, bone marrow-derived macrophages (BMDM) from wild-type (WT) and Nrf2-deficient mice, and/or splenocytes and peritoneal macrophages of obese mice fed ASTX. The effect of ASTX on M1 and M2 macrophage polarization was evaluated in BMDM. ASTX significantly decreased LPS-induced mRNA expression of interleukin 6 (Il-6) and Il-1 β by inhibiting nuclear translocation of NF κ B p65; and attenuated LPS-induced ROS with an increase in NRF2 nuclear translocation, concomitantly decreasing NADPH oxidase 2 expression in RAW 264.7 macrophages. In BMDM of WT and Nrf2-deficient mice, ASTX decreased basal and LPS-induced ROS accumulation. The induction of Il-6 mRNA by LPS was repressed by ASTX in both types of BMDM while Il-1 β mRNA was decreased only in WT BMDM. Furthermore, ASTX consumption lowered LPS sensitivity of splenocytes in obese mice. ASTX decreased M1 polarization of BMDM while increasing M2 polarization. ASTX exerts its anti-inflammatory effect by inhibiting nuclear translocation of NF κ B p65 and by preventing ROS accumulation in NRF2-dependent and -independent mechanisms. Thus, ASTX is an agent with anti-inflammatory and antioxidant properties that may be used for the prevention of inflammatory conditions.

KEYWORDS:

Anti-inflammatory; Antioxidant; Astaxanthin; Macrophages; NF κ B; NRF2

PMID: 30308382

DOI: [10.1016/j.jnutbio.2018.09.005](https://doi.org/10.1016/j.jnutbio.2018.09.005)

Astaxanthin's broad-spectrum anti-inflammatory mechanisms analyzed in buffaloes.

[Vet World](#). 2018 Jun;11(6):782-788. doi: 10.14202/vetworld.2018.782-788. Epub 2018 Jun 10.

Astaxanthin inhibits cytokines production and inflammatory gene expression by suppressing I κ B kinase-dependent nuclear factor κ B activation in pre and postpartum Murrah buffaloes during different seasons.

[Priyadarshini L¹](#), [Aggarwal A¹](#).

Author information

Abstract

AIM: We examined regulatory function of astaxanthin on mRNA expression of nuclear factor κ B (NF- κ B) p65, interleukin-6 (IL-6), tumor necrosis factor alpha (TNF- α), and interferon gamma (IFN- γ) in peripheral blood mononuclear cells in pre and postpartum Murrah buffaloes during summer (temperature-humidity index [THI]=86; relative humidity [RH]=24) and winter (THI=58.74; RH=73) seasons.

MATERIALS AND METHODS: A total of 32 Murrah buffaloes apparently healthy and in their one to four parity were selected from National Dairy Research Institute herd and equally distributed randomly into four groups (control and supplemented groups of buffaloes during summer and winter season, respectively). All groups were fed according to the nutrient requirement of buffaloes (ICAR, 2013). The treatment group was supplemented with astaxanthin at 0.25 mg/kg body weight/animal/day during the period 30 days before expected date of calving and up to 30 days postpartum.

RESULTS: There was downregulation of NF- κ B p65 gene in all the groups. NF- κ B p65 mRNA expression was lower ($p < 0.05$) in treatment than control group from prepartum to postpartum during summer, while mRNA expression was low only on day 21 after calving during winter season. The mRNA expression of IL-6, TNF- α , and IFN- γ was lower ($p < 0.05$) in treatment than a control group of buffaloes during summer and winter seasons. The mRNA expression of NF κ B p65, IL-6, TNF- α , and IFN- γ was higher ($p < 0.05$) in summer than in winter seasons.

CONCLUSION: The xanthophyll carotenoid astaxanthin a reddish-colored C-40 compound is a powerful broad-ranging antioxidant that naturally occurs in a wide variety of living organisms, such as microalgae, fungi, crustaceans, and complex plants. Astaxanthin blocked nuclear translocation of NF- κ B p65 subunit and I κ B α degradation, which correlated with its inhibitory effect on I κ B kinase (IKK) activity. These results suggest that astaxanthin, probably due to its antioxidant activity, inhibits the production of inflammatory mediators by blocking NF- κ B activation and as a consequent suppression of IKK activity and I κ B-degradation.

PMID: 30034170 PMCID: [PMC6048090](#) DOI: [10.14202/vetworld.2018.782-788](#) [Free PMC Article](#)

Astaxanthin formula reduces inflammatory markers in-vitro.

[J Med Food](#). 2016 Dec;19(12):1196-1203.

FlexPro MD, a Mixture of Krill Oil, Astaxanthin, and Hyaluronic Acid, Suppresses Lipopolysaccharide-Induced Inflammatory Cytokine Production Through Inhibition of NF- κ B.

[Park DR](#)^{1,2}, [Ko R](#)^{1,2}, [Kwon SH](#)³, [Min B](#)³, [Yun SH](#)³, [Kim MH](#)³, [Minatelli J](#)⁴, [Hill S](#)⁴, [Lee SY](#)^{1,2}.
Author information

Abstract

FlexPro MD[®] (FP-MD), a novel multi-ingredient dietary supplement formulation, has been demonstrated to relieve knee joint pain in humans. However, the mechanisms of action responsible for the activity of FP-MD have not been elucidated. In this study, we show the anti-inflammatory effects of FP-MD in RAW264.7 macrophage cells and mice challenged with lipopolysaccharide (LPS). FP-MD significantly inhibited the mRNA levels of pro-inflammatory cytokines, including interleukin-6 (IL-6), tumor necrosis factor- α (TNF- α), and IL-1 β . In contrast, it elevated the mRNA levels of anti-inflammatory cytokine IL-10 in LPS-stimulated RAW264.7 cells. FP-MD markedly reduced LPS-induced phosphorylation levels of nuclear factor- κ B (NF- κ B) p65 and inhibitor of κ B- α (I κ B- α). Importantly, the anti-inflammatory effects of FP-MD were demonstrated in mice with LPS-induced inflammatory arthritis in which FP-MD significantly reduced the expression levels of pro-inflammatory cytokines and inflammatory markers. Thus, this study suggests that FP-MD has anti-inflammatory effects by inhibiting NF- κ B that may offer a molecular basis for its pain relief property.

KEYWORDS: NF- κ B; astaxanthin; cytokines

PMID: 27982753 PMID: [PMC5312594](#) DOI: [10.1089/jmf.2016.3787](#) [Indexed for MEDLINE]

[Free PMC Article](#)

Astaxanthin is much more potent than curcumin and its derivatives in scavenging nitric oxide.

[Biol Pharm Bull.](#) 2004 Feb;27(2):170-3.

Evaluation of the nitric oxide radical scavenging activity of manganese complexes of curcumin and its derivative.

[Sumanont Y](#), [Murakami Y](#), [Tohda M](#), [Vajragupta O](#), [Matsumoto K](#), [Watanabe H](#).

Department of Pharmacology, Institute of Natural Medicine, Toyama Medical and Pharmaceutical University, 2630 Sugitani, Toyama 930-0194, Japan.

Curcumin manganese complex (CpCpx) and diacetylcurcumin manganese complex (AcylCpCpx) were determined as to their effect on the nitric oxide (NO) radical scavenging in vitro method using a sodium nitroprusside generating NO system compared with their parent compound and astaxanthin, an extreme antioxidant. All compounds effectively reduced the generation of NO radicals in a dose dependent manner. They exhibited strong NO radical scavenging activity with low IC(50) values. The IC(50) values of curcumin, diacetylcurcumin, CpCpx and AcylCpCpx obtained are 20.39 \pm 4.10 microM, 28.76 \pm 1.48 microM, 9.79 \pm 1.50 microM and 8.09 \pm 0.99 microM, respectively. CpCpx and AcylCpCpx show greater NO radical scavenging than their parent compounds, curcumin and acetylcurcumin, respectively. However, the IC(50) values of curcumin and related compounds were found to be less than astaxanthin, an extreme antioxidant, with the lower IC(50) value of 3.42 \pm 0.50 microM.

Publication Types:

- [Research Support, Non-U.S. Gov't](#)

PMID: 14758027 [PubMed - indexed for MEDLINE]

Human Clinical Research on Astaxanthin's Anti-Inflammatory Benefits

Astaxanthin decreases inflammation and oxidative stress and enhances immune response in randomized, double-blind, placebo-controlled human clinical trial.

[Nutr Metab \(Lond\)](#). 2010 Mar 5;7:18. doi: 10.1186/1743-7075-7-18.

Astaxanthin decreased oxidative stress and inflammation and enhanced immune response in humans.

[Park JS¹](#), [Chyun JH](#), [Kim YK](#), [Line LL](#), [Chew BP](#).

Author information

Abstract

BACKGROUND:

Astaxanthin modulates immune response, inhibits cancer cell growth, reduces bacterial load and gastric inflammation, and protects against UVA-induced oxidative stress in in vitro and rodent models. Similar clinical studies in humans are unavailable. Our objective is to study the action of dietary astaxanthin in modulating immune response, oxidative status and inflammation in young healthy adult female human subjects.

METHODS:

Participants (averaged 21.5 yr) received 0, 2, or 8 mg astaxanthin (n = 14/diet) daily for 8 wk in a randomized double-blind, placebo-controlled study. Immune response was assessed on wk 0, 4 and 8, and tuberculin test performed on wk 8.

RESULTS:

Plasma astaxanthin increased ($P < 0.01$) dose-dependently after 4 or 8 wk of supplementation. Astaxanthin decreased a DNA damage biomarker after 4 wk but did not affect lipid peroxidation. Plasma C-reactive protein concentration was lower ($P < 0.05$) on wk 8 in subjects given 2 mg astaxanthin. Dietary astaxanthin stimulated mitogen-induced lymphoproliferation, increased natural killer cell cytotoxic activity, and increased total T and B cell subpopulations, but did not influence populations of Thelper, Tcytotoxic or natural killer cells. A higher percentage of leukocytes expressed the LFA-1 marker in subjects given 2 mg astaxanthin on wk 8. Subjects fed 2 mg astaxanthin had a higher tuberculin response than unsupplemented subjects. There was no difference in TNF and IL-2 concentrations, but plasma IFN-gamma and IL-6 increased on wk 8 in subjects given 8 mg astaxanthin.

CONCLUSION:

Therefore, dietary astaxanthin decreases a DNA damage biomarker and acute phase protein, and enhances immune response in young healthy females.

PMID: 20205737 [PubMed] PMCID: PMC2845588 [Free PMC Article](#)

Astaxanthin reduces pain and improves satisfaction scores in patients suffering from rheumatoid arthritis in double-blind, placebo-controlled human clinical study.

EFFECT OF AN ASTAXANTHIN-CONTAINING PRODUCT ON RHEUMATOID ARTHRITIS

Nir, Y., Spiller, G., Multz, C.

Health Research and Studies Center, Los Altos, CA

Study Report, May 2002

Journal of the American College of Nutrition (October 2002) Volume 21, Number 5.

ABSTRACT

Rheumatoid arthritis (RA) is a chronic destructive disorder requiring aggressive treatment. Conventional treatments present problems in terms of safety and efficacy, and the alternative therapies so far investigated have not yielded consistent results. We investigated the effect of an extract of *Haematococcus* algae grown in Hawaii, taken three times a day, each dose supplying 4 mg of astaxanthin, 40 ug lutein, 65 IU vitamin A as beta-carotene, and 50 IU of vitamin E, on the symptoms of RA in a double-blind, placebo-controlled, parallel design study. Twenty-one subjects were randomized to receive either the extract (14 subjects) or a placebo (7 subjects) for eight weeks. Pain and satisfaction with the ability to perform daily activities were measured at the beginning of the study, and after 4 and 8 weeks of treatment. The results showed a significant difference ($P < 0.05$) both in pain and satisfaction scores between the treatment and control groups at the end of the study. Pain scores (mean \pm SD, VAS scale) at 0, 4, and 8 weeks were respectively, 0.42 ± 0.22 , 0.38 ± 0.21 , and 0.27 ± 0.25 for the treatment group, and 0.48 ± 0.23 , 0.42 ± 0.16 , and 0.45 ± 0.14 for the control group. Satisfaction scores were 1.75 ± 0.72 , 1.50 ± 0.76 , and 1.00 ± 0.60 for the treatment group, and 1.83 ± 0.69 , 1.50 ± 0.96 , and 1.67 ± 0.94 for the control group. Astaxanthin-based supplements appear to be an effective addition in the treatment of RA and further studies should be carried out with a larger population.

Astaxanthin decreases pain rate and pain duration in subjects suffering from carpal tunnel syndrome in double-blind, placebo-controlled human clinical study.

EFFECT OF AN ASTAXANTHIN-CONTAINING PRODUCT ON CARPAL TUNNEL SYNDROME

Nir, Y., Spiller, G., Multz, C.

Health Research and Studies Center, Los Altos, CA,

Study Report, May, 2002

Journal of the American College of Nutrition, Oct 2002, Volume 21, Number 5

ABSTRACT

Carpal Tunnel Syndrome (CTS) is a debilitating disease often requiring surgery. Because not all patients respond to surgery and current non-surgical treatments provide limited benefits, investigations into alternative techniques are necessary. We investigated the effect of an extract of *Haematococcus* algae grown in Hawaii, taken three times a day, each dose supplying 4 mg of astaxanthin, 40 ug lutein, 65 IU vitamin A as beta-carotene, and 50 IU of vitamin E, on the symptoms of CTS in a double-blind, placebo-controlled, parallel design study. Twenty participants were randomized to receive either the extract (13 subjects) or a placebo (7 subjects) for eight weeks. Daytime pain rate and duration were measured at the beginning of the study, and after 4 and 8 weeks of treatment, with the use of questionnaires. Results showing a trend towards decreasing pain rate and duration in the subjects receiving the extract, but because of the small number of subjects the results did not reach statistical significance ($P>0.05$). The daytime pain rates (mean \pm SD) at 0, 4 and 8 weeks were, respectively, 1.69 ± 0.99 , 1.23 ± 0.70 , and 1.00 ± 0.88 for the treatment group, and 1.67 ± 0.47 , 1.83 ± 0.37 , and 1.50 ± 0.50 for the control group. Similarly, the duration of daytime pain was 2.15 ± 1.23 , 1.69 ± 1.13 , and 1.38 ± 1.44 for the treatment group, and 2.17 ± 1.07 , 2.67 ± 1.10 , and 2.17 ± 1.34 for the control group. The positive trend observed in this pilot study suggests that an astaxanthin-containing product may be effective in treating symptoms of CTS. Further investigations in a larger-scale study are needed.

Astaxanthin helps prevent muscle damage and inflammation in young soccer players and may support immune system modulation in randomized, placebo-controlled study.

[Evid Based Complement Alternat Med.](#) 2015;2015:783761. doi: 10.1155/2015/783761. Epub 2015 Jun 18.

Effect of Astaxanthin Supplementation on Salivary IgA, Oxidative Stress, and Inflammation in Young Soccer Players.

[Baralic I¹](#), [Andjelkovic M¹](#), [Djordjevic B²](#), [Dikic N¹](#), [Radivojevic N¹](#), [Suzin-Zivkovic V³](#), [Radojevic-Skodric S⁴](#), [Pejic S⁵](#).

Author information

Abstract

The physiologic stress induced by physical activity is reflected in immune system perturbations, oxidative stress, muscle injury, and inflammation. We investigated the effect of astaxanthin (Asx) supplementation on salivary IgA (sIgA) and oxidative stress status in plasma, along with changes in biochemical parameters and total/differential white cell counts. Forty trained male soccer players were randomly assigned to Asx and placebo groups. Asx group was supplemented with 4 mg of Asx. Saliva and blood samples were collected at the baseline and after 90 days of supplementation in preexercise conditions. We observed a rise of sIgA levels at rest after 90 days of Asx supplementation, which was accompanied with a decrease in prooxidant-antioxidant balance. The plasma muscle enzymes levels were reduced significantly by Asx supplementation and by regular training. The increase in neutrophil count and hs-CRP level was found only in placebo group, indicating a significant blunting of the systemic inflammatory response in the subjects taking Asx. This study indicates that Asx supplementation improves sIgA response and attenuates muscle damage, thus preventing inflammation induced by rigorous physical training. Our findings also point that Asx could show significant physiologic modulation in individuals with mucosal immunity impairment or under conditions of increased oxidative stress and inflammation.

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Astaxanthin decreases C-reactive protein levels by 20% on average in double-blind, placebo-controlled human clinical study.

Effect of daily use natural astaxanthin on C-reactive protein.

Gene A. Spiller, PhD, Antonella Dewell, MS, RD, Sally Chaves, RN, Zaga Rakidzich
Health Research & Studies Center, Los Altos, CA

Study Report, January, 2006

Unpublished study referenced in *The Medical Research of Astaxanthin* by Capelli, B., Keily, S., Linhart, J., and Cysewski, G. (2013) and in *The World's Best Kept Health Secret: Natural Astaxanthin* by Capelli, B., and Cysewski, G. (2014).

ABSTRACT

Previous studies have provided data suggesting that daily use of natural astaxanthin can positively address inflammatory conditions such as rheumatoid arthritis and carpal tunnel syndrome. In this study, the effect of daily use of a microalgae extract containing natural astaxanthin, on C-reactive protein was evaluated. It was found that after daily use for eight weeks C-reactive protein (CRP) was significantly lowered in the treatment group as compared to the placebo group. The average decrease in patients receiving natural astaxanthin was 20%. This correlation of reduced CRP and use of astaxanthin may suggest that daily use can help reduce CRP and possibly lower inflammation levels in the body.

Astaxanthin use leads to increase in grip strength by 93% in eight weeks in patients suffering from tendonitis (tennis elbow) in double-blind, placebo-controlled human clinical trial.

Effect of daily use of natural astaxanthin on symptoms associated with Tennis Elbow (lateral humeral epicondylitis)

Gene A. Spiller, PhD, CNS, Antonella Dewell, MS, RD, Sally Chaves, RN, Zaga Rakidzich, Health Research & Studies Center, Los Altos, CA
Study Report, January, 2006

Unpublished study referenced in *The Medical Research of Astaxanthin* by Capelli, B., Keily, S., Linhart, J., and Cysewski, G. (2013) and in *The World's Best Kept Health Secret: Natural Astaxanthin* by Capelli, B., and Cysewski, G. (2014).

ABSTRACT

Previous studies have provided data suggesting that daily use of a microalgal extract containing natural astaxanthin can help alleviate pain associated with joint damage, specifically that seen in rheumatoid arthritis and carpal tunnel syndrome. For this study, the benefits of daily use natural astaxanthin for the purpose of alleviating pain associated with Tennis Elbow (lateral humeral epicondylitis) was evaluated. It was found that grip strength measurements (GSM) for those on the active product were significantly improved by the end of the study. The average grip strength improved by 93% in subjects supplementing with 12mg per day of natural astaxanthin in a period of 8 weeks. This correlation of improved GSM and use of natural astaxanthin may suggest that daily use can help alleviate pain associated with Tennis Elbow, and increase mobility. This improvement may greatly improve the standard of living for those who suffer from such joint disorders.

Astaxanthin reduces inflammation and injury to vocal fold in human volunteers after 60 minutes vocal loading in human clinical trial.

[J Voice](#). 2017 May;31(3):352-358. doi: 10.1016/j.jvoice.2016.06.017. Epub 2016 Oct 26.

Protective Effect of Astaxanthin on Vocal Fold Injury and Inflammation Due to Vocal Loading: A Clinical Trial.

[Kaneko M](#)¹, [Kishimoto Y](#)¹, [Suzuki R](#)¹, [Kawai Y](#)¹, [Tateya I](#)¹, [Hirano S](#)².

Author information

Abstract

OBJECTIVES: Professional voice users, such as singers and teachers, are at greater risk of developing vocal fold injury from excessive use of voice; thus, protection of the vocal fold is essential. One of the most important factors that aggravates injury is the production of reactive oxygen species at the wound site. The purpose of the current study was to assess the effect of astaxanthin, a strong antioxidant, on the protection of the vocal fold from injury and inflammation due to vocal loading.

STUDY DESIGN: This study is an institutional review board-approved human clinical trial.

METHODS: Ten male subjects underwent a 60-minute vocal loading session and received vocal assessments prior to, immediately after, and 30 minutes postvocal loading (AST(-) status). All subjects were then prescribed 24 mg/day of astaxanthin for 28 days, after which they received the same vocal task and assessments (AST(+) status). Phonatory parameters were compared between both groups.

RESULTS: Aerodynamic assessment, acoustic analysis, and GRBAS scale (grade, roughness, breathiness, asthenia, and strain) were significantly worse in the AST(-) status immediately after vocal loading, but improved by 30 minutes after loading. In contrast, none of the phonatory parameters in the AST(+) status were statistically worse, even when measured immediately after vocal loading. No allergic responses or adverse effects were observed after administration of astaxanthin.

CONCLUSIONS: The current results suggest that astaxanthin can protect the vocal fold from injury and inflammation caused by vocal loading possibly through the regulation of oxidative stress.

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KEYWORDS: Astaxanthin; Clinical trial; Reactive oxygen species; Vocal fold; Vocal loading

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Astaxanthin decreases joint pain after heavy exercise in double-blind, placebo-controlled human clinical trial.

Astaxanthin Clinical Trial for Delayed Onset Muscular Soreness

Fry, A. (2001). "Astaxanthin Clinical Trial for Delayed Onset Muscular Soreness." Human Performance Laboratories. The University of Memphis. Report 1, August 16, 2001. Unpublished study cited in "The World's Best Kept Health Secret: Natural Astaxanthin" Capelli, B. and Cysewski, G. (2014).

While the original goal of this study was to test for delayed onset muscle soreness, the researcher found that 4mg per day of Natural Astaxanthin over a 3-week supplementation period significantly reduced knee soreness after heavy knee exercise immediately after exercise as well as at intervals of 10 hours, 24 hours and 48 hours after exercise. The placebo group experienced a significant increase in knee pain after performing heavy exercise. However, the Astaxanthin group showed no increase in knee soreness after heavy exercise.

Astaxanthin improves visual acuity (the ability to see fine detail) and muscle soreness and fatigue in placebo-controlled human clinical trial.

Journal of Clinical Therapeutics & Medicines VOL.18;NO.9;PAGE.1085-1100(2002)

Sports Performance Benefits from Taking Natural Astaxanthin Characterized by Visual Acuity and Muscle Fatigue Improvement in Humans.

[SAWAKI KEISUKE](#); [YOSHIGI HIROSHI](#); [AOKI KAZUHIRO](#); [KOIKAWA NATSUE](#); [AZUMANE AKITO](#); [KANEKO KESATOKI](#); [YAMAGUCHI MASAHIRO](#)

The effects of astaxanthin on visual acuity and muscle fatigue were studied. Astaxanthin (3,3'-Dihydroxy-.BETA.,.BETA.-carotene-4,4'-dione) is a red pigment found in salmon and krill and has strong antioxidant properties. In the two supplementation studies, astaxanthin extracted from algae (*Haematococcus pluvialis*) was used. Four visual acuity parameters were examined in experiment A in 18 healthy adult male volunteers that were equally divided into two groups (treatment and control). The measured parameters were deep vision, critical flicker fusion, static and kinetic visual acuity before and after supplementation. A second investigation (experiment B) involved 16 adult male volunteers to establish the effect of astaxanthin supplementation on the build up of lactic acid before and after running 1200 metres. In both experiments, the treated groups ingested an astaxanthin capsule per day for 4 weeks (6mg astaxanthin per day) and the control groups received a placebo capsule. Results: In experiment A, the deep vision and the critical flicker fusion of the treated groups were significantly improved compared to the control group. No effects of treated group were observed on static and kinetic visual acuity. In experiment B, serum lactic acid concentration at 2 minutes after activity (1,200m running) of the treatment group was significantly lower than that of the control one. No other effects related to supplementation of astaxanthin on serum biological and hematological examinations were observed. Based on these preliminary findings, it suggested that supplementation of astaxanthin is effective for the improvement of visual acuity and muscle fatigue that may lead to sports performance benefits.

ASTAXANTHIN DECREASES LEVELS OF OXIDATIVE STRESS MARKER MALONDIALDEHYDE AND INFLAMMATORY CYTOKINE INTERLEUKIN-6 IN PATIENTS WITH TYPE-2 DIABETES IN RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED HUMAN CLINICAL TRIAL.

Int J Clin Pract. 2021 May;75(5):e14022.

doi: 10.1111/ijcp.14022. Epub 2021 Feb 2.

The antioxidant and anti-inflammatory effects of astaxanthin supplementation on the expression of miR-146a and miR-126 in patients with type 2 diabetes mellitus: A randomised, double-blind, placebo-controlled clinical trial

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- PMID: 33445213 DOI: [10.1111/ijcp.14022](https://doi.org/10.1111/ijcp.14022)

Abstract

Background: The pathogenesis of type 2 diabetes mellitus (T2DM) is associated with chronic oxidative stress and inflammation. It is well known that the expression of some miRNAs such as miRNA-146a is upregulated in diabetic and hyperglycaemic patients, whereas circulating miRNA-126 is reduced. Therefore, we aimed to determine the effects of astaxanthin (AST) supplementation on the circulating malondialdehyde (MDA) and interleukin 6 (IL-6) levels, and the expression of miR-146a and miR-126 in patients with T2DM.

Methods: This randomised, double-blind, placebo-controlled clinical trial was conducted in 44 patients with T2DM randomly receiving 8 mg/d of oral AST (n = 22) or placebo (n = 22) for 8 weeks.

Results: We observed that AST supplementation could decrease plasma levels of MDA and IL-6 (P < .05) and decrease the expression level of miR-146a over time (fold change: -1/388) (P < .05).

Conclusion: AST supplementation might be beneficial for improving circulating MDA and IL-6 and the down-regulation of miR-146a. However, future investigations are suggested to confirm these results.

Astaxanthin reduces delayed onset muscle soreness after weight training in placebo-controlled human clinical study.

ASTAXANTHIN SUPPLEMENTATION

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38152

Unpublished study referenced in *The Medical Research of Astaxanthin* by Capelli, B., Keily, S., Linhart, J., and Cysewski, G. (2013) and in *The World's Best Kept Health Secret: Natural Astaxanthin* by Capelli, B., and Cysewski, G. (2014).

Abstract

PURPOSE: To determine the effects of astaxanthin anti-oxidant supplementation as a counter-measure for delayed onset muscular soreness (DOMS) in currently trained individuals, nine weight trained males ($X \pm SE$: age=25.1 \pm 1.6 yrs., hgt=1.79 \pm 0.02 m, wgt=86.8 \pm 4.4 kg) participated in this study. **METHODS:** All subjects provided muscle biopsy samples from the vastus lateralis m. prior to inducing DOMS in the knee extensor mm. (10 sets x 7-10 reps, 85% eccentric 1 RM). The subjects ingested either 4 mg.d-1 of astaxanthin (Suppl; n=4) or a placebo (Con; n=5) for a 3 week loading phase prior to the DOMS-inducing protocol, and during a 12 d recovery phase. Perceptions of DOMS at 48 hrs post-eccentric exercise were quantified by muscle soreness ratings (0-10 Likert scale). Muscle fiber characteristics were determined via mATPase histochemistry and digital imaging to determine % cross-sectional areas of the major fiber types (I, IIA, IIB/B). Due to small numbers of IIB fibers in some subjects, IIB hybrid fibers were included in this fiber type population. Simple regression was used to determine relationships between fiber characteristics and perceptions of soreness. **RESULTS:** No differences in perceptions of soreness between the Suppl or Con groups were observed ($p > 0.05$), with all subjects exhibiting a mean score of > 5 . Percent fiber type areas were similar ($p > 0.05$) for both groups (type I, Suppl=47.6 \pm 8.9%, Con=41.3 \pm 2.7%; type IIA, Suppl=44.3 \pm 5.6%, Con=53.0 \pm 2.8%; type IIB/B, Suppl=8.2 \pm 3.6%, Con=5.7 \pm 1.6%). However, 48 hrs after the DOMS-inducing session, perceptions of soreness for the Suppl group were positively related to % area type I ($r=0.90$), and negatively related to % area types IIA ($r=-0.80$) and IIB/B ($r=-0.99$). A distinctly different correlational pattern was observed for the Con group (% type I area, $r=-0.58$; % type IIA area, $r=0.32$; % type IIB/B area, $r=0.40$). **CONCLUSIONS:** Collectively, these preliminary data suggest that astaxanthin supplementation may preferentially attenuate perceptions of DOMS in weight trained men with a high % area for fiber types IIA & AB/B.

Astaxanthin reduces C-reactive protein levels in individuals at high risk for cardiovascular disease.

Natural Astaxanthin reduces C-reactive protein in subjects in high-risk category for cardiovascular disease.

Mera Pharmaceuticals, Unpublished study referenced in *The World's Best Kept Health Secret: Natural Astaxanthin* by Capelli, B., and Cysewski, G. (2014).

The study (double blind, placebo controlled) was designed to test the hypothesis that supplementation with AstaFactor(TM) reduces levels of C - reactive protein (CRP). Other studies have shown that elevated levels of CRP indicate the presence of inflammation in the body and are considered by many to be a better indicator of risk of cardiovascular disease than cholesterol.

The trial subjects all had CRP levels high enough to place them in the high-risk category for heart disease. After three months in the study 43% of the subjects in the treatment group experienced enough of a reduction in their CRP levels to fall out of the high-risk category and into the average risk group. However, all of the subjects in the placebo-controlled group remained at high-risk.

Although the subject group was small, the results of the AstaFactor(TM) trial have clear significance for cardiovascular health. The control of inflammation suggested by the trial results could also be important for other diseases and conditions, ranging from arthritis to diabetes, that heavily involve inflammatory processes. Mera plans to continue the study. Mr. Kowal added "that Mera Pharmaceuticals will continually strive to produce the finest supplements available, the AstaFactor (TM) Rejuvenating, Sports and Salmon Essentials formulae to supply an increasing demand as more people become aware of the health benefits associated with astaxantin."

Astaxanthin user survey shows that 84% of respondents experiencing painful conditions found reduced joint, tendon & muscle pain and 60% experienced increased mobility.

Potential Clinical Applications of Natural Astaxanthin from Haematococcus Microalgae

Bob Capelli, Robert Corish, MD, Gerald R. Cysewski, PhD

Published at www.cyanotech.com

Natural Astaxanthin from Haematococcus Pluvialis microalgae has been used as a human nutritional supplement since the early 1990's. Researchers have studied potential benefits of Astaxanthin during and before its introduction as a commercially sold nutritional supplement. Among many different areas of research, our discussion will be limited specifically to research on antioxidant protection; anti-inflammatory applications including joint and tendon conditions; protection of the skin from UV radiation; and immune system enhancement. We first review research on Natural Astaxanthin as a potential preventative and/or curative agent in relation to the aforementioned areas of health. Additionally, we report the results of a survey of Natural Astaxanthin users. A use/benefit survey (Appendix A) was created and posted on an independent survey implementation and analysis website. A request was sent by e-mail to 1584 consumers who had purchased a commercially sold Natural Astaxanthin supplement (BioAstin® Natural Astaxanthin, Cyanotech Corporation) at least once during the last seven years. These consumers were asked to log onto the independent survey website and fill out the use/benefit survey. 423 consumers (26.7% of the total) completed the survey (full results in Appendix A). Of the 423 respondents, 121 respondents were classified as non-qualified due to three specific disqualifying factors, yielding a final total of 302 qualified respondents (qualified results in Appendix B). Respondents were surveyed about their use of the Natural Astaxanthin supplement including a) milligrams per day; b) frequency of use; c) duration of use; d) consumption with food. Respondents were further surveyed about the benefits they derived from their use of Natural Astaxanthin. Of the 302 qualified respondents, 85% experienced positive benefits from Natural Astaxanthin supplementation. Of those respondents who had experienced joint, tendon or muscle pain, 84% found that their condition ameliorated through Natural Astaxanthin supplementation; 83% experienced less pain while 60% experienced increased mobility. 75% found that Natural Astaxanthin worked the same or better than over-the-counter pain medications, while 64% found that Natural Astaxanthin worked the same or better than prescription anti-inflammatories. Additional results include: a) 68% experienced reduced UV damage from sun exposure; b) 65% experienced improvement in skin condition; c) 80% experienced improved immunity and/or resistance to colds and flu. Based on previous research and further validated by the results of this survey, we conclude that Natural Astaxanthin is a viable therapy 1) for joint and tendon conditions; 2) as a preventative for UV damage; 3) to improve immune function and increase resistance to colds and flu.

Astaxanthin leads to improvement in muscle and joint soreness in vast majority of consumers surveyed.

Mera Pharmaceuticals, Inc. Review presented at the 1st Congress of the International Society for Applied Phycology/9th International Conference on Applied Phycology, May 2002, Almeria, Spain.

Haematococcus astaxanthin: health and nutrition applications: Exercise survey with 88% reporting improvement

Guerin, M, Huntley, M, Olaizola, M.

“In March 2001, a health survey looked at the various positive effects of Astaxanthin on exercise. The survey involved 247 between the ages of 20 and 87 years. 146 of those taking part reported problems with muscle and joint soreness. When taking Astaxanthin, 88% of participants reported improvement. In all cases, the more exercise an individual did, the more benefit was experienced.”

ASTAXANTHIN-CONTAINING FORMULA REDUCES SYSTOLIC BLOOD PRESSURE; REDUCES HIGH-SENSITIVITY C-REACTIVE PROTEIN AND INTERLEUKIN-6 INFLAMMATORY MARKERS; AND IMPROVES ENDOTHELIAL FUNCTION IN HUMAN CLINICAL STUDY.

Clin Nutr ESPEN. 2020 Feb;35:174-179.
doi: 10.1016/j.clnesp.2019.09.011. Epub 2019 Oct 24.

A combined effect of Cavacurcumin, Eicosapentaenoic acid (Omega-3s), Astaxanthin and Gamma -linoleic acid (Omega-6) (CEAG) in healthy volunteers- a randomized, double-blind, placebo-controlled study

[Divya Birudaraju¹](#), [Lavanya Cherukuri¹](#), [April Kinninger¹](#), [Bhanu T Chaganti¹](#), [Kashif Shaikh¹](#), [Sajad Hamal¹](#), [Ferdinand Flores¹](#), [Sion K Roy¹](#), [Matthew J Budoff²](#)

- PMID: 31987113
- DOI: [10.1016/j.clnesp.2019.09.011](https://doi.org/10.1016/j.clnesp.2019.09.011)

Abstract

Background: Inflammation plays a key role and is one of the early steps in the pathogenesis of endothelial function, thereby increasing the risk of hypertension (HTN), coronary artery disease (CAD), stroke and several other risk factors of cardiovascular disease (CVD). We assessed the efficacy for improving cardiovascular health (blood pressure, inflammation and endothelial reactivity) over a 4-week intervention period in healthy individuals.

Methods: We performed a randomized, double-blinded, placebo-controlled, randomized clinical trial to investigate Curcumin, Eicosapentaenoic acid (EPA), Astaxanthin and Gamma -linoleic acid (GLA) (CEAG) supplements with 80 individuals (30 men and 50 women). The mean age of participants was 48.8 ± 16.0 years. Participants were enrolled and randomized to active or placebo and followed for 4 weeks. Paired

and Independent T-tests were used to analyze the mean differences between and within groups.

Results: The primary endpoints of the study were the effect on inflammatory markers (IL-6, CRP), endothelial function and blood pressure at 4 weeks. There was a significant reduction in mean SBP at 4 weeks in the CEAG group compared to placebo [mean \pm SD 4.7 ± 6.8 ($p = 0.002$)]. Relative to placebo, active group showed a significant decrease in High sensitivity C Reactive Protein (hsCRP) (-0.49 ± 1.9 vs $+ 0.51 \pm 2.5$, $p = 0.059$) and blunted increase in IL-6 ($+0.2$ vs $+ 0.4$ in placebo, $p = 0.60$).

Conclusion: Inflammatory markers were reduced or blunted by CEAG, with a robust increase in both EPA levels and the fatty acid index. Furthermore, systolic BP was reduced over 4 weeks with concurrent improvement in endothelial function.

Supporting Pre-Clinical Trials

ASTAXANTHIN REVIEWED AS AN ANTI-INFLAMMATORY WITH POTENTIAL TO TREAT PATIENTS WITH COVID-19

Review

Iran J Microbiol 2021 Aug;13(4):434-441.
doi: 10.18502/ijm.v13i4.6965.

Astaxanthin protective barrier and its ability to improve the health in patients with COVID-19

[Ali-Reza Ahmadi](#)¹, [Roya Ayazi-Nasrabadi](#)¹

- PMID: 34557270 PMCID: [PMC8421583](#) DOI: [10.18502/ijm.v13i4.6965](#)

Abstract

Inflammation acts like a double-edged sword and can be harmful if not appropriately controlled. COVID-19 is created through a novel species of coronavirus SARS-CoV-2 (2019-nCoV). Elevated levels of inflammatory factors such as interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF- α), etc. lead to Acute Respiratory Distress Syndrome (ARDS) and severe complications of infection in the lungs of coronavirus-infected patients. Astaxanthin is a natural and potent carotenoid with powerful antioxidant activity as well as an anti-inflammatory agent that supports good health. The effects of astaxanthin on the regulation of cyclooxygenase-2 (COX-2) pathways and the reduction and suppression of cytokines and other inflammatory agents such as IL-6 and TNF- α have already been identified. Therefore, these unique features can make this natural compound an excellent option to minimize inflammation and its consequences.

Astaxanthin reduces inflammation and pain behavior in mice comparatively equally to a drug commonly used to treat arthritis and gout.

[Molecules](#). 2016 Mar 19;21(3):382. doi: 10.3390/molecules21030382.

Effects of Astaxanthin from *Litopenaeus Vannamei* on Carrageenan-Induced Edema and Pain Behavior in Mice.

[Kuedo Z](#)¹, [Sangsuriyawong A](#)², [Klaypradit W](#)³, [Tipmanee V](#)⁴, [Chonpathompikunlert P](#)⁵.

Author information

Abstract

Carrageenan produces both inflammation and pain when injected in mouse paws via enhancement of reactive oxygen species formation. We have investigated an effect of astaxanthin extracted from *Litopenaeus vannamei* in carrageenan-induced mice paw edema and pain. The current study demonstrates interesting effects from astaxanthin treatment in mice: an inhibition of paw edema induced in hind paw, an increase in mechanical paw withdrawal threshold and thermal paw withdrawal latency, and a reduction in the amount of myeloperoxidase enzyme and lipid peroxidation products in the paw. Furthermore the effect was comparable to indomethacin, a standard treatment for inflammation symptoms. Due to adverse effects of indomethacin on cardiovascular and gastrointestinal systems, our study suggests promising prospect of astaxanthin extract as an anti-inflammatory alternative against carrageenan-induced paw edema and pain behavior.

KEYWORDS:

Litopenaeus vannamei; astaxanthin; carrageenan; inflammatory pain; mice; myeloperoxidase

PMID: 27007359

DOI: [10.3390/molecules21030382](https://doi.org/10.3390/molecules21030382)

[Indexed for MEDLINE]

Free PMC Article

ASTAXANTHIN IS MORE EFFECTIVE THAN CORTICOSTEROID AND HYLAURONIC ACID IN A RAT OSTEOARTHRITIS MODEL.

Cartilage 2021 Sep 16;19476035211046042. doi: 10.1177/19476035211046042. Online ahead of print.

Evaluation of Different Intraarticular Injection Therapies with Gait Analysis in a Rat Osteoarthritis Model

[Ceyhun Çağlar](#)¹, [Halil Kara](#)², [Okan Ateş](#)³, [Mahmut Uğurlu](#)⁴

- PMID: 34528494 DOI: [10.1177/19476035211046042](https://doi.org/10.1177/19476035211046042)

Abstract

Objective: Osteoarthritis (OA) is a degenerative disease that causes serious damage to joints, especially in elderly patients. The aim of study was to demonstrate the effectiveness of intraarticular therapies that are currently used or recently popularized in the treatment of OA.

Design: The baseline values were determined by walking the rats on the CatWalk system. Afterwards, a monosodium iodoacetate (MIA)-induced knee OA model was created with intraarticular MIA, and the rats were walked again on the CatWalk system and post-OA values were recorded. At this stage, the rats were divided into 4 groups, and intraarticular astaxanthin, intraarticular corticosteroid, intraarticular hyaluronic acid, and intraarticular astaxanthin + hyaluronic acid were applied to the groups, respectively. The rats were walked once more and posttreatment values were obtained. Nine different dynamic gait parameters were used in the comparison.

Results: Significant changes were measured in 6 of the 9 dynamic gait parameters after the MIA-induced knee OA model. While the best improvement was observed in run duration ($P = 0.0022$), stride length ($P < 0.0001$), and swing speed ($P = 0.0355$) in the astaxanthin group, the results closest to basal values in paw print length ($P < 0.0001$), paw print width ($P = 0.0101$), and paw print area ($P = 0.0277$) were seen in the astaxanthin + hyaluronic acid group.

Conclusion: Astaxanthin gave better outcomes than corticosteroid and hyaluronic acid in both dynamic gait parameters and histological examinations. Intraarticular astaxanthin therapy can be a good alternative to corticosteroid and hyaluronic acid currently used in intraarticular therapy to treat OA.

Astaxanthin prevents muscle atrophy by protecting membranes in rodent study.

Effect of Astaxanthin on Muscular Atrophy

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Objective: Patients wearing casts or other devices that hinder mobility are reported to have muscular atrophy. It is commonly thought that the cause is from reactive oxygen species (ROS). The use of Vitamin E, along with other antioxidants, prevents ROS from causing muscular atrophy that arises from lack of movement; however there has been conflicting reports. In this experiment, Astaxanthin (Ax), which is considered to be a more effective antioxidant than Vitamin E or beta-carotene, will be administered to subjects as food supplement to see its effect on muscular atrophy caused by lack of movement. It will also be tested if the amount of Ax intake will make a difference in its effectiveness. **Methods:** 14-week old, Wister-type, male rats were used. Mice were all the same weight after growth for one week under controlled conditions. The rats were separated into three separate groups: Control group (n=7), Ax 0.04% group, and Ax 0.2% group. 15 days after the administration of Ax, each rat had his right leg contained with a cast in an extended position to decrease muscle mass in the triceps surae muscle group for 10 days. At the end of the experiment, the weights of the rats were measured and, along with the use of Nembutal (an anesthesia), euthanized. The plantaris muscle was extracted for analysis.

Results and Analysis: Groups that were administered Ax had significantly less muscle atrophy than those in the Control group ($p < 0.05$). The level of Cu/Zn-SOD expressed was higher in the rats with casts than those without casts in the control group; however, in the Ax group, the level expressed was insignificantly different from those with casts and those without. In addition, the level expressed in the control group with casts was significantly higher than the Ax group with casts on. The level of calpain and ubiquitin expressed was higher in the control group with casts than those in the Ax group with casts, but the difference was insignificant. Also, significantly less (of calpain and ubiquitin) was expressed in the Ax 0.2% with casts compared to the control group with casts. The same pattern was seen with Capthesin L expression.

Presently, it is reported that muscular atrophy in patients who are immobile due to casts was caused by oxidative stress. The increase in oxidative stress accelerates the reaction of lipoperoxide, which causes distress in the cell membrane and sarcoendoplaxmic reticulum, leading to an increase in Ca^{2+} in the cytoplasm and concurrently causing a decrease in its discharge. An increase in Ca^{2+} concentration activates calpain along with cathepsin. In addition, the presence of lipoperoxide causes disruption in the cell membrane of the mitrocondria, causing iron ions and ROS to leak in the cytoplasm, which leads to ubiquitination (of proteins.) Ax is the same as beta-carotene in that they are both carotenoids. They both prevent lipoperoxides from

disturbing the cell membrane in many biological organisms, but Ax is more active than other antioxidants. Based on this information, we believe Ax intake prevents muscular atrophy by protecting membranes; preventing oxidative stress which results in atrophy; preventing the facilitation protease and ubiquitination. The effects due to the quantity of Ax uptake were not clear in this study.

Astaxanthin decreases pain and improves motor function in rat model of spinal cord injury.

[Eur J Pain](#). 2018 Nov 14. doi: 10.1002/ejp.1342. [Epub ahead of print]

Effects of astaxanthin on sensory-motor function in a compression model of spinal cord injury: Involvement of ERK and AKT signalling pathway.

[Fakhri S](#)¹, [Dargahi L](#)², [Abbaszadeh F](#)³, [Jorjani M](#)^{1,3}.

Author information

Abstract

BACKGROUND: Spinal cord injury (SCI) causes continuous neurological deficits and major sensory-motor impairments. There is no effective treatment to enhance sensory-motor function following SCI. Thus, it is crucial to develop novel therapeutics for this particular patient population. Astaxanthin (AST) is a strong antioxidant, anti-inflammatory and anti-apoptotic agent. In the present study, it was tested in a severe compression SCI model with emphasis on sensory-motor outcomes, signalling pathway, along with other complications.

METHODS: A severe SCI was induced by compression of the rat thoracic spinal cord with an aneurysm clip and treatment with AST or the vehicle was carried out, 30 min after injury. Behavioural tests including open field, von Frey, hot plate and BBB were performed weekly to 28 days post-injury. Rats were assigned to measure blood glucose, weight and auricle temperature. Western blot and histological analysis also were performed at the same time points.

RESULTS: AST decreased mechanical and thermal pain and also improved motor function performance, reduced blood glucose and auricle temperature increases and attenuated weight loss in SCI rats. Western blot analysis showed decreased activation of ERK1/2 and increased activation of AKT following AST treatment. The histology results revealed that AST considerably preserved myelinated white matter and the number of motor neurons following SCI.

CONCLUSION: Taken together, the beneficial effects of AST to improve sensory-motor outcomes, attenuate pathological tissue damage and modulate ERK and AKT signalling pathways following SCI, suggest it as a strong therapeutic agent towards clinical applications.

SIGNIFICANCE: Spinal cord injury (SCI) impairs sensory-motor function and causes complications, which astaxanthin (AST) has the potential to be used as a treatment for. The present study investigates the effects of AST in a compression model of SCI with emphasis on sensory-motor outcomes alongside other complications, histopathological damage and also related signalling pathways.

© 2018 European Pain Federation - EFIC®. PMID: 30427581 DOI: [10.1002/ejp.1342](https://doi.org/10.1002/ejp.1342)

Astaxanthin outperforms fish oil and krill oil in reducing neural inflammation in rats.

[Mar Drugs](#). 2015 Sep 28;13(10):6117-37. doi: 10.3390/md13106117.

Redox Status and Neuro Inflammation Indexes in Cerebellum and Motor Cortex of Wistar Rats Supplemented with Natural Sources of Omega-3 Fatty Acids and Astaxanthin: Fish Oil, Krill Oil, and Algal Biomass.

[Polotow TG](#)¹, [Poppe SC](#)², [Vardaris CV](#)³, [Ganini D](#)^{4,5}, [Guariroba M](#)⁶, [Mattei R](#)⁷, [Hatanaka E](#)⁸, [Martins MF](#)^{9,10}, [Bondan EF](#)^{11,12}, [Barros MP](#)¹³.

Author information

Abstract

Health authorities worldwide have consistently recommended the regular consumption of marine fishes and seafood to preserve memory, sustain cognitive functions, and prevent neurodegenerative processes in humans. Shrimp, crabs, lobster, and salmon are of particular interest in the human diet due to their substantial provision of omega-3 fatty acids (n-3/PUFAs) and the antioxidant carotenoid astaxanthin (ASTA). However, the optimal ratio between these nutraceuticals in natural sources is apparently the key factor for maximum protection against most neuro-motor disorders. Therefore, we aimed here to investigate the effects of a long-term supplementation with (n-3)/PUFAs-rich fish oil, ASTA-rich algal biomass, the combination of them, or krill oil (a natural combination of both nutrients) on baseline redox balance and neuro-inflammation indexes in cerebellum and motor cortex of Wistar rats. Significant changes in redox metabolism were only observed upon ASTA supplementation, which reinforces its antioxidant properties with a putative mitochondrial-centered action in rat brain. Krill oil imposed mild astrocyte activation in motor cortex of Wistar rats, although no redox or inflammatory index was concomitantly altered. In summary, there is no experimental evidence that krill oil, fish oil, or algal biomass (minor variation), drastically change the baseline oxidative conditions or the neuro-inflammatory scenario in neuromotor-associated rat brain regions.

KEYWORDS:

Alzheimer; DHA; EPA; Parkinson; aging; antioxidant; brain; carotenoid; hormesis; senescence

PMID: 26426026 PMCID: [PMC4626682](#) DOI: [10.3390/md13106117](#)

[Indexed for MEDLINE]

Free PMC Article

Astaxanthin reduces cartilage damage in rabbits and is suggested as a possible treatment for osteo arthritis.

[Mod Rheumatol.](#) 2015 Sep;25(5):768-71. doi: 10.3109/14397595.2015.1008724. Epub 2015 Jun 12.

Astaxanthin ameliorates cartilage damage in experimental osteoarthritis.

[Huang LJ](#)¹, [Chen WP](#).

[Author information](#)

Abstract

PURPOSE:

Astaxanthin is a red-pigment carotenoid found in certain marine animals and plants. Astaxanthin has been shown to inhibit matrix metalloproteinases (MMPs) expression in vitro. However, the effect of astaxanthin on cartilage is still unclear. The aim of this study was to investigate the effects of astaxanthin on cartilage in experimental osteoarthritis (OA).

METHODS:

New Zealand rabbits underwent anterior cruciate ligament transection to induce OA in right knee. Rabbits received intra-articular injection containing 0.3 ml of vehicle (dimethyl sulfoxide) or astaxanthin (50 µM). Injection was started on the day of operation, and the injection were performed once weekly for six consecutive weeks. Then, rabbits were sacrificed and the right knees were harvested for study.

RESULTS:

Cartilage degradation was reduced by astaxanthin, as assessed by morphological and histological examination. Astaxanthin inhibited the gene expression of MMP-1, MMP-3, and MMP-13 in cartilage as compared with the vehicle group.

CONCLUSIONS:

The results suggest that astaxanthin may be considered as pharmaceutical agent in OA treatment.

KEYWORDS:

Astaxanthin; Matrix metalloproteinases; Osteoarthritis

PMID: 25608048

DOI: [10.3109/14397595.2015.1008724](#)

[Indexed for MEDLINE]

Astaxanthin taken on a long-term basis reduces sarcopenia [age-related muscle atrophy] in rodents.

Long term dietary antioxidant intakes attenuate sarcopenia

Tsubasa SHIBAGUCHI, Talmo SUGIURA, Tsukasa FURUMOTO,
Koshiro IOUEI, Yoshiharu TIDA, Hieeabl AITOA, Kaeumaea GOTO',
Daijiro OHMORI, Ibshitadu YOSMOK.,V
Japanese Journal of Physical Fitness and Sports Medicine (2008), 57:541-552.

Oxidative stress is thought to be one of significant contributing factors to age-related sarcopenia. We tested the hypothesis that the long term dietary antioxidant (astaxanthin) intakes attenuate sarcopenia. Wistar strain male rats, aged 45 weeks old, were given either control (Cont) or astaxanthin feed (0.004%, Ax) for 1 year. The soleus muscle weights and muscle weight-to-body weight ratios in Ax group were significantly heavier than in Cont group, but tibialis anterior muscle mass remained similar between the two dietary groups. The level of ubiquitinated proteins was significantly lower in soleus muscles of Ax group, but not in tibialis anterior muscles when compared with Cont group. Tibialis anterior levels of cathepsin L and caspase-3 were tended to be lower in Ax group than in Cont group, especially significant differences observed in cathepsin L, whereas no differences between Cont and Ax were observed in soleus muscle levels. There were no effects of Ax supplementation on calpain 1 and 2, UBC3B, Cu/Zn SOD and nitrotyrosine levels in both soleus and tibialis anterior muscles. Our data suggest that the long term dietary astaxanthin intakes attenuate the age related muscle atrophy, due in part, to reductions in oxidative stress and ubiquitination of myofibrillar protein in slow soleus muscles, but not in fast tibialis anterior muscles.

Astaxanthin could be useful for improving chronic inflammation.

[J Clin Biochem Nutr.](#) 2015 May;56(3):171-8. doi: 10.3164/jcbrn.14-109. Epub 2015 Jan 29.

Anti-inflammatory effects of astaxanthin in the human gingival keratinocyte line NDUSD-1.

[Miyachi M](#)¹, [Matsuno T](#)¹, [Asano K](#)¹, [Mataga I](#)¹.

Author information

Abstract

Oral lichen planus is a chronic inflammatory disease that affects the mucous membrane of the oral cavity and can contribute to the development of other diseases. Inflammation in oral lichen planus is a T-cell-mediated autoimmune disease that acts through cytotoxic CD8(+) T cells to trigger apoptosis of keratinocytes. However, the specific cause of oral lichen planus remains unknown and no effective medical treatment has yet been established. Astaxanthin is a carotenoid pigment with capacity for anti-inflammatory and anti-oxidant activities. In this study, we evaluated whether astaxanthin could be used to improve the pathology of oral lichen planus by reducing inflammation. In particular, the anti-inflammatory effects of astaxanthin on the chronic inflammation caused by lipopolysaccharide derived from *Escherichia coli* O55 in human gingival keratinocytes (NDUSD-1) were evaluated. Following astaxanthin treatment, localization of nuclear factor κ B/p65 and the level of inflammatory cytokines (interleukin-6, tumor necrosis factor- α) tended to decrease, and cell proliferation significantly increased in vitro. These results suggest that astaxanthin could be useful for improving chronic inflammation such as that associated with oral lichen planus.

KEYWORDS:

astaxanthin; chronic inflammation; human gingival keratinocyte; inflammatory cytokine; nuclear factor κ B/p65

PMID:

26060346

[PubMed]

Free full text

ASTAXANTHIN REDUCES JOINT INFLAMMATION AND MAY BE A SUITABLE THERAPY FOR GOUTY ARTHRITIS IN RAT MODEL.

FASEB J. 2020 Aug;34(8):11215-11226.

doi: 10.1096/fj.202000558RR. Epub 2020 Jul 10.

Astaxanthin attenuates joint inflammation induced by monosodium urate crystals

[Yi-Jen Peng](#)¹, [Jeng-Wei Lu](#)², [Feng-Cheng Liu](#)³, [Chian-Her Lee](#)⁴, [Herng-Sheng Lee](#)⁵, [Yi-Jung Ho](#)⁶, [Tsung-Hsun Hsieh](#)¹, [Chia-Chun Wu](#)⁷, [Chih-Chien Wang](#)⁷

PMID: **32648603** DOI: [10.1096/fj.202000558RR](https://doi.org/10.1096/fj.202000558RR)

Abstract

Gouty arthritis is the one of the most painful arthritis and is caused by an inflammatory reaction. This study investigated whether astaxanthin (AXT), which has documented anti-inflammatory and antioxidant properties, exhibits protective effects against monosodium urate (MSU) crystal-induced inflammation. Cell viability of J774A.1 murine macrophages was assessed by AXT dose-dependent incubation by MTT assays, and expression levels of iNOS and COX-2 proteins as well as secretion of IL-1 β were also analyzed under MSU crystals stimulation with or without AXT treatment. The production of inflammatory mediators was found to significantly decrease with AXT treatment, and the formation of the inflammasome complex was also attenuated when cells were co-stimulated with MSU crystals and AXT. Furthermore, we found that expression of the MAPK pathway was downregulated in J774A.1 cells. AXT also inhibited the induction of COX-2 and IL-6 in human chondrocytes and synovial fibroblasts by western blots. Finally, an MSU crystal intra-articular injection rat model for gouty arthritis was utilized in which treatment groups received 5-daily intraperitoneal injections of AXT prior to MSU crystal stimulation, or once intra-articular injections of AXT following MSU crystal stimulation for 6 hours. Results of synovitis score analysis revealed that inflammation was significantly attenuated in the group which received intraperitoneal AXT injection prior to MSU crystal stimulation compared to the group which received MSU only. These results indicate that AXT attenuates the effects of MSU crystal-induced inflammation by suppressing the production of pro-inflammatory cytokines and inflammatory mediators. Our findings that the anti-inflammatory activities of AXT may be beneficial in the treatment of MSU crystal-induced arthritis.

ASTAXANTHIN SHOWS POTENTIAL AGAINST EPILEPSY AND REDUCES INFLAMMATION AND REACTIVE OXYGEN SPECIES IN RAT MODEL.

Saudi Pharm J 2021 May;29(5):418-426. doi: 10.1016/j.jsps.2021.04.002. Epub 2021 Apr 9.

The potential antiepileptic activity of astaxanthin in epileptic rats treated with valproic acid

[Yussra Ata Yaseen Abdulqader](#)^{1,2}, [Hala Salah Abdel Kawy](#)¹, [Huda Mohammed Alkreathy](#)¹, [Nisreen Abdullah Rajeh](#)³

- PMID: 34135667 PMCID: [PMC8180462](#) DOI: [10.1016/j.jsps.2021.04.002](#)

Free PMC article

Abstract

Objectives: Epilepsy is a neurological disease characterized by sudden, abnormal, and hyper- discharges in the central nervous system (CNS). Valproic acid (VPA) is commonly used as a broad-spectrum antiepileptic therapeutic. However, in many cases, patients develop resistance to VPA treatment due to overwhelming oxidative stress, which in turn might be a major catalyst for disease progression. Therefore, antioxidants can potentially become therapeutic agents by counteracting reactive oxygen species (ROS)-mediated damage. The present study is aimed to evaluate the potential antiepileptic effect of astaxanthin (ASTA) in pentylenetetrazol (PTZ) induced epileptic model rats that are chronically treated with VPA for 8 weeks.

Method: Fifty-male Wistar rats were randomly divided into five groups: Non-PTZ group, PTZ, PTZ/VPA, PTZ/ASTA, and PTZ/VPA/ASTA treated groups.

Results: PTZ/VPA treated group showed a neuroprotective effect with improvement in antioxidant levels, behavioral test, and histopathological changes induced by PTZ. VPA also exhibited an anti-inflammatory effect as its treatment resulted in the reduction of tumor necrosis factor- α (TNF- α). ASTA exhibited an anticonvulsant effect and enhanced anti-inflammatory effect as compared to VPA. During the combined therapy, ASTA potentiated the antiepileptic effect of the VPA by reducing the oxidative stress and TNF- α as well as increased the glutathione (GSH) levels. Also, there were substantial

improvements in the behavioral and histopathological changes in the VPA/ASTA treated group as compared to the VPA treated group.

Conclusion: ASTA could have an antiepileptic and anti-inflammatory effect by reducing ROS generation. Therefore, co-administration of both the therapeutics (VPA/ASTA) has a synergistic effect in treating epilepsy and could potentially minimize recurrence and/or exacerbation of seizures.

ASTAXANTHIN SHOWS POTENTIAL ANTI-ARTHRITIC EFFECT IN RAT STUDY.

Pharmacol Rep. 2020 Feb;72(1):104-114.

doi: 10.1007/s43440-019-00022-z. Epub 2019 Dec 19.

Astaxanthin attenuates oxidative stress and inflammatory responses in complete Freund-adjuvant-induced arthritis in rats

[Akshay Kumar](#)¹, [Navneet Dhaliwal](#)¹, [Jatinder Dhaliwal](#)¹, [Ravinder Naik Dharavath](#)¹, [Kanwaljit Chopra](#)^{2,3}

PMID: 32016833 DOI: [10.1007/s43440-019-00022-z](https://doi.org/10.1007/s43440-019-00022-z)

Abstract

Background: Astaxanthin (ATX), a natural xanthophyll carotenoid, has shown to exert significant protective effects against various diseases via its antioxidant and anti-inflammatory properties. However, its potential role in arthritis is still not reported. Therefore, the aim of the present study was to investigate the potential anti-arthritic properties of ATX against complete Freund's adjuvant (CFA)-induced arthritis rats.

Methods: Adjuvant arthritis was induced by single intraplantar injection of complete Freund's adjuvant (CFA) in the left hind paw of adult female Wistar rats. ATX (25, 50 and 100 mg/kg) and indomethacin (5 mg/kg) were given orally from days 14 to 28. The anti-arthritic activity was evaluated through various nociceptive behavioral tests (mechanical allodynia, mechanical hyperalgesia, cold allodynia, and thermal hyperalgesia), paw edema assessment, and arthritis scores. Serum tumor necrosis factor- α (TNF- α), C-reactive protein (CRP) and cyclic citrullinated peptide (CCP) antibody levels were assessed. Moreover, malondialdehyde (MDA), nitrite, glutathione (GSH), superoxide dismutase (SOD) and catalase (CAT) levels were also evaluated.

Results: Oral administration of ATX (50 and 100 mg/kg) exhibited significant anti-arthritic activity via enhancing the nociceptive threshold, reducing paw edema and improving arthritis scores. Moreover, ATX treatment also markedly suppressed inflammatory and oxidative mediators in adjuvant-administered rats.

Conclusions: Our findings suggest that ATX possesses potential anti-arthritic activity, which could be attributed to its anti-inflammatory and antioxidant properties.

ASTAXANTHIN PROTECTS AGAINST OSTEOARTHRITIS IN MOUSE MODEL AND MAY BE A POTENTIAL THERAPEUTIC TREATMENT.

Aging (Albany NY). 2019 Nov 26;11(22):10513-10531.
doi: 10.18632/aging.102474. Epub 2019 Nov 26.

Astaxanthin protects against osteoarthritis via Nrf2: a guardian of cartilage homeostasis

[Kai Sun](#)¹, [Jiahui Luo](#)², [Xingzhi Jing](#)¹, [Jiachao Guo](#)¹, [Xudong Yao](#)¹, [Xiaoxia Hao](#)³, [Yaping Ye](#)¹, [Shuang Liang](#)¹, [Jiamin Lin](#)¹, [Genchun Wang](#)¹, [Fengjing Guo](#)¹

PMID: 31772142 PMCID: [PMC6914430](#) DOI: [10.18632/aging.102474](#) [Free PMC article](#)

Abstract

Scope: Osteoarthritis (OA) is a progressive disease characterized by cartilage degradation. Astaxanthin (Ast), a natural compound with remarkable antioxidant activity and multiple medical applications due to its activation of Nrf2 signaling, has been studied for application to various degenerative diseases. Currently, however, little is known about its efficacy in treating OA. This study reports the effects of Ast on cartilage homeostasis in OA progression.

Methods: IL-1 β , TNF- α , and tert-butyl hydroperoxide (TBHP) were used to impair cartilage homeostasis. Modulating effects of Ast on the Nrf2 signaling pathway, and damage-associated events including extracellular matrix (ECM) degradation, inflammation, oxidative stress, chondrocyte apoptosis, and *in vivo* cartilage degradation were examined.

Results: Ast attenuated ECM degradation of OA chondrocytes through the Nrf2 signaling, and ameliorated the IL-1 β -induced inflammatory response and ECM degradation via blockade of MAPK signaling. Additionally, Ast alleviated TNF- α -induced ECM degradation and chondrocyte apoptosis by inhibiting the NF- κ B signaling, suppressed TBHP-induced oxidative stress, and subsequently reduced chondrocyte apoptosis. *In vitro* results were finally corroborated *in vivo* by demonstrating that Ast attenuates the severity of cartilage destruction in a mouse model of OA.

Conclusions: Ast could protect against osteoarthritis via the Nrf2 signaling, suggesting Ast might be a potential therapeutic supplement for OA treatment.

ASTAXANTHIN PROTECTS MITOCHONDRIA IN MOUSE SKELETAL MUSCLE.

Antioxidants (Basel). 2020 Jan 23;9(2):98.
doi: 10.3390/antiox9020098.

Improved Tetanic Force and Mitochondrial Calcium Homeostasis by Astaxanthin Treatment in Mouse Skeletal Muscle

[Mónika Sztretye](#)¹, [Zoltán Singlár](#)^{1,2}, [László Szabó](#)^{1,2}, [Ágnes Angyal](#)^{1,2}, [Norbert Balogh](#)^{1,2}, [Faranak Vakilzadeh](#)^{1,2}, [Péter Szentesi](#)¹, [Beatrix Dienes](#)¹, [László Csernoch](#)¹

PMID: 31979219 PMCID: [PMC7070261](#) DOI: [10.3390/antiox9020098](#) [Free PMC article](#)

Abstract

Background: Astaxanthin (AX) a marine carotenoid is a powerful natural antioxidant which protects against oxidative stress and improves muscle performance. Retinol and its derivatives were described to affect lipid and energy metabolism. Up to date, the effects of AX and retinol on excitation-contraction coupling (ECC) in skeletal muscle are poorly described.

Methods: 18 C57Bl6 mice were divided into two groups: Control and AX supplemented in rodent chow for 4 weeks (AstaReal A1010). In vivo and in vitro force and intracellular calcium homeostasis was studied. In some experiments acute treatment with retinol was employed.

Results: The voltage activation of calcium transients (V_{50}) were investigated in single flexor digitorum brevis isolated fibers under patch clamp and no significant changes were found following AX supplementation. Retinol shifted V_{50} towards more positive values and decreased the peak F/F_0 of the calcium transients. The amplitude of tetani in the extensor digitorum longus was significantly higher in AX than in control group. Lastly, the mitochondrial calcium uptake was found to be less prominent in AX.

Conclusion: AX supplementation increases in vitro tetanic force without affecting ECC and exerts a protecting effect on the mitochondria. Retinol treatment has an inhibitory effect on ECC in skeletal muscle.

Astaxanthin reduces pro-inflammatory cytokines and reactive oxygen species in mice.

[Mar Drugs](#). 2015 May 27;13(6):3368-87. doi: 10.3390/md13063368.

Astaxanthin Pretreatment Attenuates Hepatic Ischemia Reperfusion-Induced Apoptosis and Autophagy via the ROS/MAPK Pathway in Mice.

[Li J](#)¹, [Wang F](#)², [Xia Y](#)³, [Dai W](#)⁴, [Chen K](#)⁵, [Li S](#)⁶, [Liu T](#)⁷, [Zheng Y](#)⁸, [Wang J](#)⁹, [Lu W](#)¹⁰, [Zhou Y](#)¹¹, [Yin Q](#)¹², [Lu J](#)¹, [Zhou Y](#)⁸, [Guo C](#)¹³.

Author information

Abstract

BACKGROUND:

Hepatic ischemia reperfusion (IR) is an important issue in complex liver resection and liver transplantation. The aim of the present study was to determine the protective effect of astaxanthin (ASX), an antioxidant, on hepatic IR injury via the reactive oxygen species/mitogen-activated protein kinase (ROS/MAPK) pathway.

METHODS:

Mice were randomized into a sham, IR, ASX or IR + ASX group. The mice received ASX at different doses (30 mg/kg or 60 mg/kg) for 14 days. Serum and tissue samples at 2 h, 8 h and 24 h after abdominal surgery were collected to assess alanine aminotransferase (ALT), aspartate aminotransferase (AST), inflammation factors, ROS, and key proteins in the MAPK family.

RESULTS:

ASX reduced the release of ROS and cytokines leading to inhibition of apoptosis and autophagy via down-regulation of the activated phosphorylation of related proteins in the MAPK family, such as P38 MAPK, JNK and ERK in this model of hepatic IR injury.

CONCLUSION:

Apoptosis and autophagy caused by hepatic IR injury were inhibited by ASX following a reduction in the release of ROS and inflammatory cytokines, and the relationship between the two may be associated with the inactivation of the MAPK family.

KEYWORDS:

astaxanthin; hepatic ischemia reperfusion; oxidative stress; reactive oxygen species

PMID:

26023842

[PubMed - in process]

PMCID:

PMC4483634

[Free PMC Article](#)

Astaxanthin provides neuroprotection by inhibiting inflammation in mice.

[Cell Mol Neurobiol.](#) 2015 May 14. [Epub ahead of print]

Anti-inflammatory Effect of Astaxanthin on the Sickness Behavior Induced by Diabetes Mellitus.

[Ying CJ](#)¹, [Zhang F](#), [Zhou XY](#), [Hu XT](#), [Chen J](#), [Wen XR](#), [Sun Y](#), [Zheng KY](#), [Tang RX](#), [Song YJ](#).
Author information

Abstract

Chronic inflammation appears to play a critical role in sickness behavior caused by diabetes mellitus. Astaxanthin has been used in treating diabetes mellitus and diabetic complications because of its neuroprotective and anti-inflammatory actions. However, whether astaxanthin can improve sickness behavior induced by diabetes and its potential mechanisms are still unknown. The aim of this study was to investigate the effects of astaxanthin on diabetes-elicited abnormal behavior in mice and its corresponding mechanisms. An experimental diabetic model was induced by streptozotocin (150 mg/kg) and astaxanthin (25 mg/kg/day) was provided orally for 10 weeks. Body weight and water consumption were measured, and the sickness behavior was evaluated by the open field test (OFT) and closed field test (CFT). The expression of glial fibrillary acidic protein (GFAP) was measured, and the frontal cortical cleaved caspase-3 positive cells, interleukin-6 (IL-6), and interleukin-1 β (IL-1 β) expression levels were also investigated. Furthermore, cystathionine β -synthase (CBS) in the frontal cortex was detected to determine whether the protective effect of astaxanthin on sickness behavior in diabetic mice is closely related to CBS. As expected, we observed that astaxanthin improved general symptoms and significantly increase horizontal distance and the number of crossings in the OFT and CFT. Furthermore, data showed that astaxanthin could decrease GFAP-positive cells in the brain and down-regulate the cleaved caspase-3, IL-6, and IL-1 β , and up-regulate CBS in the frontal cortex. These results suggest that astaxanthin provides neuroprotection against diabetes-induced sickness behavior through inhibiting inflammation, and the protective effects may involve CBS expression in the brain.

PMID:

25971983

[PubMed - as supplied by publisher]

Astaxanthin reduces neuropathic pain in rat and in-vitro models.

[Neurosci Lett](#). 2018 May 1;674:162-170. doi: 10.1016/j.neulet.2018.03.030. Epub 2018 Mar 17.

Astaxanthin ameliorates behavioral and biochemical alterations in in-vitro and in-vivo model of neuropathic pain.

[Sharma K¹](#), [Sharma D¹](#), [Sharma M¹](#), [Sharma N¹](#), [Bidve P¹](#), [Prajapati N¹](#), [Kalia K¹](#), [Tiwari V²](#).

Author information

Abstract

Despite considerable advances in understanding mechanisms involved in chronic pain, effective treatment remains limited. Astaxanthin, a marine natural drug, having potent anti-oxidant and anti-inflammatory activities is known to possess neuroprotective effects. However, effects of astaxanthin against nerve injury induce chronic pain remains unknown. Overactivity of glutamatergic NMDARs results in excitotoxicity which may participate in astrocytic and microglial activation during pathology which further contribute to the development of neuropathic pain. In this study, we investigate the effects of astaxanthin on oxido-inflammatory and NMDA receptor down-regulation pathway by using in-silico, in-vitro and in-vivo models of neuropathic pain. In-silico molecular docking study ascertained the binding affinity of astaxanthin to NMDA receptors and showed antagonistic effects. Data from in-vitro studies suggest that astaxanthin significantly reduces the oxidative stress induced by the lipopolysaccharides in C6 glial cells. In male Sprague dawley rats, a significant attenuation of neuropathic pain behavior was observed in Hargreaves test and von Frey hair test after astaxanthin treatment. Findings from the current study suggest that astaxanthin can be used as potential alternative in the treatment of chronic neuropathic pain. However, more detailed investigations are required to further probe the in-depth mechanism of action of astaxanthin.

KEYWORDS:

C6 glial cells; Mechanical allodynia; NMDA receptors; Neuropathic pain; Neuroprotection; Rats

PMID: 29559419

DOI: [10.1016/j.neulet.2018.03.030](https://doi.org/10.1016/j.neulet.2018.03.030)

Astaxanthin reduces inflammation and oxidation in kidneys of mice.

[J Transl Med.](#) 2015 Jan 27;13:28. doi: 10.1186/s12967-015-0388-1.

Protective effects of astaxanthin against ischemia/reperfusion induced renal injury in mice.

[Qiu X](#)^{1,2,3}, [Fu K](#)^{4,5}, [Zhao X](#)^{6,7}, [Zhang Y](#)⁸, [Yuan Y](#)⁹, [Zhang S](#)¹⁰, [Gu X](#)¹¹, [Guo H](#)¹².

Author information

Abstract

Astaxanthin (ATX) is a powerful antioxidant that occurs naturally in a wide variety of living organisms. Previous studies have shown that ATX has effects of eliminating oxygen free radicals and can protect organs from ischemia/reperfusion (IR) induced injury. The present study was designed to further investigate the protective effects of ATX on oxidative stress induced toxicity in tubular epithelial cells and on IR induced renal injury in mice. ATX, at a concentration of 250 nM, attenuated 100 μ M H₂O₂-induced viability decrease of tubular epithelial cells. In vivo, ATX preserved renal function 12 h or 24 h post IR. Pretreatment of ATX via oral gavage for 14 consecutive days prior to IR dramatically prevented IR induced histological damage 24 h post IR. Histological results showed that the pathohistological score, number of apoptotic cells, and the expression of α -smooth muscle actin were significantly decreased by pretreatment of ATX. In addition, oxidative stress and inflammation in kidney samples were significantly reduced by ATX 24 h post IR. Taken together, the current study suggests that pretreatment of ATX is effective in preserving renal function and histology via antioxidant activity.

PMID:

25623758

[PubMed - in process]

PMCID:

PMC4323259

[Free PMC Article](#)

Astaxanthin protects against diabetes-induced hepatic inflammation and oxidative stress in rats.

[J Med Food](#). 2015 Mar;18(3):337-44. doi: 10.1089/jmf.2014.3174. Epub 2015 Jan 8.

Astaxanthin and Corni Fructus protect against diabetes-induced oxidative stress, inflammation, and advanced glycation end product in livers of streptozotocin-induced diabetic rats.

[Park CH¹](#), [Xu FH](#), [Roh SS](#), [Song YO](#), [Uebaba K](#), [Noh JS](#), [Yokozawa T](#).

Author information

Abstract

This study was conducted to compare the protective effects of astaxanthin (ASX) with Corni Fructus (CF) against diabetes-induced pathologies such as oxidative stress-induced inflammation and advanced glycation end product (AGE) formation in the liver of type 1 diabetic rats. ASX (50 mg/kg body weight/day) or CF (200 mg/kg body weight/day) was orally administered every day for 18 days to streptozotocin (STZ)-induced diabetic rats, and their effects were compared with nondiabetic and diabetic control rats. The administration of CF, but not ASX, decreased both the elevated serum and hepatic glucose concentration in diabetic rats. In diabetic rats, increased levels of AGE, reactive oxygen species, and lipid peroxidation were significantly decreased by treatment with both ASX and CF in the liver of diabetic rats. STZ treatment markedly augmented the protein expressions of AGE, and both ASX and CF efficiently attenuated these increases in hepatic protein expressions. In addition, oxidative stress and proinflammatory protein expressions were upregulated in the diabetic rats. On the contrary, these upregulations of protein expressions were decreased by the administration of ASX or CF. These results suggest that the inhibitory effect of ASX on diabetes-induced hepatic dysfunction could be derived from the blocking of AGE formation and further anti-inflammation and that CF exhibited beneficial effects through the attenuation of hyperglycemia, and thus the inhibition of AGE formation and the inflammatory responses. Therefore, ASX as well as CF may help prevent ongoing diabetes-induced hepatic injury.

KEYWORDS:

AGE; Corni Fructus; astaxanthin; inflammation; oxidative stress; streptozotocin-induced diabetes

PMID:

25569034

[PubMed - in process]

Astaxanthin inhibits the formation of pre-malignant colon lesions in mice by suppressing chronic inflammation and oxidative stress.

[BMC Gastroenterol.](#) 2014 Dec 17;14:212. doi: 10.1186/s12876-014-0212-z.

Inhibitory effects of astaxanthin on azoxymethane-induced colonic preneoplastic lesions in C57/BL/KsJ-db/db mice.

[Kochi T](#)¹, [Shimizu M](#)², [Sumi T](#)³, [Kubota M](#)⁴, [Shirakami Y](#)⁵, [Tanaka T](#)⁶, [Moriwaki H](#)⁷.

Author information

Abstract

BACKGROUND:

Obesity and related metabolic abnormalities, including excess oxidative stress and chronic inflammation, are associated with colorectal carcinogenesis. Astaxanthin, a xanthophyll carotenoid found in aquatic animals, is known to possess antioxidant, anti-inflammatory, and antineoplastic properties. The present study examined the effects of astaxanthin on the development of azoxymethane (AOM)-induced colonic premalignant lesions in C57BL/KsJ-db/db (db/db) obese mice.

METHOD:

Male db/db mice were administered 4 weekly subcutaneous injections of AOM (15 mg/kg body weight) from 5 weeks of age and subsequently, from 1 week after the last injection of AOM, were fed a diet containing 200 ppm astaxanthin throughout the experiment (8 weeks).

RESULT:

The development of colonic premalignant lesions, i.e., aberrant crypt foci and β -catenin accumulated crypts, was significantly inhibited in mice treated with astaxanthin than in mice fed the basal diet. Astaxanthin administration markedly reduced urinary levels of 8-OHdG and serum levels of d-ROMs, which are oxidative stress markers, while increasing the expression of mRNA for the antioxidant enzymes GPx1, SOD1, and CAT in the colonic mucosa of AOM-treated db/db mice. The expression levels of IL-1 β , IL-6, F4/80, CCL2, and CXCL2 mRNA in the colonic mucosa of AOM-treated mice were significantly decreased by astaxanthin. Dietary feeding with astaxanthin also resulted in a reduction in the numbers of NF- κ B- and PCNA-positive cells that were increased by AOM exposure, in the colonic epithelium.

CONCLUSION:

These findings suggest that astaxanthin inhibits the development of colonic premalignant lesions in an obesity-related colorectal carcinogenesis model by reducing oxidative stress, attenuating chronic inflammation, and inhibiting NF- κ B activation and cell proliferation in the colonic mucosa. Astaxanthin, therefore, may be a potential candidate as a chemoprevention agent against colorectal carcinogenesis in obese individuals.

PMID: 25515685 [PubMed - in process] PMCID:

PMC4273491

[Free PMC Article](#)

Astaxanthin may prevent obesity-associated metabolic disturbances and inflammation.

[Br J Nutr.](#) 2014 Dec 14;112(11):1797-804. doi: 10.1017/S0007114514002554. Epub 2014 Oct 20.

Astaxanthin lowers plasma TAG concentrations and increases hepatic antioxidant gene expression in diet-induced obesity mice.

[Yang Y¹](#), [Pham TX¹](#), [Wegner CJ¹](#), [Kim B¹](#), [Ku CS¹](#), [Park YK¹](#), [Lee JY¹](#).

Author information

Abstract

Non-alcoholic fatty liver disease (NAFLD) is significantly associated with hyperlipidaemia and oxidative stress. We have previously reported that astaxanthin (ASTX), a xanthophyll carotenoid, lowers plasma total cholesterol and TAG concentrations in apoE knockout mice. To investigate whether ASTX supplementation can prevent the development of NAFLD in obesity, male C57BL/6J mice (n 8 per group) were fed a high-fat diet (35%, w/w) supplemented with 0, 0.003, 0.01 or 0.03% of ASTX (w/w) for 12 weeks. The 0.03% ASTX-supplemented group, but not the other groups, exhibited a significant decrease in plasma TAG concentrations, suggesting that ASTX at a 0.03% supplementation dosage exerts a hypotriacylglycerolaemic effect. Although there was an increase in the mRNA expression of fatty acid synthase and diglyceride acyltransferase 2, the mRNA levels of acyl-CoA oxidase 1, a critical enzyme in peroxisomal fatty acid β -oxidation, exhibited an increase in the 0.03% ASTX-supplemented group. There was a decrease in plasma alanine transaminase (ALT) and aspartate transaminase (AST) concentrations in the 0.03% ASTX-supplemented group. There was a significant increase in the hepatic mRNA expression of nuclear factor erythroid 2-related factor 2 and its downstream genes, which are critical for endogenous antioxidant mechanism, in the 0.03% ASTX-supplemented group. Furthermore, there was a significant decrease in the mRNA abundance of IL-6 in the primary splenocytes isolated from the 0.03% ASTX-supplemented group upon lipopolysaccharide (LPS) stimulation when compared with that in the splenocytes isolated from the control group. In conclusion, ASTX supplementation lowered the plasma concentrations of TAG, ALT and AST, increased the hepatic expression of endogenous antioxidant genes, and rendered splenocytes less sensitive to LPS stimulation. Therefore, ASTX may prevent obesity-associated metabolic disturbances and inflammation.

PMID:

25328157

[PubMed - indexed for MEDLINE]

Astaxanthin found to have neuroprotective effect which may be due to suppression of cerebral inflammation.

[J Surg Res.](#) 2014 Nov;192(1):206-13. doi: 10.1016/j.jss.2014.05.029. Epub 2014 May 21.

Astaxanthin offers neuroprotection and reduces neuroinflammation in experimental subarachnoid hemorrhage.

[Zhang XS¹](#), [Zhang X²](#), [Wu Q¹](#), [Li W¹](#), [Wang CX¹](#), [Xie GB¹](#), [Zhou XM¹](#), [Shi JX¹](#), [Zhou ML³](#).

Author information

Abstract

BACKGROUND:

Neuroinflammation has been proven to play a crucial role in early brain injury pathogenesis and represents a target for treatment of subarachnoid hemorrhage (SAH). Astaxanthin (ATX), a dietary carotenoid, has been shown to have powerful anti-inflammation property in various models of tissue injury. However, the potential effects of ATX on neuroinflammation in SAH remain uninvestigated. The goal of this study was to investigate the protective effects of ATX on neuroinflammation in a rat prechiasmatic cistern SAH model.

METHODS:

Rats were randomly distributed into multiple groups undergoing the sham surgery or SAH procedures, and ATX (25 mg/kg or 75 mg/kg) or equal volume of vehicle was given by oral gavage at 30 min after SAH. All rats were sacrificed at 24 h after SAH. Neurologic scores, brain water content, blood-brain barrier permeability, and neuronal cell death were examined. Brain inflammation was evaluated by means of expression changes in myeloperoxidase, cytokines (interleukin-1 β , tumor necrosis factor- α), adhesion molecules (intercellular adhesion molecule-1), and nuclear factor kappa B DNA-binding activity.

RESULTS:

Our data indicated that post-SAH treatment with high dose of ATX could significantly downregulate the increased nuclear factor kappa B activity and the expression of inflammatory cytokines and intercellular adhesion molecule-1 in both messenger RNA transcription and protein synthesis. Moreover, these beneficial effects lead to the amelioration of the secondary brain injury cascades including cerebral edema, blood-brain barrier disruption, neurological dysfunction, and neuronal degeneration.

CONCLUSIONS:

These results indicate that ATX treatment is neuroprotective against SAH, possibly through suppression of cerebral inflammation.

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KEYWORDS:

Astaxanthin; Early brain injury; Inflammation; Subarachnoid hemorrhage

PMID:

24948541

[PubMed - indexed for MEDLINE]

Astaxanthin found to protect against fetal alcohol spectrum disorder in mice possibly due to reduction of oxidative stress and inflammation.

[Neuropharmacology](#). 2014 Sep;84:13-8. doi: 10.1016/j.neuropharm.2014.04.013. Epub 2014 Apr 26.

The protective effect of astaxanthin on fetal alcohol spectrum disorder in mice.

[Zheng D¹](#), [Li Y²](#), [He L²](#), [Tang Y²](#), [Li X²](#), [Shen Q²](#), [Yin D³](#), [Peng Y⁴](#).

Author information

Abstract

Astaxanthin is a strong antioxidant with the ability of reducing the markers of inflammation. To explore the protective effect of astaxanthin on maternal ethanol induced embryonic deficiency, and to investigate the underlying mechanisms, we detected the morphology, expression of neural marker genes, oxidative stress indexes, and inflammatory factors in mice model of fetal alcohol spectrum disorder with or without astaxanthin pretreatment. Our results showed that astaxanthin blocked maternal ethanol induced retardation of embryonic growth, and the down-regulation of neural marker genes, Otx1 and Sox2. Moreover, astaxanthin also reversed the increases of malondialdehyde (MDA), hydrogen peroxide (H₂O₂), and the decrease of glutathione peroxidase (GPx) in fetal alcohol spectrum disorder. In addition, maternal ethanol induced up-regulation of toll-like receptor 4 (TLR4), and the down-streaming myeloid differentiation factor 88 (MyD88), NF-κB, TNF-α, and IL-1β in embryos, and this was inhibited by astaxanthin pretreatment. These results demonstrated a protective effect of astaxanthin on fetal alcohol spectrum disorder, and suggested that oxidative stress and TLR4 signaling associated inflammatory reaction are involved in this process.

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KEYWORDS:

Astaxanthin; Embryo; Ethanol

PMID:

24780381

[PubMed - indexed for MEDLINE]

Astaxanthin in combination with fish oil alleviates atherosclerosis risk factors and can improve inflammation, oxidative stress and lipid abnormalities.

[Lipids Health Dis.](#) 2014 Apr 4;13:63. doi: 10.1186/1476-511X-13-63.

A combination of flaxseed oil and astaxanthin alleviates atherosclerosis risk factors in high fat diet fed rats.

[Xu J](#), [Gao H](#), [Zhang L](#), [Chen C](#), [Yang W](#), [Deng Q](#), [Huang Q](#), [Huang F](#)¹.

Author information

Abstract

BACKGROUND:

Atherosclerosis is the most common pathologic process underlying cardiovascular disease. Both flaxseed oil (FO) and astaxanthin(ASX) are believed to benefit cardiovascular system. The combined effect of FO and ASX on the atherosclerosis risk factors in rats fed a high-fat diet was investigated.

METHODS:

Astaxanthin was dissolved in flaxseed oil to a final concentration of 1g/kg (FO + ASX). Male Sprague-Dawley rats were fed a rodent diet contained 20% fat whose source was lard (HFD) or 75% lard and 25% FO + ASX (50 mg ASX/kg diet) or 50% lard and 50% FO + ASX (100 mg ASX/kg diet) or FO + ASX (200 mg ASX/kg diet) for 10 weeks.

RESULTS:

The combination of FO and ASX significantly increased the antioxidant defense capacity and decreased lipid peroxidation in plasma. Evident decreases in the levels TG, TC and LDL-C contents, as well as IL-6 and CRP were also observed in plasma of FO and ASX fed rats.

CONCLUSION:

The combination of FO and ASX can improve oxidative stress, lipid abnormalities and inflammation, providing evidence that the combination of FO and ASX could be a promising functional food in cardiovascular health promotion.

PMID:

24708887

[PubMed - indexed for MEDLINE]

PMCID:

PMC3994197

Free PMC Article

Astaxanthin protects against UV-induced inflammation.

[Exp Dermatol](#). 2014 Mar;23(3):178-83. doi: 10.1111/exd.12347.

Astaxanthin, a xanthophyll carotenoid, inhibits ultraviolet-induced apoptosis in keratinocytes.

[Yoshihisa Y¹](#), [Rehman MU](#), [Shimizu T](#).

Author information

Abstract

Intra-cellular reactive nitrogen/oxygen species and apoptosis play important roles in ultraviolet (UV)-induced inflammatory responses in the skin. Astaxanthin (AST), a xanthophyll carotenoid, exhibits diverse clinical benefits. The protective effects of AST against UV-induced apoptosis were investigated in the present study. Astaxanthin (5 μ m) caused a significant decrease in the protein content and the mRNA levels of inducible nitric oxide (iNOS) and cyclooxygenase (COX)-2, and decreased the release of prostaglandin E2 from HaCaT keratinocytes after UVB (20 mJ/cm²) or UVC (5 mJ/cm²) irradiation. No significant protective effects against UV-induced reactive oxygen species (ROS) were observed in AST-pretreated cells. Astaxanthin caused a significant inhibition of UV-irradiation-induced apoptosis, as evidenced by a DNA fragmentation assay. Furthermore, we found that the treatment with AST caused a reduction in the UVB- or UVC-induced protein and mRNA expression of macrophage migration inhibitory factor (MIF), IL-1 β and TNF- α in HaCaT keratinocytes. These results suggest that AST effectively protects against UV-induced inflammation by decreasing iNOS and COX-2, and thereby inhibiting the apoptosis of keratinocytes.

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KEYWORDS:

apoptosis; astaxanthin; keratinocyte; reactive oxygen species; ultraviolet

PMID:

24521161

[PubMed - indexed for MEDLINE]

Astaxanthin reduces inflammation and liver stress in mice fed a high fructose / high fat diet.

[Cell Stress Chaperones](#). 2014 Mar;19(2):183-91. doi: 10.1007/s12192-013-0443-x. Epub 2013 Jul 14.

Astaxanthin reduces hepatic endoplasmic reticulum stress and nuclear factor- κ B-mediated inflammation in high fructose and high fat diet-fed mice.

[Bhuvaneswari S¹](#), [Yogalakshmi B](#), [Sreeja S](#), [Anuradha CV](#).

Author information

Abstract

We recently showed that astaxanthin (ASX), a xanthophyll carotenoid, activates phosphatidylinositol 3-kinase pathway of insulin signaling and improves glucose metabolism in liver of high fructose-fat diet (HFFD)-fed mice. The aim of this study is to investigate whether ASX influences phosphorylation of c-Jun-N-terminal kinase 1 (JNK1), reactive oxygen species (ROS) production, endoplasmic reticulum (ER) stress, and inflammation in liver of HFFD-fed mice. Adult male *Mus musculus* mice were fed either with control diet or HFFD for 15 days. After this period, mice in each group were divided into two and administered ASX (2 mg/kg/day, p.o) in 0.3 ml olive oil or 0.3 ml olive oil alone for the next 45 days. At the end of 60 days, liver tissue was excised and examined for lipid accumulation (Oil red O staining), intracellular ROS production, ER stress, and inflammatory markers. Elevated ROS production, lipid accumulation, and increased hepatic expression of ER stress markers such as Ig-binding protein, PKR-like ER kinase, phosphorylated eukaryotic initiation factor 2 α , X-box binding protein 1, activating transcription factor 6, and the apoptotic marker caspase 12 were observed in the liver of the HFFD group. ASX significantly reversed these changes. This reduction was accompanied by reduced activation of JNK1 and I kappa B kinase β phosphorylation and nuclear factor-kappa B p65 nuclear translocation in ASX-treated HFFD mice. These findings suggest that alleviation of inflammation and ER stress by ASX could be a mechanism responsible for its beneficial effect in this model. ASX could be a promising treatment strategy for insulin resistant patients.

PMID:

23852435

[PubMed - indexed for MEDLINE]

PMCID:

PMC3933623

[Free PMC Article](#)

Astaxanthin may prevent inflammation-associated colon cancer in rodents.

[Curr Drug Targets](#). 2012 Dec;13(14):1689-97.

**Animal models of carcinogenesis in inflamed colorectum:
potential use in chemoprevention study.**

[Tanaka T](#)¹.

Author information

Abstract

Inflammation is a risk factor for cancer development in several tissues. In the colorectum, inflammatory bowel disease (ulcerative colitis and Crohn's disease) is a longstanding inflammatory disease with increased risk for colorectal cancer (CRC). Several molecular events involving in chronic inflammatory process contribute to multi-stage carcinogenesis of CRC in the inflamed colon. They include alterations in production of reactive oxygen and nitrogen species, upregulation of pro-inflammatory cytokines and inflammatory enzymes, and intestinal immune system. In this short review, experimental animal models of inflammation-associated CRC are described. Also, some preclinical data on chemoprevention of inflammation-associated CRC by astaxanthin and a specific inhibitor of nitric oxide synthase using these inflammation-related CRC models is briefly introduced.

PMID:

23140280

[PubMed - indexed for MEDLINE]

Astaxanthin reduces oxidation-induced pro-inflammatory cytokines.

[Mar Drugs](#). 2012 Apr;10(4):890-9. doi: 10.3390/md10040890. Epub 2012 Apr 10.

Astaxanthin treatment reduced oxidative induced pro-inflammatory cytokines secretion in U937: SHP-1 as a novel biological target.

[Speranza L](#)¹, [Pesce M](#), [Patruno A](#), [Franceschelli S](#), [de Lutiis MA](#), [Grilli A](#), [Felaco M](#).

Author information

Abstract

It has been suggested that oxidative stress activates various intracellular signaling pathways leading to secretion of a variety of pro-inflammatory cytokines and chemokines. SHP-1 is a protein tyrosine phosphatase (PTP) which acts as a negative regulator of immune cytokine signaling. However, intracellular hydrogen peroxide (H₂O₂), generated endogenously upon stimulation and exogenously from environmental oxidants, has been known to be involved in the process of intracellular signaling through inhibiting various PTPs, including SHP-1. In this study, we investigated the potential role of astaxanthin, an antioxidant marine carotenoid, in re-establishing SHP-1 negative regulation on pro-inflammatory cytokines secretion in U-937 cell line stimulated with oxidative stimulus. ELISA measurement suggested that ASTA treatment (10 μM) reduced pro-inflammatory cytokines secretion (IL-1β, IL-6 and TNF-α) induced through H₂O₂, (100 μM). Furthermore, this property is elicited by restoration of basal SHP-1 protein expression level and reduced NF-κB (p65) nuclear expression, as showed by western blotting experiments.

KEYWORDS:

SHP-1 protein; astaxanthin; carotenoids; inflammation

PMID:

22690149

[PubMed - indexed for MEDLINE]

PMCID:

PMC3366681

Free PMC Article

Astaxanthin improves status of cells that imbed in cartilage and is suggested as a possible treatment for Osteoarthritis.

[Int Immunopharmacol.](#) 2014 Mar;19(1):174-7. doi: 10.1016/j.intimp.2013.12.007. Epub 2014 Jan 27.

Astaxanthin reduces matrix metalloproteinase expression in human chondrocytes.

[Chen WP¹](#), [Xiong Y¹](#), [Shi YX¹](#), [Hu PF¹](#), [Bao JP¹](#), [Wu LD²](#).

Author information

Abstract

Astaxanthin is a red carotenoid pigment which exerts multiple biological activities. However, little is known about the effects of astaxanthin on matrix metalloproteinases (MMPs) in OA. The present study investigated the effects of astaxanthin on MMPs in human chondrocytes. Human chondrocytes were pretreated with astaxanthin at 1, 10 or 50 μ M, then, cells were stimulated with IL-1 β (10ng/ml) for 24h. MMP-1, MMP-3 and MMP-13 were observed. We found that astaxanthin reduced the expression of MMP-1, MMP-3 and MMP-13 as well as the phosphorylation of two mitogen-activated protein kinases (MAPK) (p38 and ERK1/2) in IL-1 β -stimulated chondrocytes. Astaxanthin also blocked the I κ B- α degradation. These results suggest that astaxanthin may be beneficial in the treatment of OA.

KEYWORDS:

Astaxanthin; Matrix metalloproteinase; Osteoarthritis

PMID: 24480614

DOI: [10.1016/j.intimp.2013.12.007](#)

[Indexed for MEDLINE]

Astaxanthin reduces inflammatory cytokines induced by UVB exposure.

[Exp Dermatol.](#) 2012 Jul;21 Suppl 1:11-7. doi: 10.1111/j.1600-0625.2012.01496.x.

Astaxanthin attenuates the UVB-induced secretion of prostaglandin E2 and interleukin-8 in human keratinocytes by interrupting MSK1 phosphorylation in a ROS depletion-independent manner.

[Terazawa S](#)¹, [Nakaijima H](#), [Shingo M](#), [Niwano T](#), [Imokawa G](#).

Author information

Abstract

To elucidate the effects of redox balance regulation on cutaneous inflammation, we used the potent antioxidant astaxanthin (AX) to assess its effect on the UVB-induced secretion of PGE(2) and IL-8 in human keratinocytes and analysed its biological mechanism of action. The addition of AX (at 8 μ m) to human keratinocytes even after UVB irradiation significantly down-regulated the increased secretion of PGE(2) or IL-8. Those suppressive effects were accompanied by significantly decreased expression of genes encoding COX-2 or IL-8 as well as COX-2 protein. Analysis using a specific NF- κ B translocation inhibitor demonstrated that the UVB-stimulated secretion of PGE(2) and IL-8 was significantly abolished by its treatment prior to UVB irradiation. Western blotting of phosphorylated signalling molecules revealed that UVB irradiation (80 mJ/cm²) significantly stimulated the phosphorylation of p38, ERK and JNK, which was not suppressed by treatment with AX after irradiation. In contrast, AX significantly inhibited the UVB-increased phosphorylation of mitogen- and stress-activated protein kinase (MSK)-1, NF- κ Bp65 or CREB even when treated postirradiation. Further, the MSK1 inhibitor H89 significantly down-regulated the increased secretion of PGE(2) and IL-8 in UVB-exposed human keratinocytes, following post-irradiation treatment. These findings suggest that AX attenuates the auto-phosphorylation of MSK1 required for its activation, which results in the decreased phosphorylation of NF- κ Bp65, which in turn probably leads to a deficiency of NF- κ B DNA binding activity. This may be associated with the significant suppression of PGE(2) /IL-8 secretion via the down-regulated expression of COX-2 and IL-8 at the gene and/or protein levels.

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PMID:

22626465

[PubMed - indexed for MEDLINE]

Astaxanthin and other carotenoids can improve endothelial inflammation and oxidative stress.

[Nutrition](#). 2012 Jun;28(6):605-10. doi: 10.1016/j.nut.2011.11.028. Epub 2012 Apr 4.

Novel phytonutrient contributors to antioxidant protection against cardiovascular disease.

[Riccioni G](#)¹, [Speranza L](#), [Pesce M](#), [Cusenza S](#), [D'Orazio N](#), [Glade MJ](#).

Author information

Abstract

The associations linking endothelial inflammation, endothelial oxidative stress, and atherogenesis and the potential for dietary phytonutrients to decrease the impact of these associations were assessed. A detailed literature review was conducted and summarized. A large body of scientific evidence describes the interactions among endothelial inflammation, endothelial oxidative stress, and atherogenesis. A growing body of research indicates that several dietary phytonutrients (astaxanthin, lycopene, lutein, and glabridin) can decrease the risk for atherosclerosis by decreasing endothelial inflammation and oxidative stress. The consumption of foods or dietary supplements that provide astaxanthin, lycopene, lutein, and glabridin can ameliorate endothelial inflammation and oxidative stress, retard atherogenesis, and decrease the risk for atherogenic cardiovascular disease.

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PMID:

22480801

[PubMed - indexed for MEDLINE]

Astaxanthin inhibits colitis and colon cancer formation in mice by modulation of inflammatory cytokines.

[Chem Biol Interact.](#) 2011 Aug 15;193(1):79-87. doi: 10.1016/j.cbi.2011.05.006. Epub 2011 May 20.

Dietary astaxanthin inhibits colitis and colitis-associated colon carcinogenesis in mice via modulation of the inflammatory cytokines.

[Yasui Y¹](#), [Hosokawa M](#), [Mikami N](#), [Miyashita K](#), [Tanaka T](#).

Author information

Abstract

Astaxanthin (AX) is one of the marine carotenoid pigments, which possess powerful biological antioxidant, anti-inflammatory and anti-cancer properties. The purpose of this study is to investigate possible inhibitory effect of AX against inflammation-related mouse colon carcinogenesis and dextran sulfate sodium (DSS)-induced colitis in male ICR mice. We conducted two different experiments. In the first experiment, we evaluated the effects of AX at three dose levels, 50, 100 and 200 ppm in diet, on colitis-associated colon carcinogenesis induced by azoxymethane (AOM)/DSS in mice. In the second, the effects of the AX (100 and 200 ppm) in diet on DSS-induced colitis were determined. We found that dietary AX significantly inhibited the occurrence of colonic mucosal ulcers, dysplastic crypts, and colonic adenocarcinoma at week 20. AX-feeding suppressed expression of inflammatory cytokines, including nuclear factor (NF)- κ B, tumor necrosis factor (TNF)- α and interleukin (IL)-1 β , inhibited proliferation, and induced apoptosis in the colonic adenocarcinomas. Feeding with 200 ppm AX, but not 100 ppm, significantly inhibited the development of DSS-induced colitis. AX feeding (200 ppm in diet) also lowered the protein expression of NF- κ B, and the mRNA expression of inflammatory cytokines, including IL-1 β , IL-6, and cyclooxygenase (COX)-2. Our results suggest that the dietary AX suppresses the colitis and colitis-related colon carcinogenesis in mice, partly through inhibition of the expression of inflammatory cytokine and proliferation. Our findings suggest that AX is one of the candidates for prevention of colitis and inflammation-associated colon carcinogenesis in humans.

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PMID:

21621527

[PubMed - indexed for MEDLINE]

Astaxanthin inhibits *H. pylori*-induced mitochondrial dysfunction in vitro and has anti-inflammatory activity.

[Nutrients](#). 2018 Sep 18;10(9). pii: E1320. doi: 10.3390/nu10091320.

Astaxanthin Inhibits Mitochondrial Dysfunction and Interleukin-8 Expression in *Helicobacter pylori*-Infected Gastric Epithelial Cells.

Kim SH¹, Lim JW², Kim H³.

Author information

Abstract

Helicobacter pylori (*H. pylori*) infection leads to gastric inflammation, peptic ulcer and gastric carcinoma. *H. pylori* activates NADPH oxidase and increases reactive oxygen species (ROS), which induce NF- κ B activation and IL-8 expression in gastric epithelial cells.

Dysfunctional mitochondria trigger inflammatory cytokine production. Peroxisome proliferator-activated receptors- γ (PPAR- γ) regulate inflammatory response. Astaxanthin is a powerful antioxidant that protects cells against oxidative stress. The present study was aimed at determining whether astaxanthin inhibits *H. pylori*-induced mitochondrial dysfunction, NF- κ B activation, and IL-8 expression via PPAR- γ activation in gastric epithelial cells. Gastric epithelial AGS cells were treated with astaxanthin, NADPH oxidase inhibitor apocynin and PPAR- γ antagonist GW9662, and infected with *H. pylori*. As a result, *H. pylori* caused an increase in intracellular and mitochondrial ROS, NF- κ B activation and IL-8 expression, but decreased mitochondrial membrane potential and ATP level. Astaxanthin inhibited *H. pylori*-induced alterations (increased ROS, mitochondrial dysfunction, NF- κ B activation, and IL-8 expression). Astaxanthin activated PPAR- γ and its target gene catalase in *H. pylori*-infected cells. Apocynin reduced ROS and inhibited IL-8 expression while astaxanthin did not affect NADPH oxidase activity. Inhibitory effects of astaxanthin on ROS levels and IL-8 expression were suppressed by addition of GW9662. In conclusion, astaxanthin inhibits *H. pylori*-induced mitochondrial dysfunction and ROS-mediated IL-8 expression by activating PPAR- γ and catalase in gastric epithelial cells. Astaxanthin may be beneficial for preventing oxidative stress-mediated gastric inflammation-associated *H. pylori* infection.

KEYWORDS:

Helicobacter pylori; astaxanthin; gastric epithelial cells; mitochondrial dysfunction; reactive oxygen species

PMID: 30231525 PMCID: [PMC6164770](#) DOI: [10.3390/nu10091320](#) [Indexed for MEDLINE]

[Free PMC Article](#)

Astaxanthin heightens immune response and reduces DNA damage and inflammation in dogs.

[Vet Immunol Immunopathol.](#) 2011 Apr 15;140(3-4):199-206. doi: 10.1016/j.vetimm.2010.12.004. Epub 2010 Dec 14.

Dietary astaxanthin enhances immune response in dogs.

[Chew BP¹](#), [Mathison BD](#), [Hayek MG](#), [Massimino S](#), [Reinhart GA](#), [Park JS](#).

Author information

Abstract

No information is available on the possible role of astaxanthin on immune response in domestic canine. Female Beagle dogs (9-10 mo old; 8.2 ± 0.2 kg body weight) were fed 0, 10, 20 or 40 mg astaxanthin daily and blood sampled on wk 0, 6, 12, and 16 for assessing the following: lymphoproliferation, leukocyte subpopulations, natural killer (NK) cell cytotoxicity, and concentrations of blood astaxanthin, IgG, IgM and acute phase proteins. Delayed-type hypersensitivity (DTH) response was assessed on wk 0, 12 and 16. Plasma astaxanthin increased dose-dependently and reached maximum concentrations on wk 6. Dietary astaxanthin enhanced DTH response to vaccine, concanavalin A-induced lymphocyte proliferation (with the 20mg dose at wk 12) and NK cell cytotoxic activity. In addition, dietary astaxanthin increased concentrations of IgG and IgM, and B cell population. Plasma concentrations of C reactive protein were lower in astaxanthin-fed dogs. Therefore, dietary astaxanthin heightened cell-mediated and humoral immune response and reduced DNA damage and inflammation in dogs.

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PMID:

21208664

[PubMed - indexed for MEDLINE]

Astaxanthin inhibits colon tumors and increases cancer cell death by modulating inflammatory cytokines.

[Invest New Drugs](#). 2011 Apr;29(2):207-24. doi: 10.1007/s10637-009-9342-5. Epub 2009 Oct 30.

Astaxanthin inhibits tumor invasion by decreasing extracellular matrix production and induces apoptosis in experimental rat colon carcinogenesis by modulating the expressions of ERK-2, NFkB and COX-2.

[Nagendraprabhu P¹](#), [Sudhandiran G](#).

Author information

Abstract

Colon cancer is the third most malignant neoplasm in the world and it remains an important cause of mortality in Asian and Western countries. Astaxanthin (AST), a major component of carotenoids possesses attractive remedial features. The purpose of this study is to investigate the possible mechanism of action of astaxanthin against 1, 2 dimethyl hydrazine (DMH)-induced rat colon carcinogenesis. Wistar male rats were randomized into five groups, group 1 were control rats, group 2 were rats that received AST (15 mg/kg body wt p.o. everyday), rats in group 3 were induced with DMH (40 mg/kg body wt, s.c.), DMH-induced rats in groups 4 and 5 were either pre or post initiated with AST, respectively as in group 2. DMH-induced rats exhibited elevated expressions of Nuclear factor kappa B-p65 (NF- κ B-p65), Cyclooxygenase-2 (COX-2), Matrixmetallo proteinases (MMP) 2/9, Proliferating cell nuclear antigen (PCNA), and Extracellular signal-regulated kinase-2 (ERK-2) as confirmed by immunofluorescence. Further, Westernblot analysis of MMPs-2/9, ERK-2 and Protein kinase B (Akt) revealed increased expressions of these proteins in DMH-induced groups of rats. AST-treatment decreased the expressions of all these vital proteins, involved in colon carcinogenesis. The ability of AST to induce apoptosis in the colon of DMH-induced rats was confirmed by Annexin-V/PI staining in a confocal microscopy, DNA fragmentation analysis and expression of caspase-3 by Western blotting. In conclusion, astaxanthin exhibits anti-inflammatory and anti-cancer effects by inducing apoptosis in DMH-induced rat colon carcinogenesis by modulating the expressions of NFkB, COX-2, MMPs-2/9, Akt and ERK-2.

PMID:

19876598

[PubMed - indexed for MEDLINE]

Astaxanthin protects against inflammation, oxidative stress and apoptosis in epithelial cells exposed to high levels of glucose.

[J Agric Food Chem](#). 2009 Oct 14;57(19):8793-7. doi: 10.1021/jf9019745.

Protection against oxidative stress, inflammation, and apoptosis of high-glucose-exposed proximal tubular epithelial cells by astaxanthin.

[Kim YJ](#)¹, [Kim YA](#), [Yokozawa T](#).

Author information

Abstract

Astaxanthin is a carotenoid with powerful antioxidant properties that exists naturally in various plants, algae, and seafood. The purpose of the present study is to examine the protective action of astaxanthin against high-glucose-induced oxidative stress, inflammation, and apoptosis in proximal tubular epithelial cells (PTECs). To assess the efficacy of astaxanthin, several key markers and activities were measured, including lipid peroxidation, total reactive species (RS), superoxide (*O(2)), nitric oxide (NO*), and peroxynitrite (ONOO(-)), as well as expressions of inflammatory proteins, inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2), nuclear factor-kappa B (NF-kappaB) nuclear translocation, and levels of Bcl2/Bax protein. Results showed that astaxanthin effectively suppressed lipid peroxidation, total RS, *O(2), NO*, ONOO(-), iNOS and COX-2 protein levels, NF-kappaB nuclear translocation, and pro-apoptotic Bax, whereas it increased anti-apoptotic Bcl2 protein levels. On the basis of these findings, it was concluded that in PTECs, astaxanthin has a protective efficacy against several deleterious effects caused by high glucose exposure and proposed that astaxanthin should be explored further as a potential antidiabetic remedy for the treatment of diabetic nephropathy.

PMID:

19731916

[PubMed - indexed for MEDLINE]

Astaxanthin's anti-inflammatory activity linked to possible prevention of age-related macular degeneration in mice.

[Invest Ophthalmol Vis Sci.](#) 2008 Apr;49(4):1679-85. doi: 10.1167/iovs.07-1426.

Inhibition of choroidal neovascularization with an anti-inflammatory carotenoid astaxanthin.

[Izumi-Nagai K¹](#), [Nagai N](#), [Ohgami K](#), [Satofuka S](#), [Ozawa Y](#), [Tsubota K](#), [Ohno S](#), [Oike Y](#), [Ishida S](#).

Author information

Abstract

PURPOSE:

Astaxanthin (AST) is a carotenoid found in marine animals and vegetables. The purpose of the present study was to investigate the effect of AST on the development of experimental choroidal neovascularization (CNV) with underlying cellular and molecular mechanisms.

METHODS:

Laser photocoagulation was used to induce CNV in C57BL/6J mice. Mice were pretreated with intraperitoneal injections of AST daily for 3 days before photocoagulation, and treatments were continued daily until the end of the study. CNV response was analyzed by volumetric measurements 1 week after laser injury. Retinal pigment epithelium-choroid levels of IkappaB-alpha, intercellular adhesion molecule (ICAM)-1, monocyte chemotactic protein (MCP)-1, interleukin (IL)-6, vascular endothelial growth factor (VEGF), VEGF receptor (VEGFR)-1, and VEGFR-2 were examined by Western blotting or ELISA. AST was applied to capillary endothelial (b-End3) cells, macrophages, and RPE cells to analyze the activation of NF-kappaB and the expression of inflammatory molecules.

RESULTS:

The index of CNV volume was significantly suppressed by treatment with AST compared with that in vehicle-treated animals. AST treatment led to significant inhibition of macrophage infiltration into CNV and of the in vivo and in vitro expression of inflammation-related molecules, including VEGF, IL-6, ICAM-1, MCP-1, VEGFR-1, and VEGFR-2. Importantly, AST suppressed the activation of the NF-kappaB pathway, including IkappaB-alpha degradation and p65 nuclear translocation.

CONCLUSIONS:

AST treatment, together with inflammatory processes including NF-kappaB activation, subsequent upregulation of inflammatory molecules, and macrophage infiltration, led to significant suppression of CNV development. The present study suggests the possibility of AST supplementation as a therapeutic strategy to suppress CNV associated with AMD.

PMID:

18385091

[PubMed - indexed for MEDLINE]

Astaxanthin reduces inflammation in rats' eyes.

[Exp Eye Res.](#) 2006 Feb;82(2):275-81. Epub 2005 Aug 26.

Suppressive effects of astaxanthin against rat endotoxin-induced uveitis by inhibiting the NF-kappaB signaling pathway.

[Suzuki Y¹](#), [Ohgami K](#), [Shiratori K](#), [Jin XH](#), [Ilieva I](#), [Koyama Y](#), [Yazawa K](#), [Yoshida K](#), [Kase S](#), [Ohno S](#).

Author information

Abstract

We investigated the effects of astaxanthin (AST), a carotenoid, on endotoxin-induced uveitis (EIU), and over the course of the disease measured the expression of inflammatory cytokines and chemokines in the presence or absence of AST. EIU was induced in male Lewis rats by footpad injection of lipopolysaccharide (LPS). The animals were randomly divided to 12 groups with eight animals in each. Immediately after the inoculation, AST (1, 10, or 100 mg kg⁻¹) was injected intravenously. Aqueous humour was collected at 6, 12 and 24 hr after LPS inoculation and the number of infiltrating cells in the anterior chamber was counted. In addition, we assayed the concentration of protein, nitric oxide (NO), tumour necrosis factor-alpha (TNF-alpha) and prostaglandin E2 (PGE2). Immunohistochemical staining with a monoclonal antibody against activated NF-kappaB was performed in order to evaluate the effects of AST on NF-kappaB activation. Rats injected with AST showed a significant decrease in the number of infiltrating cells in the anterior chamber and additionally there was a significantly lower concentration of protein, NO, TNF-alpha and PGE2 in the aqueous humour. Moreover, even early stages of EIU were suppressed by injection of AST. The number of activated NF-kappaB-positive cells was lower in iris-ciliary bodies treated with 10 or 100 mg kg⁻¹ AST at 3 hr after LPS injection. These results suggest that AST reduces ocularinflammation in eyes with EIU by downregulating proinflammatory factors and by inhibiting the NF-kappaB-dependent signaling pathway.

PMID:

16126197

[PubMed - indexed for MEDLINE]

Astaxanthin reduces *H. pylori* bacteria infection and lowers inflammation levels in mice.

[Antimicrob Agents Chemother.](#) 2000 Sep;44(9):2452-7.

Astaxanthin-rich algal meal and vitamin C inhibit *Helicobacter pylori* infection in BALB/cA mice.

[Wang X¹](#), [Willén R](#), [Wadström T](#).

Author information

Abstract

Helicobacter pylori infection in humans is associated with chronic type B gastritis, peptic ulcer disease, and gastric carcinoma. A high intake of carotenoids and vitamin C has been proposed to prevent development of gastric malignancies. The aim of this study was to explore if the microalga *Haematococcus pluvialis* rich in the carotenoid astaxanthin and vitamin C can inhibit experimental *H. pylori* infection in a BALB/cA mouse model. Six-week-old BALB/cA mice were infected with the mouse-passaged *H. pylori* strain 119/95. At 2 weeks postinoculation mice were treated orally once daily for 10 days (i) with different doses of algal meal rich in astaxanthin (0.4, 2, and 4 g/kg of body weight, with the astaxanthin content at 10, 50, and 100 mg/kg, respectively), (ii) with a control meal (algal meal without astaxanthin, 4 g/kg), or (iii) with vitamin C (400 mg/kg). Five mice from each group were sacrificed 1 day after the cessation of treatment, and the other five animals were sacrificed 10 days after the cessation of treatment. Culture of *H. pylori* and determination of the inflammation score of the gastric mucosae were used to determine the outcome of the treatment. Mice treated with astaxanthin-rich algal meal or vitamin C showed significantly lower colonization levels and lower inflammation scores than those of untreated or control-meal-treated animals at 1 day and 10 days after the cessation of treatment. Lipid peroxidation was significantly decreased in mice treated with the astaxanthin-rich algal meal and vitamin C compared with that of animals not treated or treated with the control meal. Both astaxanthin-rich algal meal and vitamin C showed an inhibitory effect on *H. pylori* growth in vitro. In conclusion, antioxidants may be a new strategy for treating *H. pylori* infection in humans.

PMID:

10952594

[PubMed - indexed for MEDLINE]

PMCID:

PMC90084

Free PMC Article

Astaxanthin reduces infection of *H. pylori* and gas inflammation in mice.

[Immunol Lett.](#) 1999 Dec 1;70(3):185-9.

Treatment of *H. pylori* infected mice with antioxidant astaxanthin reduces gastric inflammation, bacterial load and modulates cytokine release by splenocytes.

[Bennedsen M¹](#), [Wang X](#), [Willén R](#), [Wadström T](#), [Andersen LP](#).

Author information

Abstract

Helicobacter pylori is a gram-negative bacterium affecting about half of the world population, causing chronic gastritis type B dominated by activated phagocytes. In some patients the disease evolves into gastric ulcer, duodenal ulcer, gastric cancer or MALT lymphoma. The pathogenesis is in part caused by the immunological response. In mouse models and in human disease, the mucosal immune response is characterized by activated phagocytes. Mucosal T-lymphocytes are producing IFN-gamma thus increasing mucosal inflammation and mucosal damage. A low dietary intake of antioxidants such as carotenoids and vitamin C may be an important factor for acquisition of *H. pylori* by humans. Dietary antioxidants may also affect both acquisition of the infection and the bacterial load of *H. pylori* infected mice. Antioxidants, including carotenoids, have anti-inflammatory effects. The aim of the present study was to investigate whether dietary antioxidant induced modulation of *H. pylori* in mice affected the cytokines produced by *H. pylori* specific T-cells. We found that treatment of *H. pylori* infected mice with an algal cell extract containing the antioxidant astaxanthin reduces bacterial load and gastric inflammation. These changes are associated with a shift of the T-lymphocyte response from a predominant Th1-response dominated by IFN-gamma to a Th1/Th2-response with IFN-gamma and IL-4. To our knowledge, a switch from a Th1-response to a mixed Th1/Th2-response during an ongoing infection has not been reported previously.

PMID:

10656672

[PubMed - indexed for MEDLINE]

Fish Shellfish Immunol. 2019 Mar;86:280-286.
doi: 10.1016/j.fsi.2018.11.011. Epub 2018 Nov 15.

Astaxanthin protects lipopolysaccharide-induced inflammatory response in *Channa argus* through inhibiting NF- κ B and MAPKs signaling pathways

[Mu-Yang Li](#)¹, [Li Sun](#)², [Xiao-Tian Niu](#)¹, [Xiu-Mei Chen](#)¹, [Jia-Xin Tian](#)¹, [Yi-Di Kong](#)¹, [Gui-Qin Wang](#)³

PMID: 30448447 DOI: [10.1016/j.fsi.2018.11.011](https://doi.org/10.1016/j.fsi.2018.11.011)

Abstract

The present study was conducted to evaluate the protective effects of astaxanthin against lipopolysaccharide (LPS)-induced inflammatory responses in *Channa argus* in vivo and ex vivo. Primary hepatocytes were exposed to different concentrations of LPS for 24 h to induce an inflammatory response, and the protective effects of astaxanthin against LPS-induced inflammation were studied ex vivo and in vivo. Hepatocytes exposed to LPS (5–20 $\mu\text{g mL}^{-1}$) alone for 24 h resulted in a significant increase in lactate dehydrogenase release (LDH), Nitric oxide (NO) production and Malondialdehyde (MDA) content, 10 $\mu\text{g mL}^{-1}$ LPS could induced inflammatory response in hepatocytes. Gene expression of TLR4, NF κ Bp65, MAPKp38, TNF- α , IL-6 and IL-1 β mRNA expression were also enhanced ex vivo ($p < 0.05$). In vivo test demonstrated that pretreatment with astaxanthin prevented the LPS-induced upregulation of pro-inflammatory cytokines TNF- α , IL-6 and IL-1 β . Besides, astaxanthin blocked the expression of Toll-like receptor 4 (TLR4) and then suppressed the phosphorylation of nuclear transcription factor-kappa B (NF- κ B) p65 and degradation inhibitor of NF- κ B α (I κ B α). Further study showed that astaxanthin could suppress the phosphorylation of p38, extracellular signal-regulated kinase (ERK) and c-jun NH2-terminal kinase (JNK) in mitogen-activated protein kinase (MAPK) signal pathway. In conclusion, our results suggest that astaxanthin played an anti-inflammatory role by regulating TLR4 and the NF- κ B and MAPK signaling pathways in *C. argus*.

ASTAXANTHIN PREVENTS HEAT STRESS IN COWS DUE TO ANTI-INFLAMMATORY AND ANTIOXIDANT ACTIVITY.

Trop Anim Health Prod. 2019 Jun;51(5):1125-1134.
doi: 10.1007/s11250-018-01793-y. Epub 2019 Jan 5.

Inhibition of NF- κ B signaling pathway by astaxanthin supplementation for prevention of heat stress-induced inflammatory changes and apoptosis in Karan Fries heifers

[Sunil Kumar](#)¹, [S V Singh](#)²

PMID: 30612290 DOI: [10.1007/s11250-018-01793-y](https://doi.org/10.1007/s11250-018-01793-y)

Abstract

Present study was conducted on 12 Karan Fries (Holstein Friesian X Tharparkar) heifers (10-12 months) to assess the effect of astaxanthin supplementation on heat stress amelioration and inhibition of NF- κ B signaling pathway for prevention of heat stress-induced inflammatory changes and apoptosis in the cell during the summer season. The heifers were randomly and equally divided into two groups, i.e., control (fed as per ICAR 2013) and treatment groups (additionally supplemented astaxanthin at a dose rate of 0.25 mg/kg BW/day/animal). Temperature humidity index used to assess the levels of summer stress during the experimental period. Blood samples were collected at the fortnightly interval for quantification of plasma cortisol and IL-12 from both the groups of the heifers and from collected blood samples, RNA was isolated and transcribed into cDNA for real time PCR, for genes expression of NF- κ B, IL-2, caspase-3, and Bcl-2. Plasma cortisol, IL-12 levels, and expression pattern of NF- κ B, IL-2, and caspase-3 were significantly ($P \leq 0.05$) lower in treatment group of Karan Fries heifers than control group, whereas, Bcl-2 was higher ($P \leq 0.05$) in astaxanthin supplemented group. The temperature humidity index had a positive correlation ($P \leq 0.05$) with plasma cortisol and IL-12 and expression pattern of NF- κ B, IL-2, and caspase-3. However, it was

negatively correlated with Bcl-2. The supplementation of astaxanthin can ameliorate the impact of summer stress through NF- κ B downregulation, might be due to the quenching of free radicals, which regulates the expression of pro-inflammatory mediators and apoptotic genes.

ASTAXANTHIN DEMONSTRATES ANTI-PLATELET ACTIVITY IN RATS FED A HIGH-CHOLESTEROL DIET DUE TO ANTIOXIDANT AND ANTI-INFLAMMATORY EFFECTS.

Platelets. 2020 May 7;1-10.

doi: 10.1080/09537104.2020.1756237. Online ahead of print.

Antiplatelet activity of astaxanthin in control- and high cholesterol-fed rats mediated by down-regulation of P2Y₁₂, inhibition of NF-κB, and increasing intracellular levels of cAMP

[Huda H Satti^{1,2}](#), [Eman F Khaleel^{3,4}](#), [Rehab M Badi^{3,5}](#), [Amany O Elrefaie^{1,6}](#), [Dalia G Mostafa^{3,7}](#)

- PMID: 32379559
- DOI: [10.1080/09537104.2020.1756237](https://doi.org/10.1080/09537104.2020.1756237)

Abstract

This study evaluated the antiplatelet effect of the plant carotenoid, astaxanthin (ASTX) in rats fed either control or high cholesterol plus cholic acid diet (HCCD) and possible underlying mechanisms. Adult male Wistar rats were divided into four groups (n = 8/each), namely, control (fed normal diet), control + ASTX (10 mg/kg/day), HCCD-fed rats, and HCCD + ASTX-treated rats. Diets and treatments were orally administered daily for 30 days. In both control and HCCD-fed rats, ASTX significantly increased fecal levels of triglycerides and cholesterol, reduced platelet count, prolonged bleeding time, and inhibited platelet aggregation. It also reduced platelet levels of reactive oxygen species (ROS) and Bcl-2; thromboxane B2 (TXB2) release; and the expression of P2Y₁₂, P-selectin, and CD36 receptors. Moreover, the activity NF-κB p65 and Akt was inhibited. Concomitantly, it increased the protein levels of cleaved caspase-3 and vasodilator-stimulated phosphoprotein (*p*-VASP) as well as intracellular levels of cAMP. However, in HCCD-fed rats, the effects of ASTX were associated with reduced serum levels of ox-LDL-c and fasting plasma glucose levels. In conclusion, antiplatelet effects of ASTX involve ROS scavenging, inhibiting NF-κB activity, down-regulating P2Y₁₂ expression, and increasing intracellular levels of cAMP that are attributed to its antioxidant, hypolipidemic, and anti-inflammatory effects.

ASTAXANTHIN SHOWS POTENTIAL TO REDUCE FUNGAL INFLAMMATION IN MICE.

Int J Ophthalmol. 2020 Nov 18;13(11):1681-1688.
doi: 10.18240/ijo.2020.11.01. eCollection 2020.

Anti-inflammatory effects of astaxanthin against fungal keratitis

[Yu Huan](#)¹, [Xu-Dong Peng](#)¹, [Jing Lin](#)¹, [Ying-Xue Zhang](#)², [Lu Zhan](#)¹, [Han Gao](#)¹, [Gui-Qiu Zhao](#)¹

- PMID: [33214996](#)
- PMCID: [PMC7590883](#)
- DOI: [10.18240/ijo.2020.11.01](#)

Free PMC article

Abstract

Aim: To characterize effect of astaxanthin (ASX) in *Aspergillus fumigatus* (*A. fumigatus*) induced keratitis in mouse model.

Methods: *In vivo*, fungal keratitis mouse model was established in C57BL/6 mice using *A. fumigatus*, followed by ASX or dimethyl sulfoxide (DMSO) treatment. Clinical responses were evaluated by clinical score and myeloperoxidase (MPO) assay. Inflammatory cytokines were assessed by reverse-transcription polymerase chain reaction (RT-PCR), Western blot, immunofluorescence, and enzyme-linked immunosorbent assay (ELISA).

Results: In animal model, ASX improved corneal transparency and clinical response, suppressed the expression of inflammatory cytokine like IL-1 β , TNF- α , and HMGB-1. Neutrophil levels have been shown to decrease in ASX-treated cornea by immunofluorescence and MPO. TLR2 and TLR4 levels were lower in ASX-treated group than DMSO-treated.

Conclusion: ASX can suppress inflammatory response and reduce inflammatory cytokine production in mice model with *A. fumigatus* keratitis.

Astaxanthin inhibits carrageenan-induced inflammation in rats.

[Physiol Chem Phys Med NMR](#). 1990;22(1):27-38.

Inhibition of oxidative injury of biological membranes by astaxanthin.

[Kurashige M¹](#), [Okimasu E](#), [Inoue M](#), [Utsumi K](#).

Author information

Abstract

The value of astaxanthin, a carotenoid pigment, in the treatment of oxidative injury is assessed. Astaxanthin protects the mitochondria of vitamin E-deficient rats from damage by Fe²⁺-catalyzed lipid peroxidation both in vivo and in vitro. The inhibitory effect of astaxanthin on mitochondrial lipid peroxidation is stronger than that of alpha-tocopherol. Thin layer chromatographic analysis shows that the change in phospholipid components of erythrocytes from vitamin E-deficient rats induced by Fe²⁺ and Fe³⁺-xanthine/xanthine oxidase system was significantly suppressed by astaxanthin. Carrageenan-induced inflammation of the paw is also significantly inhibited by administration of astaxanthin. These data indicate that astaxanthin functions as a potent antioxidant both in vivo and in vitro.

PMID:

2084711

[PubMed - indexed for MEDLINE]

Astaxanthin exerts anti-inflammatory and antioxidant effects in mice with kidney injury.

[Pharmacology](#). 2015;95(3-4):193-200. doi: 10.1159/000381314. Epub 2015 Apr 22.

Astaxanthin attenuates adriamycin-induced focal segmental glomerulosclerosis.

[Liu G¹](#), [Shi Y](#), [Peng X](#), [Liu H](#), [Peng Y](#), [He L](#).

Author information

Abstract

BACKGROUND/AIM:

Focal segmental glomerulosclerosis (FSGS) is a specific pattern of chronic renal injury with progressive glomerular scarring. The phenotypic alterations that contribute to FSGS include inflammatory response and oxidative stress. Astaxanthin (ATX) has a broad range of biological functions, particularly antioxidant and anti-inflammatory ones. This study was designed to evaluate the renoprotective effect of ATX treatment on Adriamycin-induced FSGS.

METHODS:

In Balb/c mice, Adriamycin nephropathy was induced by Adriamycin (10 mg/kg body weight, diluted in normal saline) via a tail vein on day 0. Then the mice were treated with ATX (50 mg/kg body weight) once daily by oral gavage, again starting on the day of Adriamycin injection and continued for 6 weeks. At 6 weeks, the mice were sacrificed; kidneys and blood samples were collected for further analysis.

RESULTS:

Animals that underwent intermittent exposure to ATX treatment exhibited significant improvements in renal functional parameters as well as in glomerular and interstitial fibrosis compared to those undergoing saline treatment in FSGS mouse models. ATX treatment exerted anti-inflammatory and antioxidant effects by promoting Nrf2 expression and suppressing renal nucleotide-binding oligomerization domain-like receptor protein 3 inflammasome activation.

CONCLUSION:

ATX might offer a ray of hope for ameliorating FSGS.

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PMID:

25924598

[PubMed - in process]

Astaxanthin reverses increases in several inflammatory and oxidative markers in rats with systemic inflammation.

[J Surg Res.](#) 2015 May 15;195(2):559-67. doi: 10.1016/j.jss.2015.02.026. Epub 2015 Feb 18.

Protective effect of astaxanthin against multiple organ injury in a rat model of sepsis.

[Zhou L¹](#), [Gao M²](#), [Xiao Z³](#), [Zhang J¹](#), [Li X¹](#), [Wang A⁴](#).

Author information

Abstract

BACKGROUND:

Astaxanthin, a xanthophyll carotenoid, holds exceptional promise as an antioxidant, anti-inflammatory, and anticancer agent. No evidence has been published whether it has protective effects on sepsis. The study aimed to investigate the potential effects of astaxanthin on sepsis and multiple organ dysfunctions.

MATERIALS AND METHODS:

Sepsis was induced by cecal ligation and puncture (CLP) in Sprague-Dawley rats. Animals subjected to CLP and sham-operated control rats were given vehicle or astaxanthin 100 mg/kg/d by oral gavage for 7 d before the operation. The rats were killed at the indicated time points, and the specimen was collected. Cytokines and multiorgan injury-associated enzymatic and oxidative stress indicators were investigated. Multiorgan tissues were assessed histologically, the peritoneal bacterial load and the 72-h survival was observed too.

RESULTS:

Sepsis resulted in a significant increase in serum tumor necrosis factor- α , interleukin-1 β , and interleukin-6 levels showing systemic inflammatory response; it also caused a remarkable decrease in the superoxide dismutase activity and a significant increase in the malondialdehyde content showing oxidative damage; sepsis caused a great increase in organ injury-associated indicators, including blood urea nitrogen, creatinine, lactate dehydrogenase, creatine kinase isoenzyme-MB isotype, alanine aminotransferase, and aspartate aminotransferase, which was confirmed by histologic examination. And there was a dramatical increase of colony-forming units in the peritoneal cavity in septic rats. Astaxanthin reversed these inflammatory and oxidant response, alleviated the organ injury, reduced the peritoneal bacterial load, and improved the survival of septic rats induced by CLP.

CONCLUSIONS:

Astaxanthin exerts impressively protective effects on CLP-induced multiple organ injury. It might be used as a potential treatment for clinical sepsis.

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KEYWORDS:

Astaxanthin; Cecal ligation and puncture; Multiple organ dysfunction syndrome; Sepsis

PMID:

25770740

[PubMed - in process]

Astaxanthin protects against autoimmune hepatitis by reducing the release of inflammatory factors.

[PLoS One](#). 2015 Mar 11;10(3):e0120440. doi: 10.1371/journal.pone.0120440. eCollection 2015.

Protective effects of astaxanthin on ConA-induced autoimmune hepatitis by the JNK/p-JNK pathway-mediated inhibition of autophagy and apoptosis.

[Li J¹](#), [Xia Y¹](#), [Liu T¹](#), [Wang J¹](#), [Dai W¹](#), [Wang F¹](#), [Zheng Y¹](#), [Chen K¹](#), [Li S¹](#), [Abudumijiti H¹](#), [Zhou Z²](#), [Wang J²](#), [Lu W²](#), [Zhu R²](#), [Yang J¹](#), [Zhang H³](#), [Yin Q³](#), [Wang C¹](#), [Zhou Y³](#), [Lu J¹](#), [Zhou Y¹](#), [Guo C¹](#).

Author information

Abstract

OBJECTIVE:

Astaxanthin, a potent antioxidant, exhibits a wide range of biological activities, including antioxidant, atherosclerosis and antitumor activities. However, its effect on concanavalin A (ConA)-induced autoimmune hepatitis remains unclear. The aim of this study was to investigate the protective effects of astaxanthin on ConA-induced hepatitis in mice, and to elucidate the mechanisms of regulation.

MATERIALS AND METHODS:

Autoimmune hepatitis was induced in Balb/C mice using ConA (25 mg/kg), and astaxanthin was orally administered daily at two doses (20 mg/kg and 40 mg/kg) for 14 days before ConA injection. Levels of serum liver enzymes and the histopathology of inflammatory cytokines and other marker proteins were determined at three time points (2, 8 and 24 h). Primary hepatocytes were pretreated with astaxanthin (80 μ M) in vitro 24 h before stimulation with TNF- α (10 ng/ml). The apoptosis rate and related protein expression were determined 24 h after the administration of TNF- α .

RESULTS:

Astaxanthin attenuated serum liver enzymes and pathological damage by reducing the release of inflammatory factors. It performed anti-apoptotic effects via the descending phosphorylation of Bcl-2 through the down-regulation of the JNK/p-JNK pathway.

CONCLUSION:

This research firstly expounded that astaxanthin reduced immune liver injury in ConA-induced autoimmune hepatitis. The mode of action appears to be downregulation of JNK/p-JNK-mediated apoptosis and autophagy.

PMID: 25761053 [PubMed - in process]

PMCID:

PMC4356569

[Free PMC Article](#)

Astaxanthin improves symptoms of preeclampsia [a condition that occurs during pregnancy wherein the patient has high blood pressure and signs of damage to another organ system, often the kidneys] by reducing inflammation and oxidative stress.

[Yao Xue Xue Bao](#). 2014 Oct;49(10):1400-5.

[Effect of astaxanthin on preeclampsia rat model].

[Article in Chinese]

[Xuan Rong-rong](#), [Gao Xin](#), [Wu W](#), [Chen HM](#).

Abstract

The effect of astaxanthin on N(Ω)-nitro-L-arginine methyl ester (L-NAME) induced preeclampsia disease rats was investigated. Thirty pregnant Sprague-Dawley rats were randomly divided into three groups (n = 10): blank group, L-NAME group and astaxanthin group. From day 5 to 20, astaxanthin group rats were treated with astaxanthin (25 mg x kg⁻¹ x d⁻¹ x bw⁻¹) from pregnancy (day 5). To establish the preeclamptic rat model, L-NAME group and astaxanthin group rats were injected with L-NAME (125 mg x kg⁻¹ x d⁻¹ x bw⁻¹) from days 10-20 of pregnancy. The blood pressure and urine protein were recorded. Serum of each group was collected and malondialdehyde (MDA), superoxide dismutase (SOD) and nitric oxide synthase (NOS) activities were analyzed. Pathological changes were observed with HE stain. The expression of NF- κ B (nuclear factor kappa B), ROCK II (Rho-associated protein kinase II), HO-1 (heme oxygenase-1) and Caspase 3 were analyzed with immunohistochemistry. L-NAME induced typical preeclampsia symptoms, such as the increased blood pressure, urinary protein, the content of MDA, etc. Astaxanthin significantly reduced the blood pressure (P < 0.01), the content of MDA (P < 0.05), and increased the activity of SOD (P < 0.05) of preeclampsia rats. The urinary protein, NO, and NOS were also decreased. HE stain revealed that after treated with astaxanthin, the thickness of basal membrane was improved and the content of trophoblast cells and spiral arteries was reduced. Immunohistochemistry results revealed that the expressions of NF- κ B, ROCK II and Caspase 3 in placenta tissue were effectively decreased, and HO-1 was increased. Results indicated that astaxanthin can improve the preeclampsia symptoms by effectively reducing the oxidative stress and inflammatory damages of preeclampsia. It revealed that astaxanthin may be benefit for prevention and treatment of preeclampsia disease.

PMID:

25577869

[PubMed - in process]

Astaxanthin protects cells from inflammation and oxidative stress caused by lipopolysaccharide reducing O₂-production.

[PLoS One](#). 2014 Feb 10;9(2):e88359. doi: 10.1371/journal.pone.0088359. eCollection 2014.

Astaxanthin treatment confers protection against oxidative stress in U937 cells stimulated with lipopolysaccharide reducing O₂- production.

[Franceschelli S](#)¹, [Pesce M](#)¹, [Ferrone A](#)¹, [De Lutiis MA](#)¹, [Patruno A](#)¹, [Grilli A](#)², [Felaco M](#)¹, [Speranza L](#)¹.

Author information

Abstract

Recently, astaxanthin (ASTA) studies have focused on several biological functions such as radical scavenging, singlet oxygen quenching, anti-carcinogenesis, anti-diabetic, anti-obesity, anti-inflammatory, anti-melanogenesis, and immune enhancement activities. In this study, we investigated the potential role protective of ASTA, an antioxidant marine carotenoid, in restoring physiological conditions in U937 cells stimulated with LPS (10 µg/ml). Our results show that pre-treatment with ASTA (10 µM) for 1 h attenuates the LPS-induced toxicity and ROS production. The beneficial effect of ASTA is associated with a reduction intracellular O₂ (-) production by restoring the antioxidant network activity of superoxide dismutase (SOD) and catalase (CAT), which influence HO-1 expression and activity by inhibiting nuclear translocation of Nrf2. We accordingly hypothesize that ASTA has therapeutic properties protecting U937 cells from LPS-induced inflammatory and oxidative stress.

PMID:

24520374

[PubMed - indexed for MEDLINE]

PMCID:

PMC3919765

Free PMC Article

Astaxanthin prevents mitochondrial dysfunction in *H. pylori*-infected gastric cells and mediates inflammatory markers.

[Nutrients](#). 2018 Sep 18;10(9). pii: E1320. doi: 10.3390/nu10091320.

Astaxanthin Inhibits Mitochondrial Dysfunction and Interleukin-8 Expression in *Helicobacter pylori*-Infected Gastric Epithelial Cells.

Kim SH¹, Lim JW², Kim H³.

Author information

Abstract

Helicobacter pylori (*H. pylori*) infection leads to gastric inflammation, peptic ulcer and gastric carcinoma. *H. pylori* activates NADPH oxidase and increases reactive oxygen species (ROS), which induce NF- κ B activation and IL-8 expression in gastric epithelial cells. Dysfunctional mitochondria trigger inflammatory cytokine production. Peroxisome proliferator-activated receptors- γ (PPAR- γ) regulate inflammatory response. Astaxanthin is a powerful antioxidant that protects cells against oxidative stress. The present study was aimed at determining whether astaxanthin inhibits *H. pylori*-induced mitochondrial dysfunction, NF- κ B activation, and IL-8 expression via PPAR- γ activation in gastric epithelial cells. Gastric epithelial AGS cells were treated with astaxanthin, NADPH oxidase inhibitor apocynin and PPAR- γ antagonist GW9662, and infected with *H. pylori*. As a result, *H. pylori* caused an increase in intracellular and mitochondrial ROS, NF- κ B activation and IL-8 expression, but decreased mitochondrial membrane potential and ATP level. Astaxanthin inhibited *H. pylori*-induced alterations (increased ROS, mitochondrial dysfunction, NF- κ B activation, and IL-8 expression). Astaxanthin activated PPAR- γ and its target gene catalase in *H. pylori*-infected cells. Apocynin reduced ROS and inhibited IL-8 expression while astaxanthin did not affect NADPH oxidase activity. Inhibitory effects of astaxanthin on ROS levels and IL-8 expression were suppressed by addition of GW9662. In conclusion, astaxanthin inhibits *H. pylori*-induced mitochondrial dysfunction and ROS-mediated IL-8 expression by activating PPAR- γ and catalase in gastric epithelial cells. Astaxanthin may be beneficial for preventing oxidative stress-mediated gastric inflammation-associated *H. pylori* infection.

KEYWORDS:

Helicobacter pylori; astaxanthin; gastric epithelial cells; mitochondrial dysfunction; reactive oxygen species

PMID: 30231525 PMCID: [PMC6164770](#) DOI: [10.3390/nu10091320](#)

[Indexed for MEDLINE]

[Free PMC Article](#)

Astaxanthin in combination with Vitamin C reduces inflammatory and oxidative markers in human neutrophils.

[Toxicol In Vitro](#). 2012 Oct;26(7):1181-90. doi: 10.1016/j.tiv.2012.06.010. Epub 2012 Jun 30.

Carbonyl stress and a combination of astaxanthin/vitamin C induce biochemical changes in human neutrophils.

[Guerra BA¹](#), [Bolin AP](#), [Otton R](#).

Author information

Abstract

The purpose of the present study was to find out whether co-treatment of human neutrophils with high glucose and methylglyoxal (MGO) can alter the biochemical parameters of human neutrophils. We also examined if astaxanthin associated with vitamin C can improve those biochemical parameters. Neutrophils from healthy subjects were treated with 20mM of glucose and 30 μ M MGO followed or not by the addition of the antioxidants astaxanthin (2 μ M) and vitamin C (100 μ M). MGO/high glucose treatment reduced the phagocytic capacity and the G6PDH, total/SOD and GR activities. Additionally, there was an increase in the activity of myeloperoxidase (MPO) with consequent increase in the hypochlorous acid production, CAT activity and in the release of IL-6 cytokine without changes in intracellular calcium mobilization. Our study also shows that the association of astaxanthin with vitamin C greatly improved neutrophil phagocytic capacity, decreasing all reactive oxygen species measured, pro-inflammatory IL-1 β and TNF- α release, MPO activity and HClO production. The combination of astaxanthin with vitamin C alone has more antioxidant and anti-inflammatory effects than when they were in the presence of MGO/high glucose. Injury to the function of neutrophils due to high glucose and methylglyoxal appears not to involve oxidative stress or calcium release. The association of antioxidants astaxanthin and vitamin C promoted a significant improvement in the function of neutrophils and in the redox status.

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PMID:

22750055

[PubMed - indexed for MEDLINE]

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Astaxanthin exhibits anti-inflammatory and anti-coagulatory effects in diabetic rats.

[J Food Sci.](#) 2012 Feb;77(2):H76-80. doi: 10.1111/j.1750-3841.2011.02558.x. Epub 2012 Feb 6.

Anticoagulatory and antiinflammatory effects of astaxanthin in diabetic rats.

[Chan KC¹](#), [Pen PJ](#), [Yin MC](#).

Author information

Abstract

Astaxanthin at 0.01 or 0.05% of the diet was supplied to diabetic rats for 12 wk. Astaxanthin intake significantly increased its deposit in plasma, and retained glutathione content, reduced the production of reactive oxygen species, interleukin-6, tumor necrosis factor- α , and monocyte chemoattractant protein-1 in blood and kidney of diabetic rats ($P < 0.05$). Astaxanthin treatments also significantly decreased plasma levels of C-reactive protein and von Willebrand factor in diabetic rats ($P < 0.05$). Astaxanthin intake at 0.05% significantly diminished plasminogen activator inhibitor-1 and factor VII activities, enhanced antithrombin-III and protein C activities in circulation ($P < 0.05$). These results support that astaxanthin could attenuate diabetes associated coagulatory, oxidative, and inflammatory stress.

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22309505

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Astaxanthin improves insulin sensitivity by reducing inflammation, oxidation and lipid accumulation in obese mice.

[Food Funct.](#) 2012 Feb;3(2):120-6. doi: 10.1039/c1fo10161g. Epub 2011 Nov 17.

An intervention study in obese mice with astaxanthin, a marine carotenoid--effects on insulin signaling and pro-inflammatory cytokines.

[Arunkumar E¹](#), [Bhuvanewari S](#), [Anuradha CV](#).

Author information

Abstract

Astaxanthin (ASX), a xanthophyll carotenoid from the marine algae *Hematococcus pluvialis*, has anti-obesity and insulin-sensitivity effects. The specific molecular mechanisms of its actions are not yet established. The present study was designed to investigate the mechanisms underlying the insulin sensitivity effects of ASX in a non-genetic insulin resistant animal model. A group of male Swiss albino mice was divided into two and fed either a starch-based control diet or a high fat-high fructose diet (HFFD). Fifteen days later, mice in each dietary group were divided into two and were treated with either ASX (6 mg kg⁻¹ per day) in olive oil or olive oil alone. At the end of 60 days, glucose, insulin and pro-inflammatory cytokines in plasma, lipids and oxidative stress markers in skeletal muscle and adipose tissue were assessed. Further, post-receptor insulin signaling events in skeletal muscle were analyzed. Increased body weight, hyperglycemia, hyperinsulinemia and increased plasma levels of tumor necrosis factor- α and interleukin-6 observed in HFFD-fed mice were significantly improved by ASX addition. ASX treatment also reduced lipid levels and oxidative stress in skeletal muscle and adipose tissue. ASX improved insulin signaling by enhancing the autophosphorylation of insulin receptor- β (IR- β), IRS-1 associated PI3-kinase step, phospho-Akt/Akt ratio and GLUT-4 translocation in skeletal muscle. This study demonstrates for the first time that chronic ASX administration improves insulin sensitivity by activating the post-receptor insulin signaling and by reducing oxidative stress, lipid accumulation and proinflammatory cytokines in obese mice.

PMID:

22089895

[PubMed - indexed for MEDLINE]

Astaxanthin shows neuroprotective effects which are attributed to its antioxidative and anti-inflammatory properties.

[J Food Sci.](#) 2009 Sep;74(7):H225-31. doi: 10.1111/j.1750-3841.2009.01274.x.

Antioxidative and anti-inflammatory neuroprotective effects of astaxanthin and canthaxanthin in nerve growth factor differentiated PC12 cells.

[Chan KC¹](#), [Mong MC](#), [Yin MC](#).

Author information

Abstract

Nerve growth factor differentiated PC12 cells were used to examine the antioxidative and anti-inflammatory effects of astaxanthin (AX) and canthaxanthin (CX). PC12 cells were pretreated with AX or CX at 10 or 20 μ M, and followed by exposure of hydrogen peroxide (H₂O₂) or 1-methyl-4-phenylpyridinium ion (MPP(+)) to induce cell injury. H₂O₂ or MPP(+) treatment significantly decreased cell viability, increased lactate dehydrogenase (LDH) release, enhanced DNA fragmentation, and lowered mitochondrial membrane potential (MMP) ($P < 0.05$). The pretreatments from AX or CX concentration-dependently alleviated H₂O₂ or MPP(+)-induced cell death, LDH release, DNA fragmentation, and MMP reduction ($P < 0.05$). Either H₂O₂ or MPP(+) treatment significantly increased malonyldialdehyde (MDA) and reactive oxygen species (ROS) formations, decreased glutathione content, and lowered glutathione peroxidase (GPX) and catalase activities ($P < 0.05$). The pretreatments from AX or CX significantly retained GPX and catalase activities, and decreased MDA and ROS formations ($P < 0.05$). H₂O₂ or MPP(+) treatment significantly decreased Na(+)-K(+)-ATPase activity, elevated caspase-3 activity and levels of interleukin (IL)-1, IL-6, and tumor necrosis factor (TNF)-alpha ($P < 0.05$); and the pretreatments from these agents significantly restored Na(+)-K(+)-ATPase activity, suppressed caspase-3 activity and release of IL-1, IL-6, and TNF-alpha ($P < 0.05$). Based on the observed antioxidative and anti-inflammatory protection from AX and CX, these 2 compounds were potent agents against neurodegenerative disorder.

PMID:

19895474

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Astaxanthin shows potential against osteoporosis in mouse and in-vitro studies.

[Int J Mol Sci](#). 2018 Mar 19;19(3). pii: E912. doi: 10.3390/ijms19030912.

Suppression Effect of Astaxanthin on Osteoclast Formation In Vitro and Bone Loss In Vivo.

[Hwang YH¹](#), [Kim KJ²](#), [Kim SJ³](#), [Mun SK⁴](#), [Hong SG⁵](#), [Son YJ⁶](#), [Yee ST⁷](#).

Author information

Abstract

Osteoporosis is characterized by a reduction of the bone mineral density (BMD) and microarchitectural deterioration of the bone, which lead to bone fragility and susceptibility to fracture. Astaxanthin (AST) has a variety of biological activities, such as a protective effect against asthma or neuroinflammation, antioxidant effect, and decrease of the osteoclast number in the right mandibles in the periodontitis model. Although treatment with AST is known to have an effect on inflammation, no studies on the effect of AST exposure on bone loss have been performed. Thus, in the present study, we examined the antiosteoporotic effect of AST on bone mass in ovariectomized (OVX) mice and its possible mechanism of action. The administration of AST (5, 10 mg/kg) for 6 weeks suppressed the enhancement of serum calcium, inorganic phosphorus, alkaline phosphatase, total cholesterol, and tartrate-resistant acid phosphatase (TRAP) activity. The bone mineral density (BMD) and bone microarchitecture of the trabecular bone in the tibia and femur were recovered by AST exposure. Moreover, in the in vitro experiment, we demonstrated that AST inhibits osteoclast formation through the expression of the nuclear factor of activated T cells (NFAT) c1, dendritic cell-specific transmembrane protein (DC-STAMP), TRAP, and cathepsin K without any cytotoxic effects on bone marrow-derived macrophages (BMMs). Therefore, we suggest that AST may have therapeutic potential for the treatment of postmenopausal osteoporosis.

KEYWORDS:

Astaxanthin (AST); bone mineral density (BMD); nuclear factor of activated T cells c1 (NFATc1); osteoclast; osteoporosis

PMID: 29562730

PMCID: [PMC5877773](#)

DOI: [10.3390/ijms19030912](#) [Indexed for MEDLINE] [Free PMC Article](#)

Astaxanthin shows anti-inflammatory activity in fish.

[Fish Shellfish Immunol.](#) 2018 Nov 15;86:280-286. doi: 10.1016/j.fsi.2018.11.011. [Epub ahead of print]

Astaxanthin protects lipopolysaccharide-induced inflammatory response in *Channa argus* through inhibiting NF- κ B and MAPKs signaling pathways.

[Li MY](#)¹, [Sun L](#)², [Niu XT](#)¹, [Chen XM](#)¹, [Tian JX](#)¹, [Kong YD](#)¹, [Wang GQ](#)³.

Author information

Abstract

The present study was conducted to evaluate the protective effects of astaxanthin against lipopolysaccharide (LPS)-induced inflammatory responses in *Channa argus* in vivo and ex vivo. Primary hepatocytes were exposed to different concentrations of LPS for 24 h to induce an inflammatory response, and the protective effects of astaxanthin against LPS-induced inflammation were studied ex vivo and in vivo. Hepatocytes exposed to LPS (5-20 $\mu\text{g mL}^{-1}$) alone for 24 h resulted in a significant increase in lactate dehydrogenase release (LDH), Nitric oxide (NO) production and Malondialdehyde (MDA) content, 10 $\mu\text{g mL}^{-1}$ LPS could induced inflammatory response in hepatocytes. Gene expression of TLR4, NF κ Bp65, MAPKp38, TNF- α , IL-6 and IL-1 β mRNA expression were also enhanced ex vivo ($p < 0.05$). In vivo test demonstrated that pretreatment with astaxanthin prevented the LPS-induced upregulation of pro-inflammatory cytokines TNF- α , IL-6 and IL-1 β . Besides, astaxanthin blocked the expression of Toll-like receptor 4 (TLR4) and then suppressed the phosphorylation of nuclear transcription factor-kappa B (NF- κ B) p65 and degradation inhibitor of NF- κ B α (I κ B α). Further study showed that astaxanthin could suppress the phosphorylation of p38, extracellular signal-regulated kinase (ERK) and c-jun NH2-terminal kinase (JNK) in mitogen-activated protein kinase (MAPK) signal pathway. In conclusion, our results suggest that astaxanthin played an anti-inflammatory role by regulating TLR4 and the NF- κ B and MAPK signaling pathways in *C. argus*.

KEYWORDS:

Astaxanthin; *Channa argus*; Inflammatory responses; Lipopolysaccharide; NF- κ B and MAPK signaling pathways

PMID: 30448447

DOI: [10.1016/j.fsi.2018.11.011](https://doi.org/10.1016/j.fsi.2018.11.011)

Astaxanthin reduces alcohol-induced liver injury by reducing inflammation and oxidation in rodents.

[Sci Rep.](#) 2018 Sep 20;8(1):14090. doi: 10.1038/s41598-018-32497-w.

Astaxanthin alleviated ethanol-induced liver injury by inhibition of oxidative stress and inflammatory responses via blocking of STAT3 activity.

[Han JH¹](#), [Ju JH¹](#), [Lee YS¹](#), [Park JH¹](#), [Yeo IJ¹](#), [Park MH¹](#), [Roh YS¹](#), [Han SB¹](#), [Hong JT²](#).

Author information

Abstract

Astaxanthin (AXT) is classified as a xanthophyll carotenoid compound which have broader functions including potent antioxidant, anti-inflammatory and neuroprotective properties. Considerable researches have demonstrated that AXT shows preventive and therapeutic properties against for Diabetes, Osteoarthritis and Rheumatoid Arthritis. However, the protective effect of AXT on liver disease has not yet been reported. In this study, we investigated effects of AXT on ethanol-induced liver injury in chronic plus binge alcohol feeding model. The hepatic steatosis and inflammation induced by ethanol administration were alleviated by AXT. Serum levels of aspartate transaminase and alanine transaminase were decreased in the livers of AXT administrated group. The ethanol-induced expression of cytochrome P450 2E1 (CYP2E1), pro-inflammatory proteins, cytokines, chemokines and reactive oxygen species (ROS) levels were also reduced in the livers of AXT administrated group. Moreover, ethanol-induced infiltration of neutrophils was decreased in the livers of AXT administrated group. Docking model and pull-down assay showed that AXT directly binds to the DNA binding site of STAT3. Moreover, AXT decreased STAT3 phosphorylation in the liver of AXT administration group. Therefore, these results suggest that AXT could prevent ethanol-induced hepatic injury via inhibition of oxidant and inflammatory responses via blocking of STAT3 activity.

PMID: 30237578

DOI: [10.1038/s41598-018-32497-w](https://doi.org/10.1038/s41598-018-32497-w)

Free full text

Astaxanthin protects brain function and reduces inflammation and oxidative stress in rats.

[Front Pharmacol.](#) 2018 Jul 10;9:748. doi: 10.3389/fphar.2018.00748. eCollection 2018.

The Protective Effect of Astaxanthin on Cognitive Function via Inhibition of Oxidative Stress and Inflammation in the Brains of Chronic T2DM Rats.

[Feng Y¹](#), [Chu A²](#), [Luo Q³](#), [Wu M¹](#), [Shi X¹](#), [Chen Y³](#).

Author information

Abstract

Currently, there are no effective treatments for diabetes-related cognitive dysfunction. Astaxanthin (AST), the most powerful antioxidant in nature, exhibits diverse biological functions. In this study, we tried to explore whether AST would ameliorate cognitive dysfunction in chronic type 2 diabetes mellitus (T2DM) rats. The T2DM rat model was induced via intraperitoneal injection of streptozotocin. Forty Wistar rats were divided into a normal control group, an acute T2DM group, a chronic T2DM group, and an AST group (treated with AST at a dose of 25 mg/kg three times a week). The Morris water maze test showed that the percentage of time spent in the target quadrant of the AST group was identical to that of the chronic T2DM group, while the escape latency of the AST group was decreased in comparison to that of the chronic T2DM group. Histology of the hippocampus revealed that AST ameliorated the impairment in the neurons of diabetic rats. Western blot showed that AST could upregulate nuclear factor erythroid 2-related factor 2 (Nrf2) and heme oxygenase 1 (HO-1) expression and inhibit nuclear transcription factor kappa B (NF- κ B) p65 activation in the hippocampus. We found that AST increased the level of superoxide dismutase (SOD) and decreased the level of malondialdehyde (MDA) in the hippocampus. In addition, the levels of interleukin 1 beta (IL-1 β) and interleukin 6 (IL-6) were reduced in the AST group compared with those in the chronic T2DM group. The findings of this research imply that AST might inhibit oxidative stress and inflammatory responses by activating the Nrf2-ARE signaling pathway.

KEYWORDS:

Nrf2; astaxanthin; cytokines; inflammatory response; oxidative stress; type 2 diabetes mellitus

PMID: 30042685

PMCID: [PMC6048598](#)

DOI: [10.3389/fphar.2018.00748](#)

[Free PMC Article](#)

Astaxanthin exerts significant anti-aging effects, prevents liver weight loss and improves locomotive muscular function in mouse model of jet lag.

[Endocr J.](#) 2018 May 28;65(5):569-578. doi: 10.1507/endocrj.EJ17-0500. Epub 2018 Mar 10.

Protective effects of astaxanthin on a combination of D-galactose and jet lag-induced aging model in mice.

[Ni Y¹](#), [Wu T¹](#), [Yang L¹](#), [Xu Y¹](#), [Ota T²](#), [Fu Z¹](#).

Author information

Abstract

Oxidative stress caused free radical and mitochondrial damage plays a critical role in the progression of aging and age-related damage at the cellular and tissue levels. Antioxidant supplementation has received growing attention and the effects of antioxidant on aging are increasingly assessed in both animal and human studies. However, additional and more promising treatments that contribute to the expansion of anti-aging therapies are needed. Astaxanthin, a super antioxidant carotenoid and free radical scavenger, inhibits lipid peroxidation more potently than vitamin E. In the present study, we investigated the preventative effects of astaxanthin on aging using an accelerated aging model: mice chronically treated with a combination of D-galactose and jet lag. After 6 weeks of treatment, astaxanthin administration tended to protect the liver weight loss in aged mice. It is probably by upregulating the mRNA expression of galactose-1-phosphate uridylyltransferase, which contribute to the enhancement of D-galactose metabolism. Astaxanthin supplementation also improved muscle endurance of aged mice in a swimming test. These results were associated with reduced oxidative stress in serum and increased anti-oxidative enzymes activities and mRNA expression in vivo. Moreover, astaxanthin reversed the dysregulation of aging-related gene expression caused by the combination of D-galactose and jet lag in the liver and kidney of mice. In conclusion, astaxanthin prevents liver weight loss, ameliorates locomotive muscular function, exerts significant anti-aging effects by reducing oxidative stress and improving the expression of age-related genes in D-galactose and jet lag-induced aging model.

KEYWORDS:

Aging; Antioxidant; Astaxanthin; D-galactose; Jet lag

PMID: 29526991

DOI: [10.1507/endocrj.EJ17-0500](https://doi.org/10.1507/endocrj.EJ17-0500)

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Astaxanthin protects against burn progression in rats by reducing inflammation and mitochondria cell death.

[Sci Rep.](#) 2017 Jan 27;7:41440. doi: 10.1038/srep41440.

Astaxanthin protects against early burn-wound progression in rats by attenuating oxidative stress-induced inflammation and mitochondria-related apoptosis.

[Fang Q](#)^{1,2}, [Guo S](#)¹, [Zhou H](#)¹, [Han R](#)³, [Wu P](#)¹, [Han C](#)¹.

Author information

Abstract

Burn-wound progression can occur in the initial or peri-burn area after a deep burn injury. The stasis zone has a higher risk of deterioration mediated by multiple factors but is also considered salvageable. Astaxanthin (ATX), which is extracted from some marine organisms, is a natural compound with a strong antioxidant effect that has been reported to attenuate organ injuries caused by traumatic injuries. Hence, we investigated the potential effects of ATX on preventing early burn-wound progression. A classic "comb" burn rat model was established in this study for histological and biological assessments, which revealed that ATX, particularly higher doses, alleviated histological deterioration in the stasis zone. Additionally, we observed dose-dependent improvements in oxidative stress and the release of inflammatory mediators after ATX treatment. Furthermore, ATX dose-dependently attenuated burn-induced apoptosis in the wound areas, and this effect was accompanied by increases in Akt and Bad phosphorylation and a downregulation of cytochrome C and caspase expression. In addition, the administration of Ly 294002 further verified the effect of ATX. In summary, we demonstrated that ATX protected against early burn-wound progression in a rat deep-burn model. This protection might be mediated by the attenuation of oxidative stress-induced inflammation and mitochondria-related apoptosis.

PMID: 28128352

PMCID: [PMC5269753](#)

DOI: [10.1038/srep41440](#)

[Indexed for MEDLINE]

[Free PMC Article](#)

Astaxanthin protects against seizures, reduces inflammation and prevents neuronal damage in rats.

[Neurochem Int.](#) 2018 Jun;116:85-94. doi: 10.1016/j.neuint.2018.02.008. Epub 2018 Feb 21.

Astaxanthin protects against kainic acid-induced seizures and pathological consequences.

[Chang Y](#)¹, [Lu CW](#)², [Chen YJ](#)³, [Lin TY](#)², [Huang SK](#)⁴, [Wang SJ](#)⁵.

Author information

Abstract

Excitotoxic damage caused by increased glutamate levels is involved in the pathogenesis of neurodegenerative diseases. Astaxanthin, a natural carotenoid with multiple health benefits, inhibits glutamate release from the brain tissue; however, whether it possesses the ability to affect glutamate-induced brain injury is unknown. The present study investigated the neuroprotective effects of astaxanthin on kainic acid (KA)-induced excitotoxicity in rats and the possible underlying intracellular signaling pathway. The rats were orally administrated with astaxanthin (50 or 100 mg/kg) for 7 days (once a day), and KA (15 mg/kg) was administered intraperitoneally at 1 h after the final administration. The results revealed that KA induced seizures, increased the hippocampal glutamate levels, caused considerable neuronal death and microglial activation in the hippocampal CA3 regions, and increased the production of proinflammatory cytokines. Astaxanthin pretreatment prevented these changes. Furthermore, astaxanthin pretreatment increased the expression of neuronal cell survival-related factors, including phosphorylated Akt, phosphorylated glycogen synthase kinase-3 β , and Bcl-2 in the hippocampus of KA-injected rats. These results suggested that astaxanthin can attenuate seizures, mitigate inflammation, augment survival signals, and prevent hippocampal neuronal damage in the animal model of KA-induced excitotoxicity.

KEYWORDS:

Astaxanthin; Glutamate excitotoxicity; Hippocampus; Kainic acid; Neuroprotection

PMID: 29475038

DOI: [10.1016/j.neuint.2018.02.008](https://doi.org/10.1016/j.neuint.2018.02.008)

Astaxanthin protects against eye inflammation induced by UV in mice.

[Oxid Med Cell Longev.](#) 2017;2017:1956104. doi: 10.1155/2017/1956104. Epub 2017 Sep 28.

Protective Effects of Oral Astaxanthin Nanopowder against Ultraviolet-Induced Photokeratitis in Mice.

[Harada F](#)^{1,2}, [Morikawa T](#)¹, [Lennikov A](#)^{3,4}, [Mukwaya A](#)³, [Schaupper M](#)³, [Uehara O](#)⁵, [Takai R](#)⁶, [Yoshida K](#)¹, [Sato J](#)¹, [Horie Y](#)⁷, [Sakaguchi H](#)⁸, [Wu CZ](#)^{2,9,10}, [Abiko Y](#)¹, [Lagali N](#)³, [Kitaichi N](#)^{7,11}.

Author information

Abstract

PURPOSE: Astaxanthin (AST) has a strong antioxidant cellular membrane chaperone protective effect. Recently, a water-soluble nanosized AST (nano-AST) form was produced, which is expected to improve the efficacy of oral intake effects. The purpose of this study was to examine whether oral nano-AST has therapeutic effects on UV-induced photokeratitis in mice.

METHODS: C57BL/6 mice were administered twice with either nano-AST, AST oil, lutein, or bilberry extracts 3 hours before and shortly before UV irradiation (dose: 400 mJ/cm²). The corneas were collected 24 hours after irradiation and stained with H&E and TUNEL. NF- κ B, dihydroethidium (DHE), COX-2, p-I κ B- α , TNF α , and CD45 expression were evaluated through immunohistochemistry, Western blot analysis, and qPCR.

RESULTS: Corneal epithelium was significantly thicker in mice orally administered with nano-AST than in the others ($p < 0.01$), with significantly less NF- κ B nucleus translocation ($p < 0.001$), and significantly fewer TUNEL cells ($p < 0.01$). Weaker DHE signals were detected in the nano-AST group ($p < 0.05$) relative to the others. Furthermore, reduced inflammation and decreased cell death in corneal tissue were observed in the nano-AST group, as indicated by a reduction in the expression of COX-2, p-I κ B- α , TNF α , and CD45.

CONCLUSIONS: Oral administration of nano-AST demonstrated a protective effect on UV-induced photokeratitis via antioxidative, anti-inflammatory, and antiapoptotic activity.

PMID: 29104724

PMCID: [PMC5637851](#)

DOI: [10.1155/2017/1956104](#)

[Indexed for MEDLINE]

[Free PMC Article](#)

Astaxanthin inhibits neuro-inflammation in-vitro.

[Oncotarget](#). 2017 Sep 3;8(41):69370-69385. doi: 10.18632/oncotarget.20628. eCollection 2017 Sep 19.

Astaxanthin acts via LRP-1 to inhibit inflammation and reverse lipopolysaccharide-induced M1/M2 polarization of microglial cells.

[Wen X¹](#), [Xiao L¹](#), [Zhong Z²](#), [Wang L³](#), [Li Z¹](#), [Pan X¹](#), [Liu Z^{2,4}](#).

Author information

Abstract

Microglia become activated during neuroinflammation and produce neurotoxic and neurotrophic factors, depending on whether they acquire M1 proinflammatory or M2 anti-inflammatory phenotypes. Astaxanthin (ATX), a natural carotenoid, has anti-inflammatory and neuroprotective effects. We investigated whether ATX could reverse M1/M2 polarization and suppress neuroinflammation *via* low-density lipoprotein receptor-related protein-1 (LRP-1). We observed increased expression of M1 (TNF- α , IL-1 β , and CD86) and decreased expression of M2 (Arg-1, IL-10, and CD206) markers in BV2 microglial cells stimulated with lipopolysaccharide (LPS). These alterations were reversed by pretreating the cells with ATX. Activation of the NF- κ B and JNK pathways was observed upon LPS stimulation, which was reversed by ATX. ATX-induced M2 polarization was attenuated by inhibition of NF- κ B and JNK. Pretreatment of LPS-stimulated BV2 cells with ATX resulted in increased LRP-1 expression. The addition of receptor-associated protein, an LRP-1 antagonist, ameliorated ATX-induced inactivation of NF- κ B and JNK signaling, and M2 polarization. ATX promotes M2 polarization to suppress neuroinflammation *via* LRP-1 by inhibiting NF- κ B and JNK signaling. This novel mechanism may suppress neuroinflammation in diseases such as Alzheimer's disease.

KEYWORDS:

Gerotarget; M1/M2 phenotypes; astaxanthin; c-Jun N-terminal kinase; low-density lipoprotein receptor-related protein 1; nuclear factor- κ B

PMID: 29050210

PMCID: [PMC5642485](#)

DOI: [10.18632/oncotarget.20628](#)

[Free PMC Article](#)

Astaxanthin reduces cognitive impairment in rat model by decreasing inflammation, oxidation and cell death.

[Mol Neurobiol.](#) 2018 Jul;55(7):5727-5740. doi: 10.1007/s12035-017-0797-7. Epub 2017 Oct 16.

Astaxanthin Ameliorates Doxorubicin-Induced Cognitive Impairment (Chemobrain) in Experimental Rat Model: Impact on Oxidative, Inflammatory, and Apoptotic Machineries.

[El-Agamy SE¹](#), [Abdel-Aziz AK¹](#), [Wahdan S¹](#), [Esmat A¹](#), [Azab SS²](#).

Author information

Abstract

Chemobrain refers to a common sequelae experienced by 15-80% of cancer patients exposed to chemotherapeutics. The antineoplastic agent doxorubicin (DOX) has been implicated in a strenuous neurotoxicity manifested as decline in cognitive functions, most probably via cytokine-induced oxidative and nitrosative damage to brain tissues. Astaxanthin (AST), a naturally occurring carotenoid, is reputable for its outstanding antioxidant, anti-inflammatory, and antiapoptotic activities. Therefore, the aim of the current study was to investigate the potential neuroprotective and memory-enhancing effects of AST against DOX-induced behavioral and neurobiological abnormalities. Briefly, AST treatment (25 mg/kg) significantly protected against DOX-induced memory impairment. Furthermore, AST restored hippocampal histopathological architecture, halted DOX-induced oxidative and inflammatory insults, mitigated the increase in acetylcholinesterase activity, and consistently downregulated the overactive apoptotic machineries. In conclusion, these findings suggest that AST offers neuroprotection against DOX-induced cognitive impairment which could be explained at least partly by its antioxidant, anti-inflammatory, and antiapoptotic effects.

KEYWORDS:

Apoptosis; Astaxanthin; Chemobrain; Doxorubicin; Neuroinflammation; Oxidative stress

PMID: 29039023

DOI: [10.1007/s12035-017-0797-7](https://doi.org/10.1007/s12035-017-0797-7)

Astaxanthin displays anti-inflammatory and antioxidant effects in-vitro.

PLoS One. 2017 Sep 19;12(9):e0184332. doi: 10.1371/journal.pone.0184332. eCollection 2017.

Scavenging of reactive oxygen species by astaxanthin inhibits epithelial-mesenchymal transition in high glucose-stimulated mesothelial cells.

Hara K¹, Hamada C¹, Wakabayashi K¹, Kanda R^{1,2}, Kaneko K¹, Horikoshi S¹, Tomino Y^{1,2}, Suzuki Y¹.

Author information

Abstract

BACKGROUND: High glucose concentrations influence the functional and structural development of the peritoneal membrane. We previously reported that the oral administration of astaxanthin (AST) suppressed peritoneal fibrosis (PF) as well as inhibited oxidative stress, inflammation, and epithelial-mesenchymal transition (EMT) of peritoneal mesothelial cells (PMCs) in a chlorhexidine-induced PF rat model. This suggests that oxidative stress induction of EMT is a key event during peritoneal damage. The present study evaluated the therapeutic effect of AST in suppressing EMT, in response to glucose-induced oxidative stress.

METHODS: Temperature-sensitive mesothelial cells (TSMCs) were cultured in the presence or absence of AST and then treated with 140 mM glucose for 3 or 12 hours. Expression levels of TNF- α , TGF- β , and VEGF were determined at the mRNA and protein levels, and nuclear factor kappa B (NF- κ B) activity was evaluated. We measured NO₂⁻/NO₃⁻ concentrations in cellular supernatants and determined 8-hydroxy-2'-deoxyguanosine (8-OHdG) levels in mitochondrial and nuclear DNA. The expressions of E-cadherin and alpha-smooth muscle actin (α -SMA) were evaluated by double immunofluorescence and protein levels.

RESULTS: High glucose concentrations induced overproduction of reactive oxidative species (ROS), increasing 8-OHdG mitochondrial DNA and cytokine levels. The NF- κ B pathway was activated in response to high glucose concentrations, whereas de novo α -SMA expression was observed with decreased E-cadherin expression. AST treatment attenuated ROS production, inflammatory cytokine production, NF- κ B activation, and EMT.

CONCLUSION: The findings of the present study indicate that AST may have an anti-EMT effect due to anti-oxidative and anti-inflammatory activities by scavenging glucose-induced ROS from mitochondria in PMCs. AST may be an efficacious treatment for PF.

PMID: 28926603 PMCID: [PMC5604950](https://pubmed.ncbi.nlm.nih.gov/PMC5604950/) DOI: [10.1371/journal.pone.0184332](https://doi.org/10.1371/journal.pone.0184332) [Indexed for MEDLINE]

[Free PMC Article](#)

ASTAXANTHIN SHOWS ANTI-INFLAMMATORY AND ANTIOXIDANT POTENTIAL IN-VITRO.

J Nutr Biochem. 2018 Dec;62:202-209.

doi: 10.1016/j.jnutbio.2018.09.005. Epub 2018 Sep 19.

Astaxanthin exerts anti-inflammatory and antioxidant effects in macrophages in NRF2-dependent and independent manners

[Callie Farruggia¹](#), [Mi-Bo Kim¹](#), [Minkyung Bae¹](#), [Yoojin Lee¹](#), [Tho X Pham¹](#), [Yue Yang¹](#), [Myung Joo Han²](#), [Young-Ki Park¹](#), [Ji-Young Lee³](#)

PMID: 30308382 DOI: [10.1016/j.jnutbio.2018.09.005](https://doi.org/10.1016/j.jnutbio.2018.09.005)

Abstract

Although anti-inflammatory effects of astaxanthin (ASTX) have been suggested, the underlying mechanisms have not been fully understood. Particularly, the modulatory action of ASTX in the interplay between nuclear factor E2-related factor 2 (NRF2) and nuclear factor κ B (NF κ B) to exert its anti-inflammatory effect in macrophages is unknown. The effect of ASTX on mRNA and protein expression of pro-inflammatory and antioxidant genes and/or cellular reactive oxygen species (ROS) accumulation were determined in RAW 264.7 macrophages, bone marrow-derived macrophages (BMDM) from wild-type (WT) and Nrf2-deficient mice, and/or splenocytes and peritoneal macrophages of obese mice fed ASTX. The effect of ASTX on M1 and M2 macrophage polarization was evaluated in BMDM. ASTX significantly decreased LPS-induced mRNA expression of interleukin 6 (Il-6) and Il-1 β by inhibiting nuclear translocation of NF κ B p65; and attenuated LPS-induced ROS with an increase in NRF2 nuclear translocation, concomitantly decreasing NADPH oxidase 2 expression in RAW 264.7 macrophages. In BMDM of WT and Nrf2-deficient mice, ASTX decreased basal and LPS-induced ROS accumulation. The induction of Il-6 mRNA by LPS was repressed by ASTX in both types of BMDM while Il-1 β mRNA was decreased only in WT BMDM. Furthermore, ASTX consumption lowered LPS sensitivity of splenocytes in obese mice. ASTX decreased M1 polarization of BMDM while increasing M2 polarization. ASTX exerts its anti-inflammatory effect by inhibiting nuclear translocation of NF κ B p65 and by preventing ROS accumulation in NRF2-dependent and -independent mechanisms. Thus, ASTX is an agent with anti-inflammatory and antioxidant properties that may be used for the prevention of inflammatory conditions.

ASTAXANTHIN REDUCES CIGARETTE AND LIPOPOLYSACCHARIDE-INDUCED INFLAMMATION REVEALING POTENTIAL FOR AIRWAY SUPPORT.

Cell Mol Biol (Noisy-le-grand). 2019 Jan 31;65(1):94-99.

Astaxanthin suppresses cigarette smoke and lipopolysaccharide-induced airway inflammation through induction of heme oxygenase-1

[Liu Nian](#)¹, [Zhang Weidong](#)¹, [Luo Shujuan](#)², [Cao Jun](#)¹, [Peng Minlian](#)¹, [Liu Zhiguang](#)¹

- PMID: 30782300

Abstract

The present study was carried out to evolve an effective treatment strategy for chronic obstructive pulmonary disease (COPD). Astaxanthin (AS) is abundantly present in red pigments of crustaceans, and has also been proven to have considerable biological activities. The anti-inflammatory effect of AS was evaluated in lipopolysaccharide (LPS)-exposed RAW264.7 macrophages. It was found that AS markedly inhibited elevation of NO and pro-inflammatory mediators. Moreover, it downregulated iNOS in LPS-stimulated RAW264.7 cells, suppressed the release of pro-inflammatory cytokines, and decreased ROS levels in mice exposed to cigarette smoke (CS) and LPS. These results imply that AS has therapeutic and prophylactic potential in the airway inflammatory response associated with COPD.

ASTAXANTHIN REDUCES ALCOHOL-INDUCED INFLAMMATION AND OXIDATIVE STRESS.

J Nutr Biochem. 2020 Nov;85:108477.

doi: 10.1016/j.jnutbio.2020.108477. Epub 2020 Aug 12.

Astaxanthin inhibits alcohol-induced inflammation and oxidative stress in macrophages in a sirtuin 1-dependent manner

[Hyunju Kang](#)¹, [Yoojin Lee](#)¹, [Minkyung Bae](#)¹, [Young-Ki Park](#)¹, [Ji-Young Lee](#)²

- PMID: [32801029](#)
- DOI: [10.1016/j.jnutbio.2020.108477](#)

Abstract

Objectives: Alcohol induces inflammation and oxidative stress, causing cell damages. We previously demonstrated that astaxanthin (ASTX), a xanthophyll carotenoid, exerts anti-inflammatory and antioxidant properties in macrophages exposed to inflammatory insults. In this study, we investigated whether ASTX can inhibit alcohol-induced inflammation and oxidative stress in macrophages with the elucidation of mechanisms.

Methods: RAW 264.7 macrophages and mouse bone marrow-derived macrophages were treated with 80 mM ethanol in the presence or absence of 25 μ M of ASTX for 72 h. Subsequently, the expression of genes related to inflammation and oxidative stress, cellular reactive oxygen species accumulation, cellular NAD⁺ level and sirtuin 1 (SIRT1) activity were measured. In addition, RAW 264.7 macrophages were treated with sirtinol or resveratrol, which are known inhibitors or activators of SIRT1 activity, respectively, to determine the contribution of SIRT1 to the inhibitory effect of ASTX on inflammation and oxidative stress in macrophages exposed to ethanol.

Results: Ethanol increased mRNA expression of interleukin (Il)-6, Il-1b and tumor necrosis factor α with a concomitant increase in nuclear translocation of nuclear factor κ B, which was abolished by ASTX. Importantly, ethanol significantly decreased SIRT1 activity and cellular NAD⁺ level, but ASTX markedly attenuated the decreases in RAW

264.7 macrophages. Sirtinol increased the expression of proinflammatory genes in ethanol-induced RAW 264.7 macrophages. In contrast, resveratrol decreased proinflammatory gene expression.

Conclusions: ASTX showed anti-inflammatory and antioxidant properties by inhibiting decreases in SIRT1 expression and cellular NAD⁺ level in ethanol-treated macrophages. Therefore, ASTX may be used for the prevention of alcohol-induced cell damages.

ASTAXANTHIN REDUCES URIC ACID LEVELS IN RATS AND MAY BE AN ALTERNATIVE TO DRUGS USED FOR THIS PURPOSE.

Mar Drugs. 2020 Dec 1;18(12):610.
doi: 10.3390/md18120610.

Anti-Hyperuricemic Effects of Astaxanthin by Regulating Xanthine Oxidase, Adenosine Deaminase and Urate Transporters in Rats

[Yanzuo Le](#)[‡], [Xie Zhou](#)[‡], [Jiawen Zheng](#)[‡], [Fangmiao Yu](#)[‡], [Yunping Tang](#)[‡], [Zuisu Yang](#)[‡], [Guofang Ding](#)[‡], [Yan Chen](#)[‡]

- PMID: [33271765](#)
- PMCID: [PMC7759838](#)
- DOI: [10.3390/md18120610](#)

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Abstract

This study was designed to investigate the effects and underlying mechanisms of Astaxanthin (AST) on high-fructose-induced hyperuricemia (HUA) from the perspectives of the uric acid (UA) synthesis and excretion in rat models. Following six weeks of a 10% fructose diet, the level of serum UA effectively decreased in the AST groups as compared to the model group. The enzymatic activities of xanthine oxidase (XOD) and adenosine deaminase (ADA) were significantly inhibited, and the mRNA expression levels of XOD and ADA significantly decreased after the AST administration. These results suggested that the AST reduced UA synthesis by inhibiting the mRNA expressions and enzyme activities of XOD and ADA, thereby contributing to HUA improvement. On the hand, the relative expressions of the mRNA and protein of kidney reabsorption transport proteins (GLUT9 and URAT1) were significantly down-regulated by AST, while that of the kidney secretion proteins (OAT1, OAT3 and ABCG2) were significantly up-regulated by AST. These results indicated that the AST promoted UA excretion by regulating the urate transport proteins, and thus alleviated HUA. This study suggested that the AST could serve as an effective alternative to traditional medicinal drugs for the prevention of fructose-induced HUA.

ASTAXANTHIN REDUCES INFLAMMATION IN HUMAN CELL STUDY.

Zhong Nan Da Xue Xue Bao Yi Xue Ban. 2021 Mar 28;46(3):227-233.

doi: 10.11817/j.issn.1672-7347.2021.190661.

Astaxanthin inhibits inflammation of human periodontal ligament cells induced by lipopolysaccharide

[[Congman Xie](#)^{1,2}, [Min Lin](#)^{3,4}, [Haonan Tian](#)^{3,4}, [Lin Zhang](#)^{3,5}, [Aishu Ren](#)^{6,7}

- PMID: 33927068 DOI: [10.11817/j.issn.1672-7347.2021.190661](https://doi.org/10.11817/j.issn.1672-7347.2021.190661) **Free article**

Abstract

Objectives: Human periodontal ligament cells (hPDLCs) are important source of periodontal tissue reconstruction. Under chronic inflammation, the multi-directional differentiation potential and chemotaxis in hPDLCs are decreased. Therefore, inhibiting inflammatory microenvironment and improving the functional characteristics of stem cells can better promote periodontal tissue reconstruction. This study was to investigate the effect of astaxanthin (AST) on lipopolysaccharide (LPS)-induced inflammation in hPDLCs and the underlying mechanisms.

Methods: hPDLCs were isolated and cultured in vitro, and vimentin and keratin immunocytochemical staining were used to identify hPDLCs. CCK-8 assay was used to measure the effects of AST (1, 5, 10, 20, 50, 100, and 200 $\mu\text{mol/L}$) on proliferation of hPDLCs. Quantitative RT-PCR (RT-qPCR) and ELISA were used to measure the mRNA and protein expression of inflammatory factors (IL-6, IL-1 β , and TNF- α) in the control (Con) group, the LPS group, and the LPS+AST (5, 10, 20, and 50 $\mu\text{mol/L}$) group. Western blotting was used to detect the protein expression of IKB α , phosphorylated IKB α (p-IKB α), and p65 in the Con group, the LPS group, the AST (20 $\mu\text{mol/L}$) group, and the LPS+AST (20 $\mu\text{mol/L}$) group. After 10 $\mu\text{mol/L}$ PDTC treatment, the mRNA and protein expressions of IL-6, IL-1 β , and TNF- α were detected by RT-qPCR and ELISA.

Results: Cell morphology and immunocytochemical staining showed that the cells were in line with the characteristics of hPDLCs. Treatment with AST could promote the proliferation of hPDLCs, which reached the peak at 20 $\mu\text{mol/L}$. The mRNA and protein expressions of IL-6, IL-1 β , and TNF- α in the LPS group were higher than those in the

Con group (all $P < 0.05$). Compared with the LPS group, the mRNA and protein expressions of IL-6, IL-1 β , and TNF- α in the LPS+AST (5, 10, 20, and 50 $\mu\text{mol/L}$) group were down-regulated (all $P < 0.05$). Compared with the Con group, the levels of IKB α and p65 in cytoplasm of the LPS group were significantly downregulated (both $P < 0.05$), and the levels of p-IKB α in cytoplasm and p65 in nucleus of the LPS group were significantly up-regulated (both $P < 0.05$). Compared with the LPS group, the levels of IKB α and p65 in cytoplasm of the LPS+AST (20 $\mu\text{mol/L}$) group were significantly upregulated (both $P < 0.05$), and the levels of p-IKB α in cytoplasm and p65 in nucleus of the LPS+AST (20 $\mu\text{mol/L}$) group were significantly downregulated (both $P < 0.05$). The mRNA and protein expressions of IL-6, IL-1 β , and TNF- α in the LPS+PDTC (10 $\mu\text{mol/L}$) group were lower than those in the LPS group (all $P < 0.05$).

Conclusions: AST promotes the proliferation of hPDLCS, which is related to suppression of LPS-induced the secretion of inflammatory factors via inhibiting the activation of NF- κB signaling pathway.

Astaxanthin has neuroprotective effects and reduces inflammation and oxidative stress in diabetic rats.

[PLoS One](#). 2016 Jan 14;11(1):e0146438. doi: 10.1371/journal.pone.0146438. eCollection 2016.

Astaxanthin Inhibits Expression of Retinal Oxidative Stress and Inflammatory Mediators in Streptozotocin-Induced Diabetic Rats.

[Yeh PT](#)^{1,2}, [Huang HW](#)³, [Yang CM](#)^{1,4}, [Yang WS](#)^{5,6}, [Yang CH](#)^{1,4}.

Abstract

PURPOSE: We evaluated whether orally administered astaxanthin (AST) protects against oxidative damage in the ocular tissues of streptozotocin (STZ)-induced diabetic rats.

METHODS AND RESULTS: Fifty 6-week-old female Wistar rats were randomly assigned to receive an injection of STZ to induce diabetes (n = 40) or to remain uninduced (n = 10). The diabetic rats were randomly selected into four groups and they were separately administered normal saline, 0.6 mg/kg AST, 3 mg/kg AST, or 0.5 mg/kg lutein daily for eight weeks. Retinal functions of each group were evaluated by electroretinography. The expression of oxidative stress and inflammatory mediators in the ocular tissues was then assessed by immunohistochemistry, western blot analysis, ELISA, RT-PCR, and electrophoretic mobility shift assay (EMSA). Retinal functions were preserved by AST and lutein in different levels. Ocular tissues from AST- and lutein-treated rats had significantly reduced levels of oxidative stress mediators (8-hydroxy-2'-deoxyguanosine, nitrotyrosine, and acrolein) and inflammatory mediators (intercellular adhesion molecule-1, monocyte chemoattractant protein-1, and fractalkine), increased levels of antioxidant enzymes (heme oxygenase-1 and peroxiredoxin), and reduced activity of the transcription factor nuclear factor-kappaB (NF-κB).

CONCLUSION: The xanthophyll carotenoids AST and lutein have neuroprotective effects and reduce ocular oxidative stress, and inflammation in the STZ diabetic rat model, which may be mediated by downregulation of NF-κB activity.

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PMCID: [PMC4713224](#)

DOI: [10.1371/journal.pone.0146438](#)

[Indexed for MEDLINE]

[Free PMC Article](#)

Astaxanthin reduces muscle atrophy in rats.

[Exp Physiol](#). 2014 Aug;99(8):1065-77. doi: 10.1113/expphysiol.2014.079988. Epub 2014 Jun 6.

Amelioration of capillary regression and atrophy of the soleus muscle in hindlimb-unloaded rats by astaxanthin supplementation and intermittent loading.

[Kanazashi M¹](#), [Tanaka M¹](#), [Murakami S²](#), [Kondo H³](#), [Nagatomo F⁴](#), [Ishihara A⁴](#), [Roy RR⁵](#), [Fujino H⁶](#).

Author information

Abstract

A chronic decrease in neuromuscular activity (activation and/or loading) results in muscle atrophy and capillary regression that are due, in part, to the overproduction of reactive oxygen species. We have reported that antioxidant treatment with astaxanthin attenuates the overexpression of reactive oxygen species in atrophied muscles that, in turn, ameliorates capillary regression in hindlimb-unloaded rats. Astaxanthin supplementation, however, had little effect on muscle mass and fibre cross-sectional area. In contrast, intermittent loading of the hindlimbs of hindlimb-unloaded rats ameliorates muscle atrophy. Therefore, we hypothesized that the combination of astaxanthin supplementation and intermittent loading would attenuate both muscle atrophy and capillary regression during hindlimb unloading. As expected, 2 weeks of hindlimb unloading resulted in atrophy, a decrease in capillary volume and a shift towards smaller-diameter capillaries in the soleus muscle. Intermittent loading alone (1 h of cage ambulation per day) attenuated atrophy of the soleus, while astaxanthin treatment alone maintained the capillary network to near control levels. The combination of intermittent loading and astaxanthin treatment, however, ameliorated atrophy of the soleus and maintained the capillary volume and luminal diameters and the superoxide dismutase-1 protein levels near control values. These results indicate that intermittent loading combined with astaxanthin supplementation could be an effective therapy for both the muscle atrophy and the capillary regression associated with a chronic decrease in neuromuscular activity.

PMID: 24907028

DOI: [10.1113/expphysiol.2014.079988](https://doi.org/10.1113/expphysiol.2014.079988)

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Astaxanthin reduces acute lung injury by ameliorating the inflammatory and oxidative response in mice.

[Biomed Pharmacother.](#) 2017 Nov;95:974-982. doi: 10.1016/j.biopha.2017.09.012. Epub 2017 Sep 11.

Astaxanthin alleviated acute lung injury by inhibiting oxidative/nitrative stress and the inflammatory response in mice.

Bi J¹, Cui R², Li Z¹, Liu C³, Zhang J⁴.

Author information

Abstract

The purpose of the present study was to assess the effect of astaxanthin (ASX) treatment on the acute lung injury (ALI) induced by cecal ligation and puncture (CLP) in mice. Mice were randomly allocated into the following groups: (1) the saline control group, in which mice were given saline before sham operation; (2) the ASX control group, in which mice received ASX before sham operation; (3) the ALI group, in which mice were given saline before CLP operation; and (4) the ALI+ASX group, in which mice received ASX before CLP operation. ASX was dissolved in olive oil and administrated by oral gavage for 14days consecutively before the CLP or sham operation. In experiment 1, Kaplan-Meier survival analysis was conducted for 72h after CLP. In experiment 2, blood, bronchoalveolar lavage fluid (BALF) and lung tissues were collected at 24h after the CLP or sham operation to determine the severity of lung injury. The results showed that ASX treatment could significantly decrease the CLP-induced mortality rate in mice. Meanwhile, ASX treatment significantly attenuated CLP-induced lung histopathological injury, inflammatory infiltration, total protein and albumin concentration, and total cell and neutrophil counts in the BALF. Furthermore, ASX treatment alleviated oxidative/nitrative stress, inflammation levels and pulmonary apoptosis in lung tissues. In addition, ASX treatment markedly down-regulated the expression of inducible nitric oxide synthase (i-NOS), nitrotyrosine (NT) and nuclear factor-kappa B (NF-Kb) P65 in the lung tissues compared with that in the ALI group. Astaxanthin treatment had markedly protective effect against ALI in mice, and the potential mechanism is associated with its ability to inhibit the inflammatory response, oxidative/nitrative stress, and pulmonary apoptosis, as well as down-regulate NF-kB P65 expression.

KEYWORDS:

Acute lung injury; Astaxanthin; Inflammatory response; NF-kB P65; Oxidative stress; Pulmonary apoptosis

PMID: 28915539

DOI: [10.1016/j.biopha.2017.09.012](https://doi.org/10.1016/j.biopha.2017.09.012)

[Indexed for MEDLINE]

Astaxanthin exerts anti-inflammatory activity in eczema model in rodents and in-vitro.

[Exp Dermatol](#). 2018 Apr;27(4):378-385. doi: 10.1111/exd.13437.

Anti-inflammatory effect of astaxanthin in phthalic anhydride-induced atopic dermatitis animal model.

[Park JH](#)^{1,2}, [Yeo IJ](#)¹, [Han JH](#)¹, [Suh JW](#)³, [Lee HP](#)¹, [Hong JT](#)¹.

Author information

Abstract

In this study, we investigated anti-dermatitic effects of astaxanthin (AST) in phthalic anhydride (PA)-induced atopic dermatitis (AD) animal model as well as in vitro model. AD-like lesion was induced by the topical application of 5% PA to the dorsal skin or ear of Hos:HR-1 mouse. After AD induction, 100 μ L of 1 mg/mL and 2 mg/mL of AST (10 μ g or 20 μ g/cm²) was spread on the dorsum of ear or back skin three times a week for four weeks. We evaluated dermatitis severity, histopathological changes and changes in protein expression by Western blotting for inducible nitric oxide synthase (iNOS), cyclooxygenase-2 (COX-2) and nuclear factor- κ B (NF- κ B) activity. We also measured tumor necrosis factor- α (TNF- α), interleukin-1 β (IL-1 β), interleukin-6 (IL-6) and immunoglobulin E (IgE) concentration in the blood of AD mice by enzyme-linked immunosorbent assay (ELISA). AST treatment attenuated the development of PA-induced AD. Histological analysis showed that AST inhibited hyperkeratosis, mast cells and infiltration of inflammatory cells. AST treatment inhibited expression of iNOS and COX-2, and NF- κ B activity as well as release of TNF- α , IL-1 β , IL-6 and IgE. In addition, AST (5, 10 and 20 μ M) potently inhibited lipopolysaccharide (LPS) (1 μ g/mL)-induced nitric oxide (NO) production, expression of iNOS and COX-2 and NF- κ B DNA binding activities in RAW 264.7 macrophage cells. Our data demonstrated that AST could be a promising agent for AD by inhibition of NF- κ B signalling.

KEYWORDS:

IgE; NF- κ B; astaxanthin; atopic dermatitis; cytokine; skin inflammation

PMID: 28887839

DOI: [10.1111/exd.13437](https://doi.org/10.1111/exd.13437)

Astaxanthin reduces inflammation and liver fibrosis in mouse model.

[J Nutr Biochem](#). 2017 May;43:27-35. doi: 10.1016/j.jnutbio.2016.01.006. Epub 2016 Mar 2.

Astaxanthin inhibits inflammation and fibrosis in the liver and adipose tissue of mouse models of diet-induced obesity and nonalcoholic steatohepatitis.

[Kim B¹](#), [Farruggia C¹](#), [Ku CS¹](#), [Pham TX¹](#), [Yang Y¹](#), [Bae M¹](#), [Wegner CJ¹](#), [Farrell NJ¹](#), [Harness E¹](#), [Park YK¹](#), [Koo SI¹](#), [Lee JY²](#).

Author information

Abstract

The objective of this study was to determine if astaxanthin (ASTX), a xanthophyll carotenoid, can prevent obesity-associated metabolic abnormalities, inflammation and fibrosis in diet-induced obesity (DIO) and nonalcoholic steatohepatitis (NASH) mouse models. Male C57BL/6J mice were fed a low-fat (6% fat, w/w), a high-fat/high-sucrose control (HF/HS; 35% fat, 35% sucrose, w/w), or a HF/HS containing ASTX (AHF/HS; 0.03% ASTX, w/w) for 30 weeks. To induce NASH, another set of mice was fed a HF/HS diet containing 2% cholesterol (HF/HS/HC) a HF/HS/HC with 0.015% ASTX (AHF/HS/HC) for 18 weeks. Compared to LF, HF/HS significantly increased plasma total cholesterol, triglyceride and glucose, which were lowered by ASTX. ASTX decreased hepatic mRNA levels of markers of macrophages and fibrosis in both models. The effect of ASTX was more prominent in NASH than DIO mice. In epididymal fat, ASTX also decreased macrophage infiltration and M1 macrophage marker expression, and inhibited hypoxia-inducible factor 1- α and its downstream fibrogenic genes in both mouse models. ASTX significantly decreased tumor necrosis factor α mRNA in the splenocytes from DIO mice upon lipopolysaccharides stimulation compared with those from control mice fed an HF/HS diet. Additionally, ASTX significantly elevated the levels of genes that regulate fatty acid β -oxidation and mitochondrial biogenesis in the skeletal muscle compared with control obese mice, whereas no differences were noted in adipose lipogenic genes. Our results indicate that ASTX inhibits inflammation and fibrosis in the liver and adipose tissue and enhances the skeletal muscle's capacity for mitochondrial fatty acid oxidation in obese mice.

KEYWORDS:

Astaxanthin; Fibrosis; Inflammation; Macrophage infiltration; Macrophage phenotypes; Obesity

PMID: 28193580 DOI: [10.1016/j.jnutbio.2016.01.006](#) [Indexed for MEDLINE]

Astaxanthin protects against high blood pressure during pregnancy by reducing inflammation and oxidative stress in rats.

[Mol Med Rep.](#) 2016 Sep;14(3):2697-704. doi: 10.3892/mmr.2016.5569. Epub 2016 Jul 28.

Astaxanthin blocks preeclampsia progression by suppressing oxidative stress and inflammation.

[Xuan RR¹](#), [Niu TT²](#), [Chen HM²](#).

Author information

Abstract

To investigate the antioxidative effect of astaxanthin on Nω-nitro-L-arginine methyl ester (L-NAME)-induced preeclamptic rats. Cell survival, the level of reactive oxygen species (ROS) and the changes in mitochondrial membrane potential (MMP) were examined in astaxanthin and H₂O₂-treated human umbilical vein endothelial cells (HUVECs). The preeclamptic Sprague-Dawley (SD) rat model was established by injection of L-NAME and treatment with astaxanthin. The activities of malondialdehyde (MDA), superoxide dismutase (SOD) and nitric oxide synthase (NOS) in serum were analyzed. Pathological changes were examined by hematoxylin and eosin (H&E) staining. The expression of nuclear factor (NF)-κB, Rho-associated protein kinase II (ROCK II), heme oxygenase-1 (HO-1) and caspase 3 in preeclamptic placentas were examined by immunohistochemistry. Astaxanthin significantly reduced H₂O₂-induced HUVEC cell death, decreased ROS and increased MMP. Astaxanthin significantly reduced blood pressure and the content of MDA, but significantly increased the activity of SOD in preeclamptic rats. The urinary protein and the level of NO and NOS were also decreased. H&E staining revealed that the thickness of the basilar membrane was increased, while the content of trophoblast cells and spiral arteries were reduced following astaxanthin treatment. Immunohistochemistry results showed that the expression of NF-κB, ROCK II and caspase 3 in preeclamptic placentas was significantly decreased after astaxanthin treatment, while HO-1 expression was increased. In conclusion, astaxanthin inhibited H₂O₂-induced oxidative stress in HUVECs. Astaxanthin treatment significantly improved L-NAME-induced preeclamptic symptoms and reduced the oxidative stress and inflammatory damages in preeclamptic placentas. Astaxanthin treatment may effectively prevent and treat preeclampsia.

PMID: 27484589

DOI: [10.3892/mmr.2016.5569](https://doi.org/10.3892/mmr.2016.5569)

[Indexed for MEDLINE]

Astaxanthin protects against burn progression in rats by reducing inflammation and mitochondria cell death.

[Sci Rep.](#) 2017 Jan 27;7:41440. doi: 10.1038/srep41440.

Astaxanthin protects against early burn-wound progression in rats by attenuating oxidative stress-induced inflammation and mitochondria-related apoptosis.

[Fang Q](#)^{1,2}, [Guo S](#)¹, [Zhou H](#)¹, [Han R](#)³, [Wu P](#)¹, [Han C](#)¹.

Author information

Abstract

Burn-wound progression can occur in the initial or peri-burn area after a deep burn injury. The stasis zone has a higher risk of deterioration mediated by multiple factors but is also considered salvageable. Astaxanthin (ATX), which is extracted from some marine organisms, is a natural compound with a strong antioxidant effect that has been reported to attenuate organ injuries caused by traumatic injuries. Hence, we investigated the potential effects of ATX on preventing early burn-wound progression. A classic "comb" burn rat model was established in this study for histological and biological assessments, which revealed that ATX, particularly higher doses, alleviated histological deterioration in the stasis zone. Additionally, we observed dose-dependent improvements in oxidative stress and the release of inflammatory mediators after ATX treatment. Furthermore, ATX dose-dependently attenuated burn-induced apoptosis in the wound areas, and this effect was accompanied by increases in Akt and Bad phosphorylation and a downregulation of cytochrome C and caspase expression. In addition, the administration of Ly 294002 further verified the effect of ATX. In summary, we demonstrated that ATX protected against early burn-wound progression in a rat deep-burn model. This protection might be mediated by the attenuation of oxidative stress-induced inflammation and mitochondria-related apoptosis.

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PMCID: [PMC5269753](#)

DOI: [10.1038/srep41440](#)

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[Free PMC Article](#)

Astaxanthin prevents depression by reducing inflammation in diabetic mice.

Brain Res. 2017 Feb 15;1657:262-268. doi: 10.1016/j.brainres.2016.12.018. Epub 2016 Dec 22.

Depression can be prevented by astaxanthin through inhibition of hippocampal inflammation in diabetic mice.

[Zhou XY](#)¹, [Zhang F](#)¹, [Hu XT](#)¹, [Chen J](#)¹, [Tang RX](#)², [Zheng KY](#)³, [Song YJ](#)⁴.

Author information

Abstract

The critical factor considered in a depression induced by diabetes is the inflammation eliciting hippocampal, amygdala and thalamic neuronal injury. Therefore, inhibiting inflammatory reactions in the brain and reducing neuronal injury can alleviate depression in rodents suffering from diabetes mellitus. The oral administration of astaxanthin has been employed in emotional disorders and diabetic complications due to its anti-depressant, anti-inflammatory and anti-apoptotic functions. However, it has not been reported whether astaxanthin can improve diabetes-related depression-like behavior, and its potential mechanisms have not been elucidated. The objective of the present study is to elucidate the effect of astaxanthin on depression in diabetic mice and to understand the underlying molecular mechanisms. In this study, experimental diabetic mice were given a single intraperitoneal injection of streptozotocin (STZ, 150mg/kg, dissolved in citrate buffer) after fasting for 12h. The diabetic model was assessed 72h after STZ injection, and mice with a fasting blood glucose level more than or equal to 16.7mmol/L were used in this study, and oral astaxanthin (25mg/kg) was provided uninterrupted for ten weeks. Depression-like behavior was evaluated by the tail suspension test (TST) and forced swimming test (FST). The glial fibrillary acidic protein (GFAP) and cleaved caspase-3-positive cells were measured by immunohistochemistry, and the western blotting was used to test the protein levels of interleukin-6 (IL-6), interleukin-1 β (IL-1 β) and cyclooxygenase (COX-2). The results showed that astaxanthin had an anti-depressant effect on diabetic mice. Furthermore, we observed that astaxanthin significantly reduced the number of GFAP-positive cells in the hippocampus and hypothalamus, and also the expression of cleaved caspase-3 in the hippocampus, amygdala and hypothalamus was decreased as well. Moreover, astaxanthin could down-regulate the expression of IL-6, IL-1 β and COX-2 in the hippocampus. These findings suggest that the mechanism of astaxanthin in preventing depression in diabetic mice involves the inhibition of inflammation/inflammation inhibition, thereby protecting neurons in hippocampus, amygdala and hypothalamus against hyperglycemic damage.

KEYWORDS: Astaxanthin; Depression; Diabetes; Inflammation; Injury

PMID: 28017669 DOI: [10.1016/j.brainres.2016.12.018](https://doi.org/10.1016/j.brainres.2016.12.018) [Indexed for MEDLINE]

Astaxanthin effective against production of inflammatory mediators nitric oxide and COX-2 enzyme in-vitro.

[J Microbiol Biotechnol.](#) 2008 Dec;18(12):1990-6.

Effects of astaxanthin on the production of NO and the expression of COX-2 and iNOS in LPS-stimulated BV2 microglial cells.

[Choi SK¹](#), [Park YS](#), [Choi DK](#), [Chang HI](#).

Author information

Abstract

Astaxanthin has shown antioxidant, antitumor, and antiinflammatory activities; however, its molecular action and mechanism in the nervous system have yet to be elucidated. We examined the in vitro effects of astaxanthin on the production of nitric oxide (NO), as well as the expression of inducible NO synthase (iNOS) and cyclooxygenase-2 (COX-2) in lipopolysaccharide (LPS)-stimulated BV2 microglial cells. Astaxanthin inhibited the expression or formation of nitric oxide (NO), iNOS and COX-2 in lipopolysaccharide (LPS)-stimulated BV-2 microglial cells. Astaxanthin also suppressed the protein levels of iNOS and COX-2 in LPS-stimulated BV2 microglial cells. These results suggest that astaxanthin, probably due to its antioxidant activity, inhibits the production of inflammatory mediators by blocking iNOS and COX-2 activation or by the suppression of iNOS and COX-2 degradation.

PMID:

19131704

[PubMed - indexed for MEDLINE]

Free full text

Astaxanthin shows anti-inflammatory properties and may reduce C-reactive protein levels.

[Cardiovasc Drug Rev.](#) 2005 Fall;23(3):199-216.

Disodium disuccinate astaxanthin (Cardax): antioxidant and antiinflammatory cardioprotection.

[Lockwood SF](#)¹, [Gross GJ](#).

Author information

Abstract

Disodium disuccinate astaxanthin (Cardax), DDA) has cardioprotective effects in the rat, rabbit, and canine models of experimental infarction. It is highly effective by parenteral administration in subchronic and acute dosing regimens. Unpublished data in rats suggest that oral cardioprotection is also readily achievable. DDA-induced myocardial salvage in the canine can reach 100% with a 4-day subchronic dosing regimen. At a single i.v. dose DDA is cardioprotective, when given 2 h before experimental coronary occlusion, but the protection is on the average two-thirds of that achieved with the subchronic regimen in dogs. In conscious animals DDA has no effects on hemodynamic parameters. The primary mechanism of cardioprotection appears to be antioxidant activity involving direct scavenging of superoxide anion, the lynchpin radical in ischemia-reperfusion injury. In addition, modulation of serum complement activity, as well as the reduction in the levels of C-reactive protein (CRP) and the membrane attack complex (MAC) in infarcted tissue suggest a significant antiinflammatory component in the mechanism of cardioprotective action of DDA. Stoichiometric binding of the meso-form of the compound to human serum albumin (HSA) has been demonstrated in vitro. This binding capacity overcomes the supramolecular assembly of the compound in aqueous solution, which by itself improves the stability and shelf life of aqueous formulations. Non-esterified astaxanthin readily enters cardiac tissue after either oral or parenteral administration, providing a reservoir of a cardioprotective agent with a significant half-life due to favorable ADME in mammals. Due to the well-documented safety profile of non-esterified astaxanthin in humans, disodium disuccinate astaxanthin may well find clinical utility in cardiovascular indications in humans following successful completion of preclinical and clinical pharmacology and toxicology studies.

PMID:

16252014

[PubMed - indexed for MEDLINE]

Astaxanthin in combination with Vitamin C shown to suppress respiratory inflammation better than ibuprofen in rodent study.

[Phytother Res.](#) 2010 Jul 14. [Epub ahead of print]

Summative interaction between astaxanthin, Ginkgo biloba extract (EGb761) and vitamin C in Suppression of respiratory inflammation: a comparison with ibuprofen.

[Haines DD](#), [Varga B](#), [Bak I](#), [Juhasz B](#), [Mahmoud FF](#), [Kalantari H](#), [Gesztelyi R](#), [Lekli I](#), [Czompa A](#), [Tosaki A](#).

Department of Pharmacology, Faculty of Pharmacy, University of Debrecen, Debrecen, Hungary.

Abstract

In this study, combinations of Ginkgo biloba leaf extract (EGb761) plus the carotenoid antioxidant astaxanthin (ASX) and vitamin C were evaluated for a summative dose effect in the inhibition of asthma-associated inflammation in asthmatic guinea-pigs. Ovalbumin-sensitized Hartley guinea-pigs challenged with ovalbumin aerosol to induce asthma, were administered EGb761, ASX, vitamin C or ibuprofen. Following killing, bronchoalveolar lavage (BAL) fluid was evaluated for inflammatory cell infiltrates and lung tissue cyclic nucleotide content. Each parameter measured was significantly altered to a greater degree by drug combinations, than by each component acting independently. An optimal combination was identified that included astaxanthin (10 mg/kg), vitamin C (200 mg/kg) and EGb761 (10 mg/kg), resulting in counts of eosinophils and neutrophils each 1.6-fold lower; macrophages 1.8-fold lower, cAMP 1.4-fold higher; and cGMP 2.04-fold higher than levels in untreated, asthmatic animals ($p < 0.05$). In conclusion, EGb761, ASX and vitamin C are shown here to interact summatively to suppress inflammation with efficacy equal to or better than ibuprofen, a widely used non-steroidal antiinflammatory drug (NSAID). Such combinations of non-toxic phytochemicals constitute powerful tools for the prevention of onset of acute and chronic inflammatory disease if consumed regularly by healthy individuals; and may also augment the effectiveness of therapy for those with established illness. Copyright (c) 2010 John Wiley & Sons, Ltd.

PMID: 20632299 [PubMed - as supplied by publisher]

Review Articles Referencing Astaxanthin's Anti-Inflammatory Benefits

Astaxanthin's cardioprotective properties reviewed and linked to its anti-inflammatory and antioxidant activity.

[Molecules](#). 2012 Feb 20;17(2):2030-48. doi: 10.3390/molecules17022030.

Astaxanthin in cardiovascular health and disease.

[Fassett RG](#)¹, [Coombes JS](#).

[Author information](#)

Abstract

Oxidative stress and inflammation are established processes contributing to cardiovascular disease caused by atherosclerosis. However, antioxidant therapies tested in cardiovascular disease such as vitamin E, C and β -carotene have proved unsuccessful at reducing cardiovascular events and mortality. Although these outcomes may reflect limitations in trial design, new, more potent antioxidant therapies are being pursued. Astaxanthin, a carotenoid found in microalgae, fungi, complex plants, seafood, flamingos and quail is one such agent. It has antioxidant and anti-inflammatory effects. Limited, short duration and small sample size studies have assessed the effects of astaxanthin on oxidative stress and inflammation biomarkers and have investigated bioavailability and safety. So far no significant adverse events have been observed and biomarkers of oxidative stress and inflammation are attenuated with astaxanthin supplementation. Experimental investigations in a range of species using a cardiac ischaemia-reperfusion model demonstrated cardiac muscle preservation when astaxanthin is administered either orally or intravenously prior to the induction of ischaemia. Human clinical cardiovascular studies using astaxanthin therapy have not yet been reported. On the basis of the promising results of experimental cardiovascular studies and the physicochemical and antioxidant properties and safety profile of astaxanthin, clinical trials should be undertaken.

PMID:

22349894

[PubMed - indexed for MEDLINE]

Free full text

Astaxanthin reviewed including its anti-inflammatory properties.

[Trends Biotechnol.](#) 2003 May;21(5):210-6.

Haematococcus astaxanthin: applications for human health and nutrition.

[2Guerin M](#), [Huntley ME](#), [Olaizola M](#).

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The carotenoid pigment astaxanthin has important applications in the nutraceutical, cosmetics, food and feed industries. *Haematococcus pluvialis* is the richest source of natural astaxanthin and is now cultivated at industrial scale. Astaxanthin is a strong coloring agent and a potent antioxidant - its strong antioxidant activity points to its potential to target several health conditions. This article covers the antioxidant, UV-light protection, anti-inflammatory and other properties of astaxanthin and its possible role in many human health problems. The research reviewed supports the assumption that protecting body tissues from oxidative damage with daily ingestion of natural astaxanthin might be a practical and beneficial strategy in health management.

Publication Types:

- [Review](#)

PMID: 12727382 [PubMed - indexed for MEDLINE]

Astaxanthin reviewed for its anti-inflammatory and antioxidant activity in multiple species.

Am J Cardiol 2008;101[suppl]:58D– 68D

Astaxanthin: A Novel Potential Treatment for Oxidative Stress and Inflammation in Cardiovascular Disease

Fredric J. Pashkow, MD,^{a,b,*} David G. Watumull,^b and Charles L. Campbell, MD^c

Oxidative stress and inflammation are implicated in several different manifestations of cardiovascular disease (CVD). They are generated, in part, from the overproduction of reactive oxygen species (ROS) and reactive nitrogen species (RNS) that activate transcriptional messengers, such as nuclear factor- κ B, tangibly contributing to endothelial dysfunction, the initiation and progression of atherosclerosis, irreversible damage after ischemic reperfusion, and even arrhythmia, such as atrial fibrillation. Despite this connection between oxidative stress and CVD, there are currently no recognized therapeutic interventions to address this important unmet need. Antioxidants that provide a broad, “upstream” approach via ROS/RNS quenching or free radical chain breaking seem an appropriate therapeutic option based on epidemiologic, dietary, and in vivo animal model data. However, human clinical trials with several different well-known agents, such as vitamin E and β -carotene, have been disappointing. Does this mean antioxidants as a class are ineffective, or rather that the “right” compound(s) have yet to be found, their mechanisms of action understood, and their appropriate targeting and dosages determined? A large class of potent naturally-occurring antioxidants exploited by nature—the oxygenated carotenoids (xanthophylls)— have demonstrated utility in their natural form but have eluded development as successful targeted therapeutic agents up to the present time. This article characterizes the mechanism by which this novel group of antioxidants function and reviews their preclinical development. Results from multiple species support the antioxidant/anti-inflammatory properties of the prototype compound, astaxanthin, establishing it as an appropriate candidate for development as a therapeutic agent for cardiovascular oxidative stress and inflammation.

Astaxanthin reviewed for multiple benefits including anti-inflammation.

[Altern Med Rev.](#) 2011 Dec;16(4):355-64.

Astaxanthin, cell membrane nutrient with diverse clinical benefits and anti-aging potential.

[Kidd P¹.](#)

Author information

Abstract

Astaxanthin, a xanthophyll carotenoid, is a nutrient with unique cell membrane actions and diverse clinical benefits. This molecule neutralizes free radicals or other oxidants by either accepting or donating electrons, and without being destroyed or becoming a pro-oxidant in the process. Its linear, polar-nonpolar-polar molecular layout equips it to precisely insert into the membrane and span its entire width. In this position, astaxanthin can intercept reactive molecular species within the membrane's hydrophobic interior and along its hydrophilic boundaries. Clinically, astaxanthin has shown diverse benefits, with excellent safety and tolerability. In double-blind, randomized controlled trials (RCTs), astaxanthin lowered oxidative stress in overweight and obese subjects and in smokers. It blocked oxidative DNA damage, lowered C-reactive protein (CRP) and other inflammation biomarkers, and boosted immunity in the tuberculin skin test. Astaxanthin lowered triglycerides and raised HDL-cholesterol in another trial and improved blood flow in an experimental microcirculation model. It improved cognition in a small clinical trial and boosted proliferation and differentiation of cultured nerve stem cells. In several Japanese RCTs, astaxanthin improved visual acuity and eye accommodation. It improved reproductive performance in men and reflux symptoms in H. pylori patients. In preliminary trials it showed promise for sports performance (soccer). In cultured cells, astaxanthin protected the mitochondria against endogenous oxygen radicals, conserved their redox (antioxidant) capacity, and enhanced their energy production efficiency. The concentrations used in these cells would be attainable in humans by modest dietary intakes. Astaxanthin's clinical success extends beyond protection against oxidative stress and inflammation, to demonstrable promise for slowing age-related functional decline.

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22214255

[PubMed - indexed for MEDLINE]

Free full text

Astaxanthin reviewed for its effects on oxidative stress-induced mitochondrial dysfunction.

[Nutrients](#). 2018 Aug 21;10(9). pii: E1137. doi: 10.3390/nu10091137.

Inhibitory Effect of Astaxanthin on Oxidative Stress-Induced Mitochondrial Dysfunction-A Mini-Review.

[Kim SH¹](#), [Kim H²](#).

[Author information](#)

Abstract

Oxidative stress is a major contributor to the pathogenesis of various human diseases as well as to the aging process. Mitochondria, as the center of cellular metabolism and major regulators of redox balance, play a critical role in disease development and progression. Mitochondrial dysfunction involving structural and metabolic impairment is prominent in oxidative stress-related diseases. Increased oxidative stress can damage mitochondria, and subsequent mitochondrial dysfunction generates excesses of mitochondrial reactive oxygen species that cause cellular damage. Mitochondrial dysfunction also activates the mitochondrial apoptotic pathway, resulting in cellular death. Astaxanthin, a red-colored xanthophyll carotenoid, exerts an anti-oxidative and anti-inflammatory effect on various cell lines. In this manner astaxanthin maintains mitochondrial integrity under various pathological conditions. In this review, the inhibitory effects of astaxanthin on oxidative stress-induced mitochondrial dysfunction and related disease development are discussed.

KEYWORDS:

astaxanthin; disease prevention; mitochondrial dysfunction; oxidative stress

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PMCID: [PMC6165470](#)

DOI: [10.3390/nu10091137](#)

[Indexed for MEDLINE]

[Free PMC Article](#)

Astaxanthin reviewed for its beneficial effects including anti-inflammatory activity.

[Integr Blood Press Control](#). 2008;1:1-3. Epub 2008 Oct 27.

Antihypertensive effects of astaxanthin.

[Yanai H¹](#), [Ito K](#), [Yoshida H](#), [Tada N](#).

Author information

Abstract

Astaxanthin is a biological antioxidant naturally found in a wide variety of aquatic living organisms, and has shown various pharmacological activities, such as anti-inflammatory and antidiabetic activities. A recent study reported that the administration of astaxanthin induced a significant reduction in blood pressure and delayed the incidence of stroke in stroke-prone spontaneously hypertensive rats, suggesting that astaxanthin also has antihypertensive effect. In a study using aortic rings of spontaneously hypertensive rats, astaxanthin induced a significant reduction of the contractile responses of the aorta to α -adrenergic receptor agonist and angiotensin II, which may contribute to the antihypertensive effect of astaxanthin. In a histopathological study, astaxanthin decreased coronary artery wall thickness compared with the control, indicating the possibility that astaxanthin ameliorates hypertension-induced vascular remodeling. Astaxanthin has anti-inflammatory, antidiabetic, antihypertensive, and antioxidative activities; therefore, we should perform further studies to elucidate an antiatherogenic effect of astaxanthin.

KEYWORDS:

antihypertensive effect; antioxidant; astaxanthin; atherosclerosis

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21949609

[PubMed]

PMCID:

PMC3172056

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Eye Health

Astaxanthin dose-dependently improves visual acuity and eye accommodation in human clinical trial.

Japanese Journal of Clinical Ophthalmology VOL.58;NO.6;PAGE.1051-1054(2004)

Changes in visual function following peroral astaxanthin

[NAKAMURA AKIRA](#); [ISOBE RYOKO](#); [OTAKA YASUHIRO](#); [ABEMATSU YASUKO](#); [NAKATA DAISUKE](#); [HONMA CHIKA](#) ; [SAKURAI SHIZUKA](#); [SHIMADA YOSHIAKI](#); [HORIGUCHI MASAYUKI](#)

We evaluated the effect of astaxanthin on visual function in 49 eyes of 49 healthy volunteers. They were over 40 years of age. They were divided into 4 groups matched for age and gender. Each group was given peroral astaxanthin once a day. The dosage was 0mg, 2mg, 4mg, or 12mg for each group. After ingestion of astaxanthin for consecutive 28 days, the uncorrected far visual acuity significantly improved in groups receiving 4mg or 12mg. The accommodation time significantly shortened in groups receiving 4mg or 12mg. There was no change in refraction, flicker fusion frequency, or pupillary reflex.

Astaxanthin improves eye fatigue in double-blind, placebo-controlled randomized human clinical trial.

Journal of Clinical Therapeutics & Medicines VOL.22;NO.1;PAGE.41-54(2006)

The supplementation effect of Astaxanthin on Accommodation and Asthenopia

[NAGAKI YASUNORI](#); [MIHARA MIHARU](#); [TSUKAHARA HIROKI](#); [ONO SHIGEAKI](#)

This double blind randomized placebo controlled study examined the supplementation effects of Haematococcus (H) pluvialis derived astaxanthin on subjects suffering from visual display terminal (VDT) induced visual fatigue. Subjects were divided into two groups: 6 mg astaxanthin treated and placebo groups. Furthermore, the safety of astaxanthin intake was simultaneously assessed. After the 4 week supplementation period, the groups' visual accommodation was evaluated as well as a subjective questionnaire designed to evaluate visual asthenopia (eye fatigue). Twenty five subjects of the astaxanthin treated group and 23 subjects of the placebo group were examined for eye fatigue. For safety evaluation, 31 treated subjects and 28 placebo subjects were analysed. We report the following observations: 1. In the astaxanthin treated group, the change of accommodation before and after supplementation significantly improved compared with the placebo group. 2. The astaxanthin supplemented group exhibited a significant rate of change in the accommodation compared with the placebo group. 3. The subjective questionnaire evaluating visual asthenopia revealed a marked reduction in "heavy head" claims. Other typical improvements of fatigue symptoms included "dimness of sight" and "stiff shoulders and back". 4. No significant differences were detected between the treatment and the placebo groups after 4 weeks of supplementation in the safety parameters analyzed, and adverse event. These results suggest that 6 mg of astaxanthin per day from a H. pluvialis algal extract can improve eye fatigue. Moreover, astaxanthin can be safely consumed at this level by healthy adults.

Astaxanthin increases retinal capillary blood flow in double-blind, placebo-controlled randomized human clinical trial.

Journal of Clinical Therapeutics & Medicines VOL.21;NO.5;PAGE.537-542(2005)

The Effect of Astaxanthin on Retinal Capillary Blood Flow in Normal Volunteers

[NAGAKI YASUNORI](#); [MIHARA MIHARU](#); [TAKAHASHI JIRO](#); [KITAMURA AKITOSHI](#); [HORITA YOSHIHARU](#); [SUGIURA YURI](#); [TSUKAHARA HIROKI](#)

Objective: We evaluated the effect of astaxanthin on retinal circulation in healthy volunteers. Design A double blind randomized placebo controlled study. Methods: Thirty-six volunteers were randomized into two groups: Astaxanthin group that consisted of 18 subjects who received oral astaxanthin, 6mg/day, for 4 weeks and a placebo group that consisted of 18 subjects who received an identical looking oral placebo for 4 weeks. Retinal capillary blood flow was measured by the Heidelberg Retina Flowmeter. Changes in blood pressure, blood cell counts, fasting plasma glucose level, fasting plasma astaxanthin level, retinal capillary blood flow, intraocular pressure, inquiry about eye strain were examined before and after supplementation in both groups. Results: The fasting plasma astaxanthin level in the astaxanthin group was significantly ($P<0.001$) higher than before supplementation. The fasting plasma astaxanthin level in the placebo group after placebo treatment remained unchanged. After 4 weeks supplementation, retinal capillary blood flow in the astaxanthin group was significantly ($P<0.01$) higher than before supplementation in both eyes, while retinal capillary blood flow in the placebo group after placebo treatment was unchanged. Intraocular pressures in both groups remained unchanged during the supplementation period. Conclusion: Our results suggest that astaxanthin supplementation may increase retinal capillary blood flow.

Astaxanthin improves eye strain and eye accommodation in double-blind, placebo-controlled human clinical study.

Journal of Clinical Therapeutics & Medicines VOL.21;NO.6;PAGE.637-650(2005)

Effect of Astaxanthin on Accommodation and Asthenopia-Efficacy-Identification Study in Healthy Volunteers-

[SHIRATORI KENJI](#); [OGAMI KAZUHIRO](#); [NITTA TAKUYA](#); [SHINMEI YASUHIRO](#); [CHIN SHINKI](#); [YOSHIDA KAZUHIKO](#); [TSUKAHARA HIROKI](#); [TAKEHARA ISAO](#); [ONO SHIGEAKI](#)

A double-blind study was conducted to confirm the efficacy of *H. pluvialis* Astaxanthin on accommodation and asthenopia and its safety. Two groups of subjects were compared, wherein one was given 0mg of Astaxanthin (as a control group) and the other was given 6mg of Astaxanthin (AX group). The subjects were healthy volunteers who complained of asthenopia. Twenty were enrolled in each group, and the testing food was administered during 4 weeks. Sub-objective accommodation power, positive accommodation time and negative accommodation time were measured before and after administration to objectively evaluate the degree of asthenopia. Additionally, subjective degree of asthenopia by volunteers was evaluated using VAS. The safety was assessed by changes in value of laboratory tests between pre- and post-administrations and by the doctor's questions. 1) Sub-objective accommodation power (rate of change) of the AX group was significantly higher than that of the control group. 2) The AX group showed significantly higher rate of positive and negative accommodation times (rate of change) compared to those of the control group. 3) In the AX group, subjective degree of asthenopia measured by VAS showed significant improvement in two parameters, i.e., "blar-eye feeling" and "tendency of irritation" than the control group. 4) No changes in laboratory tests of clinically controversial were noted and also no adverse events suggesting causal relationship with the testing food were found. In conclusion, administration of 6mg/day (in a daily dosage of 2 capsules; 3mg/capsule) of *H. pluvialis* Astaxanthin improved accommodation power and subjective symptoms of asthenopia. Also, Astaxanthin was confirmed to be completely safe.

Astaxanthin improves eye accommodative recovery and prevents eye fatigue in human clinical trial.

Journal of Clinical Therapeutics & Medicines VOL.21;NO.4;PAGE.431-436(2005)

Effects of Astaxanthin on Accommodative Recovery

[TAKAHASHI NANAOKO](#) (Kajitaganka) [KAJITA MASAYOSHI](#) (Kajitaganka)

Effects of astaxanthin on accommodative recovery derived from a rest after VDT (visual display terminal) working was studied. Ten healthy volunteers were entered into the study, and except one subject who developed allergic conjunctivitis during the study, 9 of whom were evaluated (9 dominant eyes) by values of objective diopter, HFC (High Frequency Component in Accommodative micro-fluctuation) and accommodative reaction. Consequently, increase of HFC after the rest was significantly restrained by astaxanthin uptake compared to that shortly after working. Therefore, Astaxanthin was suggested to have effects on accommodation during recovery process of accommodative fatigue to relieve fatigue rapidly.

Astaxanthin increases blood flow velocity in the vascular layer of the eye in a double-blind, placebo-controlled randomized human clinical trial.

[Graefes Arch Clin Exp Ophthalmol](#). 2012 Feb;250(2):239-45. doi: 10.1007/s00417-011-1843-1. Epub 2011 Nov 10.

Astaxanthin increases choroidal blood flow velocity.

[Saito M¹](#), [Yoshida K](#), [Saito W](#), [Fujiya A](#), [Ohgami K](#), [Kitaichi N](#), [Tsukahara H](#), [Ishida S](#), [Ohno S](#).
Author information

Abstract

PURPOSE:

Previous studies have reported that astaxanthin (AXT) has antioxidative and anti-inflammatory effects in addition to its ability to shorten blood transit times. As laser speckle flowgraphy (LSFG) can noninvasively visualize the hemodynamics of the choroidal circulation, we used the technique to evaluate whether continuous ingestion of 12 mg of AXT per day could increase quantitative blood flow velocity.

METHODS:

In this randomized, double-blind, placebo-controlled study, we examined 20 healthy volunteers who ingested 12 mg AXT or placebo capsules over a 4-week period. LSFG was measured in the right eyes of all subjects at pre-ingestion, and at 2 and 4 weeks after the treatment of AXT. LSFG values were used to calculate the square blur rate (SBR), which is a quantitative index of relative blood flow velocity.

RESULTS:

A significant increase of the macular SBR was seen 4 weeks after AXT ingestion when compared to the pre-ingestion values (Wilcoxon signed-rank test, $P = 0.018$). In contrast, no statistical difference in the macular SBR was detected in the placebo group (Friedman test, $P = 0.598$). No subjective or objective adverse events were found after the 12-mg AXT ingestion.

CONCLUSIONS:

Results suggest that administration of AXT over a 4-week period can elevate the choroidal blood flow velocity without any adverse effects.

PMID:

22072378

[PubMed - indexed for MEDLINE]

Astaxanthin improves visual acuity (the ability to see fine detail) and muscle fatigue in placebo-controlled human clinical trial.

Journal of Clinical Therapeutics & Medicines VOL.18;NO.9;PAGE.1085-1100(2002)

Sports Performance Benefits from Taking Natural Astaxanthin Characterized by Visual Acuity and Muscle Fatigue Improvement in Humans.

[SAWAKI KEISUKE](#); [YOSHIGI HIROSHI](#); [AOKI KAZUHIRO](#); [KOIKAWA NATSUE](#); [AZUMANE AKITO](#); [KANEKO KESATOKI](#); [YAMAGUCHI MASAHIRO](#)

The effects of astaxanthin on visual acuity and muscle fatigue were studied. Astaxanthin (3,3'-Dihydroxy-.BETA.,.BETA.-carotene-4,4'-dione) is a red pigment found in salmon and krill and has strong antioxidant properties. In the two supplementation studies, astaxanthin extracted from algae (*Haematococcus pluvialis*) was used. Four visual acuity parameters were examined in experiment A in 18 healthy adult male volunteers that were equally divided into two groups (treatment and control). The measured parameters were deep vision, critical flicker fusion, static and kinetic visual acuity before and after supplementation. A second investigation (experiment B) involved 16 adult male volunteers to establish the effect of astaxanthin supplementation on the build up of lactic acid before and after running 1200 metres. In both experiments, the treated groups ingested an astaxanthin capsule per day for 4 weeks (6mg astaxanthin per day) and the control groups received a placebo capsule. Results: In experiment A, the deep vision and the critical flicker fusion of the treated groups were significantly improved compared to the control group. No effects of treated group were observed on static and kinetic visual acuity. In experiment B, serum lactic acid concentration at 2 minutes after activity (1,200m running) of the treatment group was significantly lower than that of the control one. No other effects related to supplementation of astaxanthin on serum biological and hematological examinations were observed. Based on these preliminary findings, it suggested that supplementation of astaxanthin is effective for the improvement of visual acuity and muscle fatigue that may lead to sports performance benefits.

Astaxanthin at 6mg per day improves eye fatigue and eye accommodation in double-blind, placebo-controlled human clinical trial.

Journal of Clinical Therapeutics & Medicines VOL.21;NO.5;PAGE.543-556(2005)

Effects of Astaxanthin on Accommodation and Asthenopia-Dose Finding Study in Healthy Volunteers-

[NITTA TAKUYA](#); [OGAMI KAZUHIRO](#); [SHIRATORI KENJI](#); [SHINMEI YASUHIRO](#); [CHIN SHINKI](#); [YOSHIDA KAZUHIKO](#); [TSUKAHARA HIROKI](#); [ONO SHIGEAKI](#)

A double-blind study was conducted in healthy volunteers to objectively evaluate the optimum dose and safety of astaxanthin (AX) on accommodation and asthenopia. The subjects were divided into 3 groups: 0mg (AX 0mg group), 6mg (AX 6mg group) and 12mg (AX 12mg group) of astaxanthin administered. Ten subjects, total thirty subjects were included in each group. Mean time consumed for close working (e.g., VDT working) was approximately 7 hours a day. The testing food was given to the subjects for 4 weeks. Then, the subjects were traced for 4 weeks and assessed by comparison of the observed values between pre- and post-dosing. As a result 1. Objective accommodation power of the AX 12mg group was significantly increased compared to that of pre-dosing. 2. Positive accommodation time was significantly shortened in the AX 6mg and the 12mg groups compared to those of pre-dosing, and negative accommodation time was significantly shortened in the AX 0mg and the 6mg groups compared to those of pre-dosing. 3. According to the assessment by VAS, many parameters in subjective symptoms were improved in the AX 6mg group. 4. No changes were noted in laboratory tests of controversial in clinical setting due to AX uptake. Also, there were no adverse events caused by the administration of the testing food. In conclusion, accommodation power and subjective symptoms relating asthenopia were improved by taking 6mg/day of astaxanthin, therefore more than 6mg/day was considered to be optimal dosage of astaxanthin.

Astaxanthin prevents eye strain in double-blind, placebo-controlled human crossover study.

Journal of the Eye VOL.23;NO.6;PAGE.829-834(2006)

Effects of Astaxanthin on Eyestrain Induced by Accommodative Dysfunction

[IWASAKI TSUNETO](#); [TAHARA AKIHIKO](#)

We investigated effects of astaxanthin on eyestrain induced by accommodative dysfunction. The 10 healthy subjects received 6mg/day of astaxanthin (Ax group) or 0mg/day (placebo; P group) for 14 days, and were then assigned a near visual task for 20min. Accommodative function and subjective symptoms relating to eyestrain were measured before and after the task, and after the 10-minute rest following the task. The data were then compared between Ax and P groups by the double-blind cross-over method. After the task, accommodation contraction and relaxation times were extended in both the Ax and P groups. Comparison between the two groups showed that after the task, accommodation relaxation time was significantly extended in P group, in contrast to Ax. Accommodative contraction and relaxation times were significantly prolonged after the 10-minute rest in P group as compared to Ax. The symptoms eye fatigue, eye heaviness, blurred vision and eye dryness in P group were increased, but Ax group showed increased in eye fatigue and eye heaviness. On the basis of these results, we concluded that astaxanthin has the effects of reducing and preventing eyestrain induced by accommodative dysfunction.

Astaxanthin improves eye accommodation in randomized placebo-controlled human clinical trial.

Journal of Traditional Medicines VOL.19;NO.5;PAGE.170-173(2002)

Effects of astaxanthin on accommodation, critical flicker fusion, and pattern visual evoked potential in visual display terminal workers.

[NAGAKI Y](#); [HAYASAKA S](#) ; [YAMADA T](#) ; [HAYASAKA Y](#); [SANADA M](#); [UONOMI T](#)

We evaluated the effects of astaxanthin, a red carotenoid, on accommodation, critical flicker fusion(CFF), and pattern visual evoked potential(PVEP) in visual display terminal(VDT) workers. As controls, 13 non-VDT workers received no supplementation (Group A). Twenty-six VDT workers were randomized into 2 groups: Group B consisted of 13 subjects who received oral astaxanthin, 5mg/day, for 4 weeks, and Group C consisted of 13 subjects who received an oral placebo, 5mg/day, for 4 weeks. No significant difference in age was noted among the 3 groups. A double-masked study was designed in Groups B and C. Accommodation amplitude in Group A was 3.7. \pm .1.5 diopters. Accommodation amplitudes (2.3. \pm .1.4 and 2.2. \pm .1.0 diopters) in Groups B and C before supplementation were significantly ($p < 0.05$) lower than in Group A. Accommodation amplitude (2.8. \pm .1.6 diopters) in Group B after astaxanthin treatment was significantly ($p < 0.01$) larger than before supplementation, while accommodation amplitude (2.3. \pm .1.1 diopters) in Group C after placebo supplementation was unchanged. The CFFs and amplitude and latency of P100 in PVEP in Group A were 45.0. \pm .4.2Hz, 6.5 \pm 1.8.MU.V, and 101.3. \pm .6.5msec, respectively. The CFFs in Groups B and C before supplementation were significantly ($p < 0.05$) lower than in Group A. The CFFs in Groups B and C did not change after supplementation. Amplitudes and latencies of P100 in PVEP in Groups B and C before supplementation were similar to those in Group A and did not change after supplementation. Findings of the present study indicated that accommodation amplitude improved after astaxanthin supplementation in VDT workers.

Astaxanthin reduces eye strain in 46% of subjects in 4 weeks at 5mg per day in double-blind human clinical trial.

Journal of Traditional Medicines 2002: 19 (5), 170 – 173.

Effects of Astaxanthin on accommodation, critical flicker fusion, and pattern visual evoked potential in visual display terminal workers.

Nagaki Y., Hayasaka S., Yamada T., Hayasaka Y., Sanada M., Uonomi T.

Working for long periods at visual display terminals reportedly induces various visual problems such as eye strain, blurring and diplopia (a disorder of vision in which two images of a single object are seen because of unequal action of the eye muscles – also called double vision). In a double blind study performed in Japan, after four weeks of supplementation with 5 mg of Astaxanthin per day (extracted from *Haematococcus Pluvialis* algae meal) the authors reported a 46% reduction of eye strain subjects and higher accommodation amplitude in visual display terminal subjects.

Although the mechanism of action is unclear, Astaxanthin's potent antioxidant properties may relieve chronic stress of visual display terminal use that may induce hypofunction of the ciliary body, resulting in decreased accommodation.

Astaxanthin formula may provide therapeutic benefit to patients suffering from dry eye syndrome in double-blind, placebo-controlled human clinical trial.

[Clin Ophthalmol.](#) 2016 May 9;10:813-20. doi: 10.2147/OPTH.S106455. eCollection 2016.

A randomized, double-blind, placebo-controlled study of oral antioxidant supplement therapy in patients with dry eye syndrome.

[Huang JY¹](#), [Yeh PT¹](#), [Hou YC¹](#).

Author information

Abstract

PURPOSE: To evaluate the efficacy of oral antioxidant supplementation in the treatment of patients with dry eye syndrome (DES).

METHODS: A prospective, randomized, double-blinded study compared the effects of an antioxidant supplement (containing anthocyanosides, astaxanthin, vitamins A, C, and E, and several herbal extracts, including *Cassiae semen* and *Ophiopogonis japonicus*) with placebo on patients with DES. We assessed dry eye symptoms, visual acuity, Schirmer's test, tear film breakup time, cornea and conjunctiva fluorescein staining, serum anti-SSA/anti-SSB antibodies, and the level of reactive oxygen species (ROS) in tears. The supplementation period was 8 weeks and patients were followed up every 4 weeks for 16 weeks. A linear mixed model was used to compare the groups, while within-group differences were tested by repeated-measures analysis of variance.

RESULTS: Forty-three patients, 20 and 23 in treatment and placebo groups, respectively, completed the study. Liver and renal functions were normal. Diastolic blood pressure decreased in the treatment group. There were no significant differences in systolic blood pressure, dry eye symptoms, serum anti-SSA and anti-SSB, visual acuity, intraocular pressure, or fluorescein corneal staining between the groups. Tear film breakup time scores and Schirmer's test without topical anesthesia significantly improved in the treatment group. Tear ROS level differed between the groups and decreased after treatment. Overall subjective impression revealed a significant improvement with treatment compared with placebo.

CONCLUSION: Oral antioxidant supplementations may increase tear production and improve tear film stability by reducing tear ROS. The vegetable-based antioxidant supplement used in this study is safe and can be utilized as an adjuvant therapy to conventional artificial tear therapy for patients with DES.

KEYWORDS: blood pressure; dry eye; herbal extracts; reactive oxygen species; tear

PMID: 27274185 PMCID: [PMC4869783](#) DOI: [10.2147/OPTH.S106455](#)

[Free PMC Article](#)

Astaxanthin with other nutrients can improve retinal dysfunction in patients with non-advanced age-related macular degeneration in double-blind, placebo-controlled human clinical trial.

[Ophthalmology](#). 2008 Feb;115(2):324-333.e2. Epub 2007 Aug 22.

Carotenoids and antioxidants in age-related maculopathy italian study: multifocal electroretinogram modifications after 1 year.

[Parisi V](#), [Tedeschi M](#), [Gallinaro G](#), [Varano M](#), [Saviano S](#), [Piermarocchi S](#); [CARMIS Study Group](#).

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OBJECTIVE: To evaluate the influence of short-term carotenoid and antioxidant supplementation on retinal function in nonadvanced age-related macular degeneration (AMD). **DESIGN:** Randomized controlled trial. **PARTICIPANTS:** Twenty-seven patients with nonadvanced AMD and visual acuity $>$ or $=0.2$ logarithm of the minimum angle of resolution were enrolled and randomly divided into 2 age-similar groups: 15 patients had oral supplementation of vitamin C (180 mg), vitamin E (30 mg), zinc (22.5 mg), copper (1 mg), lutein (10 mg), zeaxanthin (1 mg), and astaxanthin (4 mg) (AZYR SIFI, Catania, Italy) daily for 12 months (treated AMD [T-AMD] group; mean age, 69.4 \pm 4.31 years; 15 eyes); 12 patients had no dietary supplementation during the same period (nontreated AMD [NT-AMD] group; mean age, 69.7 \pm 6.23 years; 12 eyes). At baseline, they were compared with 15 age-similar healthy controls. **METHODS:** Multifocal electroretinograms in response to 61 M-stimuli presented to the central 20 degrees of the visual field were assessed in pretreatment (baseline) conditions and, in nonadvanced AMD patients, after 6 and 12 months. **MAIN OUTCOME MEASURES:** Multifocal electroretinogram response amplitude densities (RAD, nanovolt/deg²) of the N1-P1 component of first-order binary kernels measured from 5 retinal eccentricity areas between the fovea and midperiphery: 0 degrees to 2.5 degrees (R1), 2.5 degrees to 5 degrees (R2), 5 degrees to 10 degrees (R3), 10 degrees to 15 degrees (R4), and 15 degrees to 20 degrees (R5). **RESULTS:** At baseline, we observed highly significant reductions of N1-P1 RADs of R1 and R2 in T-AMD and NT-AMD patients when compared with healthy controls (1-way analysis of variance $P < 0.01$). N1-P1 RADs of R3-R5 observed in T-AMD and NT-AMD were not significantly different ($P > 0.05$) from controls. No significant differences ($P > 0.05$) were observed in N1-P1 RADs of R1-R5 between T-AMD and NT-AMD at baseline. After 6 and 12 months of treatment, T-AMD eyes showed highly significant increases in N1-P1 RADs of R1 and R2 ($P < 0.01$), whereas no significant ($P > 0.05$) change was observed in N1-P1 RADs of R3-R5. No significant ($P > 0.05$) changes were found in N1-P1 RADs of R1-R5 in NT-AMD eyes. **CONCLUSIONS:** In nonadvanced AMD eyes, a selective dysfunction in the central retina (0 degrees -5 degrees) can be improved by the supplementation with carotenoids and antioxidants. No functional changes are present in the more peripheral (5 degrees -20 degrees) retinal areas.

PMID: 17716735 [PubMed - indexed for MEDLINE]

Astaxanthin with other nutrients can improve visual acuity, contrast sensitivity and visual function in patients with non-advanced age-related macular degeneration in randomized human clinical trial.

[Eur J Ophthalmol](#). 2012 Mar-Apr;22(2):216-25. doi: 10.5301/ejo.5000069.

Carotenoids in Age-related Maculopathy Italian Study (CARMIS): two-year results of a randomized study.

[Piermarocchi S¹](#), [Saviano S](#), [Parisi V](#), [Tedeschi M](#), [Panozzo G](#), [Scarpa G](#), [Boschi G](#), [Lo Giudice G](#); [Carmis Study Group](#).

[Collaborators \(21\)](#)

[Author information](#)

Abstract

PURPOSE:

The high concentration of carotenoids in the macula, plus evidence linking oxidative stress to age-related macular degeneration (AMD) and carotenoids to antioxidation, generated the hypothesis that higher antioxidant intakes can prevent AMD. The aim of this study was to determine whether nutritional supplementation with a targeted nutritional supplement improves visual acuity and visual function in AMD.

METHODS:

In this multicenter, prospective open-label randomized study, 145 patients were randomly assigned to 2 different treatment groups. Interventions were lutein (10 mg), zeaxanthin (1 mg), astaxanthin (4 mg; AZYR SIFI, Catania, Italy), and antioxidants/vitamins supplementation formula or no dietary supplementation for 2 years. Primary outcome was mean changes in visual acuity (VA) at 12 and 24 months. Other measures included contrast sensitivity (CS) and National Eye Institute visual function questionnaire (NEI VFQ-25) scores at 12 and 24 months.

RESULTS:

Patients in the treated group showed stabilization of VA with significantly ($p=0.003$) better VA scores (81.4 ± 7.2) compared to the nontreated group (76.8 ± 8.9) at 24-month follow-up. An improvement in CS ($p=0.001$) and final mean NEI VFQ-25 composite scores at 12 and 24 months higher in treated group compared to nontreated group were also shown ($p<0.001$).

CONCLUSIONS:

Patients treated with lutein/zeaxanthin and astaxanthin together with other nutrients were more likely to report clinically meaningful stabilization/improvements in VA, CS, and visual function through 24 months compared with nontreated subjects. Further studies are needed with more patients and for longer periods of time.

PMID:

22009916

[PubMed - indexed for MEDLINE]

ASTAXANTHIN SHOWS POTENTIAL TO WORK AS EYE ANTIOXIDANT DURING CATARACT SURGERY IN FEMALES IN HUMAN CLINICAL STUDY.

J Clin Biochem Nutr. 2019 Jul;65(1):47-51.

doi: 10.3164/jcfn.18-110. Epub 2019 Apr 18.

Effects of astaxanthin on VEGF level and antioxidation in human aqueous humor: difference by sex

[Hirotaka Hashimoto](#)¹, [Kiyomi Arai](#)², [Jiro Takahashi](#)³, [Makoto Chikuda](#)²

- PMID: [31379413](#)
- PMCID: [PMC6667389](#)
- DOI: [10.3164/jcfn.18-110](#)

[Free PMC article](#)

Abstract

In our previous report, we showed the effect of astaxanthin intake on VEGF level in the aqueous humor and the relationship between VEGF level and reactive oxygen species-related parameters and other relevant factors. VEGF level is associated with total hydroperoxide level, and a multivariate analysis identified sex as a secondary factor affecting these relationships. Here, we analyzed the effects of astaxanthin on the relationship between VEGF level and reactive oxygen species-related parameters by sex. Patients (16 males and 19 females, aged 71.3 and 70.6, respectively) underwent bilateral cataract surgery on one side before and the other side after astaxanthin treatment (6 mg/day for 2 weeks). Levels of VEGF, hydrogen peroxide, and total hydroperoxide, and O₂⁻ scavenging activity, were measured in the aqueous humor. In females only, VEGF level was negatively correlated with O₂⁻ scavenging activity before the astaxanthin intake ($r = -0.6, p < 0.01$) and positively correlated with total hydroperoxide level before and after the astaxanthin intake ($r = 0.7$ and 0.8 , respectively, $p < 0.01$). In conclusion, astaxanthin appears to affect O₂⁻ scavenging activity in the aqueous humor in females, and is likely to be involved in the control of VEGF levels in the anterior eye.

ASTAXANTHIN FORMULA REDUCES LOSS OF ACCOMODATIVE FUNCTION IN SUBJECTS USING VIDEO DISPLAY TERMINALS IN PLACEBO-CONTROLLED HUMAN CLINICAL STUDY.

J Clin Biochem Nutr 2021 Jul;69(1):77-90. doi: 10.3164/jcbn.20-149. Epub 2021 Feb 5.

Effects of anthocyanin, astaxanthin, and lutein on eye functions: a randomized, double-blind, placebo-controlled study

[Yuki Kizawa](#)¹, [Takahiro Sekikawa](#)¹, [Masakatsu Kageyama](#)², [Haruna Tomobe](#)², [Riyo Kobashi](#)², [Takahiro Yamada](#)³

- PMID: 34376917 PMCID: [PMC8325772](#) DOI: [10.3164/jcbn.20-149](#)

Free PMC article

Abstract

We examined the effects of a test food containing anthocyanin, astaxanthin, and lutein on the eye function in healthy Japanese adults with eye fatigue after operating visual display terminals. Forty-four subjects were randomly but equally assigned to the active or placebo group. Two active or placebo capsules were taken once daily for 6 weeks. Accommodative function, tear film break-up time, visual acuity, the value of Schirmer's test, macular pigment optical density level, muscle hardness, and a questionnaire were evaluated before and after a 6-week intervention. Each group included 20 subjects in the efficacy analysis. The active group showed a significant improvement in the percentage of pupillary response of an average of both eyes and dominant eye pre- and post-visual display terminal operation at 6 weeks compared with the placebo group. Moreover, the active group showed a significant improvement in the scores of "A sensation of trouble in focusing the eyes" and "Difficulty in seeing objects in one's hand and nearby, or fine print" compared with the placebo group between before and after ingestion. Therefore, 6-weeks consumption of the test food inhibited a decrease in the accommodative function caused by visual display terminal operation (UMIN000036989).

ASTAXANTHIN REVIEWED FOR POTENTIAL TO TREAT A VARIETY OF OCULAR DISEASES IN HUMAN AND ANIMALS.

Mar Drugs. 2020 May 1;18(5):239.

doi: 10.3390/md18050239.

Clinical Applications of Astaxanthin in the Treatment of Ocular Diseases: Emerging Insights

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- PMID: [32370045](#)
- PMCID: [PMC7281326](#)
- DOI: [10.3390/md18050239](#)

Free PMC article

Abstract

Astaxanthin is a naturally occurring red carotenoid pigment belonging to the family of xanthophylls, and is typically found in marine environments, especially in microalgae and seafood such as salmonids, shrimps and lobsters. Due to its unique molecular structure, astaxanthin features some important biologic properties, mostly represented by strong antioxidant, anti-inflammatory and antiapoptotic activities. A growing body of evidence suggests that astaxanthin is efficacious in the prevention and treatment of several ocular diseases, ranging from the anterior to the posterior pole of the eye. Therefore, the present review aimed at providing a comprehensive evaluation of current clinical applications of astaxanthin in the management of ocular diseases. The efficacy of this carotenoid in the setting of retinal diseases, ocular surface disorders, uveitis, cataract and asthenopia is reported in numerous animal and human studies, which highlight its ability of modulating several metabolic pathways, subsequently restoring the cellular homeostatic balance. To maximize its multitarget therapeutic effects, further long-term clinical trials are warranted in order to define appropriate dosage, route of administration and exact composition of the final product.

Astaxanthin protects against retinal damage in mice and in-vitro.

[Curr Eye Res.](#) 2016 Nov;41(11):1465-1472. Epub 2016 May 9.

Astaxanthin Protects Against Retinal Damage: Evidence from In Vivo and In Vitro Retinal Ischemia and Reperfusion Models.

[Otsuka T¹](#), [Shimazawa M¹](#), [Inoue Y¹](#), [Nakano Y¹](#), [Ojino K¹](#), [Izawa H¹](#), [Tsuruma K¹](#), [Ishibashi T²](#), [Hara H¹](#).

Author information

Abstract

PURPOSE: Astaxanthin exhibits various pharmacological activities, including anti-oxidative, anti-tumor, and anti-inflammatory effects, and is thought to exert a neuroprotective effect via these mechanisms. The purpose of this study was to investigate the protective effects of astaxanthin on neuronal cell death using a retinal ischemia/reperfusion model.

METHODS: In vivo, retinal ischemia was induced by 5 h unilateral ligation of the pterygopalatine artery (PPA) and the external carotid artery (ECA) in ddY mice. Astaxanthin (100 mg/kg) was administered orally 1 h before induction of ischemia, immediately after reperfusion, at 6 or 12 h after reperfusion, and twice daily for the following 4 days. Histological analysis and an electroretinogram (ERG) were performed 5 days after ischemia/reperfusion. In vitro, cell death was induced in the RGC-5 (retinal precursor cells) by oxygen-glucose deprivation (OGD), and the rates of cell death and production of intracellular reactive oxygen species (ROS) were measured using nuclear staining and a ROS reactive reagent, CM-H₂DCFDA.

RESULTS: Histological studies revealed that astaxanthin significantly reduced retinal ischemic damage and ERG reduction. In in vitro studies, astaxanthin inhibited cell death and ROS production in a concentration-dependent manner.

CONCLUSIONS: Collectively, these results indicate that astaxanthin inhibits ischemia-induced retinal cell death via its antioxidant effect. Hence, astaxanthin might be effective in treating retinal ischemic pathologies.

KEYWORDS: Astaxanthin; ROS; ischemia; neuroprotection; retina

PMID: 27158842

DOI: [10.3109/02713683.2015.1127392](https://doi.org/10.3109/02713683.2015.1127392)

[Indexed for MEDLINE]

Astaxanthin protects against light-induced retinal damage in rats.

[Nippon Ganka Gakkai Zasshi](#). 2015 Feb;119(2):55-62.

[Protection effect of astaxanthin against light-induced retinal damage in rat].

[Article in Japanese]

[Yamamoto A](#), [Yuzawa M](#).

Abstract

PURPOSE: To clarify the protective effect of astaxanthin (AST) against light-induced retinal damage in rats.

METHODS: Albino rats were divided into three groups: a group treated orally with 1 mg/kg AST daily (group H), a group treated with 0.2 mg/kg AST (group L), and a control group (group C). Rats were administered AST in groups H and L and olive oil in group C followed by a 12-hour exposure to 3000-lux white light. After exposure for 7 days, the protective effect of AST was evaluated functionally by electroretinogram (ERG) and histologically by measuring outer nuclear layer (ONL) thickness and by counting rate of terminal deoxynucleotidyl transferase dUTP nick end labeling (TUNEL) stained cells.

RESULTS: After exposure to light, the b-wave amplitudes were significantly preserved in the AST groups compared to group C, Further the rate of the residual amplitude was higher in group H than in group L. The ONL thicknesses were significantly thicker in AST-treated rats compared to group C. The rates of TUNEL stained cells were significantly lower in the following order: group H, L and C.

CONCLUSION: AST may have a protective effect against light-induced retinal damage in albino rats.

PMID: 25804029

[Indexed for MEDLINE]

Astaxanthin protects the vascular layer of the eye in mice and may be a potential therapy for age-related macular degeneration.

[Invest Ophthalmol Vis Sci](#). 2008 Apr;49(4):1679-85.

Inhibition of choroidal neovascularization with an anti-inflammatory carotenoid astaxanthin.

[Izumi-Nagai K](#), [Nagai N](#), [Ohgami K](#), [Satofuka S](#), [Ozawa Y](#), [Tsubota K](#), [Ohno S](#), [Oike Y](#), [Ishida S](#).

Laboratory of Retinal Cell Biology, Keio University of Medicine, Tokyo, Japan.

PURPOSE: Astaxanthin (AST) is a carotenoid found in marine animals and vegetables. The purpose of the present study was to investigate the effect of AST on the development of experimental choroidal neovascularization (CNV) with underlying cellular and molecular mechanisms. **METHODS:** Laser photocoagulation was used to induce CNV in C57BL/6J mice. Mice were pretreated with intraperitoneal injections of AST daily for 3 days before photocoagulation, and treatments were continued daily until the end of the study. CNV response was analyzed by volumetric measurements 1 week after laser injury. Retinal pigment epithelium-choroid levels of IkappaB-alpha, intercellular adhesion molecule (ICAM)-1, monocyte chemoattractant protein (MCP)-1, interleukin (IL)-6, vascular endothelial growth factor (VEGF), VEGF receptor (VEGFR)-1, and VEGFR-2 were examined by Western blotting or ELISA. AST was applied to capillary endothelial (b-End3) cells, macrophages, and RPE cells to analyze the activation of NF-kappaB and the expression of inflammatory molecules. **RESULTS:** The index of CNV volume was significantly suppressed by treatment with AST compared with that in vehicle-treated animals. AST treatment led to significant inhibition of macrophage infiltration into CNV and of the *in vivo* and *in vitro* expression of inflammation-related molecules, including VEGF, IL-6, ICAM-1, MCP-1, VEGFR-1, and VEGFR-2. Importantly, AST suppressed the activation of the NF-kappaB pathway, including IkappaB-alpha degradation and p65 nuclear translocation. **CONCLUSIONS:** AST treatment, together with inflammatory processes including NF-kappaB activation, subsequent upregulation of inflammatory molecules, and macrophage infiltration, led to significant suppression of CNV development. The present study suggests the possibility of AST supplementation as a therapeutic strategy to suppress CNV associated with AMD.

Publication Types:

PMID: 18385091 [PubMed - indexed for MEDLINE]

Astaxanthin prevents the formation of cataracts in rats.

[Chem Res Toxicol](#). 2009 Feb 4. [Epub ahead of print]

Astaxanthin Interacts with Selenite and Attenuates Selenite-Induced Cataractogenesis.

[Liao JH](#), [Chen CS](#), [Maher TJ](#), [Liu CY](#), [Lin MH](#), [Wu TH](#), [Wu SH](#).

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Selenite, the most commonly encountered toxic form of selenium, in overdose, is used to induce cataracts in rats. This study demonstrated that selenite, but not selenate, would interact with the carotenoid astaxanthin (ASTX), as determined using isothermal titration calorimetry and NMR. The maximum absorption of ASTX decreased with increasing selenite concentration, indicating that the conjugated system of ASTX was changed by selenite. Such interactions between ASTX and selenite were also supported by the attenuation of selenite-induced turbidity by ASTX (0-12.5 μ M) in vitro. In vivo experiments also showed that ASTX attenuated selenite-induced cataractogenesis in rats. In summary, this is the first report of a direct interaction of ASTX with selenite. This interaction is supported by an in vitro assay and may be partially responsible for the ASTX observed in vivo protection against selenite-induced cataractogenesis.

PMID: 19193053 [PubMed - as supplied by publisher]

Astaxanthin protects retinal cells against oxidative stress in mice and in-vitro.

[J Pharm Pharmacol.](#) 2008 Oct;60(10):1365-74.

Astaxanthin, a dietary carotenoid, protects retinal cells against oxidative stress in-vitro and in mice in-vivo.

[Nakajima Y](#), [Inokuchi Y](#), [Shimazawa M](#), [Otsubo K](#), [Ishibashi T](#), [Hara H](#).

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We have investigated whether astaxanthin exerted neuroprotective effects in retinal ganglion cells in-vitro and in-vivo. In-vitro, retinal damage was induced by 24-h hydrogen peroxide (H₂O₂) exposure or serum deprivation, and cell viability was measured using a WST assay. In cultured retinal ganglion cells (RGC-5, a rat ganglion cell-line transformed using E1A virus), astaxanthin inhibited the neurotoxicity induced by H₂O₂ or serum deprivation, and reduced the intracellular oxidation induced by various reactive oxygen species (ROS). Furthermore, astaxanthin decreased the radical generation induced by serum deprivation in RGC-5. In mice in-vivo, astaxanthin (100 mg kg⁻¹, p.o., four times) reduced the retinal damage (a decrease in retinal ganglion cells and in thickness of inner plexiform layer) induced by intravitreal N-methyl-D-aspartate (NMDA) injection. Furthermore, astaxanthin reduced the expressions of 4-hydroxy-2-nonenal (4-HNE)-modified protein (indicator of lipid peroxidation) and 8-hydroxy-deoxyguanosine (8-OHdG; indicator of oxidative DNA damage). These findings indicated that astaxanthin had neuroprotective effects against retinal damage in-vitro and in-vivo, and that its protective effects may have been partly mediated via its antioxidant effects.

PMID: 18812030 [PubMed - indexed for MEDLINE]

Astaxanthin and other carotenoids of the macular pigment of the human retina protect against DNA damage in human neuroblastoma cells.

[J Photochem Photobiol B](#). 2007 Jul 27;88(1):1-10. Epub 2007 May 1.

Lutein, zeaxanthin and astaxanthin protect against DNA damage in SK-N-SH human neuroblastoma cells induced by reactive nitrogen species.

[Santocono M](#), [Zurria M](#), [Berrettini M](#), [Fedeli D](#), [Falcioni G](#).

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The purpose of this study was to evaluate the ability of the predominant carotenoids (lutein and zeaxanthin) of the macular pigment of the human retina, to protect SK-N-SH human neuroblastoma cells against DNA damage induced by different RNOS donors. Although astaxanthin has never been isolated from the human eye, it was included in this study because its structure is very close to that of lutein and zeaxanthin and because it affords protection from UV-light. DNA damage was induced by GSNO-MEE, a nitric oxide donor, by Na(2)N(2)O(3), a nitroxyl anion donor and by SIN-1, a peroxynitrite-generating agent. DNA damage was assessed using the comet assay, a rapid and sensitive single cell gel electrophoresis technique able to detect primary DNA damage in individual cells. The tail moment parameter was used as an index of DNA damage. The values of tail moment increased in all the samples incubated with the RNOS donors, indicating DNA impairment. Data obtained show that the ability of zeaxanthin, lutein, and astaxanthin to reduce the DNA damage depends on the type of RNOS donor and the carotenoid concentration used. All the carotenoids studied were capable of protecting against DNA damage in neuroblastoma cells when the cells were exposed to GSNO-MEE. However, a different behaviour was present when the other two RNOS donors were used. The presence of a carotenoid alone (without an RNOS donor) did not cause DNA damage. Spectrophotometric studies showed that the order with which tested carotenoids reacted with RNOS was not always in agreement with the DNA protection results. The data from this study provides additional information on the activities of the macular pigment carotenoids of the human retina.

Publication Types:

PMID: 17548202 [PubMed - indexed for MEDLINE]

Astaxanthin protects against oxidative stress and protein degradation in porcine lens cells in-vitro.

[J Agric Food Chem.](#) 2006 Mar 22;54(6):2418-23.

Astaxanthin protects against oxidative stress and calcium-induced porcine lens protein degradation.

[Wu TH](#), [Liao JH](#), [Hou WC](#), [Huang FY](#), [Maher TJ](#), [Hu CC](#).

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Astaxanthin (ASTX), a carotenoid with potent antioxidant properties, exists naturally in various plants, algae, and seafoods. In this study, we investigated the in vitro ability of ASTX to protect porcine lens crystallins from oxidative damage by iron-mediated hydroxyl radicals or by calcium ion-activated protease (calpain), in addition to the possible underlying biochemical mechanisms. ASTX (1 mM) was capable of protecting lens crystallins from being oxidized, as measured by changes in tryptophan fluorescence, in the presence of a Fenton reaction solution containing 0.2 mM Fe²⁺ and 2 mM H₂O₂. Sodium dodecyl sulfate-polyacrylamide gel electrophoresis analysis demonstrated that beta(high)-crystallin was the most vulnerable protein under these conditions of free radical exposure. The proteolysis of lens crystallins induced by calcium ion-activated calpain was also inhibited by ASTX (0.03-1 mM) as determined by daily measurement of the light-scattering intensity at 405 nm for five consecutive days. ASTX at 1 mM was as potent as a concentration of 0.1 mM calpain inhibitor E64 in protecting the oxidative damage/hydrolysis of porcine crystallins. At a concentration of 1 mM, ASTX provided better protection than the endogenous antioxidant glutathione in terms of suppressing calcium-induced turbidity of lens proteins. Thin-layer chromatography analysis indicated that ASTX interacted with calcium ions to form complexes, which we believe interfere with the hydrolysis of lens crystallins by calcium-activated calpain. This in vitro study shows that ASTX is capable of protecting porcine lens proteins from oxidative insults and degradation by calcium-induced calpain.

Publication Types:

PMID: 16536628 [PubMed - indexed for MEDLINE]

Astaxanthin protects against eye inflammation in rats.

[Exp Eye Res.](#) 2006 Feb;82(2):275-81. Epub 2005 Aug 26.

Suppressive effects of astaxanthin against rat endotoxin-induced uveitis by inhibiting the NF-kappaB signaling pathway.

[Suzuki Y](#), [Ohgami K](#), [Shiratori K](#), [Jin XH](#), [Ilieva I](#), [Koyama Y](#), [Yazawa K](#), [Yoshida K](#), [Kase S](#), [Ohno S](#).

Department of Ophthalmology and Visual Sciences, Hokkaido University Graduate School of Medicine, N15 W7, Sapporo 060-8638, Japan.

We investigated the effects of astaxanthin (AST), a carotenoid, on endotoxin-induced uveitis (EIU), and over the course of the disease measured the expression of inflammatory cytokines and chemokines in the presence or absence of AST. EIU was induced in male Lewis rats by footpad injection of lipopolysaccharide (LPS). The animals were randomly divided to 12 groups with eight animals in each. Immediately after the inoculation, AST (1, 10, or 100 mg kg⁻¹) was injected intravenously. Aqueous humour was collected at 6, 12 and 24 hr after LPS inoculation and the number of infiltrating cells in the anterior chamber was counted. In addition, we assayed the concentration of protein, nitric oxide (NO), tumour necrosis factor-alpha (TNF-alpha) and prostaglandin E2 (PGE2). Immunohistochemical staining with a monoclonal antibody against activated NF-kappaB was performed in order to evaluate the effects of AST on NF-kappaB activation. Rats injected with AST showed a significant decrease in the number of infiltrating cells in the anterior chamber and additionally there was a significantly lower concentration of protein, NO, TNF-alpha and PGE2 in the aqueous humour. Moreover, even early stages of EIU were suppressed by injection of AST. The number of activated NF-kappaB-positive cells was lower in iris-ciliary bodies treated with 10 or 100 mg kg⁻¹ AST at 3 hr after LPS injection. These results suggest that AST reduces ocular inflammation in eyes with EIU by downregulating proinflammatory factors and by inhibiting the NF-kappaB-dependent signaling pathway.

Publication Types:

PMID: 16126197 [PubMed - indexed for MEDLINE]

Astaxanthin protects against eye inflammation induced by UV in mice.

[Oxid Med Cell Longev.](#) 2017;2017:1956104. doi: 10.1155/2017/1956104. Epub 2017 Sep 28.

Protective Effects of Oral Astaxanthin Nanopowder against Ultraviolet-Induced Photokeratitis in Mice.

[Harada F](#)^{1,2}, [Morikawa T](#)¹, [Lennikov A](#)^{3,4}, [Mukwaya A](#)³, [Schaupper M](#)³, [Uehara O](#)⁵, [Takai R](#)⁶, [Yoshida K](#)¹, [Sato J](#)¹, [Horie Y](#)⁷, [Sakaguchi H](#)⁸, [Wu CZ](#)^{2,9,10}, [Abiko Y](#)¹, [Lagali N](#)³, [Kitaichi N](#)^{7,11}.

Author information

Abstract

PURPOSE: Astaxanthin (AST) has a strong antioxidant cellular membrane chaperone protective effect. Recently, a water-soluble nanosized AST (nano-AST) form was produced, which is expected to improve the efficacy of oral intake effects. The purpose of this study was to examine whether oral nano-AST has therapeutic effects on UV-induced photokeratitis in mice.

METHODS: C57BL/6 mice were administered twice with either nano-AST, AST oil, lutein, or bilberry extracts 3 hours before and shortly before UV irradiation (dose: 400 mJ/cm²). The corneas were collected 24 hours after irradiation and stained with H&E and TUNEL. NF- κ B, dihydroethidium (DHE), COX-2, p-I κ B- α , TNF α , and CD45 expression were evaluated through immunohistochemistry, Western blot analysis, and qPCR.

RESULTS: Corneal epithelium was significantly thicker in mice orally administered with nano-AST than in the others ($p < 0.01$), with significantly less NF- κ B nucleus translocation ($p < 0.001$), and significantly fewer TUNEL cells ($p < 0.01$). Weaker DHE signals were detected in the nano-AST group ($p < 0.05$) relative to the others. Furthermore, reduced inflammation and decreased cell death in corneal tissue were observed in the nano-AST group, as indicated by a reduction in the expression of COX-2, p-I κ B- α , TNF α , and CD45.

CONCLUSIONS: Oral administration of nano-AST demonstrated a protective effect on UV-induced photokeratitis via antioxidative, anti-inflammatory, and antiapoptotic activity.

PMID: 29104724

PMCID: [PMC5637851](#)

DOI: [10.1155/2017/1956104](#)

[Indexed for MEDLINE]

[Free PMC Article](#)

Astaxanthin protects retina cells in diabetic rodents fed a high-fat diet.

[Curr Eye Res.](#) 2018 Sep;43(9):1177-1189. doi: 10.1080/02713683.2018.1484143. Epub 2018 Jul 20.

Short-Term Administration of Astaxanthin Attenuates Retinal Changes in Diet-Induced Diabetic *Psammomys obesus*.

[Baccouche B](#)^{1,2}, [Benlarbi M](#)¹, [Barber AJ](#)³, [Ben Chaouacha-Chekir R](#)¹.

Author information

Abstract

OBJECTIVES: *Psammomys obesus* is a high-fat diet (HFD)-fed animal model of obesity and type 2 diabetes recently explored as a model of non-proliferative diabetic retinopathy. This study tested the protective effect of the pigment astaxanthin (AST) in the *P. obesus* diabetic retina.

METHODS: Young adult *P. obesus* were randomly assigned to two groups. The control group received a normal diet consisting of a plant-based regimen, and the HFD group received an enriched laboratory chow. After 3 months, control and diabetic rodents were administered vehicle or AST, daily for 7 days. Body weight, blood glucose, and plasma pentosidine were assessed. Frozen sections of retinas were immunolabeled for markers of oxidative stress, glial reactivity and retinal ganglion cell bodies, and imaged by confocal microscopy.

RESULTS: Retinal tissue from AST-treated control and HFD-diabetic *P. obesus* showed a greater expression of the antioxidant enzyme heme oxygenase-1 (HO-1). In retinas of HFD-diabetic AST-treated *P. obesus*, cellular retinaldehyde binding protein and glutamine synthetase in Müller cells were more intense compared to the untreated HFD-diabetic group. HFD-induced diabetes downregulated the expression of glial fibrillary acidic protein in astrocytes, the POU domain protein 3A in retinal ganglion cells, and synaptophysin throughout the plexiform layers.

DISCUSSION: Our results show that type 2-like diabetes induced by HFD affected glial and neuronal retinal cell homeostasis. AST treatment induced the antioxidant enzyme HO-1 and reduced glial reactivity. These findings suggest that diabetic *P. obesus* is a useful model of HFD-induced obesity and diabetes to evaluate early neuroglial retinal alterations and antioxidant neuroprotection mechanisms in DR.

KEYWORDS: Diabetic retinopathy; high-fat diet; neurodegeneration; neuroprotection; oxidative stress

PMID: 30028214 DOI: [10.1080/02713683.2018.1484143](https://doi.org/10.1080/02713683.2018.1484143)

Astaxanthin protects against retinal toxicity from chemotherapy drug in rats.

[Cutan Ocul Toxicol.](#) 2018 Sep 5:1-23. doi: 10.1080/15569527.2018.1518330. [Epub ahead of print]

The protective effects of astaxanthin against cisplatin-induced retinal toxicity.

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Author information

Abstract

This study investigated the toxic effects of an antineoplastic agent, Cisplatin (CIS), on retinal cells and the potential capacity of Astaxanthin(ASTA) to elicit a future therapeutic protocol in CIS-induced retinal toxicity. Six groups were formed for the assessment; control (healthy; Group 1), olive oil (olive oil only; Group 2), ASTA control group (ASTA only, Group 3), the single intraperitoneal (IP) dose of 16 mg/kg CIS (CIS only group; Group 4), 16 mg/kg CIS + 25 mg/kg (IP) ASTA (Group 5) and 16 mg/kg CIS + 75 mg/kg (IP) ASTA (Group 6). On the third day after cisplatin administration, rats in all groups were sacrificed under anesthesia and the analysis of the biochemical parameters and histopathological levels were performed. A significant decrease in GSH levels and increases in MDA, eNOS, 8-OHdG expressions were recorded. Additionally, CIS treatment had caused acidophilic staining in retinal histological appearance. ASTA treatment reduced the increases in MDA, eNOS, and 8-OHdG levels following CIS administration and increased the levels of GSH expressions, as well. These results may suggest the ASTA molecule as a promising option to prevent retinal toxicity in patients receiving CIS treatment for malignant tumors.

KEYWORDS:

Astaxanthin; chemotherapy; cisplatin toxicity; eNOS; oxidative stress; retina

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Astaxanthin and Vitamins C & E prevent formation of cataracts in salmon while pro-oxidants such as iron, copper and manganese increased the incidence of cataracts.

Cataract formation in Atlantic salmon, *Salmo salar* L., smolt relative to dietary pro- and antioxidants and lipid level.

[Waagbø R](#), [Hamre K](#), [Bjerkås E](#), [Berge R](#), [Wathne E](#), [Lie O](#), [Torstensen B](#).

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The development of cataracts in Atlantic salmon, *Salmo salar* L., was studied in 16 groups of smolts fed diets differing in prooxidant (iron, copper, manganese) and antioxidant (vitamin E, vitamin C, astaxanthin) composition and lipid level for 23 weeks in sea water, using a 2(7-3) reduced factorial design. The seven dietary variables were systematically varied at low (requirement level and 150 g lipid kg(-1)) and high levels (below known toxic levels and 320 g lipid kg(-1)). A mean endpoint cataract incidence of approximately 36% was observed. High dietary levels of vitamin C and astaxanthin reduced cataract frequency, whereas high dietary lipid level, iron and manganese were associated with increased cataract frequencies. Considering the nutritional status of selected organs of the fish, only the status of ascorbic acid correlated negatively to cataract development ($P < 0.05$). The lens glutathione (GSH) status was not correlated to cataract frequency, nor statistically explained by the dietary variables. However, the study shows that balancing the diet with respect to pro- and antioxidant nutrients may significantly protect Atlantic salmon against development of cataracts. An incidence of reversible osmotic cataract observed at week 14 was positively correlated to plasma glucose concentration.

Publication Types:

PMID: 12962230 [PubMed - indexed for MEDLINE]

Astaxanthin performs well in rat study on eye inflammation which leads to the conclusion that it may be beneficial in the treatment of conditions such as conjunctivitis.

Bechettoby ni kansuru Chosa Kenkyu Heisei 14 Nendo Sokatsu, Buntan Kenkyu Hokokusho
VOL.;NO.;PAGE.98-99(2003)

Research on the anti-inflammatory effect of astaxanthin

[ONO SHIGEAKI](#); [OGAMI KAZUHIRO](#); [SHIRATORI KENJI](#); [ILIEVA I](#); [KOTAKE SATOSHI](#); [NISHIDA TOMOMI](#); [MIZUKI NOBUHISA](#)

The effect of astaxanthin (AST) was examined in rat model of the endotoxin induced uveitis. As the result, the protein concentration in the hydatoid lowered obviously in the group which administered 10 (AST10) or 100mg/kg (AST100) of AST in comparison with control animals. The number of inflammatory cells was significantly decreased only in AST100 group. The effect of AST on protein concentration and cell numbers in the hydatoid in AST100 group was almost equivalent to those of 10mg/kg of prednisolone (PSL) administrated group. Any side effects by AST administration could not be observed. AST showed dose-dependent inhibitory effect in this model. Therefore, it was indicated that AST could be utilized as a new antiphlogistic for ophthalmia disease.

Astaxanthin performs well in a rabbit model of eye fatigue.

Atarashii Ganka, 25(10):1461-1464 (In Japanese). 2008

Intraocular penetration of astaxanthin in rabbit eyes

Fukuda et al.,

In a new study, natural astaxanthin extract derived from *Haematococcus microalgae* was detected in the iris/ciliary body of New Zealand Albino (NZW) Rabbit Eyes 24 hours after ingestion.

Astaxanthin has been reported to have many benefits in the eye. Several human clinical studies reported the alleviation of eye fatigue (by improving accommodation function) in visual display terminal (VDT) workers after oral supplementation. However, up to now there has been no intraocular kinetic information available. In collaboration between the Ophthalmology Department of Kanazawa Medical University, Japan, and Fuji Chemical Industry, Japan, researchers investigated the ocular and blood serum levels of astaxanthin in 24 NZW albino rabbits. After administering a 100 mg/kg single oral dose, astaxanthin was determined by careful extraction followed by HPLC analysis over a period of 168 hours. According to the astaxanthin detection system, the time taken to reach maximum presence (T_{max}) in serum and iris/ciliary body was 9 hours (at C_{max} 61.3 ng/mL) and 24 hours (at C_{max} 79.3) respectively. In other human studies with oral intake of astaxanthin, the T_{max} in serum ranged between 9 and 12 hours.

The intraocular penetration kinetics could have a similar pattern to humans but further study is necessary. This study adds to the growing body of science supporting astaxanthin's benefits for eye fatigue caused by VDT use.

Astaxanthin prevents eye inflammation in rats and in-vitro.

[Invest Ophthalmol Vis Sci](#). 2003 Jun;44(6):2694-701

Effects of astaxanthin on lipopolysaccharide-induced inflammation in vitro and in vivo

[Ohgami K](#), [Shiratori K](#), [Kotake S](#), [Nishida T](#), [Mizuki N](#), [Yazawa K](#), [Ohno S](#)

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PURPOSE: Astaxanthin (AST) is a carotenoid that is found in marine animals and vegetables. Several previous studies have demonstrated that AST exhibits a wide variety of biological activities including antioxidant, antitumor, and anti-*Helicobacter pylori* effects. In this study, attention was focused on the antioxidant effect of AST. The object of the present study was to investigate the efficacy of AST in endotoxin-induced uveitis (EIU) in rats. In addition, the effect of AST on endotoxin-induced nitric oxide (NO), prostaglandin E2 (PGE2), and tumor necrosis factor (TNF)-alpha production in a mouse macrophage cell line (RAW 264.7) was studied in vitro. **METHODS:** EIU was induced in male Lewis rats by a footpad injection of lipopolysaccharide (LPS). AST or prednisolone was administered intravenously at 30 minutes before, at the same time as, or at 30 minutes after LPS treatment. The number of infiltrating cells and protein concentration in the aqueous humor collected at 24 hours after LPS treatment was determined. RAW 264.7 cells were pretreated with various concentrations of AST for 24 hours and subsequently stimulated with 10 microg/mL of LPS for 24 hours. The levels of PGE2, TNF-alpha, and NO production were determined in vivo and in vitro. **RESULTS:** AST suppressed the development of EIU in a dose-dependent fashion. The anti-inflammatory effect of 100 mg/kg AST was as strong as that of 10 mg/kg prednisolone. AST also decreased production of NO, activity of inducible nitric oxide synthase (NOS), and production of PGE2 and TNF-alpha in RAW264.7 cells in vitro in a dose-dependent manner. **CONCLUSIONS:** This study suggests that AST has a dose-dependent ocular anti-inflammatory effect, by the suppression of NO, PGE2, and TNF-alpha production, through directly blocking NOS enzyme activity.

Astaxanthin prevents retinal injury in rats with high ocular blood pressure.

[Regul Toxicol Pharmacol](#). 2010 Oct;58(1):121-30. Epub 2010 May 8.

Suppressive effect of astaxanthin on retinal injury induced by elevated intraocular pressure.

[Cort A](#), [Ozturk N](#), [Akpinar D](#), [Unal M](#), [Yucel G](#), [Ciftcioglu A](#), [Yargicoglu P](#), [Aslan M](#).

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Abstract

The aim of this study was to clarify the possible protective effect of astaxanthin (ASX) on the retina in rats with elevated intraocular pressure (EIOP). Rats were randomly divided into two groups which received olive oil or 5mg/kg/day ASX for a period of 8 weeks. Elevated intraocular pressure was induced by unilaterally cauterizing three episcleral vessels and the unoperated eye served as control. At the end of the experimental period, neuroprotective effect of ASX was determined via electrophysiological measurements of visual evoked potentials (VEP) and rats were subsequently sacrificed to obtain enucleated globes which were divided into four groups including control, ASX treated, EIOP, EIOP+ASX treated. Retinoprotective properties of ASX were determined by evaluating retinal apoptosis, protein carbonyl levels and nitric oxide synthase-2 (NOS-2) expression. Latencies of all VEP components were significantly prolonged in EIOP and returned to control levels following ASX administration. When compared to controls, EIOP significantly increased retinal protein oxidation which returned to baseline levels in ASX treated EIOP group. NOS-2 expression determined by Western blot analysis and immunohistochemical staining was significantly greater in rats with EIOP compared to ASX and control groups. Retinal TUNEL staining showed apoptosis in all EIOP groups; however ASX treatment significantly decreased the percent of apoptotic cells when compared to non treated ocular hypertensive controls. The presented data confirm the role of oxidative injury in EIOP and highlight the protective effect of ASX in ocular hypertension.

Astaxanthin protects retinal cells against oxidative stress in mice and in-vitro.

[J Pharm Pharmacol](#). 2008 Oct;60(10):1365-74.

Astaxanthin, a dietary carotenoid, protects retinal cells against oxidative stress in-vitro and in mice in-vivo.

[Nakajima Y](#), [Inokuchi Y](#), [Shimazawa M](#), [Otsubo K](#), [Ishibashi T](#), [Hara H](#).

Source

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Abstract

We have investigated whether astaxanthin exerted neuroprotective effects in retinal ganglion cells in-vitro and in-vivo. In-vitro, retinal damage was induced by 24-h hydrogen peroxide (H₂O₂) exposure or serum deprivation, and cell viability was measured using a WST assay. In cultured retinal ganglion cells (RGC-5, a rat ganglion cell-line transformed using E1A virus), astaxanthin inhibited the neurotoxicity induced by H₂O₂ or serum deprivation, and reduced the intracellular oxidation induced by various reactive oxygen species (ROS). Furthermore, astaxanthin decreased the radical generation induced by serum deprivation in RGC-5. In mice in-vivo, astaxanthin (100 mg kg⁻¹, p.o., four times) reduced the retinal damage (a decrease in retinal ganglion cells and in thickness of inner plexiform layer) induced by intravitreal N-methyl-D-aspartate (NMDA) injection. Furthermore, astaxanthin reduced the expressions of 4-hydroxy-2-nonenal (4-HNE)-modified protein (indicator of lipid peroxidation) and 8-hydroxy-deoxyguanosine (8-OHdG; indicator of oxidative DNA damage). These findings indicated that astaxanthin had neuroprotective effects against retinal damage in-vitro and in-vivo, and that its protective effects may have been partly mediated via its antioxidant effects.

PMID: 18812030 [PubMed - indexed for MEDLINE]

Astaxanthin protects against ganglion cell death due to various stresses in rat retinal cells.

[Mol Vis.](#) 2014 Dec 31;20:1796-805. eCollection 2014.

Neuroprotective effect of astaxanthin against rat retinal ganglion cell death under various stresses that induce apoptosis and necrosis.

[Yamaqishi R](#)¹, [Aihara M](#)².

Author information

Abstract

PURPOSE:

Astaxanthin is a type of carotenoid known to have strong antioxidant effects. The purpose of this study was to investigate whether astaxanthin confers a neuroprotective effect against glutamate stress, oxidative stress, and hypoxia-induced apoptotic or necrotic cell death in primary cultures of rat retinal ganglion cells (RGCs).

METHODS:

Purified rat RGCs were exposed to three kinds of stressors induced by 25 μ M glutamate for 72 h, B27 medium without an antioxidant for 4 h, and a reduced oxygen level of 5% for 12 h. Each assay was repeated 12 times, with or without 1 nM, 10 nM, and 100 nM astaxanthin. The number of live RGCs was then counted using a cell viability assay. RGC viability in each condition was evaluated and compared with controls. In addition, we measured apoptosis and DNA damage.

RESULTS:

We found that under glutamate stress, RGC viability was reduced to 58%. Cultures with 1 nM, 10 nM, and 100 nM astaxanthin showed an increase in RGC viability of 63%, 74%, and 84%, respectively. Under oxidative stress, RGC viability was reduced to 40%, and astaxanthin administration resulted in increased viability of 43%, 50%, and 67%, respectively. Under hypoxia, RGC viability was reduced to 66%, and astaxanthin administration resulted in a significant increase in viability to 67%, 77%, and 93%, respectively. These results indicate that 100 nM astaxanthin leads to a statistically significant increase in RGC viability under the three kinds of stressors tested, compared to controls (Dunnett's test, $p < 0.05$). The apoptotic activity of RGCs under glutamate stress increased to 32%, but was reduced to 15% with 100 nM astaxanthin administration. Glutamate stress led to a 58% increase in DNA damage, which was reduced to 43% when cultured with 100 nM astaxanthin. Thus, 100 nM astaxanthin showed a statistically significant reduction in apoptosis and DNA damage in RGCs (Wilcoxon rank-sum test, $p < 0.05$).

CONCLUSIONS:

Our results suggest that astaxanthin has a neuroprotective effect against RGC death induced by glutamate stress, oxidative stress, and hypoxia, which induce apoptotic and necrotic cell death.

PMID: 25593507 [PubMed - in process] PMCID: PMC4287717 [Free PMC Article](#)

Astaxanthin protects against the formation of cataracts in chick embryos.

[Curr Eye Res.](#) 2015 May;40(5):535-40. doi: 10.3109/02713683.2014.935445. Epub 2014 Aug 11.

Effect of astaxanthin on cataract formation induced by glucocorticoids in the chick embryo.

[Ishikawa S¹](#), [Hashizume K](#), [Nishigori H](#), [Tezuka Y](#), [Sanbe A](#), [Kurosaka D](#).

Author information

Abstract

PURPOSE:

To examine whether astaxanthin (AST) prevent the cataract formation induced by glucocorticoid in chick embryo.

MATERIALS AND METHODS:

Hydrocortisone hemisuccinate sodium (HC) (0.5 $\mu\text{mol/egg}$) was administered directly into the air chamber in the egg shell of chick embryo day 15. The eggs were then kept in an incubator at same conditions and administered 100 μL of 50 (HC + AST50 group), 80 (HC + AST80 group), 100 (HC + AST100 group) mg/mL of AST solutions dissolved in dimethyl sulfoxide (DMSO) 3 h after administration of HC. In addition, non-HC treated group (treated with physiological saline without HC and 100 μL of DMSO), HC-alone group (treated with 0.5 μmol of HC and 100 μL of DMSO), and AST100 group (treated with physiological saline without HC and 100 μL of DMSO) were also incorporated. After 48 h of treatment, lenses were removed from embryo and classified into five stages according to developed opacity. The amounts of reduced glutathione in the lenses and the blood glucose levels were measured.

RESULTS:

The average scores of lens opacity were 2.63 ± 1.02 nmol/lens (HC-alone), 2.78 ± 0.97 nmol/lens (HC + AST50), 2.22 ± 1.20 nmol/lens (HC + AST80) and 1.84 ± 0.83 nmol/lens (HC + AST100; $p < 0.05$), respectively. Administration of AST decreased the lens opacity dose-dependently. The amounts of reduced glutathione in lenses were 11.6 ± 2.8 nmol/lens (HC-alone), 11.3 ± 2.7 nmol/lens (HC + AST50), 13.4 ± 2.4 nmol/lens (HC + AST80) and 13.7 ± 3.1 nmol/lens (HC + AST100; $p < 0.05$), respectively. Higher levels of AST prevented loss of reduced glutathione from the lens.

CONCLUSION:

These findings support that AST protects glucocorticoid-induced cataract in chick embryo.

KEYWORDS:

Astaxanthin; cataract; chick embryo; glucocorticoid; oxidative stress

PMID:

25110808

[PubMed - in process]

Astaxanthin protects against light-induced retinal damage in mice.

[J Pharmacol Sci.](#) 2013;123(3):209-18. Epub 2013 Oct 22.

Protective effects of a dietary carotenoid, astaxanthin, against light-induced retinal damage.

[Otsuka T¹](#), [Shimazawa M](#), [Nakanishi T](#), [Ohno Y](#), [Inoue Y](#), [Tsuruma K](#), [Ishibashi T](#), [Hara H](#).

Author information

Abstract

Dietary carotenoids exhibit various biological activities, including antioxidative activity. In particular, astaxanthin, a type of carotenoid, is well known as a powerful antioxidant. We investigated whether astaxanthin would protect against light-induced retinal damage. In an in vivo study, ddY male mice were exposed to white light at 8,000 lux for 3 h to induce retinal damage. Five days after light exposure, retinal damage was evaluated by measuring electroretinogram (ERG) amplitude and outer nuclear layer (ONL) thickness. Furthermore, expression of apoptotic cells, 8-hydroxy-deoxyguanosine (8-OHdG), was measured. In an in vitro study, retinal damage was induced by white light exposure at 2,500 lux for 24 h, and propidium iodide (PI)-positive cells was measured and intracellular reactive oxygen species (ROS) activity was examined. Astaxanthin at 100 mg/kg inhibited the retinal dysfunction in terms of ERG and ONL loss and reduced the expression of apoptotic and 8-OHdG-positive cells induced by light exposure. Furthermore, astaxanthin protected against increases of PI-positive cells and intracellular reactive oxygen species (ROS) activity in 661W cells. These findings suggest that astaxanthin has protective effects against light-induced retinal damage via the mechanism of its antioxidative effect.

PMID:

24152963

[PubMed - indexed for MEDLINE]

Free full text

Astaxanthin inhibits oxidative stress and may be developed as an antioxidant drug to treat diabetic retinopathy.

[Mar Drugs](#). 2013 Mar 21;11(3):960-74. doi: 10.3390/md11030960.

Astaxanthin attenuates the apoptosis of retinal ganglion cells in db/db mice by inhibition of oxidative stress.

[Dong LY¹](#), [Jin J](#), [Lu G](#), [Kang XL](#).

Author information

Abstract

Diabetic retinopathy is a common diabetic eye disease caused by changes in retinal ganglion cells (RGCs). It is an ocular manifestation of systemic disease, which affects up to 80% of all patients who have had diabetes for 10 years or more. The genetically diabetic db/db mouse, as a model of type-2 diabetes, shows diabetic retinopathy induced by apoptosis of RGCs. Astaxanthin is a carotenoid with powerful antioxidant properties that exists naturally in various plants, algae and seafood. Here, astaxanthin was shown to reduce the apoptosis of RGCs and improve the levels of oxidative stress markers, including superoxide anion, malondialdehyde (MDA, a marker of lipid peroxidation), 8-hydroxy-2-deoxyguanosine (8-OHdG, indicator of oxidative DNA damage) and MnSOD (manganese superoxide dismutase) activity in the retinal tissue of db/db mouse. In addition, astaxanthin attenuated hydrogen peroxide(H₂O₂)-induced apoptosis in the transformed rat retinal ganglion cell line RGC-5. Therefore, astaxanthin may be developed as an antioxidant drug to treat diabetic retinopathy.

PMID:

23519150

[PubMed - indexed for MEDLINE]

PMCID:

PMC3705382

Free PMC Article

Research from 1950's shows a variety of potential eye health benefits in rats.

Massonet, R. (1958). "Research on Astaxanthin's Biochemistry." Doctoral Thesis at University of Lyon, France. Available on the United States Patent and Trademark Office website at www.uspto.gov.

Weaned rats were fed a synthetic diet lacking vitamin A and: 1) just synthetic diet or 2) 10 mg/day of astaxanthin-ester oil or 3) 90 mg/day of astaxanthin-ester oil or 4) 0.9 mg/day of vitamin A

- 1) Rats developed xerophthalmia (sever eye dryness), ocular lesion, and no weight gain and died in 56 days.
- 2) Rats did not develop xerophthalmia (sever eye dryness) or ocular lesion, had no weight gain and also died in 56 days.
- 3) Rats did not develop xerophthalmia (sever eye dryness) or ocular lesion, had weight gain, appeared totally healthy and did not die.
- 4) Rats did not develop xerophthalmia (sever eye dryness) or ocular lesion, had weight gain, appeared totally healthy and did not die.

Conclusion: Low doses of astaxanthin-esters can reduce vitamin A deficiency in in the eye but not elsewhere in the body

High doses of astaxanthin esters can not only eliminate vitamin a deficiency in the eye, and also in other parts of the body.

Further findings:

- 1) 50 micrograms of astaxanthin is equivalent to 0.9 micrograms of vitamin a for preventing eye damage weather taken orally or injected.
- 2) Astaxanthin was found in the eyes, pituitary glands, thyroid, and liver

Additional research from 1950's shows a variety of potential eye health benefits in rats.

Grangaud, R. (1951). "Research on Astaxanthin, a New Vitamin A Factor." Doctoral Thesis at University of Lyon, France. Available on the United States Patent and Trademark Office website at www.uspto.gov

Rats were fed a vitamin A deficient diet since being weaned and developed vitamin A deficiency after 70 days. Vitamin A deficiency was manifested by xerophthalmia (sever eye dryness), ocular lesion, and no weight gain. Vitamin A deficient rats were fed an astaxanthin-ester oil extracted from shrimp shells. The astaxanthin-ester oil was purified by chromatography, contained no vitamin A and although the astaxanthin concentration was not determined it was probably 2.5% (as based on a subsequent publication). Rats receiving a low dose of oil (22 mg/day) showed reduced symptoms of xerophthalmia in 4 days, complete healing of ocular lesion in 15 days and had minimal weight gain and died on day 20. Rats receiving a medium dose of oil (45 mg/day) showed reduced symptoms of xerophthalmia in 4 days, complete healing of ocular lesion in 15 days and had low weight gain but died on day 35. Rats receiving a high dose of oil (90 mg/day) showed reduced symptoms of xerophthalmia in 4 days, complete healing of ocular lesion in 15 days and regained normal weight gain and remained alive.

The conclusion: Low doses of astaxanthin-esters can reduce vitamin A deficiency in in the eye but not elsewhere in the body. High doses of astaxanthin esters can not only reduce vitamin a deficiency in the eye, reverse (cure) physical eye maladies and also in other parts of the body.

Further, astaxanthin was found in the eye of rats feed astaxanthin-ester, but not in rats fed free astaxanthin.

Mice treated with Astaxanthin eye-drops improve their resistance to UV-induced eye damage.

[Mol Vis.](#) 2012;18:455-64. Epub 2012 Feb 14.

Amelioration of ultraviolet-induced photokeratitis in mice treated with astaxanthin eye drops.

[Lennikov A¹](#), [Kitaichi N](#), [Fukase R](#), [Murata M](#), [Noda K](#), [Ando R](#), [Ohguchi T](#), [Kawakita T](#), [Ohno S](#), [Ishida S](#).

Author information

Abstract

PURPOSE:

Ultraviolet (UV) acts as low-dose ionizing radiation. Acute UVB exposure causes photokeratitis and induces apoptosis in corneal cells. Astaxanthin (AST) is a carotenoid, present in seafood, that has potential clinical applications due to its high antioxidant activity. In the present study, we examined whether topical administration of AST has preventive and therapeutic effects on UV-photokeratitis in mice.

METHODS:

C57BL/6 mice were administered with AST diluted in polyethylene glycol (PEG) in instillation form (15 μ l) to the right eye. Left eyes were given vehicle alone as controls. Immediately after the instillation, the mice, under anesthesia, were irradiated with UVB at a dose of 400 mJ/cm². Eyeballs were collected 24 h after irradiation and stained with H&E and TUNEL. In an in vitro study, mouse corneal epithelial (TKE2) cells were cultured with AST before UV exposure to quantify the UV-derived cytotoxicity.

RESULTS:

UVB exposure induced cell death and thinning of the corneal epithelium. However, the epithelium was morphologically well preserved after irradiation in AST-treated corneas. Irradiated corneal epithelium was significantly thicker in eyes treated with AST eye drops, compared to those treated with vehicles ($p < 0.01$), in a dose-dependent manner. Significantly fewer apoptotic cells were observed in AST-treated eyes than controls after irradiation ($p < 0.01$). AST also reduced oxidative stress in irradiated corneas. The in vitro study showed less cytotoxicity of TKE2 cells in AST-treated cultures after UVB-irradiation ($p < 0.01$). The cytoprotective effect increased with the dose of AST.

CONCLUSIONS:

Topical AST administration may be a candidate treatment to limit the damages by UV irradiation with wide clinical applications.

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22393271

[PubMed - indexed for MEDLINE]

PMCID: PMC3291518

[Free PMC Article](#)

US Patent (currently expired) on the use of Astaxanthin for various preventative and therapeutic measures for eye and brain health including age-related macular degeneration.

Tso, M., Lam, T. (1996) "Method of Retarding and Ameliorating Central Nervous System and Eye Damage." U.S. Patent #5527533.

A method of retarding and ameliorating eye diseases and injuries is disclosed. The method comprises administering astaxanthin in a therapeutically-effective amount to prevent, retard or treat eye and central nervous system diseases or injuries, such as age-related macular degeneration and other central nervous system degenerative diseases, photic injury, ischemic diseases, and inflammatory diseases.

Astaxanthin, EPA and Lutein reviewed as potential preventive supplements for eye health.

[Nippon Ganka Gakkai Zasshi](#). 2009 Mar;113(3):403-22; discussion 423.

[Lifestyle-related diseases and anti-aging ophthalmology: suppression of retinal and choroidal pathologies by inhibiting renin-angiotensin system and inflammation]

[Article in Japanese]

Ishida S.

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Lifestyle-related diseases cause macro- and microangiopathies in the major organs including the brain, heart, kidney, and eye, and as a result, shorten the lifespan. The renin-angiotensin system (RAS) has recently been shown to contribute to the processes of accelerated aging caused by lifestyle-related diseases from visceral obesity in the early stage to late-onset organ damage. Vision-threatening diabetic retinopathy and age-related macular degeneration (AMD), associated with lifestyle-related diseases as risk factors for progression, develop retinal and choroidal neovascularization (CNV), respectively, in their advanced stages. We have found that tissue RAS is activated in the pathogenesis of diabetic retinopathy and CNV, leading to angiotensin type 1 receptor (AT1-R)-mediated expression of inflammation-related molecules including vascular endothelial growth factor (VEGF), intercellular adhesion molecule (ICAM)-1, and monocyte chemoattractant protein (MCP)-1. Neuronal dysfunction in diabetic retinopathy is also shown to result from AT1-R-mediated degradation of synaptic proteins. Moreover, we revealed for the first time that the receptor for prorenin [(pro) renin receptor] is expressed in the eye, although prorenin was until recently believed to be just an inactive precursor of renin. Prorenin binds to the receptor that causes dual activation of its intracellular signaling and tissue RAS, and this pathogenic mechanism is termed receptor-associated prorenin system (RAPS). We have demonstrated the contribution of RAPS to the pathogenesis of CNV and dual regulation of VEGF and MCP-1 by signal transduction via (pro) renin receptor and AT1-R. Next, we report the potential validity of food factor supplements as a therapeutic strategy for preventing the retinal and choroidal pathologies driven by RAS-induced inflammatory and angiogenic molecules. Functional food factors examined include lutein in yellow-green vegetables, the omega-3 polyunsaturated fatty acid eicosapentaenoic acid purified from fish oil, and red pigment astaxanthin from salmon and shrimp. We recently revealed that these food factors prevent intraocular angiogenesis and inflammation by inhibiting the expression of inflammatory molecules including VEGF, ICAM-1, and MCP-1. Preventive medicine for AMD and diabetic retinopathy, both of which have lifestyle-related diseases as a systemic background, has attracted growing attention. In the present review, we provide biological evidence for RAS inhibition and food factor supplementation in the early intervention for retinal and choroidal pathologies as an 'anti-aging ophthalmology' approach.

Brain Health

Astaxanthin shows potential efficacy for age-related decline in cognitive and psychomotor functions in human clinical trial on subjects with age-related forgetfulness.

[J Clin Biochem Nutr.](#) 2009 May;44(3):280-4. Epub 2009 Apr 25.

Preliminary Clinical Evaluation of Toxicity and Efficacy of A New Astaxanthin-rich Haematococcus pluvialis Extract.

[Sato A](#), [Tsuji S](#), [Okada Y](#), [Murakami N](#), [Urami M](#), [Nakagawa K](#), [Ishikura M](#), [Katagiri M](#), [Koga Y](#), [Shirasawa T](#).

Life Science Institute, Yamaha Motor Co., Ltd., 3001-10 Kuno, Fukuroi, Shizuoka 437-0061, Japan.

Astaxanthin (Ax), a carotenoid ubiquitously distributed in microorganisms, fish, and crustaceans, has been known to be a potent antioxidant and hence exhibit various physiological effects. We attempted in these studies to evaluate clinical toxicity and efficacy of long-term administration of a new Ax product, by measuring biochemical and hematological blood parameters and by analyzing brain function (using CogHealth and P300 measures). Ax-rich Haematococcus pluvialis extracts equivalent to 4, 8, 20 mg of Ax dialcohol were administered to 73, 38, and 16 healthy adult volunteers, respectively, once daily for 4 weeks to evaluate safety. Ten subjects with age-related forgetfulness received an extract equivalent to 12 mg in a daily dosing regimen for 12 weeks to evaluate efficacy. As a result, no abnormality was observed and efficacy for age-related decline in cognitive and psychomotor functions was suggested.

PMID: 19430618 [PubMed - in process]

PMCID: PMC2675019

Astaxanthin improves marker of dementia in placebo-controlled human clinical trial and may contribute to the prevention of dementia

[Br J Nutr.](#) 2011 Jun;105(11):1563-71. doi: 10.1017/S0007114510005398. Epub 2011 Jan 31.

Antioxidant effect of astaxanthin on phospholipid peroxidation in human erythrocytes.

[Nakagawa K¹](#), [Kiko T](#), [Miyazawa T](#), [Carpentero Burdeos G](#), [Kimura F](#), [Satoh A](#), [Miyazawa T](#).

Author information

Abstract

Phospholipid hydroperoxides (PLOOH) accumulate abnormally in the erythrocytes of dementia patients, and dietary xanthophylls (polar carotenoids such as astaxanthin) are hypothesised to prevent the accumulation. In the present study, we conducted a randomised, double-blind, placebo-controlled human trial to assess the efficacy of 12-week astaxanthin supplementation (6 or 12 mg/d) on both astaxanthin and PLOOH levels in the erythrocytes of thirty middle-aged and senior subjects. After 12 weeks of treatment, erythrocyte astaxanthin concentrations were higher in both the 6 and 12 mg astaxanthin groups than in the placebo group. In contrast, erythrocyte PLOOH concentrations were lower in the astaxanthin groups than in the placebo group. In the plasma, somewhat lower PLOOH levels were found after astaxanthin treatment. These results suggest that astaxanthin supplementation results in improved erythrocyte antioxidant status and decreased PLOOH levels, which may contribute to the prevention of dementia.

PMID:

21276280

[PubMed - indexed for MEDLINE]

Astaxanthin shows ability to improve cognitive function in healthy subjects in randomized double-blind, placebo-controlled human clinical study.

[J Clin Biochem Nutr.](#) 2012 Sep;51(2):102-7. doi: 10.3164/jcbrn.11-00017. Epub 2012 Mar 30.

Effects of astaxanthin-rich Haematococcus pluvialis extract on cognitive function: a randomised, double-blind, placebo-controlled study.

[Katagiri M](#)¹, [Satoh A](#), [Tsuji S](#), [Shirasawa T](#).

Author information

Abstract

In this study we tried to confirm the effect of an astaxanthin-rich Haematococcus pluvialis extract on cognitive function in 96 subjects by a randomised double-blind placebo-controlled study. Healthy middle-aged and elderly subjects who complained of age-related forgetfulness were recruited. Ninety-six subjects were selected from the initial screen, and ingested a capsule containing astaxanthin-rich Haematococcus pluvialis extract, or a placebo capsule for 12 weeks. Somatometry, haematology, urine screens, and CogHealth and Groton Maze Learning Test were performed before and after every 4 weeks of administration. Changes in cognitive performance and the safety of astaxanthin-rich Haematococcus pluvialis extract administration were evaluated. CogHealth battery scores improved in the high-dosage group (12 mg astaxanthin/day) after 12 weeks. Groton Maze Learning Test scores improved earlier in the low-dosage (6 mg astaxanthin/day) and high-dosage groups than in the placebo group. The sample size, however, was small to show a significant difference in cognitive function between the astaxanthin-rich Haematococcus pluvialis extract and placebo groups. No adverse effect on the subjects was observed throughout this study. In conclusion, the results suggested that astaxanthin-rich Haematococcus pluvialis extract improves cognitive function in the healthy aged individuals.

KEYWORDS:

Astaxanthin; Haematococcus pluvialis; aging; clinical efficacy; cognitive function

PMID:

22962526

[PubMed]

PMCID:

PMC3432818

[Free PMC Article](#)

Astaxanthin improves processing speed and psychomotor speed in patients with mild cognitive impairment in double-blind, placebo-controlled study.

Journal of Alzheimer's Disease 62 (2018) 1767–1775

DOI 10.3233/JAD-170969

IOS Press 1767

Effects of Composite Supplement Containing Astaxanthin and Sesamin on Cognitive Functions in People with Mild Cognitive Impairment: A Randomized, Double-Blind, Placebo-Controlled Trial

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Accepted 11 January 2018

Abstract.

Background: Dementia and its first or transitional stage, mild cognitive impairment (MCI), is a major concern for the aging Japanese society. Thus, the use of dietary supplements to improve or maintain cognitive function has become a topic of public interest.

Objective: In this study, we evaluated the effects of a composite supplement containing food-derived antioxidants, specifically astaxanthin and sesamin (AS), on cognitive function in people with MCI.

Method: Twenty-one healthy participants with MCI were recruited in our double-blind placebo-controlled pilot study. They were assigned to either an AS group, who received ingestible capsules containing AS, or a placebo group, who received identical placebo capsules. To assess cognitive functions, we performed the Japanese version of the Central Nervous System Vital Signs (CNSVS) test and the Alzheimer's Disease Assessment Scale-Cog test at baseline, after 6 weeks, and after 12 weeks of dietary supplementation.

Results: The CNSVS test revealed significant improvements in psychomotor speed and processing speed in the AS group compared with the placebo group, suggesting that the daily supplementation of AS improved cognitive functions related to the ability to comprehend, and perform complex tasks quickly and accurately.

Conclusion: Our results provide support for the use of AS as a dietary supplementation for improving cognitive functions.

Astaxanthin improves mood state in double-blind, placebo-controlled human clinical study.

Published as a poster at American College of Lifestyle Medicine and to be published as a full manuscript in 2019.

Natural Astaxanthin Supplementation Improves Mental Wellness

Talbott, S., Hantla, D., Capelli, B., Ding, L., Li, Y., Artaria, C.

Introduction: Nutrition plays a major role in the pathophysiology of many “physical” disease states, including cardiovascular disease, cancer, obesity, and diabetes. The role of nutrition is less well-known with respect to “mental” disease states, including depression, anxiety, attention deficit disorder, psychological burnout and chronic pain. Diet-related changes in psychological mood state and mental wellness may be due to cellular, biochemical, and behavioral factors – and may be mediated by lifestyle factors including diet and exercise.

Purpose: Our objective was to assess changes in mental wellness by assessing psychological mood state in response to dietary supplementation with natural astaxanthin (12mg/day for 8 weeks). Marine microalgae is the predominant source of natural astaxanthin (NAX), a red-orange carotenoid with powerful antioxidant and anti-inflammatory properties. Studies in both rodents and humans suggest that NAX supplementation improves antioxidant capacity and reduces oxidative stress – effects which may be related to mental wellness.

Methods: Using a double-blind parallel design, 28 recreational runners (male = 14, female = 14, age = 42) were supplemented with NAX (*Haematococcus pluvialis* algal extract) or a placebo. Before and after the supplementation period, subjects completed the validated Profile of Mood States (POMS) survey to assess mental wellness parameters including global mood state (GM) and related subscales: Vigor (V), Tension (T), Depression (D), Anger (A), Fatigue (F), and Confusion (C).

Results & Conclusions: Significant changes (all, $p < 0.05$) were found for improvements in positive mood state parameters: GM (+11%) & V (+5%); as well as reductions in negative mood state parameters: T (-20%), D (-57%), A (-12%), F (-36%), and C (-28%). Previous studies have shown astaxanthin supplementation to be associated with improvements in fatigue, attention, and memory – with suggestions that it may also play a role in prevention of dementia and age-related memory loss. These data are the first to suggest that astaxanthin supplementation improves mental wellness parameters associated with improvements in mood state and depression.

Astaxanthin decreases mental and physical fatigue in double-blind, placebo-controlled human clinical trial.

J. Clin. Thera & Med 32.7 (2016):277-91 (Japanese)

Randomized Controlled Trial of the Anti-Fatigue Effects of Astaxanthin on Mental and Physical Loads Simulating Daily Life.

Hongo, N. et al.

In a study designed to induce fatigue and stress encountered in daily life, natural astaxanthin from *Haematococcus pluvialis* microalgae was administered over eight weeks to the treatment group in a double-blind, placebo-controlled study. A mental challenge comprised of a number of timed calculations (the Uchida-Kraepelin test) and a physical test on a bicycle ergometer were assessed in both the placebo and treatment groups before and after the eight-week supplementation period. Participants consisted of 39 healthy subjects who were divided into two groups. The treatment group received 12mg per day of natural astaxanthin combined with 20mg of tocotrienols while the control group received 20mg of tocotrienols without any astaxanthin. A Visual Analogue Scale analysis showed that astaxanthin significantly reduced perceived symptoms of mental and physical fatigue compared to placebo. Results included improvements in clarity of thinking, concentration, motivation and mood. Irritation and feelings of body heaviness were reduced. In the mental challenge test, an increase in errors observed in the placebo group was almost eliminated in the astaxanthin group. Salivary cortisol (a marker for stress) was significantly reduced in the astaxanthin group. These results suggest that astaxanthin supplementation has beneficial effects on fatigue encountered in daily life.

ASTAXANTHIN IN COMBINATION WITH TOCOTRIENOLS LEADS TO COGNITIVE IMPROVEMENT IN ELDERLY SUBJECTS WITH MILD FORGETFULNESS IN BGG-SPONSORED HUMAN CLINICAL TRIAL.

J Clin Biochem Nutr. 2020 Nov;67(3):307-316.
doi: 10.3164/jcfn.19-116. Epub 2020 Jun 19.

Cognitive function improvement with astaxanthin and tocotrienol intake: a randomized, double-blind, placebo-controlled study

[Takahiro Sekikawa](#)¹, [Yuki Kizawa](#)¹, [Yanmei Li](#)², [Tsuyoshi Takara](#)³

PMID: 33293773 PMCID: [PMC7705074](#) DOI: [10.3164/jcfn.19-116](#) [Free PMC article](#)

Abstract

We examined the effects of the mixed ingestion of astaxanthin derived from *Haematococcus pluvialis* and tocotrienols on the cognitive function of healthy Japanese adults who feel a memory decline. Forty-four subjects were randomly but equally assigned to the astaxanthin-tocotrienols or placebo group. An astaxanthin-tocotrienols or placebo capsule was taken once daily before or after breakfast for a 12-week intervention period. The primary outcome was composite memory from the Cognitrix cognitive test, and the secondary outcomes were other cognitive functions and subjective symptoms for memory. Each group included 18 subjects in the efficacy analysis (astaxanthin-tocotrienols group, 55.4 ± 7.9 years; placebo group, 54.6 ± 6.9 years). The astaxanthin-tocotrienols group showed a significant improvement in composite memory and verbal memory in Cognitrix at Δ12 weeks compared with the placebo group. Additionally, the astaxanthin-tocotrienols group showed a significant improvement in the subjective symptom of "During the last week, have you had trouble remembering people's names or the names of things?" compared with the placebo group after 12 weeks. No adverse events were observed in this study. The results demonstrated that taking an astaxanthin-tocotrienols combination improves the composite memory and verbal memory of Japanese adults who feel a memory decline (UMIN 000031758).

ASTAXANTHIN-CONTAINING FORMULA MAY BE EFFECTIVE FOR COMBATING AGE-RELATED COGNITIVE DECLINE IN HUMAN CLINICAL STUDY.

Nutrients. 2020 Dec 27;13(1):56.
doi: 10.3390/nu13010056.

Improvement of Executive Function after Short-Term Administration of an Antioxidants Mix Containing Bacopa, Lycopene, Astaxanthin and Vitamin B12: The BLAtwelve Study

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PMID: 33375429 PMCID: [PMC7824614](#) DOI: [10.3390/nu13010056](#) [Free PMC article](#)

Abstract

During the last few years increasing interest has been focused on antioxidants as potentially useful agents in the prevention of the onset and progression of cognitive dysfunction. In this randomized, double-blind, controlled, parallel arm study, the effects of daily consumption of an antioxidant mix on cognitive function in healthy older adults were evaluated. After a 1 week run-in period, 80 subjects aged 60 years or more, and with no evidence of cognitive dysfunction, were randomly allocated to a mix of four bioactive compounds (bacopa, lycopene, astaxanthin, and vitamin B12) or matched placebo, taken orally once a day for 8 weeks. The primary objective of the study was to evaluate the changes in trail making test (TMT) scores from baseline to 8 weeks of treatment, analyzed in the following hierarchical order: TMT-B, TMT-A, and TMT-B minus TMT-A. TMT-B increased in the control group (+3.46 s) and decreased in the active group (-17.63 s). The treatment difference was -21.01 s in favor of the active group (95% C.I. -26.80 to -15.2, $p < 0.0001$). The decrease in TMT-A was significantly higher in the active group (-6.86 s) than in the control group (-0.37 s). TMT-B minus TMT-A increased in the control group (+3.84 s) and decreased in the active group (-10.46 s). The increase in letter fluency in the verbal fluency test (VFT) was also significantly higher in the active group and statistically significant (+5.28 vs. +1.07 words; $p < 0.001$). Our findings provide encouraging evidence that regular dietary supplementation with bacopa, lycopene, astaxanthin, and vitamin B12 may be an effective dietary approach for counteracting cognitive changes associated with brain aging.

Astaxanthin combined with Sesamin improves recovery from mental fatigue in double-blind, placebo-controlled crossover human clinical trial.

[Nutrients](#). 2018 Feb 28;10(3). pii: E281. doi: 10.3390/nu10030281.

Effects of Dietary Supplementation of Astaxanthin and Sesamin on Daily Fatigue: A Randomized, Double-Blind, Placebo-Controlled, Two-Way Crossover Study.

[Imai A](#)¹, [Oda Y](#)², [Ito N](#)³, [Seki S](#)⁴, [Nakagawa K](#)⁵, [Miyazawa T](#)^{6,7}, [Ueda F](#)⁸.

Author information

Abstract

Severe fatigue can negatively affect quality of life, and oxidative stress may play a role in its mechanism. The aim of this study was to evaluate the effect of dietary supplementation of astaxanthin and sesamin (AS), strong food-derived antioxidants, on fatigue. Twenty-four healthy volunteers were supplemented with AS and placebo, each for four weeks. After each supplementation period, participants underwent tasks inducing mental and physical fatigue (visual display terminal task and ergometer task, respectively). Subjective fatigue was evaluated using a visual analogue scale during and after the mental and physical tasks, and daily subjective fatigue was evaluated by the Chalder fatigue questionnaire. Secondary outcomes included other subjective feelings, work efficiency, autonomic nerve activity, levels of an oxidative stress marker (plasma phosphatidylcholine hydroperoxide (PCOOH)) and safety. AS supplementation was associated with significantly improved recovery from mental fatigue compared with placebo. Increased PCOOH levels during mental and physical tasks were attenuated by AS supplementation. No differences between AS and placebo were detected in secondary outcomes, and no adverse effects of AS supplementation were observed. In conclusion, AS supplementation may be a candidate to promote recovery from mental fatigue which is experienced by many healthy people.

KEYWORDS:

astaxanthin; fatigue; phosphatidylcholine hydroperoxide; sesame seed extract; sesamin; visual analogue scale

PMID: 29495607

PMCID: [PMC5872699](#)

DOI: [10.3390/nu10030281](#)

[Indexed for MEDLINE]

[Free PMC Article](#)

Astaxanthin formula counteracts cognitive impairment in subjects with mild cognitive impairment in human clinical trial.

[Neuropsychiatr Dis Treat.](#) 2014 Feb 3;10:225-30. doi: 10.2147/NDT.S51092. eCollection 2014.

Cognitive effects of a dietary supplement made from extract of *Bacopa monnieri*, astaxanthin, phosphatidylserine, and vitamin E in subjects with mild cognitive impairment: a noncomparative, exploratory clinical study.

[Zanotta D¹](#), [Puricelli S¹](#), [Bonoldi G¹](#).

Author information

Abstract

A prospective cohort, noncomparative, multicenter trial was conducted to explore the potential of a phytotherapeutic compound, available as a dietary supplement and containing extracts of *Bacopa monnieri* and *Haematococcus pluvialis* (astaxanthin) plus phosphatidylserine and vitamin E, in improving cognition in subjects diagnosed with mild cognitive impairment. Enrolled subjects (n=104) were aged 71.2±9.9 years and had a mini-mental state examination score of 26.0±2.0 (mean ± standard deviation). They underwent the Alzheimer's Disease Assessment Scale-cognitive subscale (ADAS-cog) test and the clock drawing test at baseline and upon completion of a 60-day period of dietary supplementation with one tablet daily of the tested compound. In 102 assessable subjects, total ADAS-cog scores improved from 13.7±5.8 at baseline to 9.7±4.9 on day 60, and the clock drawing test scores improved from 8.5±2.3 to 9.1±1.9. Both changes were statistically significant (P<0.001). Memory tasks were the individual components of ADAS-cog showing the largest improvements. In a multivariate analysis, larger improvements in total ADAS-cog score were associated with less compromised baseline mini-mental state examination scores. Perceived efficacy was rated as excellent or good by 62% of study subjects. The tested compound was well tolerated; one nonserious adverse event was reported in the overall study population, and perceived tolerability was rated excellent or good by 99% of the subjects. In conclusion, dietary supplementation with the tested compound shows potential for counteracting cognitive impairment in subjects with mild cognitive impairment and warrants further investigation in adequately controlled, longer-term studies.

KEYWORDS: ADAS-cog test; *Bacopa monnieri*; astaxanthin; clock drawing test; dietary supplement; mild cognitive impairment

PMID: 24523587 PMCID: [PMC3921088](#) DOI: [10.2147/NDT.S51092](#) [Free PMC Article](#)

ESTERIFIED ASTAXANTHIN (E.G. FOUND IN ALGAE) IS SUPERIOR TO NON-ESTERIFIED ASTAXANTHIN (E.G. SYNTHETIC ASTAXANTHIN OR THAT DERIVED FROM YEAST) IN PROTECTING AGAINST NEURONAL CELL DEATH AND PREVENTING BEHAVIORAL DEFICITS IN MOUSE MODEL OF PARKINSON'S.

Food Funct. 2020 Sep 23;11(9):8038-8050.

doi: 10.1039/d0fo01176b.

Docosahexaenoic acid-acylated astaxanthin ester exhibits superior performance over non-esterified astaxanthin in preventing behavioral deficits coupled with apoptosis in MPTP-induced mice with Parkinson's disease

[Cheng-Cheng Wang](#)¹, [Hao-Hao Shi](#)¹, [Jie Xu](#)¹, [Teruyoshi Yanagita](#)², [Chang-Hu Xue](#)³, [Tian-Tian Zhang](#)¹, [Yu-Ming Wang](#)³

PMID: 32845953 DOI: [10.1039/d0fo01176b](https://doi.org/10.1039/d0fo01176b)

Abstract

Non-esterified astaxanthin (AST) has been reported to exhibit protective effects from Parkinson's disease (PD). Notably, DHA-acylated astaxanthin ester (DHA-AST) is widely distributed in the seafood. However, whether DHA-AST has an effect on PD, and the differences between DHA-AST, non-esterified AST and the combination of non-esterified AST (AST) with DHA (DHA + AST) is unclear. In the present study, mice with PD, induced by 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP), were employed to investigate the effects of DHA-AST, AST and DHA + AST on Parkinson's disease. The rotarod test results showed that DHA-AST significantly suppressed the PD development in MPTP-induced mice, and was better than the effects of AST and DHA + AST. Further mechanistic studies indicated that all three astaxanthin supplements could inhibit oxidative stress in the brain. It was noted that DHA-AST had the best ability to suppress the apoptosis of dopaminergic neurons via the mitochondria-mediated pathway and JNK and P38 MAPK pathway in the brain among the three treated groups. DHA-AST was superior to AST in preventing behavioral deficits coupled with apoptosis rather than oxidative stress, and might provide a valuable reference for the prevention and treatment of neurodegenerative diseases.

ASTAXANTHIN-S-ALLYL CYSTEINE DIESTER SHOWS NEUROPROTECTIVE EFFECTS BY PREVENTING NEURONAL CELL DEATH AND PRESERVING COGNITIVE FUNCTION IN-VITRO AND IN-VIVO.

Neurotoxicology 2021 Sep;86:114-124. doi: 10.1016/j.neuro.2021.07.007. Epub 2021 Jul 30.

Astaxanthin-s-allyl cysteine diester against high glucose-induced neuronal toxicity in vitro and diabetes-associated cognitive decline in vivo: Effect on p53, oxidative stress and mitochondrial function

[Chitra Loganathan](#)¹, [Penislusshiyam Sakayanathan](#)¹, [Palvannan Thayumanavan](#)²

- PMID: 34339762 DOI: [10.1016/j.neuro.2021.07.007](https://doi.org/10.1016/j.neuro.2021.07.007)

Abstract

Neuroprotective effect of astaxanthin-s-allyl cysteine diester (AST-SAC) against high glucose (HG)-induced oxidative stress in in vitro and cognitive decline under diabetes conditions in in vivo has been explored. Pretreatment of AST-SAC (5, 10 and 15 μ M) dose-dependently preserved the neuronal cells (SH-SY5Y) viability against HG toxicity through i) decreasing oxidative stress (decreasing reactive oxygen species generation and increasing endogenous antioxidants level); ii) protecting mitochondrial function [oxidative phosphorylation (OXPHOS) complexes activity and mitochondrial membrane potential (MMP)]; and iii) decreasing p53 level thereby subsequently decreasing the level of apoptotic marker proteins. Male Sprague-Dawley rats were orally administered AST-SAC (1 mg/kg/day) for 45 days in streptozotocin-induced diabetes mellitus (DM) rats. AST-SAC administration prevented the loss of spatial memory in DM rats as determined using the novel object location test. AST-SAC administration alleviated the DM-induced injury in brain such as increased cholinesterases activity, elevated oxidative stress and mitochondrial dysfunction. Altogether, the results from the present study demonstrated that AST-SAC averted the neuronal apoptosis and preserved the cognitive function against HG toxicity under DM conditions.

Astaxanthin reduces traumatic brain injury in brain tissue in mice.

[BMC Neurosci.](#) 2016 Aug 31;17(1):60. doi: 10.1186/s12868-016-0295-2.

Astaxanthin alleviates cerebral edema by modulating NKCC1 and AQP4 expression after traumatic brain injury in mice.

[Zhang M](#)¹, [Cui Z](#)², [Cui H](#)¹, [Cao Y](#)¹, [Zhong C](#)³, [Wang Y](#)⁴.

[Author information](#)

Abstract

BACKGROUND:

Astaxanthin is a carotenoid pigment that possesses potent antioxidative, anti-inflammatory, antitumor, and immunomodulatory activities. Previous studies have demonstrated that astaxanthin displays potential neuroprotective properties for the treatment of central nervous system diseases, such as ischemic brain injury and subarachnoid hemorrhage. This study explored whether astaxanthin is neuroprotective and ameliorates neurological deficits following traumatic brain injury (TBI).

RESULTS:

Our results showed that, following CCI, treatment with astaxanthin compared to vehicle ameliorated neurologic dysfunctions after day 3 and alleviated cerebral edema and Evans blue extravasation at 24 h ($p < 0.05$). Astaxanthin treatment decreased AQP4 and NKCC1 mRNA levels in a dose-dependent manner at 24 h. AQP4 and NKCC1 protein expressions in the peri-contusional cortex were significantly reduced by astaxanthin at 24 h ($p < 0.05$). Furthermore, we also found that bumetanide (BU), an inhibitor of NKCC1, inhibited trauma-induced AQP4 upregulation ($p < 0.05$).

CONCLUSIONS:

Our data suggest that astaxanthin reduces TBI-related injury in brain tissue by ameliorating AQP4/NKCC1-mediated cerebral edema and that NKCC1 contributes to the upregulation of AQP4 after TBI.

KEYWORDS:

Aquaporin-4; Astaxanthin; Cerebral edema; Na⁺-K⁺-2Cl⁻ co-transporter-1; Traumatic brain injury

PMID: [27581370](#) PMID: [PMC5007682](#)

DOI: [10.1186/s12868-016-0295-2](#)

[PubMed - in process]

[Free PMC Article](#)

Astaxanthin shows neuroprotective properties in mouse model of Parkinson's disease.

[Oncotarget](#). 2017 Dec 28;9(12):10388-10401. doi: 10.18632/oncotarget.23737. eCollection 2018 Feb 13.

Astaxanthin is neuroprotective in an aged mouse model of Parkinson's disease.

[Grimmig B](#)^{1,2}, [Daly L](#)¹, [Subbarayan M](#)^{1,2}, [Hudson C](#)³, [Williamson R](#)⁴, [Nash K](#)^{2,5}, [Bickford PC](#)^{1,2,3}.

Author information

Abstract

Parkinson's disease (PD) is the second most common neurodegenerative disorder and prevalence increases with age. Normal physiological changes that occur during the aging process reflect the pathological characteristics of Parkinson's disease. It is also recognized that age related changes significantly interact with the pathological mechanisms that underlie the neurodegeneration in PD and perpetuate the disease process. Despite the fact that aging is considered to be a primary risk factor for developing PD, the use of aged animal models are still under-utilized in pre-clinical research, thus reducing the translatability of experimental findings. Here, we use a natural compound astaxanthin (AXT) with multiple biological activities to attenuate neurotoxicity in a mouse model of Parkinson's disease in both young and aged mice. We observed that AXT preserved neurons in the substantia nigra of both young and aged mice that were exposed to the MPTP neurotoxin. However, AXT was less efficacious in the aged animals, as AXT was not able to protect against the MPTP induced loss of tyrosine hydroxylase (TH) throughout the aged nigro-striatal circuit. This disparity in the neuroprotective effect of AXT suggests that aging is a critical factor to consider during the development of novel therapeutics for neurodegenerative diseases and should be more rigorously evaluated in preclinical models.

KEYWORDS:

aging; astaxanthin; neurodegeneration; neuroinflammation; neuroprotection

PMID: 29535814

PMCID: [PMC5828206](#)

DOI: [10.18632/oncotarget.23737](#)

[Free PMC Article](#)

Astaxanthin may serve as a therapeutic agent for lipopolysaccharide-induced depressive-like behavior via its potent anti-inflammatory activity based on mouse study.

[Brain Res.](#) 2016 Aug 21. pii: S0006-8993(16)30582-0. doi: 10.1016/j.brainres.2016.08.029. [Epub ahead of print]

Trans-astaxanthin attenuates lipopolysaccharide-induced neuroinflammation and depressive-like behavior in mice.

[Jiang X](#)¹, [Chen L](#)², [Shen L](#)², [Chen Z](#)², [Xu L](#)², [Zhang J](#)², [Yu X](#)³.

[Author information](#)

Abstract

Mounting evidence supports that inflammation and increased cytokine levels are associated with depression-like symptoms and neuropsychological disturbances in humans. Trans-astaxanthin has anti-inflammatory and antioxidative activity, also has the ability to cross the blood-brain barrier in rodents. Here, we investigated the effects of trans-astaxanthin on lipopolysaccharide (LPS)-induced depressive-like behavior in mice. In both the forced swimming test (FST) and tail suspension test (TST), the immobility time was increased when mice were administrated with a single dose of LPS (0.83mg/kg, i.p.). However, this alteration can be reversed by pretreatment of trans-astaxanthin at doses of 20, 40 and 80mg/kg (p.o.) for 7 days. Further neurochemical assays suggested that LPS-induced overexpression of pro-inflammatory cytokines (IL-1 β , IL-6 and TNF- α) in the hippocampus and the prefrontal cortex (PFC) can also be reversed by trans-astaxanthin treatment. Moreover, trans-astaxanthin at 80mg/kg was demonstrated to effectively antagonize iNOS, nNOS and COX-2 expression, both at mRNA and protein levels, nitric oxide (NO) levels, via regulating NF- κ B in the hippocampus and PFC. Taken together, trans-astaxanthin may serve as an effective therapeutic agent for LPS-induced depressive-like behavior via its potent anti-inflammatory property.

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KEYWORDS:

NF- κ B; Trans-astaxanthin; depressive-like behavior; inflammation; lipopolysaccharide (LPS)

PMID:

[27559013](#)

DOI: [10.1016/j.brainres.2016.08.029](#)

Astaxanthin improves spatial memory marker of Alzheimer's Disease in mice.

[Brain Res.](#) 2018 Dec 12. pii: S0006-8993(18)30630-9. doi: 10.1016/j.brainres.2018.12.014. [Epub ahead of print]

Astaxanthin ameliorates scopolamine-induced spatial memory via reduced cortical-striato-hippocampal oxidative stress.

[Al-Amin MM¹](#), [Mahmud W¹](#), [Pervin MS²](#), [Islam SMR³](#), [Rahman MA⁴](#), [Zinchenko A⁵](#).

Author information

Abstract

Alzheimer's disease is characterized by progressive disruption of cholinergic neurotransmission and impaired cognitive functions. In rodents, scopolamine has been used to induce cholinergic dysfunction resulting in cognitive impairments and an increment of oxidative stress in the brain. Here we tested whether oxidative stress can be attenuated via an antioxidant (astaxanthin) to rescue scopolamine-induced spatial memory. For this purpose, we administered either 0.9% saline (control), or scopolamine (SCP), or scopolamine plus astaxanthin (SCP+AST) to Swiss albino mice (ten weeks old; n = 20) for 28 consecutive days and subsequently examined animals' locomotor activity, spatial learning, and memory performance. The mice were then euthanized and prefrontal cortex (PFC), striatum (ST), hippocampus (HP), and liver tissues were assayed for antioxidant enzymes, glutathione (GSH), superoxide dismutase (SOD), catalase (CAT), and nitric oxide (NO). The SCP group exhibited impaired spatial learning and significantly altered levels of antioxidant enzymes and NO in the PFC, ST, and HP. In contrast, SCP+AST treatment did not cause spatial learning deficits. Furthermore, this condition also showed unaltered levels of SOD and NO in the ST and HP. Taken together, our results show that scopolamine may interrupt the striatal-hippocampal cholinergic activity resulting in impaired spatial memory. At the same time, these impairments are extinguished with astaxanthin by preventing oxidative damage in the striatal-hippocampal cholinergic neurons. Therefore, we suggest astaxanthin as a potential treatment to slow the onset or progression of cognitive dysfunctions that are elicited by abnormal cholinergic neurotransmission in Alzheimer's disease.

KEYWORDS:

Antioxidant; Cholinergic neurotransmission; Hippocampus; Spatial memory

PMID: 30552898

DOI: [10.1016/j.brainres.2018.12.014](https://doi.org/10.1016/j.brainres.2018.12.014)

Astaxanthin shows neuroprotective properties in rat model.

[Biomed Pharmacother.](#) 2018 Nov 18;110:47-58. doi: 10.1016/j.biopha.2018.11.043. [Epub ahead of print]

Neuroprotective role of astaxanthin in hippocampal insulin resistance induced by A β peptides in animal model of Alzheimer's disease.

[Rahman SO](#)¹, [Panda BP](#)², [Parvez S](#)³, [Kaundal M](#)⁴, [Hussain S](#)¹, [Akhtar M](#)⁴, [Najmi AK](#)⁵.

Author information

Abstract

With the constant failure of the clinical trials continuous exploration of a therapeutic target against Alzheimer's disease (AD) is the utmost need. Numerous studies have supported the hypothesis that central insulin resistance plays a significant role in AD. Serine phosphorylation of Insulin Receptor Substrate-1 (IRS-1) has been found to be a contributing factor in neuronal insulin resistance. Astaxanthin (ASX) is xanthophyll carotenoid which has previously demonstrated significant antidiabetic and neuroprotective actions. In the present study, AD was induced by i.c.v administration of Amyloid- β (1-42) peptides in Wistar rats. After 7 days of recovery, rats were treated with 0.5 mg/kg and 1 mg/kg of ASX orally for 28 days. Behavioral analysis was done in the last week of our experimental study. On the 36th day, rats were sacrificed and their hippocampus were separated from the whole brain, then homogenized and stored for biochemical estimations. ASX significantly and dose-dependently reversed the cognitive and memory impairment, assessed by Morris water maze test and Novel object Recognition test, A β (1-42) peptides infused Wistar rats. ASX also significantly attenuated soluble A β (1-42) level, IRS-S307 activity, GSK-3 β activity, TNF- α level, AChE level, nitrite level and oxidative stress in the hippocampus. Histopathological evaluation, done through H&E and Congo red staining, also demonstrated neuroprotective and anti-amyloidogenic effects of ASX in hippocampus. Our study concludes preventive action of Astaxanthin against hippocampal insulin resistance and Alzheimer's disease complications, supporting potential role of hippocampal insulin resistance targeting against AD.

KEYWORDS:

Alzheimer's disease; Astaxanthin; A β (1-42) peptides; Insulin receptor substrate-1; Neuronal insulin resistance; Type-3 diabetes

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Free full text

Astaxanthin improves behavioral disorder and oxidative stress in mouse model for autism.

[Behav Brain Res.](#) 2015 Feb 28;286:112-121. Doi: 10.1016/j.bbr.2015.02.041. [Epub ahead of print]

Astaxanthin improves behavioral disorder and oxidative stress in prenatal valproic acid-induced mice model of autism.

[Al-Amin MM](#)¹, [Rahman MM](#)¹, [Khan FR](#)¹, [Zaman F](#)¹, [Mahmud Reza H](#)².

Author information

Abstract

Prenatal exposure to valproic acid on gestational day 12.5 may lead to the impaired behavior in the offspring, which is similar to the human autistic symptoms. To the contrary, astaxanthin shows neuroprotective effect by its antioxidant mechanism. We aimed to (i) develop mice model of autism and (ii) investigate the effect of astaxanthin on such model animals. Valproic acid (600mg/kg) was administered intraperitoneally to the pregnant mice on gestational day 12.5. Prenatal valproic acid-exposed mice were divided into 2 groups on postnatal day 25 and astaxanthin (2mg/kg) was given to the experimental group (VPA_AST, n=10) while saline was given to the control group (VPA, n=10) for 4 weeks. Behavioral test including social interaction, open field and hot-plate were conducted on postnatal day 25 and oxidative stress markers such as lipid peroxidation, advanced protein oxidation product, nitric oxide, glutathione, and activity of superoxide dismutase and catalase were estimated on postnatal day 26 to confirm mice model of autism and on postnatal day 56 to assess the effect of astaxanthin. On postnatal day 25, prenatal valproic acid-exposed mice exhibited (i) delayed eye opening (ii) longer latency to respond painful stimuli, (iii) poor sociability and social novelty and (iv) high level of anxiety. In addition, an increased level of oxidative stress was found by determining different oxidative stress markers. Treatment with astaxanthin significantly ($p < 0.05$) improved the behavioral disorder and reduced the oxidative stress in brain and liver. In conclusion, prenatal exposure to valproic acid in pregnant mice leads to the development of autism-like features. Astaxanthin improves the impaired behavior in animal model of autism presumably by its antioxidant activity.

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KEYWORDS:

Astaxanthin; Autism; Oxidative stress; Valproic acid

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25732953

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Astaxanthin superior to canthaxanthin and beta-carotene in antioxidant neuroprotective activity and shows merit as a potential neuron protectant.

[Kaohsiung J Med Sci](#). 2013 Aug;29(8):412-21. doi: 10.1016/j.kjms.2012.12.002. Epub 2013 Feb 8.

Reactive oxygen species scavenging activities in a chemiluminescence model and neuroprotection in rat pheochromocytoma cells by astaxanthin, beta-carotene, and canthaxanthin.

[Chang CS](#)¹, [Chang CL](#), [Lai GH](#).

Author information

Abstract

The objective of this study was to determine chemiluminescence (CL) antioxidant activities and neuroprotective effects of astaxanthin, beta-carotene (β -carotene), and canthaxanthin on undifferentiated rat pheochromocytoma (PC12) cells. We performed three CL antioxidant assays, and the three carotenoids showed varying degrees of antioxidant activity, with astaxanthin exhibiting the highest antioxidant activity than the other two samples. Results of a pyrogallol-luminol assay revealed β -carotene to have higher antioxidant activity than canthaxanthin, whereas cupric sulfate-Phen-Vc-hydrogen peroxide (H_2O_2) assay showed canthaxanthin to have higher antioxidant activity than β -carotene. Luminol- H_2O_2 assay showed the antioxidant activity series as canthaxanthin > β -carotene at 62.5-1000 μ g/mL and β -carotene > canthaxanthin at 1000-4000 μ g/mL. Astaxanthin exhibited partial neuroprotective activity against H_2O_2 and the strongest neuroprotective activity against amyloid beta-peptide(25-35) [$A\beta$ (25-35)]-induced undifferentiated PC12 cell deaths at 0.5-5.0 μ M. Canthaxanthin showed partial neuroprotective activity in $A\beta$ (25-35)-induced undifferentiated PC12 cell deaths at 1.0-5.0 μ M. Astaxanthin protected undifferentiated PC12 cells from the damaging effects of H_2O_2 and $A\beta$ (25-35) by the following ways: (1) scavenging superoxide anion radicals, hydroxyl radicals, and H_2O_2 ; (2) securing cell viability; (3) suppressing the production of reactive oxygen species; and (4) eliminating calcium ion influx. Our results conclusively show that astaxanthin has the merit as a potential neuron protectant.

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KEYWORDS:

Astaxanthin; Canthaxanthin; Chemiluminescence antioxidant activity; Neuroprotective effect; β -carotene

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Astaxanthin protects against early brain injury and improves neuron survival in rats.

[Acta Histochem.](#) 2019 Jan;121(1):56-63. doi: 10.1016/j.acthis.2018.10.014. Epub 2018 Nov 2.

Protective effects of astaxanthin on subarachnoid hemorrhage-induced early brain injury: Reduction of cerebral vasospasm and improvement of neuron survival and mitochondrial function.

[Wang Y¹](#), [Liu Y¹](#), [Li Y¹](#), [Liu B¹](#), [Wu P¹](#), [Xu S¹](#), [Shi H²](#).

Author information

Abstract

The purpose of this study was to evaluate the neuroprotective effects of astaxanthin on early brain injury (EBI) caused by subarachnoid hemorrhage (SAH) in rats and to explore possible molecular mechanisms. Experimental SAH model was introduced in adult male SD rats by injecting autologous arterial blood into the prechiasmatic cistern. Astaxanthin (75 mg/kg bodyweight) or olive oil was administered by oral gavage at 3 h after SAH. Our results showed that astaxanthin attenuated SAH-induced cerebral vasospasm and reduced neuronal apoptosis. Astaxanthin inhibited mitochondria-associated neuron apoptosis in the prefrontal cortex after SAH: increased mitochondrial membrane potential, decreased Bax/Bcl-2 ratio, inhibited cytochrome C release in cytoplasm, and suppressed caspase-3 enzyme activity. Furthermore, the cerebral expression levels of synaptic proteins (Synapsin-1, postsynaptic density-95 and growth-associated protein-43) and nerve growth and neuronal differentiation factors (brain-derived neurotropic factor and purine-rich binding protein- α) were reduced following SAH. Astaxanthin partly restored their expression. In conclusion, our current work demonstrates that astaxanthin attenuates SAH-induced EBI, possibly by improving neuronal survival and mitochondrial function.

KEYWORDS:

Apoptosis; Astaxanthin; Cerebral vasospasm; Early brain injury; Mitochondria; Subarachnoid hemorrhage

PMID: 30392635

DOI: [10.1016/j.acthis.2018.10.014](https://doi.org/10.1016/j.acthis.2018.10.014)

Astaxanthin attenuates early brain injury in rats by inducing antioxidant and detoxifying enzymes.

[Mar Drugs](#). 2014 Dec 18;12(12):6125-41. Doi: 10.3390/md12126125.

Astaxanthin activates nuclear factor erythroid-related factor 2 and the antioxidant responsive element (Nrf2-ARE) pathway in the brain after subarachnoid hemorrhage in rats and attenuates early brain injury.

[Wu Q](#)¹, [Zhang XS](#)², [Wang HD](#)³, [Zhang X](#)⁴, [Yu Q](#)⁵, [Li W](#)⁶, [Zhou ML](#)⁷, [Wang XL](#)⁸.

Author information

Abstract

Astaxanthin (ATX) has been proven to ameliorate early brain injury (EBI) after experimental subarachnoid hemorrhage (SAH) by modulating cerebral oxidative stress. This study was performed to assess the effect of ATX on the Nrf2-ARE pathway and to explore the underlying molecular mechanisms of antioxidant properties of ATX in EBI after SAH. A total of 96 male SD rats were randomly divided into four groups. Autologous blood was injected into the prechiasmatic cistern of the rat to induce an experimental SAH model. Rats in each group were sacrificed at 24 h after SAH. Expressions of Nrf2 and heme oxygenase-1 (HO-1) were measured by Western blot and immunohistochemistry analysis. The mRNA levels of HO-1, NAD (P) H: quinone oxidoreductase 1 (NQO-1), and glutathione S-transferase- α 1 (GST- α 1) were determined by real-time polymerase chain reaction (PCR). It was observed that administration of ATX post-SAH could up-regulate the cortical expression of these agents, mediated in the Nrf2-ARE pathway at both pretranscriptional and posttranscriptional levels. Meanwhile, oxidative damage was reduced. Furthermore, ATX treatment significantly attenuated brain edema, blood-brain barrier (BBB) disruption, cellular apoptosis, and neurological dysfunction in SAH models. This study demonstrated that ATX treatment alleviated EBI in SAH model, possibly through activating the Nrf2-ARE pathway by inducing antioxidant and detoxifying enzymes.

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25528957

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[Free PMC Article](#)

Astaxanthin alleviates cognitive deficits and protects neurons against inflammation in diabetic mice.

[Physiol Behav.](#) 2015 Nov 1;151:412-20. doi: 10.1016/j.physbeh.2015.08.015. Epub 2015 Aug 10.

Inhibition of inflammation by astaxanthin alleviates cognition deficits in diabetic mice.

[Zhou X¹](#), [Zhang F¹](#), [Hu X¹](#), [Chen J¹](#), [Wen X²](#), [Sun Y³](#), [Liu Y³](#), [Tang R⁴](#), [Zheng K⁵](#), [Song Y⁶](#).

Author information

Abstract

Neurons in the hippocampal and cortical functional regions are more susceptible to damage induced by hyperglycemia, which can result in severe spatial learning and memory impairment. Neuroprotection ameliorates cognitive impairment induced by hyperglycemia in diabetic encephalopathy (DE). Astaxanthin has been widely studied in diabetes mellitus and diabetic complications due to its hypoglycemic, antioxidant and anti-apoptotic effects. However, whether astaxanthin can alleviate cognition deficits induced by DE and its precise mechanisms remain undetermined. In this study, DE was induced by streptozotocin (STZ, 150 mg/kg) in ICR mice. We observed the effect of astaxanthin on cognition and investigated its potential mechanisms in DE mice. Results showed that astaxanthin treatment significantly decreased the latency and enhanced the distance and time spent in the target quadrant in the Morris water maze test. Furthermore, neuronal survival was significantly increased in the hippocampal CA3 region and the frontal cortex following treatment with astaxanthin. Meanwhile, immunoblotting was used to observe the nuclear translocation of nuclear factor-kappaB (NF- κ B) p65 and the expression of tumor necrosis factor- α (TNF- α) in the hippocampus and frontal cortex. The results indicated that astaxanthin could inhibit NF- κ B nuclear translocation and downregulate TNF- α expression in the hippocampus and frontal cortex. Overall, the present study implied that astaxanthin could improve cognition by protecting neurons against inflammation injury potentially through inhibiting the nuclear translocation of NF- κ B and down-regulating TNF- α .

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KEYWORDS:

Astaxanthin; Cognition deficits; Diabetic encephalopathy; Inflammation; Nuclear factor- κ B; Tumor necrosis factor- α

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DOI: [10.1016/j.physbeh.2015.08.015](#)

Astaxanthin has a protective effect on the brain cells of diabetic rats and improves cognitive deficits.

[Int J Clin Exp Pathol](#). 2015 Jun 1;8(6):6083-94. eCollection 2015.

Astaxanthin improves cognitive deficits from oxidative stress, nitric oxide synthase and inflammation through upregulation of PI3K/Akt in diabetes rat.

[Xu L](#)¹, [Zhu J](#)², [Yin W](#)³, [Ding X](#)³.

Author information

Abstract

Diabetes-induced cognitive deficit (DICD) is a prevalent disease with substantial morbidity and mortality and as a global health problem with serious economic burdens. Astaxanthin (AST) has a good prospect in production of nutritional, medical, and particularly functional health drug. The present study was aimed to study the effect of AST on DICD in diabetes mellitus (DM) rat through suppression of oxidative stress, nitric oxide synthase (NOS) pathway, inflammatory reaction and upregulation of PI3K/Akt. In the study, Morris water maze test was used to detect the cognitive function of DM rat. Afterwards, we measured the body weight and blood glucose levels of DM rats. Then, oxidative stress, the activities of eNOS and iNOS, and inflammatory factors were analyzed using a commercial kit in cerebral cortex and hippocampus. Finally, the caspase-3/9 and phosphoinositide 3-kinase (PI3K)/Akt expressions were also checked out with Real Time PCR and immunoblotting, respectively. In this experiment, AST could availablely enhance the body weight and reduce blood glucose levels of DM rats. Moreover, AST could observably perfect cognitive function of DM rat. Next, the activities of oxidative stress, nitric oxide synthase and inflammation were distinctly diminution in DM rat, after the treatment of AST. Furthermore, our present results demonstrated that AST had the protective effect on the brain cell of DM rat, decreased the caspase-3/9 expression and promoted the expression of PI3K/Akt in cerebral cortex and hippocampus.

KEYWORDS:

Diabetes-induced cognitive deficit; PI3K/Akt; astaxanthin; inflammatory; nitric oxide synthase; oxidative stress

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PMCID: [PMC4525820](#)

[PubMed - indexed for MEDLINE]

Free PMC Article

Astaxanthin protects brain cells from glutamate-induced cytotoxicity and may be useful for the treatment of neurodegenerative disorders such as Alzheimer's Disease.

[Neuroscience](#). 2015 Sep 10;303:558-68. doi: 10.1016/j.neuroscience.2015.07.034. Epub 2015 Jul 18.

Neuroprotective effect of astaxanthin against glutamate-induced cytotoxicity in HT22 cells: Involvement of the Akt/GSK-3 β pathway.

[Wen X](#)¹, [Huang A](#)², [Hu J](#)³, [Zhong Z](#)³, [Liu Y](#)⁴, [Li Z](#)¹, [Pan X](#)⁵, [Liu Z](#)⁶.

Author information

Abstract

Oxidative stress (OS) mediated the pathogenesis of Alzheimer's disease (AD). Astaxanthin (ATX) has been reported to exert antioxidant activities as well as neuroprotective effects in vivo and in vitro. But it is still unknown whether the Akt/glycogen synthase kinase-3 β (GSK-3 β) signaling mediated the neuroprotective effect of ATX in HT22 cells. Flow cytometric analysis was used to evaluate reactive oxygen species (ROS) generation. Caspase and PARP activity was measured. The expressions of heme oxygenase-1 (HO-1), nuclear factor-E2-related factor 2 (Nrf2), Bcl-2, Bax, apoptosis-inducing factor (AIF), cytochrome-c (Cyto-c), p-Akt and p-GSK-3 β were evaluated to elucidate the underlying mechanism. Our results showed that ATX significantly attenuated glutamate-induced cell viability loss and lactate dehydrogenase (LDH) release, decreased the expression of caspase-3/8/9 activity and cleaved PARP, and suppressed the intracellular accumulation of ROS in HT22 cells after exposure to glutamate. ATX also increased the mitochondrial expression of AIF, Cyto-c as well as Bax while decreased Bcl-2. Moreover, ATX also induced the HO-1 expression in a dose and time-dependent manner, increased the antioxidant-responsive element (ARE) activity and nuclear Nrf2 expression. Furthermore, treatment with ATX restored the p-Akt and p-GSK-3 β (Ser9) as well as HO-1 expression reduced by glutamate. This protective effect was partially blocked by the inhibitors lithium chloride treatment in HT22, indicating the involvement of Akt/GSK-3 β inactivation during the neuroprotective effect of ATX. Our results provide the first evidence that ATX can protect glutamate-induced cytotoxicity in HT22 via attenuating caspase activation and mitochondrial dysfunction and modulating the Akt/GSK-3 β signaling, indicating ATX may be useful for the treatment of neurodegenerative disorders such as AD.

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KEYWORDS:

Akt; GSK-3 β ; Nrf2; astaxanthin; oxidative stress

PMID: [26197224](#) DOI: [10.1016/j.neuroscience.2015.07.034](#)

Astaxanthin reduces brain cell death in rats given a substance to induce brain damage.

[Mol Med Rep](#). 2016 May;13(5):4073-8. doi: 10.3892/mmr.2016.5035. Epub 2016 Mar 21.

Astaxanthin reduces isoflurane-induced neuroapoptosis via the PI3K/Akt pathway.

[Wang CM](#)¹, [Cai XL](#)¹, [Wen QP](#)¹.

Author information

Abstract

Astaxanthin is an oxygen-containing derivative of carotenoids that effectively suppresses reactive oxygen and has nutritional and medicinal value. The mechanisms underlying the effects of astaxanthin on isoflurane-induced neuroapoptosis remain to be fully understood. The present study was conducted to evaluate the protective effect of astaxanthin to reduce isoflurane-induced neuroapoptosis and to investigate the underlying mechanisms. The results demonstrated that isoflurane induced brain damage, increased caspase-3 activity and suppressed the phosphatidylinositol 3-kinase (PI3K)/protein kinase B (Akt) signaling pathway in an in vivo model. However, treatment with astaxanthin significantly inhibited brain damage, suppressed caspase-3 activity and upregulated the PI3K/Akt pathway in the isoflurane-induced rats. Furthermore, isoflurane suppressed cell growth, induced cell apoptosis, enhanced caspase-3 activity and downregulated the PI3K/Akt pathway in organotypic hippocampal slice culture. Administration of astaxanthin significantly promoted cell growth, reduced cell apoptosis and caspase-3 activity, and upregulated the PI3K/Akt pathway and isoflurane-induced neuroapoptosis. The present study demonstrated that downregulation of the PI3K/Akt pathway reduced the effect of astaxanthin to protect against isoflurane-induced neuroapoptosis in the in vitro model. The results of the current study suggested that the protective effect of astaxanthin reduces the isoflurane-induced neuroapoptosis via activation of the PI3K/Akt signaling pathway.

PMID:

[27035665](#)

DOI:

[10.3892/mmr.2016.5035](#)

Astaxanthin improves spatial memory impairment and neuronal oxidative stress in mice exposed to aluminum chloride.

[Eur J Pharmacol.](#) 2016 Apr 15;777:60-9. doi: 10.1016/j.ejphar.2016.02.062. Epub 2016 Feb 27.

Astaxanthin ameliorates aluminum chloride-induced spatial memory impairment and neuronal oxidative stress in mice.

[Al-Amin MM¹](#), [Reza HM²](#), [Saadi HM²](#), [Mahmud W²](#), [Ibrahim AA²](#), [Alam MM²](#), [Kabir N²](#), [Saifullah AR²](#), [Tropa ST²](#), [Quddus AH³](#).

Author information

Abstract

Aluminum chloride induces neurodegenerative disease in animal model. Evidence suggests that aluminum intake results in the activation of glial cells and generation of reactive oxygen species. By contrast, astaxanthin is an antioxidant having potential neuroprotective activity. In this study, we investigate the effect of astaxanthin on aluminum chloride-exposed behavioral brain function and neuronal oxidative stress (OS). Male Swiss albino mice (4 months old) were divided into 4 groups: (i) control (distilled water), (ii) aluminum chloride, (iii) astaxanthin+aluminum chloride, and (iv) astaxanthin. Two behavioral tests; radial arm maze and open field test were conducted, and OS markers were assayed from the brain and liver tissues following 42 days of treatment. Aluminum exposed group showed a significant reduction in spatial memory performance and anxiety-like behavior. Moreover, aluminum group exhibited a marked deterioration of oxidative markers; lipid peroxidation (MDA), nitric oxide (NO), glutathione (GSH) and advanced oxidation of protein products (AOPP) in the brain. To the contrary, co-administration of astaxanthin and aluminum has shown improved spatial memory, locomotor activity, and OS. These results indicate that astaxanthin improves aluminum-induced impaired memory performances presumably by the reduction of OS in the distinct brain regions. We suggest a future study to determine the underlying mechanism of astaxanthin in improving aluminum-exposed behavioral deficits.

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KEYWORDS:

Behavior; Glutathione; Memory; Nitric oxide; Superoxide dismutase

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[26927754](#)

DOI: [10.1016/j.ejphar.2016.02.062](#)

Astaxanthin improves behavioral deficits in mice exposed to lipopolysaccharide exposure.

[BMC Neurosci.](#) 2016 Feb 8;17:11. doi: 10.1186/s12868-016-0245-z.

Astaxanthin ameliorates prenatal LPS-exposed behavioral deficits and oxidative stress in adult offspring.

[Al-Amin MM](#)^{1,2}, [Sultana R](#)³, [Sultana S](#)⁴, [Rahman MM](#)⁵, [Reza HM](#)⁶.

Author information

Abstract

BACKGROUND:

Prenatal maternal lipopolysaccharide (LPS) exposure leads to behavioral deficits such as depression, anxiety, and schizophrenia in the adult lives. LPS-exposure resulted in the production of cytokines and oxidative damage. On the contrary, astaxanthin is a carotenoid compound, showed neuroprotective properties via its antioxidant capacity. This study examines the effect of astaxanthin on the prenatal maternal LPS-induced postnatal behavioral deficit in mice.

RESULTS:

We found that prenatal LPS-exposed mice showed extensive immobile phase in the tail suspension test, higher frequent head dipping in the hole-board test and greater hypolocomotion in the open field test. All these values were statistically significant ($p < 0.05$). In addition, a marked elevation of the level of lipid peroxidation, advanced protein oxidation product, nitric oxide, while a pronounced depletion of antioxidant enzymes (superoxide dismutase, catalase and glutathione) were observed in the adult offspring mice that were prenatally exposed to LPS. To the contrary, 6-weeks long treatment with astaxanthin significantly improved all behavioral deficits ($p < 0.05$) and diminished prenatal LPS-induced oxidative stress markers in the brain and liver.

CONCLUSIONS:

Taken together, these results suggest that prenatal maternal LPS-exposure leads to behavioral deficits in the adults, while astaxanthin ameliorates the behavioral deficits presumably via its antioxidant property.

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PMCID: [PMC4746928](#)

DOI: [10.1186/s12868-016-0245-z](#)

[PubMed - in process]

[Free PMC Article](#)

Astaxanthin provides neuroprotection and inhibits oxidation in a model of Parkinson's disease.

[Mar Drugs](#). 2013 Mar 28;11(4):1019-34. doi: 10.3390/md11041019.

Astaxanthin suppresses MPP(+)-induced oxidative damage in PC12 cells through a Sp1/NR1 signaling pathway.

[Ye Q](#)¹, [Zhang X](#), [Huang B](#), [Zhu Y](#), [Chen X](#).

Author information

Abstract

OBJECTIVE:

To investigate astaxanthin (ATX) neuroprotection, and its mechanism, on a 1-methyl-4-phenyl-pyridine ion (MPP+)-induced cell model of Parkinson's disease.

METHODS:

Mature, differentiated PC12 cells treated with MPP+ were used as an in vitro cell model. The MTT assay was used to investigate cell viability after ATX treatment, and western blot analysis was used to observe Sp1 (activated transcription factor 1) and NR1 (NMDA receptor subunit 1) protein expression, real-time PCR was used to monitor Sp1 and NR1 mRNA, and cell immunofluorescence was used to determine the location of Sp1 and NR1 protein and the nuclear translocation of Sp1.

RESULTS:

PC12 cell viability was significantly reduced by MPP+ treatment. The expression of Sp1 and NR1 mRNA and protein were increased compared with the control ($p < 0.01$). Following co-treatment with ATX and MPP+, cell viability was significantly increased, and Sp1 and NR1 mRNA and protein were decreased, compared with the MPP+ groups ($p < 0.01$). In addition, mithracyclin A protected PC12 cells from oxidative stress caused by MPP+ by specifically inhibiting the expression of Sp1. Moreover, cell immunofluorescence revealed that ATX could suppress Sp1 nuclear transfer.

CONCLUSION:

ATX inhibited oxidative stress induced by MPP+ in PC12 cells, via the SP1/NR1 signaling pathway.

PMID: [23538867](#)

PMCID: [PMC3705385](#)

DOI: [10.3390/md11041019](#)

[PubMed - indexed for MEDLINE]

Free PMC Article

Astaxanthin reduces diabetes type-2-associated cognitive decline in rats.

[Mol Med Rep](#). 2016 Jan;13(1):973-9. doi: 10.3892/mmr.2015.4615. Epub 2015 Nov 25.

Astaxanthin reduces type 2 diabetic-associated cognitive decline in rats via activation of PI3K/Akt and attenuation of oxidative stress.

[Li X](#)¹, [Qi Z](#)², [Zhao L](#)³, [Yu Z](#)⁴.

Author information

Abstract

Astaxanthin (AST) is an oxygenated derivative of carotenoid, which possesses a strong antioxidant activity. AST can effectively remove active oxygen from the body, and is thus considered to have an important role in disease prevention and treatment. The present study aimed to determine the effects of AST on type 2 diabetic-associated cognitive decline (DACD) in rats. Rats were intraperitoneally injected with streptozotocin (STZ), in order to establish a model of diabetes mellitus (DM). A total of 40 rats were randomly divided into five groups: The control group, the DM group, the AST (50 mg/kg) group, the AST (100 mg/kg) group, and the AST+LY294002 group (AST, 50 mg/kg and LY, 0.25 µg/100 g). Following a 14-day treatment with AST, the body weight, blood glucose levels and cognitive function were determined. In addition, the protein expression levels of phosphatidylinositol 3-kinase (PI3K)/Akt, glutathione peroxidase and superoxide dismutase activity, glutathione and malondialdehyde content, and inducible nitric oxide synthase (iNOS), caspase-3 and caspase-9 activity were detected in the rats with DM. AST clearly augmented body weight and reduced blood glucose levels in rats with DM. Furthermore, treatment with AST significantly improved the cognitive function of rats with DM. Treatment with AST activated the PI3K/Akt pathway, and suppressed oxidative stress in the DM rats. In the cerebral cortex and hippocampus of the rats with DM, the activities of iNOS, caspase-3 and caspase-9 were markedly reduced. Furthermore, treatment with the Akt inhibitor LY294002 reduced the effectiveness of AST on DACD in rats. In conclusion, AST may reduce type 2 DACD in rats via activation of PI3K/Akt and attenuation of oxidative stress.

PMID:

[26648531](#)

DOI:

[10.3892/mmr.2015.4615](#)

Astaxanthin protects brain cells from the damaging effect of alcohol and may be effective for preventing neurotoxicity associated with excessive alcohol consumption.

[Mar Drugs](#). 2016 Mar 10;14(3). pii: E56. doi: 10.3390/md14030056.

Astaxanthin Inhibits Acetaldehyde-Induced Cytotoxicity in SH-SY5Y Cells by Modulating Akt/CREB and p38MAPK/ERK Signaling Pathways.

[Yan T](#)¹, [Zhao Y](#)², [Zhang X](#)³, [Lin X](#)⁴.

Author information

Abstract

Excessive alcohol consumption can lead to brain tissue damage and cognitive dysfunction. Acetaldehyde, the most toxic metabolite of ethanol, mediates the brain tissue damage and cognitive dysfunction induced by chronic excessive alcohol consumption. In this study, the effect of astaxanthin, a marine bioactive compound, on acetaldehyde-induced cytotoxicity was investigated in SH-SY5Y cells. It was found that astaxanthin protected cells from apoptosis by ameliorating the effect of acetaldehyde on the expression of Bcl-2 family proteins, preventing the reduction of anti-apoptotic protein Bcl-2 and the increase of pro-apoptotic protein Bak induced by acetaldehyde. Further analyses showed that astaxanthin treatment inhibited acetaldehyde-induced reduction of the levels of activated Akt and cyclic AMP-responsive element binding protein (CREB). Astaxanthin treatment also prevented acetaldehyde-induced increase of the level of activated p38 mitogen-activated protein kinase (MAPK) and decrease of the level of activated extracellular signal-regulated kinases (ERKs). Activation of Akt/CREB pathway promotes cell survival and is involved in the upregulation of Bcl-2 gene. P38MAPK plays a critical role in apoptotic events while ERKs mediates the inhibition of apoptosis. Thus, astaxanthin may inhibit acetaldehyde-induced apoptosis through promoting the activation of Akt/CREB and ERKs and blocking the activation of p38MAPK. In addition, astaxanthin treatment suppressed the oxidative stress induced by acetaldehyde and restored the antioxidative capacity of SH-SY5Y cells. Therefore, astaxanthin may protect cells against acetaldehyde-induced cytotoxicity through maintaining redox balance and modulating apoptotic and survival signals. The results suggest that astaxanthin treatment may be beneficial for preventing neurotoxicity associated with acetaldehyde and excessive alcohol consumption.

KEYWORDS:

Akt; MAPK; acetaldehyde; apoptosis; astaxanthin; oxidative stress

PMID: [26978376](#) PMCID: [PMC4820310](#) DOI: [10.3390/md14030056](#)

Astaxanthin provides neurovascular protection in rats.

[Brain Res.](#) 2015 Oct 22;1624:113-24. doi: 10.1016/j.brainres.2015.07.020. Epub 2015 Jul 23.

Astaxanthin reduces matrix metalloproteinase-9 expression and activity in the brain after experimental subarachnoid hemorrhage in rats.

[Zhang XS](#)¹, [Zhang X](#)², [Zhang QR](#)¹, [Wu Q](#)¹, [Li W](#)¹, [Jiang TW](#)¹, [Hang CH](#)³.

Author information

Abstract

We have previously shown that astaxanthin (ATX) reduces the blood-brain barrier (BBB) disruption and neurovascular dysfunction following subarachnoid hemorrhage (SAH) insults. However, the underlying mechanisms remain unclear. It is known that the matrix metalloproteinases (MMPs), especially matrix metalloproteinase-9 (MMP-9) plays a crucial role in the pathogenesis of secondary brain injury after SAH. And ATX has the ability to regulate MMP-9 in other models. Herein, we investigated whether ATX could ameliorate MMP-9 activation and expression in a rat model of SAH. A total of 144 rats were randomly divided into the following groups: control group (n=36), SAH group (n=36), SAH+vehicle group (n=36), and SAH+ATX group (n=36). The SAH model was induced by injection of 0.3 ml autologous blood into the prechiasmatic cistern. ATX (20 μ l of 0.1 mmol) or vehicle was administered intracerebroventricularly 30 min after SAH induction. Mortality, neurological function, brain edema and blood-brain barrier (BBB) permeability were measured at 24 and 72 h after SAH. Biochemical and zymographic methods were used to analyze MMP-9 expression and activity in brain samples. Immunohistochemistry and terminal deoxynucleotidyl transferase-mediated dUTP nick-end labeling (TUNEL) staining were also evaluated at 24h. Our data indicated that ATX could significantly reduce the expression and activity of MMP-9, leading to the amelioration of brain edema, BBB impairment, neurological deficits and TUNEL-positive cells at 24h but not 72 h after SAH. The ATX-mediated down-regulation of MMP-9 was correlated with the decreased levels of IL-1 β , TNF- α , oxidative stress, activated microglia and infiltrating neutrophils. These results suggest that the neurovascular protection of ATX in SAH is partly associated with the inhibition of MMP-9 expression and activity.

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KEYWORDS:

Astaxanthin; Early brain injury; Matrix metalloproteinase-9; Subarachnoid hemorrhage

PMID: [26210617](#) DOI: [10.1016/j.brainres.2015.07.020](#)

Astaxanthin positively affects the hippocampus of adult mice.

[Genom Data](#). 2015 Nov 7;7:32-7. doi: 10.1016/j.gdata.2015.11.001. eCollection 2016.

DNA microarray-based experimental strategy for trustworthy expression profiling of the hippocampal genes byastaxanthin supplementation in adult mouse.

[Yook JS](#)¹, [Shibato J](#)², [Rakwal R](#)³, [Soya H](#)¹.

[Author information](#)

Abstract

Naturally occurring astaxanthin (ASX) is one of the noticeable carotenoid and dietary supplement, which has strong antioxidant and anti-inflammatory properties, and neuroprotective effects in the brain through crossing the blood-brain barrier. Specially, we are interested in the role of ASX as a brain food. Although ASX has been suggested to have potential benefit to the brain function, the underlying molecular mechanisms and events mediating such effect remain unknown. Here we examined molecular factors in the hippocampus of adult mouse fed ASX diets (0.1% and 0.5% doses) using DNA microarray (Agilent 4 × 44 K whole mouse genome chip) analysis. In this study, we described in detail our experimental workflow and protocol, and validated quality controls with the housekeeping gene expression (Gapdh and Beta-actin) on the dye-swap based approach to advocate our microarray data, which have been uploaded to Gene Expression Omnibus (accession number GSE62197) as a gene resource for the scientific community. This data will also form an important basis for further detailed experiments and bioinformatics analysis with an aim to unravel the potential molecular pathways or mechanisms underlying the positive effects of ASX supplementation on the brain, in particular the hippocampus.

KEYWORDS:

Astaxanthin supplementation; Dose-dependent; Hippocampal genes; Housekeeping gene, RT-PCR

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[26981356](#)

PMCID:

[PMC4778586](#)

DOI:

[10.1016/j.gdata.2015.11.001](#)

Astaxanthin reduces inflammatory markers in the brains of mice that were injected with a neurodegenerative agent.

[Inflamm Res.](#) 2016 Aug;65(8):623-34. doi: 10.1007/s00011-016-0945-y. Epub 2016 Apr 6.

K(+) channel blocker-induced neuroinflammatory response and neurological disorders: immunomodulatory effects of astaxanthin.

[Sifi N¹](#), [Martin-Eauclaire MF²](#), [Laraba-Djebari F³](#).

Author information

Abstract

OBJECTIVE:

Channelopathies due to the brain ion channel dysfunction is considered to be an important mechanism involved in various neurodegenerative diseases. In this study, we evaluated the ability of kaliotoxin (KTX) as K(+) channel blocker to induce neuro-inflammatory response and neurodegenerative alteration. We also investigate the effects of astaxanthin (ATX) against KTX disorders.

MATERIAL AND TREATMENT:

NMRI mice were injected with KTX (1 pg/kg, by i.c.v route) with or without pretreatment using ATX (80 mg/kg, o.p route).

RESULTS:

Results showed that KTX was detected in cerebral cortex area due to its binding to the specific receptors (immunofluorescence analysis). It induced an activation of inflammatory cascade characterized by an increase of IL-6, TNF α , NO, MDA levels and NF- κ B expression associated to a decrease of GSH level. The neuroinflammatory response is accompanied with cerebral alterations and blood-brain barrier (BBB) disruption. The use of ATX prior to the KTX exerts a preventive effect not only on the neuroinflammation but also on altered tissues and the BBB disruption.

CONCLUSIONS:

Kaliotoxin is able to induce neurological disorders by blocking the K(+) ion channel, and ATX suppresses this alterations with down regulation of IL-6, TNF- α and NF- κ B expression in the brain.

KEYWORDS:

Astaxanthin; Blood–brain barrier; K+ channel blocker; Neurodegeneration; Neuroinflammatory response; Neurotoxin

PMID: [27052008](#)

DOI: [10.1007/s00011-016-0945-y](#)

Astaxanthin alleviates early brain injury after subarachnoid hemorrhage in rats.

[Mar Drugs](#). 2014 Jul 28;12(8):4291-310. Doi: 10.3390/md12084291.

Astaxanthin alleviates early brain injury following subarachnoid hemorrhage in rats: possible involvement of Akt/bad signaling.

[Zhang XS](#)¹, [Zhang X](#)², [Wu Q](#)³, [Li W](#)⁴, [Zhang QR](#)⁵, [Wang CX](#)⁶, [Zhou XM](#)¹, [Li H](#)⁷, [Shi JX](#)⁸, [Zhou ML](#)⁹.

Author information

Abstract

Apoptosis has been proven to play a crucial role in early brain injury pathogenesis and to represent a target for the treatment of subarachnoid hemorrhage (SAH). Previously, we demonstrated that astaxanthin (ATX) administration markedly reduced neuronal apoptosis in the early period after SAH. However, the underlying molecular mechanisms remain obscure. In the present study, we tried to investigate whether ATX administration is associated with the phosphatidylinositol 3-kinase-Akt (PI3K/Akt) pathway, which can play an important role in the signaling of apoptosis. Our results showed that post-SAH treatment with ATX could cause a significant increase of phosphorylated Akt and Bad levels, along with a significant decrease of cleaved caspase-3 levels in the cortex after SAH. In addition to the reduced neuronal apoptosis, treatment with ATX could also significantly reduce secondary brain injury characterized by neurological dysfunction, cerebral edema and blood-brain barrier disruption. In contrast, the PI3K/Akt inhibitor, LY294002, could partially reverse the neuroprotection of ATX in the early period after SAH by downregulating ATX-induced activation of Akt/Bad and upregulating cleaved caspase-3 levels. These results provided the evidence that ATX could attenuate apoptosis in a rat SAH model, potentially, in part, through modulating the Akt/Bad pathway.

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25072152

[PubMed – in process]

PMCID:

PMC4145317

[Free PMC Article](#)

Astaxanthin offers neuroprotection and reduces neuro-inflammation in rats.

[J Surg Res](#). 2014 Nov;192(1):206-13. Doi: 10.1016/j.jss.2014.05.029. Epub 2014 May 21.

Astaxanthin offers neuroprotection and reduces neuroinflammation in experimental subarachnoid hemorrhage.

[Zhang XS](#)¹, [Zhang X](#)², [Wu Q](#)¹, [Li W](#)¹, [Wang CX](#)¹, [Xie GB](#)¹, [Zhou XM](#)¹, [Shi JX](#)¹, [Zhou ML](#)³.

Author information

Abstract

BACKGROUND:

Neuroinflammation has been proven to play a crucial role in early brain injury pathogenesis and represents a target for treatment of subarachnoid hemorrhage (SAH). Astaxanthin (ATX), a dietary carotenoid, has been shown to have powerful anti-inflammation property in various models of tissue injury. However, the potential effects of ATX on neuroinflammation in SAH remain uninvestigated. The goal of this study was to investigate the protective effects of ATX on neuroinflammation in a rat prechiasmatic cistern SAH model.

METHODS:

Rats were randomly distributed into multiple groups undergoing the sham surgery or SAH procedures, and ATX (25 mg/kg or 75 mg/kg) or equal volume of vehicle was given by oral gavage at 30 min after SAH. All rats were sacrificed at 24 h after SAH. Neurologic scores, brain water content, blood-brain barrier permeability, and neuronal cell death were examined. Brain inflammation was evaluated by means of expression changes in myeloperoxidase, cytokines (interleukin-1 β , tumor necrosis factor- α), adhesion molecules (intercellular adhesion molecule-1), and nuclear factor kappa B DNA-binding activity.

RESULTS:

Our data indicated that post-SAH treatment with high dose of ATX could significantly downregulate the increased nuclear factor kappa B activity and the expression of inflammatory cytokines and intercellular adhesion molecule-1 in both messenger RNA transcription and protein synthesis. Moreover, these beneficial effects lead to the amelioration of the secondary brain injury cascades including cerebral edema, blood-brainbarrier disruption, neurological dysfunction, and neuronal degeneration.

CONCLUSIONS:

These results indicate that ATX treatment is neuroprotective against SAH, possibly through suppression of cerebral inflammation.

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KEYWORDS:

Astaxanthin; Early brain injury; Inflammation; Subarachnoid hemorrhage

PMID:

24948541

[PubMed – indexed for MEDLINE]

Astaxanthin protects against neuronal loss due to epilepsy in rat hippocampus.

[Neurosci Lett.](#) 2015 Jun 15;597:49-53. doi: 10.1016/j.neulet.2015.04.018. Epub 2015 Apr 15.

Astaxanthin rescues neuron loss and attenuates oxidative stress induced by amygdala kindling in adult rat hippocampus.

[Lu Y](#)¹, [Xie T](#)², [He XX](#)³, [Mao ZF](#)², [Jia LJ](#)², [Wang WP](#)⁴, [Zhen JL](#)², [Liu LM](#)².

Author information

Abstract

Oxidative stress plays an important role in the neuronal damage induced by epilepsy. The present study assessed the possible neuroprotective effects of astaxanthin (ATX) on neuronal damage, in hippocampal CA3 neurons following amygdala kindling. Male Sprague-Dawley rats were chronically kindled in the amygdala and ATX or equal volume of vehicle was given by intraperitoneally. Twenty-four hours after the last stimulation, the rats were sacrificed by decapitation. Histopathological changes and the levels of reactive oxygen species (ROS), malondialdehyde (MDA) and reduced glutathione (GSH) were measured, cytosolic cytochrome c (CytC) and caspase-3 activities in the hippocampus were also recorded. We found extensive neuronal damage in the CA3 region in the kindling group, which was preceded by increases of ROS level and MDA concentration and was followed by caspase-3 activation and an increase in cytosolic CytC. Treatment with ATX markedly attenuated the neuronal damage. In addition, ATX significantly decreased ROS and MDA concentrations and increased GSH levels. Moreover, ATX suppressed the translation of CytC release and caspase-3 activation in hippocampus. Together, these results suggest that ATX protects against neuronal loss due to epilepsy in the rat hippocampus by attenuating oxidative damage, lipid peroxidation and inhibiting the mitochondrion-related apoptotic pathway.

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KEYWORDS:

Astaxanthin; Hippocampus; Neuroprotection; Oxidative stress; Seizure

PMID:

[25888816](#)

DOI:

[10.1016/j.neulet.2015.04.018](#)

Astaxanthin protects against fetal alcohol spectrum disorder in mice.

[Neuropharmacology](#). 2014 Sep;84:13-8. Doi: 10.1016/j.neuropharm.2014.04.013. Epub 2014 Apr 26.

The protective effect of astaxanthin on fetal alcohol spectrum disorder in mice.

[Zheng D](#)¹, [Li Y](#)², [He L](#)², [Tang Y](#)², [Li X](#)², [Shen Q](#)², [Yin D](#)³, [Peng Y](#)⁴.

Author information

Abstract

Astaxanthin is a strong antioxidant with the ability of reducing the markers of inflammation. To explore the protective effect of astaxanthin on maternal ethanol induced embryonic deficiency, and to investigate the underlying mechanisms, we detected the morphology, expression of neural marker genes, oxidative stress indexes, and inflammatory factors in mice model of fetal alcohol spectrum disorder with or without astaxanthin pretreatment. Our results showed that astaxanthin blocked maternal ethanol induced retardation of embryonic growth, and the down-regulation of neural marker genes, Otx1 and Sox2. Moreover, astaxanthin also reversed the increases of malondialdehyde (MDA), hydrogen peroxide (H₂O₂), and the decrease of glutathione peroxidase (GPx) in fetal alcohol spectrum disorder. In addition, maternal ethanol induced up-regulation of toll-like receptor 4 (TLR4), and the down-streaming myeloid differentiation factor 88 (MyD88), NF-κB, TNF-α, and IL-1β in embryos, and this was inhibited by astaxanthin pretreatment. These results demonstrated a protective effect of astaxanthin on fetal alcohol spectrum disorder, and suggested that oxidative stress and TLR4 signaling associated inflammatory reaction are involved in this process.

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KEYWORDS:

Astaxanthin; Embryo; Ethanol

PMID:

24780381

[PubMed – indexed for MEDLINE]

Astaxanthin reduces cognitive impairment in rat model by decreasing inflammation, oxidation and cell death.

[Mol Neurobiol.](#) 2018 Jul;55(7):5727-5740. doi: 10.1007/s12035-017-0797-7. Epub 2017 Oct 16.

Astaxanthin Ameliorates Doxorubicin-Induced Cognitive Impairment (Chemobrain) in Experimental Rat Model: Impact on Oxidative, Inflammatory, and Apoptotic Machineries.

[El-Agamy SE¹](#), [Abdel-Aziz AK¹](#), [Wahdan S¹](#), [Esmat A¹](#), [Azab SS²](#).

Author information

Abstract

Chemobrain refers to a common sequelae experienced by 15-80% of cancer patients exposed to chemotherapeutics. The antineoplastic agent doxorubicin (DOX) has been implicated in a strenuous neurotoxicity manifested as decline in cognitive functions, most probably via cytokine-induced oxidative and nitrosative damage to brain tissues. Astaxanthin (AST), a naturally occurring carotenoid, is reputable for its outstanding antioxidant, anti-inflammatory, and antiapoptotic activities. Therefore, the aim of the current study was to investigate the potential neuroprotective and memory-enhancing effects of AST against DOX-induced behavioral and neurobiological abnormalities. Briefly, AST treatment (25 mg/kg) significantly protected against DOX-induced memory impairment. Furthermore, AST restored hippocampal histopathological architecture, halted DOX-induced oxidative and inflammatory insults, mitigated the increase in acetylcholinesterase activity, and consistently downregulated the overactive apoptotic machineries. In conclusion, these findings suggest that AST offers neuroprotection against DOX-induced cognitive impairment which could be explained at least partly by its antioxidant, anti-inflammatory, and antiapoptotic effects.

KEYWORDS:

Apoptosis; Astaxanthin; Chemobrain; Doxorubicin; Neuroinflammation; Oxidative stress

PMID: 29039023

DOI: [10.1007/s12035-017-0797-7](https://doi.org/10.1007/s12035-017-0797-7)

Astaxanthin demonstrates anti-depressive effect in mice.

[Neurosci Lett.](#) 2018 Jan 1;662:36-43. doi: 10.1016/j.neulet.2017.09.064. Epub 2017 Oct 2.

Chronic trans-astaxanthin treatment exerts antihyperalgesic effect and corrects co-morbid depressive like behaviors in mice with chronic pain.

[Jiang X¹](#), [Yan Q²](#), [Liu F³](#), [Jing C⁴](#), [Ding L⁵](#), [Zhang L⁶](#), [Pang C⁷](#).

Author information

Abstract

Patients suffering from chronic neuropathic pain are at high risk of co-morbid depression, which burdens healthcare. Trans-astaxanthin has been shown in our previous studies to exert antidepressant-like effect. This work aimed to investigate the effects of trans-astaxanthin on pain-related depressive-like behaviors in mice and explored the mechanism(s). Chronic constriction injury (CCI) model was used in this research. Chronic pain was evaluated by thermal hyperalgesia in Hargreaves test and mechanical allodynia in von Frey test, depressive-like behaviors were evaluated by immobility time in forced swim test and tail suspension test. Chronic trans-astaxanthin treatment ameliorated mechanical allodynia and thermal hyperalgesia, as well as decreasing immobility time in forced swim test and tail suspension test in CCI mice, and these actions were abolished by co-treatment with P-Chlorophenylalanine (PCPA). Subsequent study indicated that indoleamine 2,3-dioxygenase (IDO) expression increased after CCI surgery in hippocampus and spinal cord, accompanied by increase of kynurenine (KYN)/tryptophan (TRY) ratio, decrease of serotonin (5-HT)/TRY ratio and decrease of 5-HT/5-HIAA ratio. The above results affected by CCI surgery were reversed by trans-astaxanthin treatment. Moreover, trans-astaxanthin at 80mg/kg was demonstrated to effectively antagonize IL-1 β , IL-6 and TNF- α expression in hippocampus and spinal cord of CCI mice. Taken together, chronic trans-astaxanthin administration exerts therapeutic effects on thermal hyperalgesia and co-morbid depressive-like behaviors in CCI mice. These effects of trans-astaxanthin involves the serotonergic system, and also may be owing to its potent anti-inflammatory property.

KEYWORDS:

5-HT; Depression; Inflammation; Neuropathic pain; Trans-astaxanthin

PMID: 28982597

DOI: [10.1016/j.neulet.2017.09.064](https://doi.org/10.1016/j.neulet.2017.09.064)

[Indexed for MEDLINE]

Astaxanthin prevents central nervous system cell death after traumatic injury.

[BMC Neurosci.](#) 2017 May 10;18(1):42. doi: 10.1186/s12868-017-0358-z.

Astaxanthin protects astrocytes against trauma-induced apoptosis through inhibition of NKCC1 expression via the NF- κ B signaling pathway.

[Zhang M](#)^{1,2}, [Cui Z](#)^{2,3}, [Cui H](#)¹, [Wang Y](#)⁴, [Zhong C](#)⁵.

Author information

Abstract

BACKGROUND: Astaxanthin (ATX) is a carotenoid pigment with pleiotropic pharmacological properties that is seen as a possible drug for treating cerebral ischemic injury and subarachnoid hemorrhage. Na⁺-K⁺-2Cl⁻ co-transporter-1 (NKCC1), an intrinsic membrane protein expressed by many cell types, is activated by various insults, leading to the formation of cell swelling and brain edema. We previously established that ATX attenuated brain edema and improved neurological outcomes by modulating NKCC1 expression after traumatic brain injury in mice. This paper explored the molecular mechanism of ATX-mediated inhibition of NKCC1 utilizing an in vitro astrocyte stretch injury model.

RESULTS: Stretch injury in cultured astrocytes lowered cell viability time-dependently, which was substantially reduced by pretreating with ATX (50 μ mol/L). Stretch injury increased Bax level and cleaved caspase-3 activity, and decreased Bcl-2 level and pro-caspase 3 activity, resulting in the apoptosis of astrocytes. Additionally, stretch injury substantially raised the gene and protein expressions of interleukin (IL)-1 β , IL-6, and tumor necrosis factor (TNF)- α and prompted the expression and nuclear translocation of NF- κ B. Pretreatment with ATX remarkably prevented the trauma-induced initiation of NF- κ B, expressions of pro-inflammatory cytokines, and cell apoptosis. Moreover, stretch injury markedly elevated the gene and protein expression of NKCC1, which was partly blocked by co-treatment with ATX (50 μ mol/L) or an NF- κ B inhibitor (PDTC, 10 μ mol/L). Cleaved caspase-3 activity was partially reduced by PDTC (10 μ mol/L) or an NKCC1 inhibitor (bumetanide, 50 μ mol/L).

CONCLUSIONS: ATX attenuates apoptosis after stretch injury in cultured astrocytes by inhibiting NKCC1 expression, and it acts by reducing the expression of NF- κ B-mediated pro-inflammatory factors.

KEYWORDS: Apoptosis; Astaxanthin; Astrocyte; NF- κ B; Na⁺-K⁺-2Cl⁻ co-transporter-1; Traumatic brain injury

PMID: 28490320 PMCID: [PMC5425995](#) DOI: [10.1186/s12868-017-0358-z](#)

[Indexed for MEDLINE]

[Free PMC Article](#)

Astaxanthin prevents learning and memory impairment in rats after inducement of stroke.

[Brain Res Bull.](#) 2017 May;131:221-228. doi: 10.1016/j.brainresbull.2017.04.019. Epub 2017 May 4.

The protective effect of astaxanthin on learning and memory deficits and oxidative stress in a mouse model of repeated cerebral ischemia/reperfusion.

[Xue Y¹](#), [Qu Z¹](#), [Fu J²](#), [Zhen J¹](#), [Wang W¹](#), [Cai Y¹](#), [Wang W³](#).

Author information

Abstract

Oxidative stress has been implicated in the pathogenesis of neurodegenerative disorders, such as vascular cognitive impairment (VCI). The present study was performed to investigate the potential neuroprotective effect of the antioxidant astaxanthin (ATX) in a mouse model of VCI. VCI was induced in male ICR mice by repeated occlusion of the bilateral common carotid artery, leading to repeated cerebral ischemia/reperfusion (IR) injury. After surgery, the mice received ATX or an equal volume of vehicle by daily intragastric administration for 28days. The results showed that ATX treatment ameliorated learning and memory deficits after repeated cerebral IR. ATX administration rescued the number of surviving pyramidal neurons in the CA1 and CA3 regions. The concentration of malondialdehyde was decreased, and the levels of reduced glutathione and superoxide dismutase in the hippocampus were increased. Electron microphotography revealed that damage to the ultrastructure of neurons was also reduced by ATX administration. In addition, the expression levels of Cytochrome C (Cyt C), cleaved Caspase-3 and Bax were lower and the expression of Bcl-2 was higher compared to control IR mice. Our findings demonstrate that ATX is able to suppress learning and memory impairment caused by repeated cerebral IR and that this effect is associated with attenuation of oxidative stress.

KEYWORDS:

Astaxanthin; Oxidative stress; Repeated cerebral ischemia/reperfusion; Vascular cognitive impairment

PMID: 28479214

DOI: [10.1016/j.brainresbull.2017.04.019](https://doi.org/10.1016/j.brainresbull.2017.04.019)

[Indexed for MEDLINE]

Astaxanthin improves oxidative stress levels and protects against early brain injury in both rats and rabbits.

[J Neurosurg](#). 2014 Jul;121(1):42-54. doi: 10.3171/2014.2.JNS13730. Epub 2014 Apr 11.

Amelioration of oxidative stress and protection against early brain injury by astaxanthin after experimental subarachnoid hemorrhage.

[Zhang XS](#)¹, [Zhang X](#), [Zhou ML](#), [Zhou XM](#), [Li N](#), [Li W](#), [Cong ZX](#), [Sun Q](#), [Zhuang Z](#), [Wang CX](#), [Shi JX](#).

Author information

Abstract

OBJECT.: Aneurysmal subarachnoid hemorrhage (SAH) causes devastating rates of mortality and morbidity. Accumulating studies indicate that early brain injury (EBI) greatly contributes to poor outcomes after SAH and that oxidative stress plays an important role in the development of EBI following SAH. Astaxanthin (ATX), one of the most common carotenoids, has a powerful antioxidative property. However, the potential role of ATX in protecting against EBI after SAH remains obscure. The goal of this study was to assess whether ATX can attenuate SAH-induced brain edema, blood-brain barrier permeability, neural cell death, and neurological deficits, and to elucidate whether the mechanisms of ATX against EBI are related to its powerful antioxidant property.

METHODS:

Two experimental SAH models were established, including a prechiasmatic cistern SAH model in rats and a one-hemorrhage SAH model in rabbits. Both intracerebroventricular injection and oral administration of ATX were evaluated in this experiment. Posttreatment assessments included neurological scores, body weight loss, brain edema, Evans blue extravasation, Western blot analysis, histopathological study, and biochemical estimation.

RESULTS:

It was observed that an ATX intracerebroventricular injection 30 minutes post-SAH could significantly attenuate EBI (including brainedema, blood-brain barrier disruption, neural cell apoptosis, and neurological dysfunction) after SAH in rats. Meanwhile, delayed treatment with ATX 3 hours post-SAH by oral administration was also neuroprotective in both rats and rabbits. In addition, the authors found that ATX treatment could prevent oxidative damage and upregulate the endogenous antioxidant levels in the rat cerebral cortex following SAH.

CONCLUSIONS:

These results suggest that ATX administration could alleviate EBI after SAH, potentially through its powerful antioxidant property. The authors conclude that ATX might be a promising therapeutic agent for EBI following SAH.

PMID: 24724856

[PubMed - indexed for MEDLINE]

ASTAXANTHIN SHOWS BRAIN HEALTH POTENTIAL BY REDUCING SUBARACHNOID HEMORRHAGE INJURY IN RODENTS.

FASEB J. 2019 Jan;33(1):722-737.

doi: 10.1096/fj.201800642RR. Epub 2018 Jul 26.

Astaxanthin mitigates subarachnoid hemorrhage injury primarily by increasing sirtuin 1 and inhibiting the Toll-like receptor 4 signaling pathway

[Xiangsheng Zhang](#)^{1,2}, [Yue Lu](#)¹, [Qi Wu](#)³, [Haibin Dai](#)¹, [Wei Li](#)¹, [Shengyin Lv](#)³, [Xiaoming Zhou](#)⁴, [Xin Zhang](#)³, [Chunhua Hang](#)¹, [Jian Wang](#)²

PMID: 30048156 DOI: [10.1096/fj.201800642RR](https://doi.org/10.1096/fj.201800642RR)

Abstract

Inflammation plays a key role in the progression of subarachnoid hemorrhage (SAH). Here, we examined the effects of astaxanthin (ATX) on the inflammatory response and secondary damage after SAH and the underlying mechanisms of action. In vivo, a prechiasmatic cistern injection model was established in rats and mice. In addition, neuron-microglia cocultures were exposed to oxyhemoglobin to mimic SAH in vitro. Western blotting revealed that protein expression of TLR4 was markedly increased in microglia at 24 h after SAH, with consequent increases in the downstream molecules myeloid differentiation factor 88 and NF- κ B. Treatment with ATX significantly inhibited the TLR4 activation, increased sirtuin 1 expression, and inhibited the subsequent inflammatory response both in vivo and in vitro. ATX also significantly decreased high-mobility group box 1 nuclear translocation and secretion in neurons, an effect that was reversed by the sirtuin 1-specific inhibitor sirtinol. ATX administered 4 h after SAH ameliorated cerebral inflammation, brain edema, and neuronal death and improved neurologic function. ATX reduced neuronal death but did not improve neurologic function in TLR4 knockout mice. These results suggest that ATX reduces the proinflammatory response and secondary brain injury after SAH, primarily by increasing sirtuin 1 levels and inhibiting the TLR4 signaling pathway.-Zhang, X., Lu, Y., Wu, Q., Dai, H., Li, W., Lv, S., Zhou, X., Zhang, X., Hang, C., Wang, J. Astaxanthin mitigates subarachnoid hemorrhage injury primarily by increasing sirtuin 1 and inhibiting the Toll-like receptor 4 signaling pathway.

ASTAXANTHIN IMPROVES SEVERAL COGNITIVE FUNCTIONS IN AGING MICE.

Geroscience. 2019 Feb;41(1):77-87.

doi: 10.1007/s11357-019-00051-9. Epub 2019 Feb 9.

Astaxanthin supplementation modulates cognitive function and synaptic plasticity in young and aged mice

[Bethany Grimmig](#)^{1,2}, [Charles Hudson](#)³, [Lauren Moss](#)², [Melinda Peters](#)¹, [Meena Subbarayan](#)^{1,2}, [Edwin J Weeber](#)¹, [Paula C Bickford](#)^{4,5,6}

- PMID: [30739297](#)
- PMCID: [PMC6423184](#)
- DOI: [10.1007/s11357-019-00051-9](#)

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Abstract

The incidence of neurodegenerative disorders and cognitive impairment is increasing. Rising prevalence of age-related medical conditions is associated with a dramatic economic burden; therefore, developing strategies to manage these health concerns is of great public health interest. Nutritionally based interventions have shown promise in treatment of these age-associated conditions. Astaxanthin is a carotenoid with reputed neuroprotective properties in the context of disease and injury, while emerging evidence suggests that astaxanthin may also have additional biological activities relating to neurogenesis and synaptic plasticity. Here, we investigate the potential for astaxanthin to modulate cognitive function and neural plasticity in young and aged mice. We show that feeding astaxanthin to aged mice for 1 month improves performance on several hippocampal-dependent cognitive tasks and increases long-term potentiation. However, we did not observe an alteration in neurogenesis, nor did we observe a change in microglial-associated IBA1 immunostaining. This demonstrates the potential for astaxanthin to modulate neural plasticity and cognitive function in aging.

ASTAXANTHIN PREVENTS NEURONAL DAMAGE AND MEMORY DYSFUNCTION AND REDUCES OXIDATIVE STRESS IN MOUSE MODEL.

Mar Drugs. 2019 Feb 18;17(2):123.
doi: 10.3390/md17020123.

Astaxanthin Ameliorates Lipopolysaccharide-Induced Neuroinflammation, Oxidative Stress and Memory Dysfunction through Inactivation of the Signal Transducer and Activator of Transcription 3 Pathway

[Ji Hye Han](#)¹, [Yong Sun Lee](#)², [Jun Hyung Im](#)³, [Young Wan Ham](#)⁴, [Hee Pom Lee](#)⁵, [Sang Bae Han](#)⁶, [Jin Tae Hong](#)⁷

PMID: 30781690 PMCID: [PMC6410230](#) DOI: [10.3390/md17020123](#) [Free PMC article](#)

Abstract

Astaxanthin (AXT), a xanthophyll carotenoid compound, has potent antioxidant, anti-inflammatory and neuroprotective properties. Neuroinflammation and oxidative stress are significant in the pathogenesis and development of Alzheimer's disease (AD). Here, we studied whether AXT could alleviate neuroinflammation, oxidative stress and memory loss in lipopolysaccharide (LPS) administered mice model. Additionally, we investigated the anti-oxidant activity and the anti-neuroinflammatory response of AXT in LPS-treated BV-2 microglial cells. The AXT administration ameliorated LPS-induced memory loss. This effect was associated with the reduction of LPS-induced expression of inflammatory proteins, as well as the production of reactive oxygen species (ROS), nitric oxide (NO), cytokines and chemokines both in vivo and in vitro. AXT also reduced LPS-induced β -secretase and $A\beta_{1-42}$ generation through the down-regulation of amyloidogenic proteins both in vivo and in vitro. Furthermore, AXT suppressed the DNA binding activities of the signal transducer and activator of transcription 3 (STAT3). We found that AXT directly bound to the DNA-binding domain (DBD) and linker domain (LD) domains of STAT3 using docking studies. The oxidative stress and inflammatory responses were not downregulated in BV-2 cells transfected with DBD-null STAT3 and LD-null STAT3. These results indicated AXT inhibits LPS-induced oxidant activity, neuroinflammatory response and amyloidogenesis via the blocking of STAT3 activity through direct binding.

ASTAXANTHIN IMPROVES COGNITIVE FUNCTION AND PREVENTS NEURODEGENERATION IN RAT MODEL OF ALZHEIMER'S DISEASE.

Mar Drugs. 2019 Nov 4;17(11):628.

doi: 10.3390/md17110628.

Effects of Astaxanthin from Shrimp Shell on Oxidative Stress and Behavior in Animal Model of Alzheimer's Disease

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PMID: 31690015 PMCID: [PMC6891431](#) DOI: [10.3390/md17110628](#) [Free PMC article](#)

Abstract

This study aimed to investigate the effect of astaxanthin (ASX) extracted and ASX powder from shrimp (*Litopenaeus vannamei*) shells on Wistar rats with Alzheimer's disease, induced by amyloid- β (1-42) peptides. In this task, the rats were divided into eight groups: (1) Control, (2) sham operate, (3) negative control (vehicle) + $A\beta_{1-42}$, (4) ASX extract + $A\beta_{1-42}$, (5) commercial ASX + $A\beta_{1-42}$, (6) ASX powder + $A\beta_{1-42}$, (7) blank powder + $A\beta_{1-42}$, and (8) vitamin E + $A\beta_{1-42}$. All treatments were orally administrated for 30 days. At 14- and 29-days post injection, animals were observed in behavioral tests. On the 31st day, animals were sacrificed; the hippocampus and cortex were collected. Those two brain areas were then homogenized and stored for biochemical and histological analysis. The results showed that the $A\beta_{1-42}$ infused group significantly reduced cognitive ability and increased memory loss, as assessed by the Morris water maze test, novel object recognition test, and novel object location test. Moreover, the $A\beta_{1-42}$ infused group exhibited a deterioration of oxidative markers, including glutathione peroxidase enzymes (GPx), lipid peroxidation (MDA), products of protein oxidation, and superoxide anion in the cortex and the hippocampus. Meanwhile, ASX powder (10 mg/kg body weight) showed a significant reduction in cognitive and memory impairments and oxidative stress which is greater than ASX extract in the same dose of compound or vitamin E (100 mg/kg body weight). Our study indicates the beneficial properties of ASX in alleviation of cognitive functions and reducing neurodegeneration in Wistar rats induced by amyloid- β (1-42) peptides.

ASTAXANTHIN IMPROVES NEURON DEFICITS AND PROTECTS AGAINST ALZHEIMER'S DISEASE-RELATED PATHOLOGICAL PROGRESS IN MICE.

Front Pharmacol. 2020 Mar 11;11:307.

doi: 10.3389/fphar.2020.00307. eCollection 2020.

Astaxanthin Ameliorated Parvalbumin-Positive Neuron Deficits and Alzheimer's Disease-Related Pathological Progression in the Hippocampus of *App*^{NL-G-F/NL-G-F} Mice

[Nobuko Hongo](#)¹, [Yusaku Takamura](#)¹, [Hiroshi Nishimaru](#)¹, [Jumpei Matsumoto](#)¹, [Kazuyuki Tobe](#)², [Takashi Saito](#)^{3,4}, [Takaomi C Saïdo](#)³, [Hisao Nishijo](#)¹

- PMID: [32218736](#)
- PMCID: [PMC7078363](#)
- DOI: [10.3389/fphar.2020.00307](#)

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Abstract

Growing evidence suggests that oxidative stress due to amyloid β ($A\beta$) accumulation is involved in Alzheimer's disease (AD) through the formation of amyloid plaque, which leads to hyperphosphorylation of tau, microglial activation, and cognitive deficits. The dysfunction or phenotypic loss of parvalbumin (PV)-positive neurons has been implicated in cognitive deficits. Astaxanthin is one of carotenoids and known as a highly potent antioxidant. We hypothesized that astaxanthin's antioxidant effects may prevent the onset of cognitive deficits in AD by preventing AD pathological processes associated with oxidative stress. In the present study, we investigated the effects of astaxanthin intake on the cognitive and pathological progression of AD in a mouse model of AD. The *App*^{NL-G-F/NL-G-F} mice were fed with or without astaxanthin from 5-to-6 weeks old, and cognitive functions were evaluated using a Barnes maze test at 6 months old. PV-positive neurons were investigated in the hippocampus. $A\beta$ 42 deposits, accumulation of microglia, and phosphorylated tau (pTau) were immunohistochemically analyzed in the

hippocampus. The hippocampal anti-oxidant status was also investigated. The Barnes maze test indicated that astaxanthin significantly ameliorated memory deficits. Astaxanthin reduced A β 42 deposition and pTau-positive areal fraction, while it increased PV-positive neuron density and microglial accumulation per unit fraction of A β 42 deposition in the hippocampus. Furthermore, astaxanthin increased total glutathione (GSH) levels, although 4-hydroxy-2,3-trans-nonenal (4-HNE) protein adduct levels (oxidative stress marker) remained high in the astaxanthin supplemented mice. The results indicated that astaxanthin ameliorated memory deficits and significantly reversed AD pathological processes (A β 42 deposition, pTau formation, GSH decrease, and PV-positive neuronal deficits). The elevated GSH levels and resultant recovery of PV-positive neuron density, as well as microglial activation, may prevent these pathological processes.

ASTAXANTHIN PREVENTS BRAIN AGING IN RATS BY REDUCING MITOCHONDRIAL DYSFUNCTION AND OXIDATIVE STRESS AND REGULATING METABOLIC MARKER.

Food Funct. 2020 May 1;11(5):4103-4113.
doi: 10.1039/d0fo00633e. Epub 2020 Apr 28.

Astaxanthin attenuates d-galactose-induced brain aging in rats by ameliorating oxidative stress, mitochondrial dysfunction, and regulating metabolic markers

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PMID: 32343758 DOI: [10.1039/d0fo00633e](https://doi.org/10.1039/d0fo00633e)

Abstract

Astaxanthin (AX) is a red-colored xanthophyll carotenoid with potent antioxidant, anti-inflammatory, and neuroprotective properties. However, the underlying *in vivo* mechanism by which AX protects the brain from oxidative stress remains unclear. In this study, we investigated the protective effect of AX on brain oxidative damage in a d-galactose-induced rat model of aging. We also explored its possible mechanism of action by analyzing the resulting serum metabolic profiles. Our results showed that AX significantly increased the activities of catalase (CAT), superoxide dismutase (SOD), and glutathione peroxidase (GSH-Px) by 26%, 30%, and 53%, respectively. AX also significantly increased the mitochondrial membrane potential by 18% when compared with the model group. Additionally, treatment with AX (15 mg kg⁻¹) increased the activities of respiratory chain complexes I and IV by 50.17% and 122.87%, respectively. Furthermore, AX also improved age-related morphological changes in the cerebral cortex and hippocampus. Significant differences in serum metabolic profiles were observed between the d-galactose and AX treatment groups. AX corrected amino acid metabolic problems by increasing the levels of N-acetyl-l-leucine, N-acetyl-l-tyrosine, and methionine sulfoxide to protect nerve cells. This also allowed AX to regulate the pentose phosphate pathway by acting on ergothione, d-xylose-5-phosphoric, and thiamine, to against oxidative stress and apoptosis. Moreover, AX reduced the levels of both hyodeoxycholic acid and chenodeoxycholic acid through the primary bile acid biosynthesis pathway, resulting in improved brain mitochondrial dysfunction. In conclusion, AX likely enhances the brain's antioxidant defenses through these potential metabolic means, enabling the brain to resist mitochondrial dysfunction, improve neuronal damage, and protect the electron transmission of mitochondrial respiratory chain, thus preventing brain aging.

ASTAXANTHIN PROTECTS AGAINST ACUTE CEREBRAL INFARCTION IN RATS BY SUPPRESSING INFLAMMATION, OXIDATION AND CELL DEATH.

Curr Res Transl Med. 2021 Jan 18;69(2):103271.

doi: 10.1016/j.retram.2020.103271. Online ahead of print.

Astaxanthin attenuates acute cerebral infarction via Nrf-2/HO-1 pathway in rats

[Bin-Bin Yang](#)¹, [Mei Zou](#)², [Long Zhao](#)³, [Ya-Kun Zhang](#)⁴

- PMID: 33476935
- DOI: [10.1016/j.retram.2020.103271](https://doi.org/10.1016/j.retram.2020.103271)

Abstract

Objective: Acute cerebral infarction (ACI) is susceptible to cause disability or death of people. Astaxanthin (ATX) possesses the protective effect of organ injury. Therefore, the study was to explore the potential mechanism of protective effect with ATX on ACI.

Methods: 30 SD rats were divided into Sham, ACI, and ATX groups. The rats in the ATX group were pretreated with ATX by gavage for three days before surgery, while the rats in the other two groups were pretreated with saline. The model of ACI was established by thread embolization. 24 h after the operation, the neurological function was scored, and cerebral infarct area and pathological morphology of brains were measured; the edema of the brain was detected by dry/wet method; Western blot was applied to measure the translocation of Nrf-2 and the protein expression of HO-1, Bax and BCL-2; Brain cell apoptosis was assessed through TUNEL; ELISA was used to detect the oxidative stress factors of catalase (CAT) superoxide dismutase (SOD), glutathione peroxidase (GPX) and malondialdehyde (MDA), and the inflammatory factors of TNF- α , IL-1 β , IL-6.

Result: Compared with the ACI group, ATX pretreatment can significantly improve neurological function; reduce the edema index of the brain, cerebral infarct area, cerebral pathological damage and apoptosis of brain cells. Moreover, ATX also can increase the protein expression of nuclear Nrf-2, HO-1, BCL-2, CAT, SOD, and GPX by decreasing the content of TNF- α , IL-1 β , IL-6, MDA, Bax and cytosolic Nrf-2.

Conclusion: ATX might have a protective effect of acute cerebral infarction, and the mechanism is probably associated with suppressing oxidative stress, inflammation, and apoptosis by activating Nrf-2/HO-1 signalling.

ASTAXANTHIN EFFECTIVE AGAINST BRAIN CANCER IN A MOUSE MODEL AND MAY HAVE POTENTIAL AS A BRAIN CANCER TREATMENT.

Mar Drugs. 2020 Sep 18;18(9):474.

doi: 10.3390/md18090474.

Antitumour Effects of Astaxanthin and Adonixanthin on Glioblastoma

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- PMID: **32962073**
- PMCID: [PMC7551886](#)
- DOI: [10.3390/md18090474](#)

Free PMC article

Abstract

Several antitumour drugs have been isolated from natural products and many clinical trials are underway to evaluate their potential. There have been numerous reports about the antitumour effects of astaxanthin against several tumours but no studies into its effects against glioblastoma. Astaxanthin is a red pigment found in crustaceans and fish and is also synthesized in *Haematococcus pluvialis*; adonixanthin is an intermediate product of astaxanthin. It is known that both astaxanthin and adonixanthin possess radical scavenging activity and can confer a protective effect on several damages. In this study, we clarified the antitumour effects of astaxanthin and adonixanthin using glioblastoma models. Specifically, astaxanthin and adonixanthin showed an ability to suppress cell proliferation and migration in three types of glioblastoma cells. Furthermore, these compounds were confirmed to transfer to the brain in a murine model. In the murine orthotopic glioblastoma model, glioblastoma progression was suppressed by the oral administration of astaxanthin and adonixanthin at 10 and 30 mg/kg, respectively, for 10 days. These results suggest that both astaxanthin and adonixanthin have potential as treatments for glioblastoma.

ASTAXANTHIN BENEFITS BRAIN TISSUE IN RAT MODEL OF ALZHEIMER'S DISEASE AND MAY HAVE THERAPEUTIC CLINICAL POTENTIAL.

Mol Cell Biochem. 2021 May;476(5):2233-2249.

doi: 10.1007/s11010-021-04079-4. Epub 2021 Feb 11.

Ameliorative effects of astaxanthin on brain tissues of alzheimer's disease-like model: cross talk between neuronal-specific microRNA-124 and related pathways

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- PMID: 33575874 DOI: [10.1007/s11010-021-04079-4](https://doi.org/10.1007/s11010-021-04079-4)

Abstract

Alzheimer's disease (AD) is a chronic, progressive, multifactorial, and the most common neurodegenerative disease which causes dementia and mental deterioration in the elderly. The available treatments for AD are not disease-modifying drugs and only provide symptomatic relief. Astaxanthin (ATX), a second-generation antioxidant, is a dark red carotenoid and exhibits the highest antioxidant capacity, anti-inflammatory, neuroprotective, and antiapoptotic effects. In this study, we investigated the therapeutic effect of different doses of ATX on the cerebral cortex and hippocampus of AD-like rats. The AD-like model was induced in rats using hydrated aluminum chloride ($\text{AlCl}_3 \cdot 6\text{H}_2\text{O}$) solution that was given orally at a dose of 75 mg/kg daily for 6 weeks. Morris water maze (MWM) behavioral test was performed to confirm the cognitive dysfunction then AD-like rats were orally treated with different doses of ATX (5, 10, and 15 mg/kg) dissolved in dimethyl sulfoxide (DMSO) for six weeks. The results indicated that ATX significantly and dose-dependently improved the performance of AD-like rats treated with ATX during MWM and suppress the accumulation of amyloid β_{1-42} and malondialdehyde. Also, significantly inhibit acetylcholinesterase and monoamine oxidase activities and the expression of β -site amyloid precursor protein cleaving enzyme 1 (BACE 1). ATX also significantly elevated the content of acetylcholine, serotonin, and nuclear factor erythroid-2-related factor 2 (Nrf2) and miRNA-124 expression. The effect of ATX treatment was confirmed by histopathological observations using H&E stain and morphometric tissue analysis. From this study, we concluded that ATX may be a promising therapeutic agent for AD through targeting different pathogenic pathways.

ASTAXANTHIN IMPROVES NEUROLOGICAL FUNCTION IN MOUSE MODEL OF BRAIN AGING.

Neural Regen Res. 2021 Jun;16(6):1062-1067.

doi: 10.4103/1673-5374.300460.

Astaxanthin alleviates pathological brain aging through the upregulation of hippocampal synaptic proteins

[Ning Liu](#)¹, [Liang Zeng](#)², [Yi-Ming Zhang](#)³, [Wang Pan](#)⁴, [Hong Lai](#)³

- PMID: [33269751](#)
- PMCID: [PMC8224122](#)
- DOI: [10.4103/1673-5374.300460](#)

Abstract

Oxidative stress is currently considered to be the main cause of brain aging. Astaxanthin can improve oxidative stress under multiple pathological conditions. It is therefore hypothesized that astaxanthin might have therapeutic effects on brain aging. To validate this hypothesis and investigate the underlying mechanisms, a mouse model of brain aging was established by injecting amyloid beta (A β)₂₅₋₃₅ (5 μ M, 3 μ L/injection, six injections given every other day) into the right lateral ventricle. After 3 days of A β ₂₅₋₃₅ injections, the mouse models were intragastrically administered astaxanthin (0.1 mL/d, 10 mg/kg) for 30 successive days. Astaxanthin greatly reduced the latency to find the platform in the Morris water maze, increased the number of crossings of the target platform, and increased the expression of brain-derived neurotrophic factor, synaptophysin, sirtuin 1, and peroxisome proliferator-activated receptor- γ coactivator 1 α . Intraperitoneal injection of the sirtuin 1 inhibitor nicotinamide (500 μ M/d) for 7 successive days after astaxanthin intervention inhibited these phenomena. These findings suggest that astaxanthin can regulate the expression of synaptic proteins in mouse hippocampus through the sirtuin 1/peroxisome proliferator-activated receptor- γ coactivator 1 α signaling pathway, which leads to improvements in the learning, cognitive, and memory abilities of mice. The study was approved by the Animal Ethics Committee, China Medical University, China (approval No. CMU2019294) on January 15, 2019.

Astaxanthin alleviates brain aging in rats by controlling oxidative stress and ameliorating hippocampus damage.

[Food Funct.](#) 2014 Jan;5(1):158-66. Doi: 10.1039/c3fo60400d.

Astaxanthin alleviates brain aging in rats by attenuating oxidative stress and increasing BDNF levels.

[Wu W¹](#), [Wang X](#), [Xiang Q](#), [Meng X](#), [Peng Y](#), [Du N](#), [Liu Z](#), [Sun Q](#), [Wang C](#), [Liu X](#).

Author information

Abstract

Astaxanthin (AST) is a carotenoid pigment which possesses potent antioxidative, anti-inflammatory, and neuroprotective properties. The aim of this study was to investigate whether administration of AST had protective effects on D-galactose-induced brain aging in rats, and further examined its protective mechanisms. The results showed that AST treatment significantly restored the activities of glutathione peroxidase (GSH-PX) and superoxide dismutase (SOD), and increased glutathione (GSH) contents and total antioxidant capacity (T-AOC), but decreased malondialdehyde (MDA), protein carbonylation and 8-hydroxy-2- deoxyguanosine (8-OhdG) levels in the brains of aging rats. Furthermore, AST increased the ratio of Bcl-2/Bax, but decreased the expression of Cyclooxygenase-2 (COX-2) in the brains of aging rats. Additionally, AST ameliorated histopathological changes in the hippocampus and restored brain derived neurotrophic factor (BDNF) levels in both the brains and hippocampus of aging rats. These results suggested that AST could alleviate brain aging, which may be due to attenuating oxidative stress, ameliorating hippocampus damage, and upregulating BDNF expression.

PMID:

24326685

[PubMed – indexed for MEDLINE]

Astaxanthin protects against oxidative stress in-vitro and may be a therapeutic agent and neuroprotective for patients with Parkinson's disease.

[BMC Neurosci.](#) 2012 Dec 29;13:156. doi: 10.1186/1471-2202-13-156.

Astaxanthin protects against MPP(+)-induced oxidative stress in PC12 cells via the HO-1/NOX2 axis.

[Ye Q¹](#), [Huang B](#), [Zhang X](#), [Zhu Y](#), [Chen X](#).

Author information

Abstract

BACKGROUND:

Although the etiology of PD remains unclear, increasing evidence has shown that oxidative stress plays an important role in its pathogenesis and that of other neurodegenerative disorders. NOX2, a cytochrome subunit of NOX, transports electrons across the plasma membrane to generate ROS, leading to physiological and pathological processes. Heme oxygenase-1 (HO-1) can be rapidly induced by oxidative stress and other noxious stimuli in the brain or other tissues. Astaxanthin (ATX), a carotenoid with antioxidant properties, is 100-1000 times more effective than vitamin E. The present study investigated the neuroprotective effects of ATX on MPP(+)-induced oxidative stress in PC12 cells.

RESULTS:

MPP(+) significantly decreased MTT levels in a concentration-dependent manner. Hemin, SnPPIX and ATX didn't exhibit any cytotoxic effects on PC12 cells. Pretreatment with ATX (5, 10, 20 μ M), caused intracellular ROS production in the MPP(+) group to decrease by 13.06%, 22.13%, and 27.86%, respectively. MPP(+) increased NOX2, NRF2 and HO-1 protein expression compared with control ($p < 0.05$). Co-treatment with hemin or ATX suppressed NOX2 expression ($p < 0.01$), and greatly increased NRF2 and HO-1 expression ($p < 0.01$). MPP(+) treatment up-regulated both NOX2 ($p < 0.01$) and HO-1 ($p < 0.01$) mRNA levels. Co-treatment with hemin or ATX significantly increased HO-1 mRNA levels ($p < 0.01$), and decreased NOX2 mRNA levels ($p < 0.01$). MPP(+) increased NOX2 and HO-1 expression with considerable fluorescence extending out from the perinuclear region toward the periphery; this was attenuated by DPI. Co-treatment with hemin or ATX significantly up-regulated HO-1 expression and decreased NOX2 expression with considerable fluorescence intensity (stronger than the control and MPP(+) groups).

CONCLUSIONS:

ATX suppresses MPP(+)-induced oxidative stress in PC12 cells via the HO-1/NOX2 axis. ATX should be strongly considered as a potential neuroprotectant and adjuvant therapy for patients with Parkinson's disease.

PMID: 23272707

[PubMed - indexed for MEDLINE]

PMCID:

PMC3541259

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Astaxanthin protects neurons against molecule indicated in Alzheimer's disease in rodents.

[Neural Plast.](#) 2016;2016:3456783. doi: 10.1155/2016/3456783. Epub 2016 Mar 1.

Astaxanthin Protects Primary Hippocampal Neurons against Noxious Effects of A β -Oligomers.

[Lobos P¹](#), [Bruna B¹](#), [Cordova A¹](#), [Barattini P¹](#), [Galáz JL¹](#), [Adasme T¹](#), [Hidalgo C²](#), [Muñoz P³](#), [Paula-Lima A⁴](#).

Author information

Abstract

Increased reactive oxygen species (ROS) generation and the ensuing oxidative stress contribute to Alzheimer's disease pathology. We reported previously that amyloid- β peptide oligomers (A β Os) produce aberrant Ca(2+) signals at sublethal concentrations and decrease the expression of type-2 ryanodine receptors (RyR2), which are crucial for hippocampal synaptic plasticity and memory. Here, we investigated whether the antioxidant agent astaxanthin (ATX) protects neurons from A β Os-induced excessive mitochondrial ROS generation, NFATc4 activation, and RyR2 mRNA downregulation. To determine mitochondrial H₂O₂ production or NFATc4 nuclear translocation, neurons were transfected with plasmids coding for HyperMito or NFATc4-eGFP, respectively. Primary hippocampal cultures were incubated with 0.1 μ M ATX for 1.5 h prior to A β Os addition (500 nM). We found that incubation with ATX (\leq 10 μ M) for \leq 24 h was nontoxic to neurons, evaluated by the live/dead assay. Preincubation with 0.1 μ M ATX also prevented the neuronal mitochondrial H₂O₂ generation induced within minutes of A β Os addition. Longer exposures to A β Os (6 h) promoted NFATc4-eGFP nuclear translocation and decreased RyR2 mRNA levels, evaluated by detection of the eGFP-tagged fluorescent plasmid and qPCR, respectively. Preincubation with 0.1 μ M ATX prevented both effects. These results indicate that ATX protects neurons from the noxious effects of A β Os on mitochondrial ROS production, NFATc4 activation, and RyR2 gene expression downregulation.

PMID: 27034843

PMCID: [PMC4791503](#)

DOI: [10.1155/2016/3456783](#)

[Indexed for MEDLINE]

[Free PMC Article](#)

Astaxanthin protects neuronal cells against oxidative damage and is a “potential candidate for natural brain food.”

[Forum Nutr.](#) 2009;61:129-35. Epub 2009 Apr 7.

Astaxanthin protects neuronal cells against oxidative damage and is a potent candidate for brain food.

[Liu X](#), [Osawa T](#).

Graduate School of Bioagricultural Science, Nagoya University, Nagoya, Japan.

Astaxanthin (AST) is a powerful antioxidant that occurs naturally in a wide variety of living organisms. Based on the report claiming that AST could cross the brain-blood barrier, the aim of this study was to investigate the neuroprotective effect of AST by using an oxidative stress-induced neuronal cell damage system. The treatment with DHA hydroperoxide (DHA-OOH) or 6-hydroxydopamine (6-OHDA), either of which is a reactive oxygen species (ROS)-inducing neurotoxin, led to a significant decrease in viable dopaminergic SH-SY5Y cells by the MTT assay, whereas a significant protection was shown when the cells were pretreated with AST. Moreover, 100 nM AST pretreatment significantly inhibited intracellular ROS generation that occurred in either DHA-OOH- or 6-OHDA-treated cells. The neuroprotective effect of AST is suggested to be dependent upon its antioxidant potential and mitochondria protection; therefore, it is strongly suggested that treatment with AST may be effective for oxidative stress-associated neurodegeneration and a potential candidate for natural brain food.

PMID: 19367117 [PubMed - in process]

Astaxanthin reduces ischemic brain injury in rats.

[FASEB J.](#) 2009 Jun;23(6):1958-68. Epub 2009 Feb 13.

Astaxanthin reduces ischemic brain injury in adult rats.

[Shen H](#), [Kuo CC](#), [Chou J](#), [Delvolve A](#), [Jackson SN](#), [Post J](#), [Woods AS](#), [Hoffer BJ](#), [Wang Y](#), [Harvey BK](#).

National Institute on Drug Abuse, NIH, 251 Bayview Blvd., Baltimore, MD 21224, USA.

Astaxanthin (ATX) is a dietary carotenoid of crustaceans and fish that contributes to their coloration. Dietary ATX is important for development and survival of salmonids and crustaceans and has been shown to reduce cardiac ischemic injury in rodents. The purpose of this study was to examine whether ATX can protect against ischemic injury in the mammalian brain. Adult rats were injected intracerebroventricularly with ATX or vehicle prior to a 60-min middle cerebral artery occlusion (MCAo). ATX was present in the infarction area at 70-75 min after onset of MCAo. Treatment with ATX, compared to vehicle, increased locomotor activity in stroke rats and reduced cerebral infarction at 2 d after MCAo. To evaluate the protective mechanisms of ATX against stroke, brain tissues were assayed for free radical damage, apoptosis, and excitotoxicity. ATX antagonized ischemia-mediated loss of aconitase activity and reduced glutamate release, lipid peroxidation, translocation of cytochrome c, and TUNEL labeling in the ischemic cortex. ATX did not alter physiological parameters, such as body temperature, brain temperature, cerebral blood flow, blood gases, blood pressure, and pH. Collectively, our data suggest that ATX can reduce ischemia-related injury in brain tissue through the inhibition of oxidative stress, reduction of glutamate release, and antiapoptosis. ATX may be clinically useful for patients vulnerable or prone to ischemic events.

Publication Types:

PMID: 19218497 [PubMed – indexed for MEDLINE]

PMCID: PMC2698661 [Available on 2010/06/01]

Astaxanthin improves brain function in undernourished rats.

[Nutr Neurosci](#). 2018 Sep 11:1-10. doi: 10.1080/1028415X.2018.1515301. [Epub ahead of print]

Role of astaxanthin in the modulation of brain-derived neurotrophic factor and spatial learning behavior in perinatally undernourished Wistar rats.

[Damodara Gowda KM¹](#), [Suchetha Kumari N²](#), [Ullal H³](#).

Author information

Abstract

OBJECTIVE: Maternal health and nutrition during the perinatal period is the predominant factor influencing the functional development of the brain. Maternal malnutrition during the perinatal period causes retardation of brain development. The current study investigates the role of Astaxanthin (AsX) in spatial learning and memory and BDNF in perinatally undernourished Wistar rats.

METHODS: The albino wistar rats were perinatally undernourished and administered with different dosages of AsX. The spatial learning and memory performance and BDNF level were assessed. Data were collected and analysed.

RESULTS: The % Correct choice during the acquisition phase, performance at the end of the acquisition phase and the mean BDNF level at the Hippocampus, Cerebellum, and Cerebral cortex showed significant decline ($P < 0.001$) in the PUN group and significantly high ($P < 0.001$) in the PUNA2 group compared to the control. However, the mean RME and mean WME during different days of the acquisition phase were significantly high ($P < 0.001$) in the PUN group and insignificant ($P > 0.05$) in PUNA2 compared to the control.

DISCUSSION: The results showed that AsX effectively modulated the cognitive deficit that occurred in perinatally undernourished rats. This can be attributed to BDNF upregulation as evidenced by the significant increase of the BDNF level.

KEYWORDS: AsX: Astaxanthin, BDNF: Brain-Derived Neurotropic Factor, ELISA: Enzyme-Linked Immuno Sorbent Assay, FDA: Food and Drug Administration, NA1: Normal rats supplemented with AsX (6 mg/kg bw), NA2: Normal rats supplemented with AsX (12 mg/kg bw), PUN: Perinatally Undernourished, PUNA1: Perinatally Undernourished rats but supplemented with AsX (6 mg/kg bw), PUNA2: Perinatally Undernourished but supplemented with AsX (12 mg/kg bw), RME: Reference Memory Error, WME: Working Memory Error, RM-ANOVA: Repeated Measures of ANOVA; Astaxanthin; Brain-derived neurotrophic factor; Perinatal undernutrition; Reference memory error and working memory error; Spatial learning

PMID: 30200858 DOI: [10.1080/1028415X.2018.1515301](https://doi.org/10.1080/1028415X.2018.1515301)

Astaxanthin improves cognitive performance in mice subjected to traumatic brain injury.

[Brain Res.](#) 2017 Mar 15;1659:88-95. doi: 10.1016/j.brainres.2016.12.031. Epub 2016 Dec 31.

Astaxanthin improves cognitive performance in mice following mild traumatic brain injury.

Ji X¹, Peng D², Zhang Y¹, Zhang J¹, Wang Y¹, Gao Y¹, Lu N³, Tang P⁴.

Author information

Abstract

BACKGROUND: Traumatic brain injury (TBI) produces lasting neurological deficits that plague patients and physicians. To date, there is no effective method to combat the source of this problem. Here, we utilized a mild, closed head TBI model to determine the modulatory effects of a natural dietary compound, astaxanthin (AST). AST is centrally active following oral administration and is neuroprotective in experimental brain ischemia/stroke and subarachnoid hemorrhage (SAH) models. We examined the effects of oral AST on the long-term neurological functional recovery and histological outcomes following moderate TBI in a mice model.

METHODS: Male adult ICR mice were divided into 3 groups: (1) Sham+olive oil vehicle treated, (2) TBI+olive oil vehicle treated, and (3) TBI+AST. The olive oil vehicle or AST were administered via oral gavage at scheduled time points. Closed head brain injury was applied using M.A. Flierl weight-drop method. NSS, Rotarod, ORT, and Y-maze were performed to test the behavioral or neurological outcome. The brain sections from the mice were stained with H&E and cresyl-violet to test the injured lesion volume and neuronal loss. Western blot analysis was performed to investigate the mechanisms of neuronal cell survival and neurological function improvement.

RESULTS: AST administration improved the sensorimotor performance on the Neurological Severity Score (NSS) and rotarod test and enhanced cognitive function recovery in the object recognition test (ORT) and Y-maze test. Moreover, AST treatment reduced the lesion size and neuronal loss in the cortex compared with the vehicle-treated TBI group. AST also restored the levels of brain-derived neurotrophic factor (BDNF), growth-associated protein-43 (GAP-43), synapsin, and synaptophysin (SYP) in the cerebral cortex, which indicates the promotion of neuronal survival and plasticity.

CONCLUSION: To the best of our knowledge, this is the first study to demonstrate the protective role and the underlining mechanism of AST in TBI. Based on these neuroprotective actions and considering its longstanding clinical use, AST should be considered for the clinical treatment of TBI.

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KEYWORDS: Astaxanthin; Growth-associated protein; NSS; Object recognition test; Rotarod test; Synaptic protein; Traumatic brain injury; Y-maze

PMID: 28048972 DOI: [10.1016/j.brainres.2016.12.031](https://doi.org/10.1016/j.brainres.2016.12.031)

Astaxanthin's neuroprotective effect may be due to its mitochondria protection and antioxidant potential and it may be an effective treatment for oxidative stress-associated neurodegeneration.

[Brain Res.](#) 2009 Feb 13;1254:18-27. Epub 2008 Dec 3.

Astaxanthin inhibits reactive oxygen species-mediated cellular toxicity in dopaminergic SH-SY5Y cells via mitochondria-targeted protective mechanism.

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Astaxanthin is a powerful antioxidant that occurs naturally in a wide variety of living organisms. The aim of this study is to investigate the effect and the mechanism of astaxanthin on reactive oxygen species (ROS)-mediated apoptosis in dopaminergic SH-SY5Y cells. The treatment with DHA hydroperoxide (DHA-OOH) or 6-hydroxydopamine (6-OHDA), either of which is ROS-inducing neurotoxin, led to a significant decrease in viable dopaminergic SH-SY5Y cells by MTT assay, whereas a significant protection was shown while the cells were pretreated with astaxanthin. Moreover, 100 nM astaxanthin pretreatment significantly inhibited apoptosis, mitochondrial abnormalities and intracellular ROS generation occurred in either DHA-OOH- or 6-OHDA-treated cells. The neuroprotective effect of astaxanthin is suggested to be dependent upon its antioxidant potential and mitochondria protection; therefore, it is suggested that astaxanthin may be an effective treatment for oxidative stress-associated neurodegeneration.

PMID: 19101523 [PubMed - indexed for MEDLINE]

Astaxanthin protects human brain cells against cell death.

[J Neurochem.](#) 2008 Dec;107(6):1730-40. Epub 2008 Nov 7.

Protective effects of astaxanthin on 6-hydroxydopamine-induced apoptosis in human neuroblastoma SH-SY5Y cells.

[Ikeda Y](#), [Tsuji S](#), [Satoh A](#), [Ishikura M](#), [Shirasawa T](#), [Shimizu T](#).

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Parkinson's disease (PD) is a neurodegenerative disorder characterized by selective loss of dopaminergic neurons in the substantia nigra pars compacta. Although understanding of the pathogenesis of PD remains incomplete, increasing evidence from human and animal studies has suggested that oxidative stress is an important mediator in its pathogenesis. Astaxanthin (Asx), a potent antioxidant, has been thought to provide health benefits by decreasing the risk of oxidative stress-related diseases. This study examined the protective effects of Asx on 6-hydroxydopamine (6-OHDA)-induced apoptosis in the human neuroblastoma cell line SH-SY5Y. Pre-treatment of SH-SY5Y cells with Asx suppressed 6-OHDA-induced apoptosis in a dose-dependent manner. In addition, Asx strikingly inhibited 6-OHDA-induced mitochondrial dysfunctions, including lowered membrane potential and the cleavage of caspase 9, caspase 3, and poly(ADP-ribose) polymerase. In western blot analysis, 6-OHDA activated p38 MAPK, c-jun NH(2)-terminal kinase 1/2, and extracellular signal-regulated kinase 1/2, while Asx blocked the phosphorylation of p38 MAPK but not c-jun NH(2)-terminal kinase 1/2 and extracellular signal-regulated kinase 1/2. Pharmacological approaches showed that the activation of p38 MAPK has a critical role in 6-OHDA-induced mitochondrial dysfunctions and apoptosis. Furthermore, Asx markedly abolished 6-OHDA-induced reactive oxygen species generation, which resulted in the blockade of p38 MAPK activation and apoptosis induced by 6-OHDA treatment. Taken together, the present results indicated that the protective effects of Asx on apoptosis in SH-SY5Y cells may be, at least in part, attributable to its potent antioxidative ability.

Publication Types:

PMID: 19014378 [PubMed – indexed for MEDLINE]

Astaxanthin protects brain function and reduces inflammation and oxidative stress in rats.

[Front Pharmacol.](#) 2018 Jul 10;9:748. doi: 10.3389/fphar.2018.00748. eCollection 2018.

The Protective Effect of Astaxanthin on Cognitive Function via Inhibition of Oxidative Stress and Inflammation in the Brains of Chronic T2DM Rats.

[Feng Y¹](#), [Chu A²](#), [Luo Q³](#), [Wu M¹](#), [Shi X¹](#), [Chen Y³](#).

Author information

Abstract

Currently, there are no effective treatments for diabetes-related cognitive dysfunction. Astaxanthin (AST), the most powerful antioxidant in nature, exhibits diverse biological functions. In this study, we tried to explore whether AST would ameliorate cognitive dysfunction in chronic type 2 diabetes mellitus (T2DM) rats. The T2DM rat model was induced via intraperitoneal injection of streptozotocin. Forty Wistar rats were divided into a normal control group, an acute T2DM group, a chronic T2DM group, and an AST group (treated with AST at a dose of 25 mg/kg three times a week). The Morris water maze test showed that the percentage of time spent in the target quadrant of the AST group was identical to that of the chronic T2DM group, while the escape latency of the AST group was decreased in comparison to that of the chronic T2DM group. Histology of the hippocampus revealed that AST ameliorated the impairment in the neurons of diabetic rats. Western blot showed that AST could upregulate nuclear factor erythroid 2-related factor 2 (Nrf2) and heme oxygenase 1 (HO-1) expression and inhibit nuclear transcription factor kappa B (NF- κ B) p65 activation in the hippocampus. We found that AST increased the level of superoxide dismutase (SOD) and decreased the level of malondialdehyde (MDA) in the hippocampus. In addition, the levels of interleukin 1 beta (IL-1 β) and interleukin 6 (IL-6) were reduced in the AST group compared with those in the chronic T2DM group. The findings of this research imply that AST might inhibit oxidative stress and inflammatory responses by activating the Nrf2-ARE signaling pathway.

KEYWORDS:

Nrf2; astaxanthin; cytokines; inflammatory response; oxidative stress; type 2 diabetes mellitus

PMID: 30042685

PMCID: [PMC6048598](#)

DOI: [10.3389/fphar.2018.00748](#)

Free PMC Article

Astaxanthin dose-dependently reduces cortical spreading depression in ethanol-treated rats.

[Alcohol Clin Exp Res.](#) 2008 Aug;32(8):1417-21. Epub 2008 Jun 6.

Dose-dependent effects of astaxanthin on cortical spreading depression in chronically ethanol-treated adult rats.

[Abadie-Guedes R](#), [Santos SD](#), [Cahú TB](#), [Guedes RC](#), [de Souza Bezerra R](#).

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BACKGROUND: The consumption of alcoholic drinks is a frequent drug-abuse situation, which is associated to a wide variety of pathological disturbances affecting several organs, including the brain. We have previously shown in the developing rat brain that ethanol intake facilitates the propagation of cortical spreading depression (CSD), an excitability-related neural phenomenon present in several animal species. This electrophysiological effect was attenuated by a shrimp (*Litopenaeus vannamei*) carotenoids extract. Here we investigated the effects of pure astaxanthin, the main carotenoid found in shrimp, on CSD. **METHODS:** Adult Wistar rats were treated per gavage, during 18 days, with 2.5, 10 or 90 microg/kg/d astaxanthin dissolved in ethanol (3 g/kg) and CSD was recorded on the cortical surface 1 to 3 days thereafter. Four groups, treated respectively with ethanol, distilled water and soybean oil with- and without astaxanthin were also studied for comparison with the ethanol + astaxanthin groups. **RESULTS:** Ethanol-treated rats displayed higher CSD-velocities (mean values, in mm/min, per hour of recording ranging from 4.08 +/- 0.09 to 4.12 +/- 0.16), compared to the distilled water-group (from 3.19 +/- 0.13 to 3.27 +/- 0.06). Addition of astaxanthin to ethanol lead to lower CSD-velocities in a dose-dependent manner, ranging from 3.68 +/- 0.09 to 3.97 +/- 0.22 for the 2.5 microg/kg/d-dose, from 3.29 +/- 0.09 to 3.32 +/- 0.07 for the 10 microg/kg/d-dose, and from 2.89 +/- 0.13 to 2.92 +/- 0.11 for the 90 microg/kg/d-dose. The velocities of the soybean oil groups (with and without astaxanthin) were not statistically different from the 10 microg/kg/d astaxanthin + ethanol and distilled water groups. **CONCLUSION:** The results demonstrate the antagonistic effect of astaxanthin against the ethanol-induced facilitation of CSD propagation. Probably carotenoid antioxidant properties are involved in such effects.

Publication Types:

PMID: 18540920 [PubMed - indexed for MEDLINE]

Astaxanthin decreases pain and improves motor function in rat model of spinal cord injury.

[Eur J Pain](#). 2018 Nov 14. doi: 10.1002/ejp.1342. [Epub ahead of print]

Effects of astaxanthin on sensory-motor function in a compression model of spinal cord injury: Involvement of ERK and AKT signalling pathway.

[Fakhri S](#)¹, [Dargahi L](#)², [Abbaszadeh F](#)³, [Jorjani M](#)^{1,3}.

Author information

Abstract

BACKGROUND: Spinal cord injury (SCI) causes continuous neurological deficits and major sensory-motor impairments. There is no effective treatment to enhance sensory-motor function following SCI. Thus, it is crucial to develop novel therapeutics for this particular patient population. Astaxanthin (AST) is a strong antioxidant, anti-inflammatory and anti-apoptotic agent. In the present study, it was tested in a severe compression SCI model with emphasis on sensory-motor outcomes, signalling pathway, along with other complications.

METHODS: A severe SCI was induced by compression of the rat thoracic spinal cord with an aneurysm clip and treatment with AST or the vehicle was carried out, 30 min after injury. Behavioural tests including open field, von Frey, hot plate and BBB were performed weekly to 28 days post-injury. Rats were assigned to measure blood glucose, weight and auricle temperature. Western blot and histological analysis also were performed at the same time points.

RESULTS: AST decreased mechanical and thermal pain and also improved motor function performance, reduced blood glucose and auricle temperature increases and attenuated weight loss in SCI rats. Western blot analysis showed decreased activation of ERK1/2 and increased activation of AKT following AST treatment. The histology results revealed that AST considerably preserved myelinated white matter and the number of motor neurons following SCI.

CONCLUSION: Taken together, the beneficial effects of AST to improve sensory-motor outcomes, attenuate pathological tissue damage and modulate ERK and AKT signalling pathways following SCI, suggest it as a strong therapeutic agent towards clinical applications.

SIGNIFICANCE: Spinal cord injury (SCI) impairs sensory-motor function and causes complications, which astaxanthin (AST) has the potential to be used as a treatment for. The present study investigates the effects of AST in a compression model of SCI with emphasis on sensory-motor outcomes alongside other complications, histopathological damage and also related signalling pathways.

© 2018 European Pain Federation - EFIC®. PMID: 30427581 DOI: [10.1002/ejp.1342](#)

Astaxanthin helps protect both young and old rats against impairing effect of ethanol.

[Alcohol Clin Exp Res.](#) 2012 Sep;36(9):1563-7. doi: 10.1111/j.1530-0277.2012.01766. Epub 2012 Mar 20.

The impairing effect of acute ethanol on spreading depression is antagonized by astaxanthin in rats of 2 young-adult ages.

[Abadie-Guedes R¹](#), [Guedes RC](#), [Bezerra RS](#).

Author information

Abstract

BACKGROUND:

Ethanol (EtOH) abuse and insufficient ingestion of antioxidants are external factors that can alter brain electrophysiology. Our previous studies have demonstrated that the excitability-related brain electrophysiological phenomenon known as cortical spreading depression (CSD) was facilitated by chronic EtOH intake, and chronic treatment with carotenoids attenuated this effect. Here, we investigated the acute effect of a single EtOH administration on CSD in young and adult rats previously (1 hour) treated with 10 µg/kg of astaxanthin.

METHODS:

Male Wistar rats (5 young- and 5 adult groups, 60 to 80 and 150 to 180 days of age, respectively) were treated by 2 gavage procedures at 1-hour interval as follows: groups 1 and 2 received astaxanthin in gavage I combined with EtOH (group 1) or water (group 2) in gavage II; groups 3 and 4 received olive oil (the vehicle in which astaxanthin was dissolved) in gavage I combined with EtOH (group 3) or water (group 4) in gavage II; group 5 received water in gavage I combined with EtOH in gavage II. CSD was recorded on the cortical surface for 4 hours.

RESULTS:

Compared to the respective water and oil controls (groups 2 and 4; CSD velocities: 3.73 ± 0.09 and 3.78 ± 0.07 mm/min in the young groups; 2.99 ± 0.10 and 3.05 ± 0.19 mm/min in the adult groups), a single dose of EtOH (groups 3 and 5) decreased CSD propagation velocities (3.29 ± 0.23 and 3.16 ± 0.10 mm/min in the young groups; 2.71 ± 0.27 and 2.75 ± 0.31 mm/min in the adult groups). Astaxanthin antagonized the impairing effect of acute EtOH on CSD (group 1; mean velocity: 3.70 ± 0.19 and 3.13 ± 0.16 mm/min for the young and adult groups, respectively).

CONCLUSIONS:

The results showed an antagonistic effect of acute EtOH treatment on CSD propagation that was reverted by astaxanthin. The EtOH-astaxanthin interaction was not influenced by the age, as it was found in both young and adult animals.

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PMID: [22432539](#) DOI: [10.1111/j.1530-0277.2012.01766.x](#)

Astaxanthin supplementation improves spatial memory and enhances hippocampal neurogenesis in mice.

[Mol Nutr Food Res.](#) 2016 Mar;60(3):589-99. doi: 10.1002/mnfr.201500634. Epub 2016 Jan 7.

Astaxanthin supplementation enhances adult hippocampal neurogenesis and spatial memory in mice.

[Yook JS¹](#), [Okamoto M¹](#), [Rakwal R²](#), [Shibato J¹](#), [Lee MC^{1,3}](#), [Matsui T¹](#), [Chang H⁴](#), [Cho JY⁵](#), [Soya H¹](#).

Author information

Abstract

SCOPE:

There is a growing necessity for efficacious natural supplements with antioxidant effects on the brain, in particular, hippocampal function. One such compound, which also has a neuroprotective effect, is the carotenoid astaxanthin (ASX). Despite ASX's potential benefit to the brain, very little is known about its effect on hippocampal plasticity and cognition. Thus, we investigated the effect of ASX on adult hippocampal neurogenesis (AHN) and spatial memory using a mouse model.

METHODS AND RESULTS:

Dose-response was examined in mice fed ASX-supplemented diets (0, 0.02, 0.1, and 0.5%) to define the effect of ASX on AHN. In conjunction with AHN results, hippocampus-dependent cognitive function was assessed. We delineated molecular mechanisms associated with ASX-enhanced AHN using DNA microarray analysis. Results revealed that ASX enhanced cell proliferation and survival at 0.1% and 0.5% doses. Newborn mature neurons were higher only with 0.5% ASX, which also enhanced spatial memory. Transcriptomic profiling revealed potential AHN-associated molecules (Prl, Itga4, and Il4) that were ASX induced. Their downstream factors, identified through Ingenuity Pathway Analysis, were positively correlated with ASX-induced increases in spatial memory.

CONCLUSION:

ASX supplementation enhanced AHN and spatial memory, and a DNA microarray approach provided, for the first time, novel molecular insights into ASX action.

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KEYWORDS:

Adult hippocampal neurogenesis; Astaxanthin; DNA microarray; Spatial memory; Transcriptomic profile

PMID: [26643409](#)

DOI: [10.1002/mnfr.201500634](#)

Astaxanthin improves memory in mice dose-dependently and is very effective for improving memory at low doses.

[Environ Geochem Health](#). 2007 Dec;29(6):483-9. Epub 2007 Aug 25.

Impact of astaxanthin-enriched algal powder of *Haematococcus pluvialis* on memory improvement in BALB/c mice.

[Zhang X](#), [Pan L](#), [Wei X](#), [Gao H](#), [Liu J](#).

Research and Development Center of Marine Biotechnology, Institute of Oceanology, Chinese Academy of Sciences, 7 Nanhai Road, Qingdao, 266071, China.

The impact of astaxanthin-enriched algal powder on auxiliary memory improvement was assessed in BALB/c mice pre-supplemented with different dosages of cracked green algal (*Haematococcus pluvialis*) powder daily for 30 days. The supplemented mice were first tested over 8 days to find a hidden platform by swimming in a Morris water maze. Then, for 5 days, the mice were used to search for a visible platform in a Morris water maze. After that, the mice practised finding a safe place--an insulated platform in a chamber--for 2 days. During these animal experimental periods, similar algal meals containing astaxanthin at 0, 0.26, 1.3 and 6.4 mg/kg body weight were continuously fed to each group of tested mice. Profiles of latency, distance, speed and the direction angle to the platforms as well as the diving frequency in each group were measured and analyzed. The process of mice jumping up onto the insulated platform and diving down to the copper-shuttered bottom with a 36 V electrical charge were also monitored by automatic video recording. The results of the Morris maze experiment showed that middle dosage of *H. pluvialis* meals (1.3 mg astaxanthin/kg body weight) significantly shortened the latency and distance required for mice to find a hidden platform. However, there was no obvious change in swim velocity in any of the supplemented groups. In contrast, the visible platform test showed a significant increase in latency and swim distance, and a significant decrease in swim speed for all groups of mice orally supplemented with *H. pluvialis* powder compared to the placebo group ($P < 0.05$ or $P < 0.01$). Mice supplemented with the algal meal hesitantly turned around the original hidden platform, in contrast to mice supplemented with placebo, who easily forgot the original location and accepted the visible platform as a new safe place. These results illustrate that astaxanthin-enriched *H. pluvialis* powder has the auxiliary property of memory improvement. The results from the platform diving test showed that the low and middle dosage of *H. pluvialis* powder, rather than the high dosage, increased the latency and reduced the frequency of diving from the safe insulated platform to the electrically stimulated copper shutter, especially in the low treatment group ($P < 0.05$). These results indicate that *H. pluvialis* powder is associated with dose-dependent memory improvement and that a low dosage of algal powder (low or middle treatment group) is really good for improving the memory.

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Astaxanthin prevents brain damage due to ischemia in rats

Effects of astaxanthin on brain damage due to ischemia

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Brain requires high energy-supply to keep its normal function. Well-developed blood vessels in the brain supply enough glucose and oxygen to generate required energy. When some part of blood vessels were closed or occluded by some reason, the area supported by those blood vessels will fall into ischemia and the neuronal cells distributed in the area will be damaged or die. Since neuronal cells have no neogenetic properties, the functions supported by the area will be lost forever. We know and take care of large scale of neuronal cell death which will cause severe loss of brain function, but we ignore small scale of ischemia which may have no apparent dysfunction. However senile dementia will be formed due to the accumulation of such small scale ischemic neuronal cell death. Although big efforts have been made to develop some drugs to rescue the cells exposed to ischemia from death, we have no effective drugs so far. Since astaxanthin has been known to have antioxidant effects, we expected this drug to rescue the cell damage during ischemia and re-perfusion.

In the present study we used slice preparations (300 μ m) of hippocampus obtained from young adult rats. To measure intracellular Ca^{2+} concentration before, during and after ischemia we stained the slice preparation by fura-2, a Ca^{2+} indicator. The fluorescence of loaded fura-2 was analyzed by an image processor (Argus 50; Hamamatsu photonics). To examine brain edema during ischemia we used self-made device, which is consisted of an infra-red differential interference microscope with an infra-red camera and an image processor and measured "contrast value" as indices of edema. Astaxanthin (0.003%) pretreated for ten minutes before ischemia reduced the increase in intracellular Ca^{2+} concentration during ischemia and accelerate the recovery from the abnormal increase in Ca^{2+} concentration. Pretreated astaxanthin (0.01%) also reduced the edema developed during ischemia.

Although present results were still preliminary, astaxanthin can be expected to have effective rescuing effects on neuronal damages induced by ischemia.

Astaxanthin reverses neurotoxicity in rat neurons exposed to homocysteine.

[Cell Death Discov.](#) 2018 Oct 22;4:50. doi: 10.1038/s41420-018-0114-x. eCollection 2018.

Reversal of homocysteine-induced neurotoxicity in rat hippocampal neurons by astaxanthin: evidences for mitochondrial dysfunction and signaling crosstalk.

[Wang XJ](#)^{#1}, [Chen W](#)^{#1}, [Fu XT](#)^{#2}, [Ma JK](#)³, [Wang MH](#)⁴, [Hou YJ](#)², [Tian DC](#)¹, [Fu XY](#)², [Fan CD](#)².

Author information

Abstract

Elevated plasma level of homocysteine (Hcy) represents an independent risk for neurological diseases, and induction of oxidative damage is considered as one of the most important pathomechanisms. Astaxanthin (ATX) exhibits strong antioxidant activity in kinds of experimental models. However, the potential of ATX against Hcy-induced neurotoxicity has not been well explored yet. Herein, the neuroprotective effect of ATX against Hcy-induced neurotoxicity in rat hippocampal neurons was examined, and the underlying mechanism was evaluated. The results showed that ATX pre-treatment completely reversed Hcy-induced neurotoxicity through inhibiting cell apoptosis in rat primary hippocampal neurons. The mechanical investigation revealed that ATX effectively blocked Hcy-induced mitochondrial dysfunction by regulating Bcl-2 family and opening of mitochondrial permeability transition pore (MPTP). ATX pre-treatment also attenuated Hcy-induced oxidative damage via inhibiting the release of intracellular reactive oxide species (ROS) and superoxide anion through regulating MPTP opening. Moreover, normalization of MAPKs and PI3K/AKT pathways also contributed to ATX-mediated protective effects. Taken together, these results above suggested that ATX has the potential to reverse Hcy-induced neurotoxicity and apoptosis by inhibiting mitochondrial dysfunction, ROS-mediated oxidative damage and regulation of MAPKs and AKT pathways, which validated the strategy of using ATX could be a highly effective way in combating Hcy-mediated neurological disorders.

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PMCID: [PMC6197197](#)

DOI: [10.1038/s41420-018-0114-x](#)

[Free PMC Article](#)

Astaxanthin reduces brain inflammation in rat model of spinal cord injury.

[Brain Res Bull.](#) 2018 Oct;143:217-224. doi: 10.1016/j.brainresbull.2018.09.011. Epub 2018 Sep 19.

Astaxanthin attenuates neuroinflammation contributed to the neuropathic pain and motor dysfunction following compression spinal cord injury.

[Fakhri S](#)¹, [Dargahi L](#)², [Abbaszadeh F](#)³, [Jorjani M](#)⁴.

Author information

Abstract

Spinal cord injury (SCI) is a debilitating condition in which inflammatory responses in the secondary phase of injury leads to long lasting sensory-motor dysfunction. The medicinal therapy of SCI complications is still a clinical challenge. Understanding the molecular pathways underlying the progress of damage will help to find new therapeutic candidates. Astaxanthin (AST) is a ketocarotenoid which has shown anti-inflammatory effects in models of traumatic brain injury. In the present study, we examined its potential in the elimination of SCI damage through glutamatergic-phospho p38 mitogen-activated protein kinase (p-p38MAPK) signaling pathway. Inflammatory response, histopathological changes and sensory-motor function were also investigated in a severe compression model of SCI in male rats. The results of acetone drop and inclined plane tests indicated the promising role of AST in improving sensory and motor function of SCI rats. AST decreased the expression of n-methyl-d-aspartate receptor subunit 2B (NR2B) and p-p38MAPK as inflammatory signaling mediators as well as tumor necrosis factor- α (TNF- α) as an inflammatory cytokine, following compression SCI. The histopathological study culminated in preserved white matter and motor neurons beyond the injury level in rostral and caudal parts. The results show the potential of AST to inhibit glutamate-initiated signaling pathway and inflammatory reactions in the secondary phase of SCI, and suggest it as a promising candidate to enhance functional recovery after SCI.

KEYWORDS:

Astaxanthin; Glutamate signaling; Neuroinflammation; Rat; Sensory-motor function; Spinal cord injury

PMID: 30243665

DOI: [10.1016/j.brainresbull.2018.09.011](https://doi.org/10.1016/j.brainresbull.2018.09.011)

Astaxanthin provides neuroprotection against diabetes-induced sickness behavior in mice by inhibiting inflammation.

[Cell Mol Neurobiol.](#) 2015 Oct;35(7):1027-37. doi: 10.1007/s10571-015-0197-3. Epub 2015 May 14.

Anti-inflammatory Effect of Astaxanthin on the Sickness Behavior Induced by Diabetes Mellitus.

[Ying CJ](#)¹, [Zhang F](#)², [Zhou XY](#)², [Hu XT](#)², [Chen J](#)², [Wen XR](#)³, [Sun Y](#)⁴, [Zheng KY](#)⁵, [Tang RX](#)^{6,7}, [Song YJ](#)^{8,9}.

Author information

Abstract

Chronic inflammation appears to play a critical role in sickness behavior caused by diabetes mellitus. Astaxanthin has been used in treating diabetes mellitus and diabetic complications because of its neuroprotective and anti-inflammatory actions. However, whether astaxanthin can improve sickness behavior induced by diabetes and its potential mechanisms are still unknown. The aim of this study was to investigate the effects of astaxanthin on diabetes-elicited abnormal behavior in mice and its corresponding mechanisms. An experimental diabetic model was induced by streptozotocin (150 mg/kg) and astaxanthin (25 mg/kg/day) was provided orally for 10 weeks. Body weight and water consumption were measured, and the sickness behavior was evaluated by the open field test (OFT) and closed field test (CFT). The expression of glial fibrillary acidic protein (GFAP) was measured, and the frontal cortical cleaved caspase-3 positive cells, interleukin-6 (IL-6), and interleukin-1 β (IL-1 β) expression levels were also investigated. Furthermore, cystathionine β -synthase (CBS) in the frontal cortex was detected to determine whether the protective effect of astaxanthin on sickness behavior in diabetic mice is closely related to CBS. As expected, we observed that astaxanthin improved general symptoms and significantly increase horizontal distance and the number of crossings in the OFT and CFT. Furthermore, data showed that astaxanthin could decrease GFAP-positive cells in the brain and down-regulate the cleaved caspase-3, IL-6, and IL-1 β , and up-regulate CBS in the frontal cortex. These results suggest that astaxanthin provides neuroprotection against diabetes-induced sickness behavior through inhibiting inflammation, and the protective effects may involve CBS expression in the brain.

KEYWORDS:

Astaxanthin; Cystathionine β -synthase; Diabetes; Inflammation

PMID:

[25971983](#)

DOI: [10.1007/s10571-015-0197-3](#)

ASTAXANTHIN SHOWS NEUROLOGICAL POTENTIAL IN RATS DUE TO ITS ANTIOXIDANT ACTIVITY.

J Orthop Surg Res. 2020 Jul 23;15(1):275.
doi: 10.1186/s13018-020-01790-8.

Astaxanthin alleviates spinal cord ischemia-reperfusion injury via activation of PI3K/Akt/GSK-3 β pathway in rats

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- PMID: [32703256](#)
- PMCID: [PMC7376638](#)
- DOI: [10.1186/s13018-020-01790-8](#)

[Free PMC article](#)

Abstract

Background: Ischemia-reperfusion injury of the spinal cord (SCII) often leads to unalterable neurological deficits, which may be associated with apoptosis induced by oxidative stress and inflammation. Astaxanthin (AST) is a strong antioxidant and anti-inflammatory agent with multitarget neuroprotective effects. This study aimed to investigate the potential therapeutic effects of AST for SCII and the molecular mechanism.

Methods: Rat models of SCII with abdominal aortic occlusion for 40 min were carried out to investigate the effects of AST on the recovery of SCII. Tarlov's scores were used to assess the neuronal function; HE and TUNEL staining were used to observe the pathological morphology of lesions. Neuron oxidative stress and inflammation were measured using commercial detection kits. Flow cytometry was conducted to assess the mitochondrial swelling degree. Besides, Western blot assay was used to detect the expression of PI3K/Akt/GSK-3 β pathway-related proteins, as well as NOX2 and NLRP3 proteins.

Results: The results demonstrated that AST pretreatment promoted the hind limb motor function recovery and alleviated the pathological damage induced by SCII. Moreover, AST significantly enhanced the antioxidative stress response and attenuated mitochondrial swelling. However, AST pretreatment hardly inhibited the levels of proinflammatory cytokines after SCII. Most importantly, AST activated p-Akt and p-GSK-3 β expression levels. Meanwhile, cotreatment with LY294002 (a PI3K inhibitor) was found to abolish the above protective effects observed with the AST pretreatment.

Conclusion: Overall, these results suggest that AST pretreatment not only mitigates pathological tissue damage but also effectively improves neural functional recovery following SCII, primarily by alleviating oxidative stress but not inhibiting inflammation. A possible underlying molecular mechanism of AST may be mainly attributed to the activation of PI3K/Akt/GSK-3 β pathway.

ASTAXANTHIN SHOWS NEUROPROTECTIVE PROPERTIES AGAINST OPTIC- NERVE ISCHEMIA IN RATS.

Mar Drugs. 2020 Jan 28;18(2):85.
doi: 10.3390/md18020085.

***Haematococcus pluvialis*- Derived Astaxanthin Is a Potential Neuroprotective Agent against Optic Nerve Ischemia**

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PMID: [32012819](#) PMCID: [PMC7074344](#) DOI: [10.3390/md18020085](#) [Free PMC article](#)

Abstract

Astaxanthin, a xanthophyll belonging to the family of carotenoids, is a potent antioxidant. However, much less is known about its protective effects on the oxidative stress of ischemic optic nerve. We hypothesized that astaxanthin treatment could protect retinal ganglion cells (RGCs) from death via anti-oxidative and anti-apoptotic responses. Adult male Wistar rats were fed astaxanthin (100 mg/kg/day) by daily gavage for seven consecutive days, either before or after inducing oxidative stress in the retina by photodynamic treatment. The visual function, RGC apoptosis, macrophage infiltration in the optic nerve, expression of p-Akt, p-mTOR, SGK1, pS6K, Nrf2, p62, TNF α , Il1 β in retinas were investigated. The visual function and the RGC densities were significantly higher in both pre- and post-treatment groups. The numbers of apoptotic RGCs and extrinsic macrophage infiltration in the optic nerve were significantly decreased in both astaxanthin-treated groups. Furthermore, pre- and post-treatment of astaxanthin showed a higher expression of p-Akt, p-mTOR, Nrf2 and superoxide dismutase activity, and a lower expression of cleaved caspase-3, suggesting anti-apoptotic and anti-oxidative roles. Our findings indicate that astaxanthin can preserve visual function and reduce RGC apoptosis after ischemic insults. Including astaxanthin in daily diet as a supplement may be beneficiary for ischemic optic neuropathy.

ASTAXANTHIN IMPROVED COGNITIVE DEFICIT IN UNDERNOURISHED RATS.

Nutr Neurosci. 2020 Jun;23(6):422-431.

doi: 10.1080/1028415X.2018.1515301. Epub 2018 Sep 11.

Role of astaxanthin in the modulation of brain-derived neurotrophic factor and spatial learning behavior in perinatally undernourished Wistar rats

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PMID: 30200858 DOI: [10.1080/1028415X.2018.1515301](https://doi.org/10.1080/1028415X.2018.1515301)

Abstract

Objective: Maternal health and nutrition during the perinatal period is the predominant factor influencing the functional development of the brain. Maternal malnutrition during the perinatal period causes retardation of brain development. The current study investigates the role of Astaxanthin (AsX) in spatial learning and memory and BDNF in perinatally undernourished Wistar rats.

Methods: The albino wistar rats were perinatally undernourished and administered with different dosages of AsX. The spatial learning and memory performance and BDNF level were assessed. Data were collected and analysed.

Results: The % Correct choice during the acquisition phase, performance at the end of the acquisition phase and the mean BDNF level at the Hippocampus, Cerebellum, and Cerebral cortex showed significant decline ($P < 0.001$) in the PUN group and significantly high ($P < 0.001$) in the PUNA2 group compared to the control. However, the mean RME and mean WME during different days of the acquisition phase were significantly high ($P < 0.001$) in the PUN group and insignificant ($P > 0.05$) in PUNA2 compared to the control.

Discussion: The results showed that AsX effectively modulated the cognitive deficit that occurred in perinatally undernourished rats. This can be attributed to BDNF upregulation as evidenced by the significant increase of the BDNF level.

ASTAXANTHIN PROTECTS AGAINST HEMORRHAGE-INDUCED BRAIN INJURY IN RAT MODEL.

Acta Histochem. 2019 Jan;121(1):56-63.

doi: 10.1016/j.acthis.2018.10.014. Epub 2018 Nov 2.

Protective effects of astaxanthin on subarachnoid hemorrhage-induced early brain injury: Reduction of cerebral vasospasm and improvement of neuron survival and mitochondrial function

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Abstract

The purpose of this study was to evaluate the neuroprotective effects of astaxanthin on early brain injury (EBI) caused by subarachnoid hemorrhage (SAH) in rats and to explore possible molecular mechanisms. Experimental SAH model was introduced in adult male SD rats by injecting autologous arterial blood into the prechiasmatic cistern. Astaxanthin (75 mg/kg bodyweight) or olive oil was administered by oral gavage at 3 h after SAH. Our results showed that astaxanthin attenuated SAH-induced cerebral vasospasm and reduced neuronal apoptosis. Astaxanthin inhibited mitochondria-associated neuron apoptosis in the prefrontal cortex after SAH: increased mitochondrial membrane potential, decreased Bax/Bcl-2 ratio, inhibited cytochrome C release in cytoplasm, and suppressed caspase-3 enzyme activity. Furthermore, the cerebral expression levels of synaptic proteins (Synapsin-1, postsynaptic density-95 and growth-associated protein-43) and nerve growth and neuronal differentiation factors (brain-derived neurotrophic factor and purine-rich binding protein- α) were reduced following SAH. Astaxanthin partly restored their expression. In conclusion, our current work demonstrates that astaxanthin attenuates SAH-induced EBI, possibly by improving neuronal survival and mitochondrial function.

ASTAXANTHIN SHOWS POTENTIAL AGAINST ALZHEIMER'S DISEASE IN RAT MODEL OF HIPPOCAMPAL INSULIN RESISTANCE.

Biomed Pharmacother. 2019 Feb;110:47-58.

doi: 10.1016/j.biopha.2018.11.043. Epub 2018 Nov 18.

Neuroprotective role of astaxanthin in hippocampal insulin resistance induced by A β peptides in animal model of Alzheimer's disease

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PMID: 30463045 DOI: [10.1016/j.biopha.2018.11.043](https://doi.org/10.1016/j.biopha.2018.11.043) **Free article**

Abstract

With the constant failure of the clinical trials continuous exploration of a therapeutic target against Alzheimer's disease (AD) is the utmost need. Numerous studies have supported the hypothesis that central insulin resistance plays a significant role in AD. Serine phosphorylation of Insulin Receptor Substrate-1 (IRS-1) has been found to be a contributing factor in neuronal insulin resistance. Astaxanthin (ASX) is xanthophyll carotenoid which has previously demonstrated significant antidiabetic and neuroprotective actions. In the present study, AD was induced by i.c.v administration of Amyloid- β (1-42) peptides in Wistar rats. After 7 days of recovery, rats were treated with 0.5 mg/kg and 1 mg/kg of ASX orally for 28 days. Behavioral analysis was done in the last week of our experimental study. On the 36th day, rats were sacrificed and their hippocampus were separated from the whole brain, then homogenized and stored for biochemical estimations. ASX significantly and dose-dependently reversed the cognitive and memory impairment, assessed by Morris water maze test and Novel object Recognition test, A β (1-42) peptides infused Wistar rats. ASX also significantly attenuated soluble A β (1-42) level, IRS-S307 activity, GSK-3 β activity, TNF- α level, AChE level, nitrite level and oxidative stress in the hippocampus. Histopathological evaluation, done through H&E and Congo red staining, also demonstrated neuroprotective and anti-amyloidogenic effects of ASX in hippocampus. Our study concludes preventive action of Astaxanthin against hippocampal insulin resistance and Alzheimer's disease complications, supporting potential role of hippocampal insulin resistance targeting against AD.

ASTAXANTHIN DEMONSTRATES POTENTIAL TO SLOW THE ONSET OR PROGRESSION OF COGNITIVE DYSFUNCTION IN MOUSE MODEL.

Brain Res. 2019 May 1;1710:74-81.

doi: 10.1016/j.brainres.2018.12.014. Epub 2018 Dec 12.

Astaxanthin ameliorates scopolamine-induced spatial memory deficit via reduced cortical-striato-hippocampal oxidative stress

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PMID: 30552898 DOI: [10.1016/j.brainres.2018.12.014](https://doi.org/10.1016/j.brainres.2018.12.014)

Abstract

Alzheimer's disease is characterized by progressive disruption of cholinergic neurotransmission and impaired cognitive functions. In rodents, scopolamine has been used to induce cholinergic dysfunction resulting in cognitive impairments and an increment of oxidative stress in the brain. Here we tested whether oxidative stress can be attenuated via an antioxidant (astaxanthin) to rescue scopolamine-induced spatial memory. For this purpose, we administered either 0.9% saline (control), or scopolamine (SCP), or scopolamine plus astaxanthin (SCP + AST) to Swiss albino mice (ten weeks old; n = 20) for 28 consecutive days and subsequently examined animals' locomotor activity, spatial learning, and memory performance. The mice were then euthanized and prefrontal cortex (PFC), striatum (ST), hippocampus (HP), and liver tissues were assayed for antioxidant enzymes, glutathione (GSH), superoxide dismutase (SOD), catalase (CAT), and nitric oxide (NO). The SCP group exhibited impaired spatial learning and significantly altered levels of antioxidant enzymes and NO in the PFC, ST, and HP. In contrast, SCP + AST treatment did not cause spatial learning deficits. Furthermore, this condition also showed unaltered levels of SOD and NO in the ST and HP. Taken together, our results show that scopolamine may interrupt the striatal-hippocampal cholinergic activity resulting in impaired spatial memory. At the same time, these impairments are extinguished with astaxanthin by preventing oxidative damage in the striatal-hippocampal cholinergic neurons. Therefore, we suggest astaxanthin as a potential treatment to slow the onset or progression of cognitive dysfunctions that are elicited by abnormal cholinergic neurotransmission in Alzheimer's disease.

ASTAXANTHIN REDUCES TOBACCO-RELATED COGNITIVE DEFICITS IN MOUSE MODEL.

Mar Drugs. 2019 Jan 3;17(1):24.

doi: 10.3390/md17010024.

Astaxanthin Attenuates Environmental Tobacco Smoke-Induced Cognitive Deficits: A Critical Role of p38 MAPK

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PMID: 30609815 PMCID: [PMC6356379](#) DOI: [10.3390/md17010024](#) [Free PMC article](#)

Abstract

Increasing evidence indicates that environmental tobacco smoke (ETS) impairs cognitive function and induces oxidative stress in the brain. Recently, astaxanthin (ATX), a marine bioactive compound, has been reported to ameliorate cognitive deficits. However, the underlying pathogenesis remains unclear. In this study, ATX administration (40 mg/kg and 80 mg/kg, oral gavage) and cigarette smoking were carried out once a day for 10 weeks to investigate whether the p38 MAPK is involved in cognitive function in response to ATX treatment in the cortex and hippocampus of ETS mice. Results indicated that ATX administration improved spatial learning and memory of ETS mice ($p < 0.05$ or $p < 0.01$). Furthermore, exposure to ATX prevented the increases in the protein levels of the p38mitogen-activated protein kinase (p38 MAPK; $p < 0.05$ or $p < 0.01$) and nuclear factor-kappa B (NF- κ B p65; $p < 0.05$ or $p < 0.01$), reversed the decreases in the mRNA and protein levels of synapsin I (SYN) and postsynaptic density protein 95 (PSD-95) (all $p < 0.05$ or $p < 0.01$). Moreover, ATX significantly down-regulated the increased levels of pro-inflammatory cytokines including interleukin-6 (IL-6) and tumor necrosis factor (TNF- α) (all $p < 0.05$ or $p < 0.01$). Meanwhile, the increased level of malondialdehyde (MDA) and the decreased activities of superoxide dismutase (SOD), glutathione (GSH), and catalase (CAT) were suppressed after exposure to ATX (all $p < 0.05$ or $p < 0.01$). Also, the results of the molecular docking study of ATX into the p38 MAPK binding site revealed that its mechanism was possibly similar to that of PH797804, a p38 MAPK inhibitor. Therefore, our results indicated that the ATX might be a critical agent in protecting the brain against neuroinflammation, synaptic plasticity impairment, and oxidative stress in the cortex and hippocampus of ETS mice.

ASTAXANTHIN MAY SERVE TO PROTECT FROM BRAIN DAMAGE (FINDINGS OF RAT STUDY).

Brain Res Bull. 2019 May;148:63-69.

doi: 10.1016/j.brainresbull.2019.03.009. Epub 2019 Mar 22.

Neuroprotective effect of astaxanthin on newborn rats exposed to prenatal maternal seizures

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- PMID: [30910691](#)
- DOI: [10.1016/j.brainresbull.2019.03.009](#)

Abstract

Maternal epilepsy during pregnancy is associated with an increased incidence of brain damage and cognitive deficits in offspring. Oxidative stress is believed to play a critical role in this process. Astaxanthin, a natural carotenoid and dietary supplement, possesses potent antioxidant properties. This study was designed to investigate whether astaxanthin ameliorates the hippocampal damage in newborn rats induced by maternal epileptic seizures in utero and to explore the underlying mechanisms. Female Sprague-Dawley rats underwent chronic amygdalar kindling. After being fully kindled, all rats were allowed to mate, and electrical stimulation in the amygdala was performed every other day throughout the pregnancy. Astaxanthin was intraperitoneally injected at a dose of 30 mg/kg/d throughout pregnancy. Prenatal astaxanthin administration ameliorated neuronal lesions, decreased oxidative stress and induced the expression of cAMP response element-binding protein (CREB) and brain-derived neurotrophic factor (BDNF) in the hippocampus of pups. Astaxanthin also ameliorated placental ischemic damage in epileptic mothers. Based on the results of the present study, we concluded that astaxanthin might serve as a therapeutic agent for preventing brain damage in offspring exposed to prenatal maternal seizures.

ASTAXANTHIN ENHANCES THE EFFECTS OF LOW-INTENSITY EXERCISE ON NEURAL FUNCTIONS RELATED TO MEMORY IN MOUSE MODEL.

Proc Natl Acad Sci U S A. 2019 May 28;116(22):10988-10993.
doi: 10.1073/pnas.1815197116. Epub 2019 May 13.

Leptin in hippocampus mediates benefits of mild exercise by an antioxidant on neurogenesis and memory

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PMID: 31085646 PMCID: [PMC6561194](#) DOI: [10.1073/pnas.1815197116](#) [Free PMC article](#)

Abstract

Regular exercise and dietary supplements with antioxidants each have the potential to improve cognitive function and attenuate cognitive decline, and, in some cases, they enhance each other. Our current results reveal that low-intensity exercise (mild exercise, ME) and the natural antioxidant carotenoid astaxanthin (AX) each have equivalent beneficial effects on hippocampal neurogenesis and memory function. We found that the enhancement by ME combined with AX in potentiating hippocampus-based plasticity and cognition is mediated by leptin (LEP) made and acting in the hippocampus. In assessing the combined effects upon wild-type (WT) mice undergoing ME with or without an AX diet for four weeks, we found that, when administered alone, ME and AX separately enhanced neurogenesis and spatial memory, and when combined they were at least additive in their effects. DNA microarray and bioinformatics analyses revealed not only the up-regulation of an antioxidant gene, *ABHD3*, but also that the up-regulation of *LEP* gene expression in the hippocampus of WT mice with ME alone is further enhanced by AX. Together, they also increased hippocampal LEP (h-LEP) protein levels and enhanced spatial memory mediated through AKT/STAT3 signaling. AX treatment also has direct action on human neuroblastoma cell lines to increase cell viability associated with increased LEP expression. In LEP-deficient mice (*ob/ob*), chronic infusion of LEP into the lateral ventricles restored the synergy. Collectively, our findings suggest that not only h-LEP but also exogenous LEP mediates effects of ME on neural functions underlying memory, which is further enhanced by the antioxidant AX.

ASTAXANTHIN PREVENTS ISCHEMIC DAMAGE IN MOUSE MODEL IN-VIVO AND IN-VITRO.

Int J Mol Sci. 2019 Dec 6;20(24):6168.

doi: 10.3390/ijms20246168.

Astaxanthin Ameliorates Ischemic-Hypoxic-Induced Neurotrophin Receptor p75 Upregulation in the Endothelial Cells of Neonatal Mouse Brains

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- PMID: 31817750
- PMCID: [PMC6940833](#)
- DOI: [10.3390/ijms20246168](#)

[Free PMC article](#)

Abstract

Ischemic stroke is a leading cause of human death in present times. Two phases of pathological impact occur during an ischemic stroke, namely, ischemia and reperfusion. Both periods include individual characteristic effects on cell injury and apoptosis. Moreover, these conditions can cause severe cell defects and harm the blood-brain barrier (BBB). Also, the BBB components are the major targets in ischemia-reperfusion injury. The BBB owes its enhanced protective roles to capillary endothelial cells, which maintain BBB permeability. One of the nerve growth factor (NGF) receptors initiating cell signaling, once activated, is the p75 neurotrophin receptor (p75NTR). This receptor is involved in both the survival and apoptosis of neurons. Although many studies have attempted to explain the role of p75NTR in neurons, the mechanisms in endothelial cells remain unclear. Endothelial cells are the first cells to encounter p75NTR stimuli. In this study, we found the upregulated p75NTR expression and reductive expression of tight junction proteins after in vivo and in vitro ischemia-reperfusion injury. Moreover, astaxanthin (AXT), an antioxidant drug, was utilized and was found to reduce p75NTR expression and the number of apoptotic cells. This study verified that p75NTR plays a prominent role in endothelial cell death and provides a novel downstream target for AXT.

ASTAXANTHIN PROTECTS AGAINST BRAIN DAMAGE DUE TO ISCHEMIC INJURY IN RAT MODEL.

Comb Chem High Throughput Screen. 2020;23(3):214-224.
doi: 10.2174/1386207323666200219121600.

Favorable Effects of Astaxanthin on Brain Damage due to Ischemia- Reperfusion Injury

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PMID: 32072893 DOI: [10.2174/1386207323666200219121600](https://doi.org/10.2174/1386207323666200219121600)

Abstract

Background: Activated inflammation and oxidant stress during cerebral ischemia reperfusion injury (IRI) lead to brain damage. Astaxanthin (ASX) is a type of carotenoid with a strong antioxidant effect.

Objective: The aim of this study was to investigate the role of ASX on brain IRI.

Methods: A total of 42 adult male Sprague-Dawley rats were divided into 3 groups as control (n=14) group, IRI (n=14) group and IRI + ASX (n=14) group. Cerebral ischemia was instituted by occluding middle cerebral artery for 120 minutes and subsequently, reperfusion was performed for 48 hours. Oxidant parameter levels and protein degradation products were evaluated. Hippocampal and cortex cell apoptosis, neuronal cell count, neurological deficit score were evaluated.

Results: In the IRI group, oxidant parameter levels and protein degradation products in the tissue were increased compared to control group. However, these values were significantly decreased in the IRI + ASX group ($p < 0.05$). There was a significant decrease in hippocampal and cortex cell apoptosis and a significant increase in the number of neuronal cells in the IRI + ASX group compared to the IRI group alone ($p < 0.05$). The neurological deficit score which was significantly lower in the IRI group compared to the control group was found to be significantly improved in the IRI + ASX group ($p < 0.05$).

Conclusion: Astaxanthin protects the brain from oxidative damage and reduces neuronal deficits due to IRI injury.

ASTAXANTHIN REDUCES NEUROINFLAMMATION IN RATS.

Drug Des Devel Ther. 2020 Apr 30;14:1651-1662.
doi: 10.2147/DDDT.S249162. eCollection 2020.

Astaxanthin Attenuates Neuroinflammation in Status Epilepticus Rats by Regulating the ATP-P2X7R Signal

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- PMID: [32431490](#)
- PMCID: [PMC7201036](#)
- DOI: [10.2147/DDDT.S249162](#)

[Free PMC article](#)

Abstract

Background: As a life-threatening neurological emergency, status epilepticus (SE) is often refractory to available treatment. Current studies have shown a causal role of neuroinflammation in patients with lower seizure thresholds and driving seizures. The ATP-gated purinergic P2X7 receptor (P2X7R) is mainly expressed on the microglia, which function as gatekeepers of inflammation. Although emerging evidence has demonstrated significant anti-inflammatory effects of astaxanthin (AST) in SE, the associated mechanism remains unclear. Therefore, this study aimed to clarify the effects of AST on P2X7R-related inflammation in SE.

Methods: SE was induced in rats using lithium-pilocarpine, and AST was administered 1 h after SE induction. Rat microglia were treated with lipopolysaccharide (LPS), AST, ATP, 2,3-O-4-benzoyl-4-benzoyl-ATP (BzATP) and oxidized ATP (oxATP). The Morris water maze, immunohistochemistry, and Nissl staining were performed in rats. Expressions of P2X7R and inflammatory cytokines (such as cyclooxygenase-2 (Cox-2), interleukin-1 β (IL-1 β), and tumor necrosis factor- α (TNF- α)) were detected using real-time polymerase

chain reaction (RT-PCR) and Western blot (WB) both in rats and microglia. ATP concentration in the microglia was evaluated using ELISA.

Results: The AST alleviated hippocampal injury and improved cognitive dysfunction induced by SE. AST also effectively inhibited inflammation and downregulated P2X7R expression in both rat brain and microglia. The results also showed that AST reduced the extracellular ATP levels and that P2X7R expression could be increased by extracellular ATP. In addition, BzATP upregulates the expression of P2X7R and inflammatory factors in microglia. Conversely, it downregulates the expression of P2X7R and inflammatory factors.

Conclusion: Our study suggests that AST attenuated ATP-P2X7R mediated inflammation in SE.

ASTAXANTHIN PROTECTS AGAINST NEUROTOXICITY IN MICE.

Food Chem Toxicol. 2020 Oct;144:111582.

doi: 10.1016/j.fct.2020.111582. Epub 2020 Jul 13.

Protective effect of astaxanthin against La₂O₃ nanoparticles induced neurotoxicity by activating PI3K/AKT/Nrf-2 signaling in mice

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Affiliations expand

- PMID: **32673631**
- DOI: [10.1016/j.fct.2020.111582](https://doi.org/10.1016/j.fct.2020.111582)

Abstract

Lanthanum oxide nanoparticles (La₂O₃ NPs) are used in photoelectric and catalytic applications. Astaxanthin (ASX) is a red carotenoid pigment with antioxidant and anti-inflammatory properties, and the antioxidant activities promote neuroprotection. This study explored the effect of ASX supplementation on La₂O₃ NP-induced neurotoxicity in mice and the molecular mechanisms of such protective effects. Amongst our findings, we determined that ASX treatment significantly attenuated La₂O₃ NP-induced behavioural abnormalities, histopathological evidence of hippocampal injury and ultrastructural changes in the CA1 region of the hippocampus. ASX treatment also markedly inhibited the production of ROS and activated PI3K/AKT signaling, which facilitated the nuclear translocation of Nrf-2 and reversed the down-regulation of HO-1, NQO1 and GCLM proteins in the hippocampus that were induced by sub-chronic exposure to La₂O₃ NPs. Administration of ASX to mice receiving La₂O₃ NPs also resulted in decreased expression of iNOS, IL-1 β , TNF- α , COX-2, Bax and Caspase-3 and in increased expression of BDNF, NGF and Bcl-2 observed in response to La₂O₃ NPs. In conclusion, ASX had a markedly protective effect against the negative sequelae associated with La₂O₃ NP-induced neurotoxicity. This may result from the activation of the PI3K/AKT/Nrf-2 signaling and via the inhibition of oxidative stress, neuroinflammation and cellular apoptosis.

ASTAXANTHIN PREVENTS COGNITIVE DEFICITS IN MICE.

J Neuroimmune Pharmacol. 2020 Sep 18.

doi: 10.1007/s11481-020-09953-4. Online ahead of print.

Astaxanthin Improved the Cognitive Deficits in APP/PS1 Transgenic Mice Via Selective Activation of mTOR

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- PMID: 32944864
- DOI: [10.1007/s11481-020-09953-4](https://doi.org/10.1007/s11481-020-09953-4)

Abstract

Astaxanthin (Ast) is an effective neuroprotective and antioxidant compound used to treat Alzheimer's disease (AD); however, the underlying in vivo molecular mechanisms remain unknown. In this study, we report that Ast can activate the mammalian target of rapamycin (mTOR) pathway in the 8-month-old APP/PS1 transgenic mouse model of AD. Our results suggest that Ast could ameliorate the cognitive defects in APP/PS1 mice by activating the mTOR pathway. Moreover, mTOR activation perturbed the mitochondrial dynamics, increased the synaptic plasticity after 21 days of treatment with Ast (10 mg/kg/day), and increased the expression of A β -degrading enzymes, mitochondrial fusion, and synapse-associated proteins and decreased the expression of mitochondrial fission proteins. Intraperitoneal injection of the mTOR inhibitor, rapamycin, abolished the effects of Ast. In conclusion, Ast activates the mTOR pathway, which is necessary for mitochondrial dynamics and synaptic plasticity, leading to improved learning and memory. Our results support the use of Ast for the treatment of cognitive deficits. Graphical abstract In summary, Ast ameliorates cognitive deficits via facilitating the mTOR-dependent mitochondrial dynamics and synaptic damage, and reducing A β accumulation. This model supports the use of Ast for the treatment of cognitive deficits.

ASTAXANTHIN PRETREATMENT IMPROVES RECOVERY FROM TRAUMATIC BRAIN INJURY IN MICE.

Front Neurol. 2020 Oct 15;11:999.

doi: 10.3389/fneur.2020.00999. eCollection 2020.

Cognitive Effects of Astaxanthin Pretreatment on Recovery From Traumatic Brain Injury

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- PMID: 33178093 PMCID: [PMC7593578](#) DOI: [10.3389/fneur.2020.00999](#) [Free PMC article](#)

Abstract

Traumatic brain injury (TBI), caused by mechanical impact to the brain, is a leading cause of death and disability among young adults, with slow and often incomplete recovery. Preemptive treatment strategies may increase the injury resilience of high-risk populations such as soldiers and athletes. In this work, the xanthophyll carotenoid Astaxanthin was examined as a potential nutritional preconditioning method in mice (sabra strain) to increase their resilience prior to TBI in a closed head injury (CHI) model. The effect of Astaxanthin pretreatment on heat shock protein (HSP) dynamics and functional outcome after CHI was explored by gavage or free eating (in pellet form) for 2 weeks before CHI. Assessment of neuromotor function by the neurological severity score (NSS) revealed significant improvement in the Astaxanthin gavage-treated group (100 mg/kg, ATX) during recovery compared to the gavage-treated olive oil group (OIL), beginning at 24 h post-CHI and lasting throughout 28 days ($p < 0.007$). Astaxanthin pretreatment in pellet form produced a smaller improvement in NSS vs. posttreatment at 7 days post-CHI ($p < 0.05$). Cognitive and behavioral evaluation using the novel object recognition test (ORT) and the Y Maze test revealed an advantage for Astaxanthin administration via free eating vs. standard chow during recovery post-CHI (ORT at 3 days, $p < 0.035$; improvement in Y Maze score from 2 to 29 days, $p < 0.02$). HSP profile and anxiety (open field test) were not significantly affected by Astaxanthin. In conclusion, astaxanthin pretreatment may contribute to improved recovery post-TBI in mice and is influenced by the form of administration.

ASTAXANTHIN PROTECTS COGNITIVE FUNCTION IN MOUSE MODEL OF VASCULAR DEMENTIA.

Behav Brain Funct. 2020 Nov 18;16(1):10.

doi: 10.1186/s12993-020-00172-8.

Astaxanthin protects cognitive function of vascular dementia

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PMID: [33208152](#) PMCID: [PMC7672991](#) DOI: [10.1186/s12993-020-00172-8](#) [Free PMC article](#)

Abstract

Objective: The purpose of this study was to evaluate the effect of astaxanthin (AST) on cognition function, inflammatory response and oxidative stress in vascular dementia (VD) mice.

Method: VD mice model was established by left unilateral common carotid arteries occlusion (LUCCAO). Following LUCCAO, AST was intragastrically administered for 30 days. Object recognition test and morris water maze test were used to evaluate cognitive function. Hematoxylin and eosin staining was performed to observe the hippocampal neuron structure. Enzyme-linked immunosorbent assay kit and bicinchoninic acid kit were respectively adopted to measure IL-1 β and IL-4 protein expression and superoxide dismutase (SOD) activity and malondialdehyde (MDA) content in hippocampus and prefrontal cortex.

Results: AST improved the discrimination ability of VD mice. The escape latency and path length of VD mice treated with AST were dramatically reduced. Besides, AST 200 mg/kg enhanced crossing platform time and the number of times crossing the platform quadrant, and alleviated the morphological impairment in VD mice. Moreover, we found that AST inhibited IL-1 β expression and MDA content, whereas promoted IL-4 expression and SOD activity in a dose-dependent manner.

Conclusion: AST could improve cognitive impairment and hippocampal neurons in VD mice, which may be related to suppression of inflammatory response and oxidative stress.

ASTAXANTHIN PREVENTS NEURON CELL DEATH, PROTECTS FROM BRAIN INJURY, AND REDUCES OXIDATIVE STRESS AFTER TRAUMATIC BRAIN INJURY IN MICE.

Br J Pharmacol. 2021 Mar;178(5):1114-1132.
doi: 10.1111/bph.15346. Epub 2021 Jan 15.

Astaxanthin ameliorates oxidative stress and neuronal apoptosis via SIRT1/NRF2/Prx2/ASK1/p38 after traumatic brain injury in mice

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PMID: 33326114 DOI: [10.1111/bph.15346](https://doi.org/10.1111/bph.15346)

Abstract

Background and Purpose: Oxidative stress and neuronal apoptosis play key roles in traumatic brain injury. We investigated the protective effects of astaxanthin against traumatic brain injury and its underlying mechanisms of action.

Experimental approach: A weight-drop model of traumatic brain injury in vivo and hydrogen peroxide exposure in vitro model were established. Brain oedema, behaviour tests, western blot, biochemical analysis, lesion volume, histopathological study and cell viability were performed.

Key Results: Astaxanthin significantly reduced oxidative insults on Days 1, 3 and 7 after traumatic brain injury. Neuronal apoptosis was also ameliorated on Day 3. Additionally, astaxanthin improved neurological functions up to 3 weeks after traumatic brain injury. Astaxanthin treatment dramatically enhanced the expression of peroxiredoxin 2 (Prx2), nuclear factor-erythroid 2-related factor 2 (NRF2/Nrf2) and sirtuin 1 (SIRT1), while it down-regulated the phosphorylation of apoptosis signal-regulating kinase 1 (ASK1) and p38. Inhibition of Prx2 by siRNA injection reversed the beneficial effects of astaxanthin against traumatic brain injury. Additionally, Nrf2 knockout prevented the neuroprotective effects of astaxanthin in traumatic brain injury. In contrast, overexpression of Prx2 in Nrf2 knockout mice attenuated the secondary brain injury after traumatic brain injury. Moreover, inhibiting SIRT1 by EX527 dramatically inhibited the neuroprotective effects of astaxanthin and suppressed SIRT1/Nrf2/Prx2/ASK1/p38 pathway both in vivo and in vitro.

Conclusion and implications: Astaxanthin improved the neurological functions and protected the brain from injury after traumatic brain injury, primarily by reducing oxidative stress and neuronal death via SIRT1/Nrf2/Prx2/ASK1/p38 signalling pathway and might be a new candidate to ameliorate traumatic brain injury.

ASTAXANTHIN PROTECTS BRAIN TISSUE IN RAT MODEL OF ALZHEIMER'S DISEASE.

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doi: 10.1007/s11010-021-04079-4. Online ahead of print.

Ameliorative effects of astaxanthin on brain tissues of alzheimer's disease-like model: cross talk between neuronal-specific microRNA-124 and related pathways

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Abstract

Alzheimer's disease (AD) is a chronic, progressive, multifactorial, and the most common neurodegenerative disease which causes dementia and mental deterioration in the elderly. The available treatments for AD are not disease-modifying drugs and only provide symptomatic relief. Astaxanthin (ATX), a second-generation antioxidant, is a dark red carotenoid and exhibits the highest antioxidant capacity, anti-inflammatory, neuroprotective, and antiapoptotic effects. In this study, we investigated the therapeutic effect of different doses of ATX on the cerebral cortex and hippocampus of AD-like rats. The AD-like model was induced in rats using hydrated aluminum chloride ($\text{AlCl}_3 \cdot 6\text{H}_2\text{O}$) solution that was given orally at a dose of 75 mg/kg daily for 6 weeks. Morris water maze (MWM) behavioral test was performed to confirm the cognitive dysfunction then AD-like rats were orally treated with different doses of ATX (5, 10, and 15 mg/kg) dissolved in dimethyl sulfoxide (DMSO) for six weeks. The results indicated that ATX significantly and dose-dependently improved the performance of AD-like rats treated with ATX during MWM and suppress the accumulation of amyloid β_{1-42} and malondialdehyde. Also, significantly inhibit acetylcholinesterase and monoamine oxidase activities and the expression of β -site amyloid precursor protein cleaving enzyme 1 (BACE 1). ATX also significantly elevated the content of acetylcholine, serotonin, and nuclear factor erythroid-2-related factor 2 (Nrf2) and miRNA-124 expression. The effect of ATX treatment was confirmed by histopathological observations using H&E stain and morphometric tissue analysis. From this study, we concluded that ATX may be a promising therapeutic agent for AD through targeting different pathogenic pathways.

ASTAXANTHIN WORKS ON MULTIPLE MALADIES ASSOCIATED WITH SPINAL CORD INJURY IN RAT MODEL AND APPEARS TO BE A STRONG POTENTIAL THERAPEUTIC AGENT FOR CLINICAL APPLICATIONS.

Eur J Pain. 2019 Apr;23(4):750-764.
doi: 10.1002/ejp.1342. Epub 2018 Dec 10.

Effects of astaxanthin on sensory-motor function in a compression model of spinal cord injury: Involvement of ERK and AKT signalling pathway

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- PMID: [30427581](#)
- DOI: [10.1002/ejp.1342](#)

Abstract

Background: Spinal cord injury (SCI) causes continuous neurological deficits and major sensory-motor impairments. There is no effective treatment to enhance sensory-motor function following SCI. Thus, it is crucial to develop novel therapeutics for this particular patient population. Astaxanthin (AST) is a strong antioxidant, anti-inflammatory and anti-apoptotic agent. In the present study, it was tested in a severe compression SCI model with emphasis on sensory-motor outcomes, signalling pathway, along with other complications.

Methods: A severe SCI was induced by compression of the rat thoracic spinal cord with an aneurysm clip and treatment with AST or the vehicle was carried out, 30 min after injury. Behavioural tests including open field, von Frey, hot plate and BBB were performed weekly to 28 days post-injury. Rats were assigned to measure blood glucose, weight and auricle temperature. Western blot and histological analysis also were performed at the same time points.

Results: AST decreased mechanical and thermal pain and also improved motor function performance, reduced blood glucose and auricle temperature increases and attenuated weight loss in SCI rats. Western blot analysis showed decreased activation of ERK1/2 and increased activation of AKT following AST treatment. The histology results revealed that AST considerably preserved myelinated white matter and the number of motor neurons following SCI.

Conclusion: Taken together, the beneficial effects of AST to improve sensory-motor outcomes, attenuate pathological tissue damage and modulate ERK and AKT signalling pathways following SCI, suggest it as a strong therapeutic agent towards clinical applications.

Significance: Spinal cord injury (SCI) impairs sensory-motor function and causes complications, which astaxanthin (AST) has the potential to be used as a treatment for. The present study investigates the effects of AST in a compression model of SCI with emphasis on sensory-motor outcomes alongside other complications, histopathological damage and also related signalling pathways.

ASTAXANTHIN SHOWS NEUROPROTECTIVE EFFECT IN RAT STUDY.

Front Cell Neurosci. 2019 Mar 29;13:123.

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The Neuroprotective Effect of Astaxanthin on Pilocarpine-Induced Status Epilepticus in Rats

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- PMCID: [PMC6449650](#)
- DOI: [10.3389/fncel.2019.00123](#)

Free PMC article

Abstract

Cognitive dysfunction is one of the serious complications induced by status epilepticus (SE), which has a significant negative impact on patients' quality of life. Previous studies demonstrated that the pathophysiological changes after SE such as oxidative stress, inflammatory reaction contribute to neuronal damage. A recent study indicated that preventive astaxanthin (AST) alleviated epilepsy-induced oxidative stress and neuronal apoptosis in the brain. In the present study, rats were treated with vehicle or AST 1 h after SE onset and were injected once every other day for 2 weeks (total of seven times). The results showed that the cognitive function in SE rats was significantly impaired, and AST treatment improved cognitive function in the Morris water maze (MWM). Magnetic resonance imaging (MRI), hematoxylin-eosin (HE) staining and TdT-mediated dUTP Nick-End Labeling (TUNEL) staining showed obvious damage in the hippocampus of SE rats, and AST alleviated the damage. Subsequently, we evaluated the effect of AST on relative pathophysiology to elucidate the possible mechanisms. To evaluate the oxidative stress, the expression of malondialdehyde (MDA) and superoxide dismutase (SOD) in plasma were detected using commercially available kits. NADPH oxidase-4 (Nox-4), p22phox, NF-E2-related factor 2 (Nrf-2), heme oxygenase 1 (Ho-1) and sod1 in the parahippocampal cortex and hippocampus were detected using western blot and real-time polymerase chain reaction (RT-PCR). The levels of MDA in plasma and Nox-4

and p22phox in the brain increased in SE rats, and the levels of SOD in plasma and Nrf-2, Ho-1 and sod1 in the brain decreased. Treatment with AST alleviated these changes. We also detected the levels of inflammatory mediators like cyclooxygenase-2 (cox-2), interleukin-1 β (IL-1 β), tumor necrosis factor- α (TNF- α) and NF- κ B phosphorylation p65 (p-p65)/p65 in the brain. The inflammatory reaction was significantly activated in the brain of SE rats, and AST alleviated neuroinflammation. We detected the levels of p-Akt, Akt, B-cell lymphoma-2 (Bcl-2), Bax, cleaved caspase-3, and caspase-3 in the parahippocampal cortex and hippocampus using western blot. The levels of p-Akt/Akt and Bcl-2 decreased in SE rats, Bax and cleaved caspase-3/caspase-3 increased, while AST alleviated these changes. The present study indicated that AST exerted an obvious neuroprotective effect in pilocarpine-induced SE rats.

ASTAXANTHIN IMPROVES EFFICACY OF STEM CELL THERAPY FOR BEHAVIORAL DYSFUNCTION AND MOTOR NEURON LOSS IN RAT MODEL OF SPINAL CORD INJURY.

Mitochondrion. 2020 May;52:125-134.
doi: 10.1016/j.mito.2020.03.002. Epub 2020 Mar 6.

Combination therapy with astaxanthin and epidermal neural crest stem cells improves motor impairments and activates mitochondrial biogenesis in a rat model of spinal cord injury

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PMID: 32151747 DOI: [10.1016/j.mito.2020.03.002](https://doi.org/10.1016/j.mito.2020.03.002)

Abstract

Spinal cord injury (SCI), a multifactorial disease, can lead to irreversible motor and sensory disabilities. Cell therapy in combination with pharmacological agents can be a promising approach to attenuate SCI damages. Epidermal neural crest stem cells (EPI-NCSCs) extracted from bulge hair follicle in adults are attractive candidates due to the possibility of autologous transplantation. This study evaluated the effect of EPI-NCSCs combined with astaxanthin (Ast), a potent antioxidant, on damages induced by SCI. Male rats were treated with Ast (0.2 mM) and EPI-NCSCs ($10^6/10 \mu\text{l}$ PBS) alone and combined together after SCI contusion. Motor function was assessed by Basso, Beattie and Bresnahan (BBB) test on days 1, 3, 7, 14, 21, 28, 35 and 42 post-injury. Motor neurons number and myelin level were evaluated on days 14 and 42 using Nissl and Luxol Fast Blue staining. The gene expression of mitochondrial biogenesis involved factors (PGC1 α , NRF1 and TFAM) was measured by qPCR. All treatments improved motor function, with the highest BBB score in Ast + Cell compared to Ast and Cell. Decreased motor neurons number and myelin level following SCI, were increased by Ast, Cell and Ast + Cell, but combination therapy significantly had a better effect. We observed reduction in PGC1 α , NRF1, and TFAM expression in spinal tissue after SCI, and treatment with Cell and Ast + Cell significantly restored NRF1 and TFAM mRNA levels. These results suggested that Ast in combination with EPI-NCSCs has better effects on behavioral dysfunction, motor neuron loss and demyelination after SCI. These protective effects may be attributed to mitochondrial biogenesis activation.

ASTAXANTHIN SHOWS POTENTIAL ANTI-EPILEPTIC EFFECT IN RATS TREATED WITH ANTI-EPILEPSY DRUG VALPROIC ACID BY REDUCING OXIDATIVE STRESS.

Saudi Pharm J. 2021 May;29(5):418-426.

doi: 10.1016/j.jsps.2021.04.002. Epub 2021 Apr 9.

The potential antiepileptic activity of astaxanthin in epileptic rats treated with valproic acid

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- PMID: [34135667](#)
- PMCID: [PMC8180462](#)
- DOI: [10.1016/j.jsps.2021.04.002](#)

Free PMC article

Abstract

Objectives: Epilepsy is a neurological disease characterized by sudden, abnormal, and hyper- discharges in the central nervous system (CNS). Valproic acid (VPA) is commonly used as a broad-spectrum antiepileptic therapeutic. However, in many cases, patients develop resistance to VPA treatment due to overwhelming oxidative stress, which in turn might be a major catalyst for disease progression. Therefore, antioxidants can potentially become therapeutic agents by counteracting reactive oxygen species (ROS)-mediated damage. The present study is aimed to evaluate the potential antiepileptic effect of astaxanthin (ASTA) in pentylenetetrazol (PTZ) induced epileptic model rats that are chronically treated with VPA for 8 weeks.

Method: Fifty-male Wistar rats were randomly divided into five groups: Non-PTZ group, PTZ, PTZ/VPA, PTZ/ASTA, and PTZ/VPA/ASTA treated groups.

Results: PTZ/VPA treated group showed a neuroprotective effect with improvement in antioxidant levels, behavioral test, and histopathological changes induced by PTZ. VPA also exhibited an anti-inflammatory effect as its treatment resulted in the reduction of tumor necrosis factor- α (TNF- α). ASTA exhibited an anticonvulsant effect and enhanced

anti-inflammatory effect as compared to VPA. During the combined therapy, ASTA potentiated the antiepileptic effect of the VPA by reducing the oxidative stress and TNF- α as well as increased the glutathione (GSH) levels. Also, there were substantial improvements in the behavioral and histopathological changes in the VPA/ASTA treated group as compared to the VPA treated group.

Conclusion: ASTA could have an antiepileptic and anti-inflammatory effect by reducing ROS generation. Therefore, co-administration of both the therapeutics (VPA/ASTA) has a synergistic effect in treating epilepsy and could potentially minimize recurrence and/or exacerbation of seizures.

ASTAXANTHIN IMPROVES COGNITION AND LEARNING IN MICE WITH NEUROINFLAMMATION.

Food Funct. 2021 Jun 21;12(12):5333-5350.

doi: 10.1039/d0fo03018j. Epub 2021 May 12.

Development of astaxanthin-loaded layer-by-layer emulsions: physicochemical properties and improvement of LPS-induced neuroinflammation in mice

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- PMID: 33977957 DOI: [10.1039/d0fo03018j](https://doi.org/10.1039/d0fo03018j)

Abstract

Astaxanthin (AST) has been shown to have neuroprotective effects; however, its bioavailability in vivo is low due to its hydrophobic properties. In this study, lactoferrin (LF) was prepared by heat-treatment at different temperatures, and on this basis, a layer-by-layer self-assembly method was used to construct double-layer emulsions with LF as the inner layer and polysaccharide (beet pectin, BP or carboxymethyl chitosan, CMCS) as the outer layer. Then AST was encapsulated in the emulsions and their physicochemical properties and function were investigated. The results indicated that high temperature heated LF (95 °C) showed a more stable structure than the lower temperature one, and the exposed internal nonpolar groups of LF could give the emulsion an enhanced stability. The rheology results showed that compared with CMCS, the double-layer emulsion formed by BP had a higher viscosity. In addition, the 95 °C LF-AST-BP emulsion showed the best stability among all the bilayer emulsions. The best emulsion was then used as a model drug to investigate its effects on lipopolysaccharide (LPS)-induced neuroinflammation and learning-memory loss in C57BL/6J mice. Through animal behavioral experiments, it was found that dietary supplementation with the AST emulsion could effectively improve the brain cognitive and learning memory impairment caused by inflammation. Transmission electron microscopy, mRNA and western blotting results also illustrated that the AST emulsion could alleviate neuroinflammation caused by LPS. This study provides a feasible scheme for exploring an AST loaded system and may be suitable for food and drug applications.

ASTAXANTHIN LOADED LEPIDIC NANOPARTICULATE GEL SHOWS POTENTIAL AGAINST PARKINSON'S DISEASE IN RATS SUFFERING FROM NEUROTOXICITY.

Curr Drug Deliv. 2021 May 10.

doi: 10.2174/1567201818666210510173524. Online ahead of print.

Appraisal of Nano-lipidic Astaxanthin cum Thermoreversible Gel and its Efficacy in Haloperidol Induced Parkinsonism

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- PMID: 33970844 DOI: [10.2174/1567201818666210510173524](https://doi.org/10.2174/1567201818666210510173524)

Abstract

Background: Parkinsonism has a toxic cascade of neurodegeneration, with akinesia as a major manifestation. Some antioxidants have shown promise against the disease. Astaxanthin is a powerful antioxidant, demonstrates free radical scavenging, and is also a potential neuroprotective agent.

Objective: To formulate astaxanthin laden nanostructured lipid carriers based thermoreversible gel for better neuronal uptake and better neuronal efficacy.

Methods: The method for fabricating astaxanthin-nanostructured lipid carriers (ATX-NLC) was melt-emulsification, and these were optimized using factorial design and further evaluated for diverse parameters. Neurotoxicity was induced in rats by haloperidol. The treated and non-treated rats were then witnessed for their behaviour. TBARs and GSH levels were also determined. Pharmacokinetics was studied via HPLC.

Results: The average particle size (by DLS), entrapment efficiency and zeta potential of optimized ATX-NLC were 225.6 ± 3.04 nm, 65.91 ± 1.22 % and -52.64 mV respectively. Astaxanthin release (after 24 h in simulated nasal fluid) from optimized ATX-NLC was 92.5 ± 5.42 %. Its thermo-reversible nasal gel (ATX-NLC in-situ gel) was prepared using poloxamer-127. The obtained gel showed in-vivo betterment in the behaviour of animals when studied using rotarod and akinesia test. Pharmacokinetic studies showed

better availability of astaxanthin in the brain on the rats treated with ATX-NLC in-situ gel as compared to those treated with ATX-in-situ gel.

Conclusion: Astaxanthin loaded lipidic nanoparticulate gel can be a hopeful adjuvant therapy for Parkinsonism and holds scope for future studies.

ASTAXANTHIN SHOWS POTENTIAL TO SLOW THE PROGRESSION OF ALZHEIMER'S DISEASE IN RAT MODEL.

Brain Res Bull. 2021 Jul;172:151-163.

doi: 10.1016/j.brainresbull.2021.04.020. Epub 2021 Apr 28.

The effects of astaxanthin treatment on a rat model of Alzheimer's disease

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- PMID: 33932491 DOI: [10.1016/j.brainresbull.2021.04.020](https://doi.org/10.1016/j.brainresbull.2021.04.020) **Free article**

Abstract

Alzheimer's disease (AD), a progressive neurodegenerative disorder characterized by memory loss and dementia, could be a consequence of the abnormalities of cortical milieu, such as oxidative stress, inflammation, and/or accompanied with the aggregation of β -amyloid. The majority of AD patients are sporadic, late-onset AD, which predominantly occurs over 65 years of age. Our results revealed that the ferrous amyloid buthionine (FAB)-infused sporadic AD-like model showed deficits in spatial learning and memory and with apparent loss of choline acetyltransferase (ChAT) expression in medial septal (MS) nucleus. In hippocampal CA1 region, the loss of pyramidal neurons was accompanied with cholinergic fiber loss and neuroinflammatory responses including glial reaction and enhanced expression of inducible nitric oxide synthase (iNOS). Surviving hippocampal CA1 pyramidal neurons showed the reduction of dendritic spines as well. Astaxanthin (ATX), a potent antioxidant, reported to improve the outcome of oxidative-stress-related diseases. The ATX treatment in FAB-infused rats decreased neuroinflammation and restored the ChAT + fibers in hippocampal CA1 region and the ChAT expression in MS nucleus. It also partly recovered the spine loss on hippocampal CA1 pyramidal neurons and ameliorated the behavioral deficits in AD-like rats. From these data, we believed that the ATX can be a potential option for slowing the progression of Alzheimer's disease.

ASTAXANTHIN SHOWS NEUROPROTECTIVE EFFECTS IN A MOUSE MODEL OF TRAUMATIC BRAIN INJURY.

Am J Transl Res. 2021 Mar 15;13(3):1483-1493.

eCollection 2021.

Astaxanthin provides neuroprotection in an experimental model of traumatic brain injury via the Nrf2/HO-1 pathway

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- PMID: [33841672](#) PMCID: [PMC8014407](#) [Free PMC article](#)

Abstract

Background: Astaxanthin (ATX) is a carotenoid pigment with effective antioxidant, anti-inflammatory, antitumor and immunomodulatory actions. ATX has been proposed to exert neuroprotective effects and attenuate oxidative stress in mice after traumatic brain injury (TBI). The nuclear factor erythroid 2-related factor 2 (Nrf2)-heme oxygenase 1 (HO-1) signaling pathway is stimulated after TBI and activates a compensatory mechanism against TBI. Nevertheless, the effect of ATX on the pathophysiology of TBI in mice is limited. Our present study evaluated the neuroprotection afforded by ATX and the possible role of the Nrf2/HO-1 pathway in experimental TBI.

Materials and methods: Mice were casually separated into 3 groups: the sham, TBI + vehicle, and TBI + ATX (100 mg/kg, intraperitoneally administered) groups. Neurobehaviors of the mice were assessed using the neurological severity scores (NSSs), the forced swimming test (FST) and the rotarod test. Levels of the Nrf2, HO-1, NAD(P)H: quinine oxidoreductase-1 (NQO1), cleaved caspase3 (C-caspase3), and superoxide dismutase1 (SOD1) proteins and levels of the Nrf2 and HO-1 mRNAs were assessed. In addition, Nrf2 nuclear import and apoptosis were measured after TBI.

Results: The ATX treatment significantly improved the neurological status, promoted Nrf2 activation, and upregulated the expression of the Nrf2 and HO-1 mRNAs and the levels of the Nrf2, HO-1, and NQO1 proteins after TBI. The level of the SOD1 protein was decreased after TBI and increased after ATX treatment; however, the difference was not significant. ATX markedly reduced the level of the C-caspase3 protein and the number of TUNEL-positive cells, indicating that it exerted an antiapoptotic effect. Immunofluorescence staining confirmed that ATX promoted Nrf2 nuclear import.

ASTAXANTHIN IMPROVES NEUROLOGICAL FUNCTION AND REDUCES BRAIN DAMAGE IN RATS THAT SUFFER A STROKE.

Curr Res Transl Med. 2021 May;69(2):103271.

doi: 10.1016/j.retram.2020.103271. Epub 2021 Jan 18.

Astaxanthin attenuates acute cerebral infarction via Nrf-2/HO-1 pathway in rats

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- PMID: 33476935 DOI: [10.1016/j.retram.2020.103271](https://doi.org/10.1016/j.retram.2020.103271)

Abstract

Objective: Acute cerebral infarction (ACI) is susceptible to cause disability or death of people. Astaxanthin (ATX) possesses the protective effect of organ injury. Therefore, the study was to explore the potential mechanism of protective effect with ATX on ACI.

Methods: 30 SD rats were divided into Sham, ACI, and ATX groups. The rats in the ATX group were pretreated with ATX by gavage for three days before surgery, while the rats in the other two groups were pretreated with saline. The model of ACI was established by thread embolization. 24 h after the operation, the neurological function was scored, and cerebral infarct area and pathological morphology of brains were measured; the edema of the brain was detected by dry/wet method; Western blot was applied to measure the translocation of Nrf-2 and the protein expression of HO-1, Bax and BCL-2; Brain cell apoptosis was assessed through TUNEL; ELISA was used to detect the oxidative stress factors of catalase (CAT) superoxide dismutase (SOD), glutathione peroxidase (GPX) and malondialdehyde (MDA), and the inflammatory factors of TNF- α , IL-1 β , IL-6.

Result: Compared with the ACI group, ATX pretreatment can significantly improve neurological function; reduce the edema index of the brain, cerebral infarct area, cerebral pathological damage and apoptosis of brain cells. Moreover, ATX also can increase the protein expression of nuclear Nrf-2, HO-1, BCL-2, CAT, SOD, and GPX by decreasing the content of TNF- α , IL-1 β , IL-6, MDA, Bax and cytosolic Nrf-2.

Conclusion: ATX might have a protective effect of acute cerebral infarction, and the mechanism is probably associated with suppressing oxidative stress, inflammation, and apoptosis by activating Nrf-2/HO-1 signalling.

Astaxanthin shows anti-hypertensive and neuroprotective effects in rats.

January 2005 Biol. Pharm. Bull. 28(1) 47—52 (2005) 47

Antihypertensive and Neuroprotective Effects of Astaxanthin in Experimental Animals

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Astaxanthin is a natural antioxidant carotenoid that occurs in a wide variety of living organisms. We investigated, for the first time, antihypertensive effects of astaxanthin (ASX-O) in spontaneously hypertensive rats (SHR). Oral administration of ASX-O for 14 d induced a significant reduction in the arterial blood pressure (BP) in SHR but not in normotensive Wistar Kyoto (WKY) strain. The long-term administration of ASX-O (50 mg/kg) for 5 weeks in stroke prone SHR (SHR-SP) induced a significant reduction in the BP. It also delayed the incidence of stroke in the SHR-SP. To investigate the action mechanism of ASX-O, the effects on PGF₂a-induced contractions of rat aorta treated with NG-nitro-l-arginine methyl ester (L-NAME) were studied in vitro. ASX-O (1 to 10mM) induced vasorelaxation mediated by nitric oxide (NO). The results suggest that the antihypertensive effect of ASX-O may be due to a NO-related mechanism. ASX-O also showed significant neuroprotective effects in ischemic mice, presumably due to its antioxidant potential. Pretreatment of the mice with ASX-O significantly shortened the latency of escaping onto the platform in the Morris water maze learning performance test. In conclusion, these results indicate that astaxanthin can exert beneficial effects in protection against hypertension and stroke and in improving memory in vascular dementia.

Astaxanthin's neuroprotective effects demonstrated in rat model of spinal cord injury.

[Behav Brain Res.](#) 2017 Jun 30;329:104-110. doi: 10.1016/j.bbr.2017.04.026. Epub 2017 Apr 23.

Neuroprotective effects of astaxanthin in a rat model of spinal cord injury.

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Author information

Abstract

Spinal cord injury (SCI) often leads to constant neurological deficits and long-term unalterable disability. Apoptosis plays an important role in the initiation of the secondary injury cascades leading to progressive tissue damage and severely functional deficits after SCI. Although the primary mechanical destructive events cannot be reversed, a therapeutic intervention could be carried out in order to moderate the secondary injury damage several hours to weeks after injury. Astaxanthin (AST) is a strong antioxidant and anti-inflammatory agents with the potential to render anti-apoptotic and neuroprotective effects. In the current study, we examined the therapeutic potential of AST on adult rats after severe SCI contusion. Results of BBB scores showed that AST improved motor function after SCI compared to control groups. Western blot analysis showed reduced expression of Bax and Cleaved-caspase-3 proteins and increased expression of the Bcl-2 protein in response to AST treatment ($p < 0.05$). The histology results also showed that AST considerably preserved myelinated white matter and the number of motor neurons. This study is the first to report that AST reduces neuronal apoptosis, diminishes pathological tissue damage and improves functional recovery after SCI. The observed prominent neuroprotective effects, introduces AST as a promising therapy for SCI.

KEYWORDS:

Apoptosis; Astaxanthin; Neuroprotection; Spinal cord injury

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[Indexed for MEDLINE]

Astaxanthin in the trans form shows antidepressant potential in rodent model.

[Oncotarget](#). 2017 Apr 11;8(15):25552-25563. doi: 10.18632/oncotarget.16069.

The antidepressant-like effect of trans-astaxanthin involves the serotonergic system.

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Author information

Abstract

The antidepressant-like effect of trans-astaxanthin, a compound present rich in algae, was evaluated through behavioral and neurochemical methods. Results showed that trans-astaxanthin treatment significantly decreased the immobility time in force swim test and tail suspension test, but did not influence locomotor activity. Trans-astaxanthin treatment did not effectively antagonize hypothermia and ptosis induced by reserpine. However, pre-treatment with para-chlorophenylalanine abolished the anti-immobility effect of trans-astaxanthin in force swim and tail suspension test. These results suggested that the mechanism of antidepressant-like effect of trans-astaxanthin may involve the serotonergic system, but not noradrenaline system. This hypothesis was confirmed by neurochemical assays which showed that trans-astaxanthin increased serotonin levels in the hippocampus, frontal cortex, striatum and hypothalamus. Furthermore, our data suggested that trans-astaxanthin decreased indoleamine 2, 3-dioxygenase activity in the hippocampus, frontal cortex and hypothalamus. Inhibition of indoleamine 2,3-dioxygenase activity subsequently decreased the kynurenine/tryptophan ratio and increased the serotonin/tryptophan ratio in these brain regions. Taken together, these findings indicate that the antidepressant-like effect of trans-astaxanthin involves the serotonergic system.

KEYWORDS:

3-dioxygenase (IDO); depression; indoleamine 2; monoamine oxidase (MAO); serotonin (5-HT); trans-astaxanthin

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PMCID: [PMC5421950](#)

DOI: [10.18632/oncotarget.16069](#)

[Indexed for MEDLINE]

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Astaxanthin has neuroprotective effects and reduces inflammation and oxidative stress in diabetic rats.

[PLoS One](#). 2016 Jan 14;11(1):e0146438. doi: 10.1371/journal.pone.0146438. eCollection 2016.

Astaxanthin Inhibits Expression of Retinal Oxidative Stress and Inflammatory Mediators in Streptozotocin-Induced Diabetic Rats.

[Yeh PT](#)^{1,2}, [Huang HW](#)³, [Yang CM](#)^{1,4}, [Yang WS](#)^{5,6}, [Yang CH](#)^{1,4}.

Abstract

PURPOSE: We evaluated whether orally administered astaxanthin (AST) protects against oxidative damage in the ocular tissues of streptozotocin (STZ)-induced diabetic rats.

METHODS AND RESULTS: Fifty 6-week-old female Wistar rats were randomly assigned to receive an injection of STZ to induce diabetes (n = 40) or to remain uninduced (n = 10). The diabetic rats were randomly selected into four groups and they were separately administered normal saline, 0.6 mg/kg AST, 3 mg/kg AST, or 0.5 mg/kg lutein daily for eight weeks. Retinal functions of each group were evaluated by electroretinography. The expression of oxidative stress and inflammatory mediators in the ocular tissues was then assessed by immunohistochemistry, western blot analysis, ELISA, RT-PCR, and electrophoretic mobility shift assay (EMSA). Retinal functions were preserved by AST and lutein in different levels. Ocular tissues from AST- and lutein-treated rats had significantly reduced levels of oxidative stress mediators (8-hydroxy-2'-deoxyguanosine, nitrotyrosine, and acrolein) and inflammatory mediators (intercellular adhesion molecule-1, monocyte chemoattractant protein-1, and fractalkine), increased levels of antioxidant enzymes (heme oxygenase-1 and peroxiredoxin), and reduced activity of the transcription factor nuclear factor-kappaB (NF-κB).

CONCLUSION: The xanthophyll carotenoids AST and lutein have neuroprotective effects and reduce ocular oxidative stress, and inflammation in the STZ diabetic rat model, which may be mediated by downregulation of NF-κB activity.

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PMCID: [PMC4713224](#)

DOI: [10.1371/journal.pone.0146438](#)

[Indexed for MEDLINE]

[Free PMC Article](#)

Astaxanthin outperforms fish oil and krill oil in reducing neural inflammation in rats.

[Mar Drugs](#). 2015 Sep 28;13(10):6117-37. doi: 10.3390/md13106117.

Redox Status and Neuro Inflammation Indexes in Cerebellum and Motor Cortex of Wistar Rats Supplemented with Natural Sources of Omega-3 Fatty Acids and Astaxanthin: Fish Oil, Krill Oil, and Algal Biomass.

[Polotow TG](#)¹, [Poppe SC](#)², [Vardaris CV](#)³, [Ganini D](#)^{4,5}, [Guariroba M](#)⁶, [Mattei R](#)⁷, [Hatanaka E](#)⁸, [Martins MF](#)^{9,10}, [Bondan EF](#)^{11,12}, [Barros MP](#)¹³.

Author information

Abstract

Health authorities worldwide have consistently recommended the regular consumption of marine fishes and seafood to preserve memory, sustain cognitive functions, and prevent neurodegenerative processes in humans. Shrimp, crabs, lobster, and salmon are of particular interest in the human diet due to their substantial provision of omega-3 fatty acids (n-3/PUFAs) and the antioxidant carotenoid astaxanthin (ASTA). However, the optimal ratio between these nutraceuticals in natural sources is apparently the key factor for maximum protection against most neuro-motor disorders. Therefore, we aimed here to investigate the effects of a long-term supplementation with (n-3)/PUFAs-rich fish oil, ASTA-rich algal biomass, the combination of them, or krill oil (a natural combination of both nutrients) on baseline redox balance and neuro-inflammation indexes in cerebellum and motor cortex of Wistar rats. Significant changes in redox metabolism were only observed upon ASTA supplementation, which reinforce its antioxidant properties with a putative mitochondrial-centered action in rat brain. Krill oil imposed mild astrocyte activation in motor cortex of Wistar rats, although no redox or inflammatory index was concomitantly altered. In summary, there is no experimental evidence that krill oil, fish oil, or algal biomass (minor variation), drastically change the baseline oxidative conditions or the neuro-inflammatory scenario in neuromotor-associated rat brain regions.

KEYWORDS:

Alzheimer; DHA; EPA; Parkinson; aging; antioxidant; brain; carotenoid; hormesis; senescence

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Free PMC Article

Astaxanthin provides neuroprotection by suppressing reactive oxygen species in rats after stroke was induced.

[Brain Res Bull.](#) 2017 Apr;130:211-220. doi: 10.1016/j.brainresbull.2017.01.024. Epub 2017 Feb 1.

Preventive treatment of astaxanthin provides neuroprotection through suppression of reactive oxygen species and activation of antioxidant defense pathway after stroke in rats.

[Pan L](#)¹, [Zhou Y](#)², [Li XF](#)³, [Wan QJ](#)⁴, [Yu LH](#)⁵.

Author information

Abstract

Astaxanthin, a natural antioxidant carotenoid, has been shown to reduce cerebral ischemic injury in rodents. However, there have not been any studies specifically addressing whether preventive administration of astaxanthin can protect against cerebral ischemia. The purpose of this study was to examine whether pretreatment of astaxanthin can protect against ischemic injuries in the adult rats. The rats were pre-administered intragastrically with astaxanthin for seven days (once a day), and middle cerebral artery occlusion was performed at 1h after the final administration. It was found that astaxanthin prevented neurological deficits and reduced cerebral infarction volume. To evaluate the mechanisms underlying this protection, brain tissues were assayed for free radical damage, antioxidant gene expression, cell apoptosis and regeneration. The results showed that the mechanisms involved suppression of reactive oxygen species, activation of antioxidant defense pathway, and inhibition of apoptosis as well as promotion of neural regeneration. Astaxanthin did not alter body weights and the protective effect was found to be dose-dependent. Collectively, our data suggest that pretreatment of astaxanthin can protect against ischemia-related damages in brain tissue through multiple mechanisms, hinting that astaxanthin may have significant protective effects for patients vulnerable or prone to ischemic events.

KEYWORDS:

Astaxanthin; Cerebral ischemia; Mechanisms; Protective effects; Rats

PMID: 28161193

DOI: [10.1016/j.brainresbull.2017.01.024](https://doi.org/10.1016/j.brainresbull.2017.01.024)

[Indexed for MEDLINE]

Astaxanthin improves proliferative capacity in neural stem cells.

[Food Chem Toxicol.](#) 2010 Jun;48(6):1741-5. Epub 2010 Apr 9.

Astaxanthin improves the proliferative capacity as well as the osteogenic and adipogenic differentiation potential in neural stem cells.

[Kim JH](#), [Nam SW](#), [Kim BW](#), [Kim WJ](#), [Choi YH](#).

Department of Biomaterial Control, Dong-Eui University, Busan, South Korea.

Abstract

In the present study, the effect of astaxanthin on improvement of the proliferative capacity as well as the osteogenic and adipogenic differentiation potential in neural stem cells (NSCs) was evaluated. Treatment of astaxanthin-induced activates cell growth in a dose-dependent and time-dependent manner. Results from a clonogenic assay clearly indicated that astaxanthin can actively stimulate proliferation of NSCs. Astaxanthin-induced improvement in the proliferative capacity of NSCs resulted in overexpression of several proliferation-related proteins.

Astaxanthin-induced activation of PI3K and its downstream mediators, p-MEK, p-ERK, and p-Stat3 in NSCs resulted in subsequent induction of expression of proliferation-related transcription factors (Rex1, CDK1, and CDK2) and stemness genes (OCT4, SOX2, Nanog, and KLF4). Astaxanthin also improved the osteogenic and adipogenic differentiation potential of NSCs. Astaxanthin-treated NSCs showed prominent calcium deposits and fat formation. These results were consistent with overexpression of osteogenesis-related genes (osteonectin, RXR, and osteopontin) and adipogenesis-related genes (AP and PPAR-gamma) after astaxanthin treatment. These findings clearly demonstrated that astaxanthin acts synergistically on the regulatory circuitry that controls proliferation and differentiation of NSCs. Copyright 2010 Elsevier Ltd. All rights reserved.

PMID: 20385192 [PubMed – in process]

Astaxanthin shows a protective effect against cytotoxicity in neuroblastoma cells.

[Brain Res.](#) 2010 Sep 7. [Epub ahead of print]

Astaxanthin upregulates heme oxygenase-1 expression through ERK1/2 pathway and its protective effect against beta-amyloid-induced cytotoxicity in SH-SY5Y cells.

[Wang HQ](#), [Sun XB](#), [Xu YX](#), [Zhao H](#), [Zhu QY](#), [Zhu CQ](#).

Abstract

Astaxanthin (ATX), the most abundant flavonoids in propolis, has been proven to exert neuroprotective property against glutamate-induced neurotoxicity and ischemia-reperfusion-induced apoptosis. Previous study have revealed that ATX can rescue PC12 cells from A β (25-35)-induced apoptotic death. However, the mechanisms by which ATX mediates its therapeutic effects in vitro are unclear. In the present study, we explored the underlying mechanisms involved in the protective effects of ATX on the A β (25-35)-induced cytotoxicity in SH-SY5Y cells. Pre-treatment with ATX for 4h significantly reduced the A β (25-35)-induced viability loss, apoptotic rate and attenuated A β -mediated ROS production. In addition, ATX inhibited A β (25-35)-induced lowered membrane potential, decreased Bcl-2/Bax ratio. We also demonstrated that ATX could prevent the activation of p38MAPK kinase pathways induced by A β . Moreover, we for the first time have revealed the ATX increased antioxidant enzyme heme oxygenase-1 (HO-1) expression in concentration-dependent and time-dependent manners, which were correlated with its protective effect against A β (25-35)-induced injury. Because the inhibitor of HO-1 activity, ZnPP reversed the protective effect of ATX against A β (25-35)-induced cell death. We also demonstrated that the specific ERK inhibitor, PD98059, concentration-dependently blocked on ATX-induced HO-1 expression, and meanwhile PD98059 reversed the protective effect of ATX against A β 25-35-induced cell death. Taken together, these findings suggest that astaxanthin can induce HO-1 expression through activation of ERK signal pathways, thereby protecting the SH-SY5Y cells from A β (25-35)-induced oxidative cell death.

PMID: 20828541 [PubMed - as supplied by publisher]

Astaxanthin shows neuroprotective, antioxidative and anti-inflammatory effects in-vitro.

[J Food Sci.](#) 2009 Sep;74(7):H225-31.

Antioxidative and anti-inflammatory neuroprotective effects of astaxanthin and canthaxanthin in nerve growth factor differentiated PC12 cells.

[Chan KC](#), [Mong MC](#), [Yin MC](#).

Dept of Food and Nutrition, Providence Univ, Taichung County, Taiwan.

Abstract

Nerve growth factor differentiated PC12 cells were used to examine the antioxidative and anti-inflammatory effects of astaxanthin (AX) and canthaxanthin (CX). PC12 cells were pretreated with AX or CX at 10 or 20 μ M, and followed by exposure of hydrogen peroxide (H_2O_2) or 1-methyl-4-phenylpyridinium ion (MPP⁺) to induce cell injury. H_2O_2 or MPP⁺ treatment significantly decreased cell viability, increased lactate dehydrogenase (LDH) release, enhanced DNA fragmentation, and lowered mitochondrial membrane potential (MMP) ($P < 0.05$). The pretreatments from AX or CX concentration-dependently alleviated H_2O_2 or MPP⁺-induced cell death, LDH release, DNA fragmentation, and MMP reduction ($P < 0.05$). Either H_2O_2 or MPP⁺ treatment significantly increased malonyldialdehyde (MDA) and reactive oxygen species (ROS) formations, decreased glutathione content, and lowered glutathione peroxidase (GPX) and catalase activities ($P < 0.05$). The pretreatments from AX or CX significantly retained GPX and catalase activities, and decreased MDA and ROS formations ($P < 0.05$). H_2O_2 or MPP⁺ treatment significantly decreased Na⁺-K⁺-ATPase activity, elevated caspase-3 activity and levels of interleukin (IL)-1, IL-6, and tumor necrosis factor (TNF)- α ($P < 0.05$); and the pretreatments from these agents significantly restored Na⁺-K⁺-ATPase activity, suppressed caspase-3 activity and release of IL-1, IL-6, and TNF- α ($P < 0.05$). Based on the observed antioxidative and anti-inflammatory protection from AX and CX, these 2 compounds were potent agents against neurodegenerative disorder.

PMID: 19895474 [PubMed - indexed for MEDLINE]

Astaxanthin prevents depression by reducing inflammation in diabetic mice.

Brain Res. 2017 Feb 15;1657:262-268. doi: 10.1016/j.brainres.2016.12.018. Epub 2016 Dec 22.

Depression can be prevented by astaxanthin through inhibition of hippocampal inflammation in diabetic mice.

[Zhou XY](#)¹, [Zhang F](#)¹, [Hu XT](#)¹, [Chen J](#)¹, [Tang RX](#)², [Zheng KY](#)³, [Song YJ](#)⁴.

Author information

Abstract

The critical factor considered in a depression induced by diabetes is the inflammation eliciting hippocampal, amygdala and thalamic neuronal injury. Therefore, inhibiting inflammatory reactions in the brain and reducing neuronal injury can alleviate depression in rodents suffering from diabetes mellitus. The oral administration of astaxanthin has been employed in emotional disorders and diabetic complications due to its anti-depressant, anti-inflammatory and anti-apoptotic functions. However, it has not been reported whether astaxanthin can improve diabetes-related depression-like behavior, and its potential mechanisms have not been elucidated. The objective of the present study is to elucidate the effect of astaxanthin on depression in diabetic mice and to understand the underlying molecular mechanisms. In this study, experimental diabetic mice were given a single intraperitoneal injection of streptozotocin (STZ, 150mg/kg, dissolved in citrate buffer) after fasting for 12h. The diabetic model was assessed 72h after STZ injection, and mice with a fasting blood glucose level more than or equal to 16.7mmol/L were used in this study, and oral astaxanthin (25mg/kg) was provided uninterrupted for ten weeks. Depression-like behavior was evaluated by the tail suspension test (TST) and forced swimming test (FST). The glial fibrillary acidic protein (GFAP) and cleaved caspase-3-positive cells were measured by immunohistochemistry, and the western blotting was used to test the protein levels of interleukin-6 (IL-6), interleukin-1 β (IL-1 β) and cyclooxygenase (COX-2). The results showed that astaxanthin had an anti-depressant effect on diabetic mice. Furthermore, we observed that astaxanthin significantly reduced the number of GFAP-positive cells in the hippocampus and hypothalamus, and also the expression of cleaved caspase-3 in the hippocampus, amygdala and hypothalamus was decreased as well. Moreover, astaxanthin could down-regulate the expression of IL-6, IL-1 β and COX-2 in the hippocampus. These findings suggest that the mechanism of astaxanthin in preventing depression in diabetic mice involves the inhibition of inflammation/inflammation inhibition, thereby protecting neurons in hippocampus, amygdala and hypothalamus against hyperglycemic damage.

KEYWORDS: Astaxanthin; Depression; Diabetes; Inflammation; Injury

PMID: 28017669 DOI: [10.1016/j.brainres.2016.12.018](https://doi.org/10.1016/j.brainres.2016.12.018) [Indexed for MEDLINE]

Astaxanthin shows neuroprotective effects against cerebral ischemia in rats.

[J Clin Biochem Nutr.](#) 2010 Sep;47(2):121-9. Epub 2010 Jul 6.

Neuroprotective Effects of Astaxanthin in Oxygen-Glucose Deprivation in SH-SY5Y Cells and Global Cerebral Ischemia in Rat.

[Lee DH](#), [Lee YJ](#), [Kwon KH](#).

Departments of Surgery and Pharmacology, School of Medicine, University of Pittsburgh, Pittsburgh, Pennsylvania 15213, USA.

Abstract

Astaxanthin (ATX), a naturally occurring carotenoid pigment, is a powerful biological antioxidant. In the present study, we investigated whether ATX pharmacologically offers neuroprotection against oxidative stress by cerebral ischemia. We found that the neuroprotective efficacy of ATX at the dose of 30 mg/kg (n = 8) was 59.5% compared with the control group (n = 3). In order to make clear the mechanism of ATX neuroprotection, the up-regulation inducible nitric oxide synthase (iNOS) and heat shock proteins (HSPs) together with the oxygen glucose deprivation (OGD) in SH-SY5Y cells were also investigated. The induction of various factors involved in oxidative stress processes such as iNOS was suppressed by the treatment of ATX at 25 and 50 μ M after OGD-induced oxidative stress. In addition, Western blots showed that ATX elevated of heme oxygenase-1 (HO-1; Hsp32) and Hsp70 protein levels in in vitro. These results suggest that the neuroprotective effects of ATX were related to anti-oxidant activities in global ischemia.

PMID: 20838567 [PubMed – in process]PMCID: PMC2935152

Astaxanthin protects against seizures, reduces inflammation and prevents neuronal damage in rats.

[Neurochem Int.](#) 2018 Jun;116:85-94. doi: 10.1016/j.neuint.2018.02.008. Epub 2018 Feb 21.

Astaxanthin protects against kainic acid-induced seizures and pathological consequences.

[Chang Y](#)¹, [Lu CW](#)², [Chen YJ](#)³, [Lin TY](#)², [Huang SK](#)⁴, [Wang SJ](#)⁵.

Author information

Abstract

Excitotoxic damage caused by increased glutamate levels is involved in the pathogenesis of neurodegenerative diseases. Astaxanthin, a natural carotenoid with multiple health benefits, inhibits glutamate release from the brain tissue; however, whether it possesses the ability to affect glutamate-induced brain injury is unknown. The present study investigated the neuroprotective effects of astaxanthin on kainic acid (KA)-induced excitotoxicity in rats and the possible underlying intracellular signaling pathway. The rats were orally administrated with astaxanthin (50 or 100 mg/kg) for 7 days (once a day), and KA (15 mg/kg) was administered intraperitoneally at 1 h after the final administration. The results revealed that KA induced seizures, increased the hippocampal glutamate levels, caused considerable neuronal death and microglial activation in the hippocampal CA3 regions, and increased the production of proinflammatory cytokines. Astaxanthin pretreatment prevented these changes. Furthermore, astaxanthin pretreatment increased the expression of neuronal cell survival-related factors, including phosphorylated Akt, phosphorylated glycogen synthase kinase-3 β , and Bcl-2 in the hippocampus of KA-injected rats. These results suggested that astaxanthin can attenuate seizures, mitigate inflammation, augment survival signals, and prevent hippocampal neuronal damage in the animal model of KA-induced excitotoxicity.

KEYWORDS:

Astaxanthin; Glutamate excitotoxicity; Hippocampus; Kainic acid; Neuroprotection

PMID: 29475038

DOI: [10.1016/j.neuint.2018.02.008](https://doi.org/10.1016/j.neuint.2018.02.008)

Astaxanthin protects from cerebral infarction in rats.

[Hum Exp Toxicol](#). 2018 Sep;37(9):929-936. doi: 10.1177/0960327117745693. Epub 2017 Dec 8.

Protective effect of astaxanthin on acute cerebral infarction in rats.

[Nai Y¹](#), [Liu H¹](#), [Bi X¹](#), [Gao H²](#), [Ren C¹](#).

Author information

Abstract

The aim of the study was to investigate the effect of astaxanthin and its possible mechanisms on acute cerebral infarction (ACI) in rat model. Male Sprague Dawley rats were randomly divided into sham group, model group, and astaxanthin-treated groups (20, 40, and 80 mg/kg). Neurological examination, the ratio of cerebral edema, and histopathology changes were assessed. Moreover, some oxidative stress markers were obtained for biochemical analysis, and the expression of neurotrophic factors gene was detected by real-time polymerase chain reaction (RT-PCR) method. The results showed that treatment with astaxanthin notably reduced neurological deficit scores and the ratio of cerebral edema compared with the model group. Meanwhile, astaxanthin increased the activity of catalase, superoxide dismutase, and glutathioneperoxidase as well as decreased the content of malondialdehyde in brain tissue. RT-PCR results showed that the expression of brain-derived neurotrophic factor (BDNF) and nerve growth factor (NGF) mRNA were increased with astaxanthin treatment. The results indicated that astaxanthin could ameliorate ACI followed by suppressing oxidative stress and upregulating the expression of BDNF and NGF mRNA.

KEYWORDS:

Astaxanthin; acute cerebral infarction; neurological factors; oxidative stress

PMID: 29216762

DOI: [10.1177/0960327117745693](https://doi.org/10.1177/0960327117745693)

[Indexed for MEDLINE]

Astaxanthin may have potential neuron protective effects and may serve as an early stage Alzheimer's treatment.

[J Med Food](#). 2010 Jun;13(3):548-56.

Astaxanthine secured apoptotic death of PC12 cells induced by beta-amyloid peptide 25-35: its molecular action targets.

[Chang CH](#), [Chen CY](#), [Chiou JY](#), [Peng RY](#), [Peng CH](#).

Research Institute of Biotechnology, Hungkuang University, Taichung Hsien, Taiwan.

Abstract

Astaxanthine (ASTx) is a novel carotenoid nutraceutical occurring in many crustaceans and red yeasts. It has potent antioxidant, photoprotective, hepatodetoxicant, and anti-inflammatory activities. Documented effect of ASTx on treatment of neurodegenerative disease is still lacking. We used the beta-amyloid peptide (Abeta) 25-35-treated PC12 model to investigate the neuron-protective effect of ASTx. The parameters examined included cell viability, caspase activation, and various apoptotic biomarkers that play their critical roles in the transduction pathways independently or synergistically. Results indicated that Abeta25-35 at 30 microM suppressed cell viability by 55%, whereas ASTx was totally nontoxic below a dose of 5.00 microM. ASTx at 0.1 microM protected PC12 cells from damaging effects of Abeta25-35 in several ways: (1) by securing the cell viability; (2) by partially down-regulating the activation of caspase 3; (3) by inhibiting the expression of Bax; (4) by completely eliminating the elevation of interleukin-1beta and tumor necrosis factor-alpha; (5) by inhibiting the nuclear translocation of nuclear factor kappaB; (6) by completely suppressing the phosphorylation of p38 mitogen-activated protein kinase; (7) by completely abolishing the calcium ion influx to effectively maintain calcium homeostasis; and (8) by suppressing the majority (about 75%) of reactive oxygen species production. Conclusively, ASTx may have merit to be used as a very potential neuron protectant and an anti-early-stage Alzheimer's disease adjuvant therapy.

PMID: 20521980 [PubMed - indexed for MEDLINE]

ASTAXANTHIN SHOWS NEUROPROTECTIVE PROPERTIES IN-VITRO.

Noro Psikiyatı Ars. 2018 Dec;55(4):295-300.
doi: 10.29399/npa.23259. Epub 2018 Jul 14.

The Role of Astaxanthin on Transcriptional Regulation of NMDA Receptors Voltage Sensitive Calcium Channels and Calcium Binding Proteins in Primary Cortical Neurons

[Muhittin Emre Altunrende](#)¹, [Duygu Gezen-Ak](#)², [İrem L Atasoy](#)², [Esin Candaş](#)², [Erdinç Dursun](#)²

PMID: 30622383 PMCID: [PMC6300839](#) DOI: [10.29399/npa.23259](#) [Free PMC article](#)

Abstract

Introduction: Calcium (Ca) is the phenomenon intracellular molecule that regulate many cellular process in neurons physiologically. Calcium dysregulation may occur in neurons due to excessive synaptic release of glutamate or other reasons related with neurodegeneration. Astaxanthin is a carotenoid that has antioxidant effect in cell. The purpose of this study was to investigate whether astaxanthin affects NMDA subunits, calcium binding proteins and L Type voltage sensitive Ca-channels (LVSCC) in primary cortical neuron cultures in order to see its role in calcium metabolism.

Methods: Primary cortical neurons were prepared from embryonic day 16-Sprague Dawley rat embryos. The cultures were treated with 10 nM and 20 nM astaxanthin on day 7. NMDA subunits, LVSCC-A1C and LVSCC-A1D, calbindinD28k and parvalbumin mRNA expression levels was determined by qRT-PCR at 4, 24 and 48 hours.

Results: Our findings indicate that astaxanthin could have direct or indirect outcome on calcium homeostasis by regulating mRNA expression levels of NMDA subunits, LVSCC-A1C and LVSCC-A1D, calbindinD28k and parvalbumin by a dose and time dependent manner.

Conclusion: Neuroprotective effects of astaxanthin as a Ca homeostasis regulator should be noted throughout neurodegenerative disorders, and neurosurgery applications.

ASTAXANTHIN PROTECTS ENDOTHELIAL CELLS FROM INDUCED DYSFUNCTION INDICATING POTENTIAL FOR CEREBRAL VASCULAR DISEASES.

Mol Med Rep. 2019 Jun;19(6):4753-4760.
doi: 10.3892/mmr.2019.10162. Epub 2019 Apr 12.

Astaxanthin inhibits homocysteine-induced endothelial cell dysfunction via the regulation of the reactive oxygen species-dependent VEGF-VEGFR2-FAK signaling pathway

[Xian-Jun Wang¹](#), [Da-Chen Tian¹](#), [Feng-Wen Wang²](#), [Meng-Hao Zhang²](#), [Cun-Dong Fan²](#), [Wang Chen¹](#), [Mei-Hong Wang¹](#), [Xiao-Yan Fu²](#), [Jin-Kui Ma³](#)

PMID: 31059085 PMCID: [PMC6522805](#) DOI: [10.3892/mmr.2019.10162](#) **Free PMC article**

Abstract

Increased plasma levels of homocysteine (Hcy) can cause severe damage to vascular endothelial cells. Hcy-induced endothelial cell dysfunction contributes to the occurrence and development of human cerebrovascular diseases (CVDs). Our previous studies have revealed that astaxanthin (ATX) exhibits novel cardioprotective activity against Hcy-induced cardiotoxicity in vitro and in vivo. However, the protective effect and mechanism of ATX against Hcy-induced endothelial cell dysfunction requires further investigation. In the present study, treatment of human umbilical vascular endothelial cells (HUVECs) with Hcy inhibited the migration, invasive and tube formation potentials of these cells in a dose-dependent manner. Hcy treatment further induced a time-dependent increase in the production of reactive oxygen species (ROS), and downregulated the expression of vascular endothelial growth factor (VEGF), phosphorylated (p)-Tyr-VEGF receptor 2 (VEGFR2) and p-Tyr397-focal adhesion kinase (FAK). On the contrary, ATX pre-treatment significantly inhibited Hcy-induced cytotoxicity and increased HUVEC migration, invasion and tube formation following Hcy treatment. The mechanism of action may involve the effective inhibition of Hcy-induced ROS generation and the recovery of FAK phosphorylation. Collectively, our findings suggested that ATX could inhibit Hcy-induced endothelial dysfunction by suppressing Hcy-induced activation of the VEGF-VEGFR2-FAK signaling axis, which indicates the novel therapeutic potential of ATX in treating Hcy-mediated CVD.

ASTAXANTHIN IMPROVES MOTOR FUNCTION IN MICE BY INCREASING CYCLIC ADENOSINE MONOPHOSPHATE IN BRAIN TISSUE.

Eur Rev Med Pharmacol Sci. 2019 Aug;23(3 Suppl):135-143.
doi: 10.26355/eurrev_201908_18640.

Effects of astaxanthin on axonal regeneration via cAMP/PKA signaling pathway in mice with focal cerebral infarction

[Y-L Wang](#)¹, [X-L Zhu](#), [M-H Sun](#), [Y-K Dang](#)

- PMID: 31389584
- DOI: [10.26355/eurrev_201908_18640](https://doi.org/10.26355/eurrev_201908_18640)

Free article

Abstract

Objective: To investigate the effect of astaxanthin on the neurological function of the middle cerebral artery occlusion (MCAO) mice and its possible mechanism.

Materials and Methods: The male C57BL/6 mice were selected to establish the model of MCAO via electrocoagulation, and they were randomly divided into 4 groups: the sham operation group (Sham group), the cerebral ischemia model group (MCAO group), the astaxanthin intervention group (gavage with 30 mg/kg astaxanthin for 28 days, twice a day; Ast group), and astaxanthin + H89 group (Ast + H89 group). At 3, 7, 14, and 28 d after the operation, the Rotarod test and the balance beam footstep error test were performed. The brain tissues were taken for immunofluorescence to observe the expression of the growth-associated protein 43 (GAP43) in the cortex around the infarction. The GAP43 protein and mRNA levels in the cortex around the infarction were detected via Western blotting, and the Reverse Transcription-Polymerase Chain Reaction (RT-PCR), the levels of cyclic adenosine monophosphate (cAMP) and protein kinase A (PKA) in the bilateral cerebral cortex were detected via enzyme-linked immunosorbent assay (ELISA), and the PKAc and phosphorylated-cAMP-response element-binding protein (p-CREB) levels in the bilateral cerebral cortex were detected via Western

blotting. Biotin dextran amine (BDA) was injected at 14 d after the operation, and the brain was taken at 28 d. The BDA-labeled neurons or axons were observed in the bilateral cortex via immunohistochemistry and immunofluorescence, and the colocalization of BDA and GAP43 in the cortex around the infarction was observed using double immunofluorescence staining.

Results: Compared with those in the MCAO group, the mean residence time in the Rotarod test was significantly increased, and the times of the footstep error on the balance beam were significantly reduced in the Ast group. In the Ast group, the expression of GAP43 in the cortex around the infarction, the GAP43 protein, and the mRNA levels were all significantly elevated. Immunofluorescence showed that in the Ast group, the number of the labeled neurons and axons in the bilateral cortex was slightly larger than that in the other groups, and the number of labeled axonal fibers in the ischemic cortex was significantly increased. The colocalization area of BDA and GAP43 was observed, and it was found that the positive area in the Ast group was significantly larger than that in the MCAO group. The cAMP level was higher in the Ast group and Ast + H89 group at 7, 14, and 28 d after operation, while the PKA level was lower in the Ast + H89 group at 7 and 14 d after operation and higher in the Ast group at 7, 14, and 28 d after operation. The results of the Western blotting manifested that the PKAc and p-CREB levels were upregulated in the Ast group at 7, 14, and 28 d after the operation, and downregulated in the Ast + H89 group at 7, 14, and 28 d after the operation.

Conclusions: Astaxanthin activates the cAMP/PKA/CREB signaling pathway by increasing the cAMP concentration in brain tissues, ultimately promoting the axonal regeneration in the cerebral cortex and improving the motor function.

ASTAXANTHIN PROTECTS NEURONAL CELLS AGAINST INDUCED NEUROTOXICITY.

Molecules. 2020 Jan 5;25(1):214.
doi: 10.3390/molecules25010214.

Astaxanthin Protects PC12 Cells against Homocysteine- and Glutamate-Induced Neurotoxicity

[Chi-Huang Chang](#)¹, [Kuan-Chou Chen](#)^{2,3,4}, [Kuo-Chun Liaw](#)¹, [Chiung-Chi Peng](#)⁴, [Robert Y Peng](#)¹

- PMID: 31948056
- PMCID: [PMC6982875](#)
- DOI: [10.3390/molecules25010214](#)

[Free PMC article](#)

Abstract

Memory impairment has been shown to be associated with glutamate (Glu) excitotoxicity, homocysteine (Hcy) accumulation, and oxidative stress. We hypothesize that Glu and Hcy could damage neuronal cells, while astaxanthin (ATX) could be beneficial to alleviate the adverse effects. Using PC12 cell model, we showed that Glu and Hcy provoked a huge amount of reactive oxygen species (ROS) production, causing mitochondrial damage at EC₅₀ 20 and 10 μM, respectively. The mechanisms of action include: (1) increasing calcium influx; (2) producing ROS; (3) initiating lipid peroxidation; (4) causing imbalance of the Bcl-2/Bax homeostasis; and (5) activating cascade of caspases involving caspases 12 and 3. Conclusively, the damages caused by Glu and Hcy to PC12 cells can be alleviated by the potent antioxidant ATX.

ASTAXANTHIN SHOWS TWO DISTINCT BENEFITS IN CELL STUDY OF PARKINSON'S DISEASE.

Neurosci Res. 2020 Apr 22;S0168-0102(20)30018-3.

doi: 10.1016/j.neures.2020.04.003. Online ahead of print.

Astaxanthin suppresses endoplasmic reticulum stress and protects against neuron damage in Parkinson's disease by regulating miR-7/SNCA axis

[Dong-Fang Shen](#)¹, [Hui-Ping Qi](#)¹, [Chi Ma](#)¹, [Ming-Xiu Chang](#)¹, [Wei-Na Zhang](#)¹, [Rong-Rong Song](#)²

- PMID: 32333925
- DOI: [10.1016/j.neures.2020.04.003](https://doi.org/10.1016/j.neures.2020.04.003)

Abstract

Parkinson's disease (PD) is a common neurodegenerative disorder that featured by the loss of dopaminergic neurons. Astaxanthin (AST), an important antioxidant, is demonstrated to be a neuroprotective agent for PD. However, the underlying mechanisms of AST in PD remain largely unclear. In this study, we found that AST treatment significantly not only abolished the cell viability inhibition and apoptosis promotion induced by 1-methyl-4-phenylpyridinium (MPP+) in SH-SY5Y cells via inhibiting endoplasmic reticulum (ER) stress, but also reversed the MPP+ caused dysregulation of miR-7 and SNCA expression. MiR-7 knockdown and SNCA overexpression were achieved by treating SH-SY5Y cells with miR-7 inhibitor and pcDNA3.1-SNCA plasmids, respectively. MiR-7 could bind to and negatively regulate SNCA in SH-SY5Y cells. Treated SH-SY5Y cells with miR-7 inhibitor or pcDNA3.1-SNCA abrogated the protective effects of AST on MPP+ induced cytotoxicity. Knockdown of miR-7 aggravated 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) induced neuron injury in vivo suggested by athletic performance, histopathological morphology, expression of tyrosine hydroxylase (TH) and TUNEL positive cells, however, AST treatment could reverse these effects of miR-7 knockdown. Collectively, AST suppressed ER stress and protected against PD-caused neuron damage by targeting miR-7/SNCA axis, implying that AST might be a potential effective therapeutic agent for PD.

ASTAXANTHIN PROTECTS NEURONS AGAINST OXYGEN AND GLUCOSE DEPRIVATION IN-VITRO.

J Cell Mol Med. 2020 Aug;24(16):8977-8985.
doi: 10.1111/jcmm.15531. Epub 2020 Jun 21.

Neuroprotective effects of astaxanthin against oxygen and glucose deprivation damage via the PI3K/Akt/GSK3 β /Nrf2 signalling pathway in vitro

[Jie Zhang](#)¹, [Changling Ding](#)², [Shuping Zhang](#)³, [Yangyang Xu](#)²

- PMID: 32567157
- PMCID: [PMC7417723](#)
- DOI: [10.1111/jcmm.15531](#)

Free PMC article

Abstract

Astaxanthin (ATX), which is the most abundant flavonoid in propolis, has previously shown neuroprotective properties against cerebral ischaemia-induced apoptosis. However, the mechanisms by which ATX mediates its therapeutic effects are unclear. At present, we explored the underlying mechanisms involved in the protective effects of ATX via the phosphoinositide 3-kinase (PI3K)/Akt/glycogen synthase kinase 3 beta (GSK3 β)/nuclear factor erythroid 2-related factor 2 (Nrf2) signalling pathway in SH-SY5Y cells. The PI3K/Akt inhibitor LY294002 and GSK3 β inhibitor LiCl were employed in this study. Pre-treatment with ATX for 24 hours significantly decreased the oxygen and glucose deprivation (OGD)-induced viability loss, reduced the proportion of apoptosis and regulated OGD-mediated reactive oxygen species (ROS) production. Furthermore, ATX suppressed OGD-caused mitochondrial membrane potential and decomposition of caspase-3 to cleaved caspase-3, and heightened the B-cell lymphoma 2 (Bcl-2)/Bax ratio. PI3K/Akt/GSK3 β /Nrf2 signalling pathway activation in SH-SY5Y cells was verified by Western blot. ATX and LiCl treatment raised the protein levels of p-Akt, p-GSK3 β ,

nucleus Nrf2 and haeme oxygenase 1 (HO-1). However, these protein expression levels decreased by treatment of LY294002. The above in vitro data indicate that ATX can confer neuroprotection against OGD-induced apoptosis via the PI3K/Akt/GSK3 β /Nrf2 signalling pathway.

ASTAXANTHIN PROTECTS NEURONS AGAINST EXCITOTOXICITY AND REDUCES OXIDATION OF MITOCHONDRIA.

Mar Drugs. 2020 Jun 26;18(6):335.
doi: 10.3390/md18060335.

Astaxanthin Counteracts Excitotoxicity and Reduces the Ensuing Increases in Calcium Levels and Mitochondrial Reactive Oxygen Species Generation

[Francisca García](#)^{1,2,3}, [Pedro Lobos](#)⁴, [Alejandra Ponce](#)^{1,2,3}, [Karla Cataldo](#)^{1,2,3}, [Daniela Meza](#)^{1,2,3}, [Patricio Farías](#)^{1,2,3}, [Carolina Estay](#)^{1,2,3}, [Felipe Oyarzun-Ampuero](#)⁵, [Rodrigo Herrera-Molina](#)^{6,7}, [Andrea Paula-Lima](#)^{4,8}, [Álvaro O Ardiles](#)^{1,9,10}, [Cecilia Hidalgo](#)^{4,11,12}, [Tatiana Adasme](#)⁷, [Pablo Muñoz](#)^{1,2,3}

PMID: **32604880** PMCID: [PMC7345213](#) DOI: [10.3390/md18060335](#) **Free PMC article**

Abstract

Astaxanthin (ASX) is a carotenoid pigment with strong antioxidant properties. We have reported previously that ASX protects neurons from the noxious effects of amyloid- β peptide oligomers, which promote excessive mitochondrial reactive oxygen species (mROS) production and induce a sustained increase in cytoplasmic Ca^{2+} concentration. These properties make ASX a promising therapeutic agent against pathological conditions that entail oxidative and Ca^{2+} dysregulation. Here, we studied whether ASX protects neurons from N-methyl-D-aspartate (NMDA)-induced excitotoxicity, a noxious process which decreases cellular viability, alters gene expression and promotes excessive mROS production. Incubation of the neuronal cell line SH-SY5Y with NMDA decreased cellular viability and increased mitochondrial superoxide production; pre-incubation with ASX prevented these effects. Additionally, incubation of SH-SY5Y cells with ASX effectively reduced the basal mROS production and prevented hydrogen peroxide-induced cell death. In primary hippocampal neurons, transfected with a genetically encoded cytoplasmic Ca^{2+} sensor, ASX also prevented the increase in intracellular Ca^{2+} concentration induced by NMDA. We suggest that, by preventing the noxious mROS and Ca^{2+} increases that occur under excitotoxic conditions, ASX could be useful as a therapeutic agent in neurodegenerative pathologies that involve alterations in Ca^{2+} homeostasis and ROS generation.

Astaxanthin Suppresses PM2.5-Induced Neuroinflammation by Regulating Akt Phosphorylation in BV-2 Microglial Cells

[Ryeong-Eun Kim](#)¹, [Chan Young Shin](#)², [Seol-Heui Han](#)^{1,3}, [Kyoung Ja Kwon](#)^{1,3}

- PMID: [33008094](#)
- PMCID: [PMC7582569](#)
- DOI: [10.3390/ijms21197227](#)

Free PMC article

Abstract

Air pollution has become one of the most serious issues for human health and has been shown to be particularly concerning for neural and cognitive health. Recent studies suggest that fine particulate matter of less than 2.5 (PM2.5), common in air pollution, can reach the brain, potentially resulting in the development and acceleration of various neurological disorders including Alzheimer's disease, Parkinson's disease, and other forms of dementia, but the underlying pathological mechanisms are not clear.

Astaxanthin is a red-colored phytonutrient carotenoid that has been known for anti-inflammatory and neuroprotective effects. In this study, we demonstrated that exposure to PM2.5 increases the neuroinflammation, the expression of proinflammatory M1, and disease-associated microglia (DAM) signature markers in microglial cells, and that treatment with astaxanthin can prevent the neurotoxic effects of this exposure through anti-inflammatory properties. Diesel particulate matter (Sigma-Aldrich) was used as a fine particulate matter 2.5 in the present study. Cultured rat glial cells and BV-2 microglial cells were treated with various concentrations of PM2.5, and then the expression of various inflammatory mediators and signaling pathways were measured using qRT-PCR and Western blot. Astaxanthin was then added and assayed as above to evaluate its effects on microglial changes, inflammation, and toxicity induced by PM2.5.

PM2.5 increased the production of nitric oxide and reactive oxygen species and upregulated the transcription of various proinflammatory markers including Interleukin-1 β (IL-1 β), Interleukin-6 (IL-6), Tumor necrosis factor α (TNF α), inducible nitric oxide synthase (iNOS), triggering receptor expressed on myeloid cells 2 (TREM2), Toll-like receptor 2/4 (TLR2/4), and cyclooxygenase-2 (COX-2) in BV-2 microglial cells. However, the mRNA expression of IL-10 and arginase-1 decreased following PM2.5 treatment. PM2.5 treatment increased c-Jun N-terminal kinases (JNK) phosphorylation and decreased Akt phosphorylation. Astaxanthin attenuated these PM2.5-induced responses, reducing transcription of the proinflammatory markers iNOS and heme oxygenase-1 (HO-1), which prevented neuronal cell death. Our results indicate that PM2.5 exposure reformulates microglia via proinflammatory M1 and DAM phenotype, leading to neurotoxicity, and the fact that astaxanthin treatment can prevent neurotoxicity by inhibiting transition to the proinflammatory M1 and DAM phenotypes. These results demonstrate that PM2.5 exposure can induce brain damage through the change of proinflammatory M1 and DAM signatures in the microglial cells, as well as the fact that astaxanthin can have a potential beneficial effect on PM2.5 exposure of the brain.

ASTAXANTHIN SHOWS EFFICACY AGAINST HUMAN BRAIN CANCER CELLS AND MAY BE APPLICABLE FOR THE PROTECTION OF CANCER METASTASIS.

Asian Pac J Cancer Prev. 2020 Jul 1;21(7):2029-2033.
doi: 10.31557/APJCP.2020.21.7.2029.

Anti-Migration and Invasion Effects of Astaxanthin against A172 Human Glioblastoma Cell Line

[Tanapan Siangcham](#)¹, [Pornpun Vivithanaporn](#)², [Kant Sangpairoj](#)^{3,4}

- PMID: 32711429
- PMCID: [PMC7573402](#)
- DOI: [10.31557/APJCP.2020.21.7.2029](#)

Free PMC article

Abstract

Objectives: The study was to investigate anti-migration and invasion effects of astaxanthin (ATX), a natural carotenoid derivative distributed in marine environments, against A172 human glioblastoma cells.

Materials and Methods: Cell viability after ATX treatment was measured by MTT assays. Tumor cell migration and invasion were observed by scratch and Boyden chamber assays, respectively. Expression of MMP-2 and activity of MMP-9 were observed by immunoblotting and gelatin zymography, respectively.

Results: ATX up to 150 μ M was not toxic to A172 cells at 48 h post-treatment. In contrast, ATX at 50 and 100 μ M significantly decreased migration and invasion of A172 cells at 24 and 48 h post-treatment. Metastatic-reducing effect of ATX is associated with the reduction of MMP-2 and MMP-9 expressions in a dose-dependent manner.

Conclusion: This finding indicated that ATX has anti-migration and invasion effects against human glioblastoma cells and might be applicable for the protection against metastasis of glioblastoma.

ASTAXANTHIN PROTECTS AGAINST NEURONAL DAMAGE IN CELL STUDY MODELING PARKINSON'S DISEASE.

Neurosci Res. 2021 Apr;165:51-60.

doi: 10.1016/j.neures.2020.04.003. Epub 2020 Apr 22.

Astaxanthin suppresses endoplasmic reticulum stress and protects against neuron damage in Parkinson's disease by regulating miR-7/SNCA axis

[Dong-Fang Shen](#)¹, [Hui-Ping Qi](#)¹, [Chi Ma](#)¹, [Ming-Xiu Chang](#)¹, [Wei-Na Zhang](#)¹, [Rong-Rong Song](#)²

- PMID: [32333925](#)
- DOI: [10.1016/j.neures.2020.04.003](#)

Abstract

Parkinson's disease (PD) is a common neurodegenerative disorder that featured by the loss of dopaminergic neurons. Astaxanthin (AST), an important antioxidant, is demonstrated to be a neuroprotective agent for PD. However, the underlying mechanisms of AST in PD remain largely unclear. In this study, we found that AST treatment significantly not only abolished the cell viability inhibition and apoptosis promotion induced by 1-methyl-4-phenylpyridinium (MPP+) in SH-SY5Y cells via inhibiting endoplasmic reticulum (ER) stress, but also reversed the MPP+ caused dysregulation of miR-7 and SNCA expression. MiR-7 knockdown and SNCA overexpression were achieved by treating SH-SY5Y cells with miR-7 inhibitor and pcDNA3.1-SNCA plasmids, respectively. MiR-7 could bind to and negatively regulate SNCA in SH-SY5Y cells. Treated SH-SY5Y cells with miR-7 inhibitor or pcDNA3.1-SNCA abrogated the protective effects of AST on MPP+ induced cytotoxicity. Knockdown of miR-7 aggravated 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) induced neuron injury in vivo suggested by athletic performance, histopathological morphology, expression of tyrosine hydroxylase (TH) and TUNEL positive cells, however, AST treatment could reverse these effects of miR-7 knockdown. Collectively, AST suppressed ER stress and protected against PD-caused neuron damage by targeting miR-7/SNCA axis, implying that AST might be a potential effective therapeutic agent for PD.

Astaxanthin inhibits neuro-inflammation in-vitro.

[Oncotarget](#). 2017 Sep 3;8(41):69370-69385. doi: 10.18632/oncotarget.20628. eCollection 2017 Sep 19.

Astaxanthin acts via LRP-1 to inhibit inflammation and reverse lipopolysaccharide-induced M1/M2 polarization of microglial cells.

[Wen X¹](#), [Xiao L¹](#), [Zhong Z²](#), [Wang L³](#), [Li Z¹](#), [Pan X¹](#), [Liu Z^{2,4}](#).

Author information

Abstract

Microglia become activated during neuroinflammation and produce neurotoxic and neurotrophic factors, depending on whether they acquire M1 proinflammatory or M2 anti-inflammatory phenotypes. Astaxanthin (ATX), a natural carotenoid, has anti-inflammatory and neuroprotective effects. We investigated whether ATX could reverse M1/M2 polarization and suppress neuroinflammation *via* low-density lipoprotein receptor-related protein-1 (LRP-1). We observed increased expression of M1 (TNF- α , IL-1 β , and CD86) and decreased expression of M2 (Arg-1, IL-10, and CD206) markers in BV2 microglial cells stimulated with lipopolysaccharide (LPS). These alterations were reversed by pretreating the cells with ATX. Activation of the NF- κ B and JNK pathways was observed upon LPS stimulation, which was reversed by ATX. ATX-induced M2 polarization was attenuated by inhibition of NF- κ B and JNK. Pretreatment of LPS-stimulated BV2 cells with ATX resulted in increased LRP-1 expression. The addition of receptor-associated protein, an LRP-1 antagonist, ameliorated ATX-induced inactivation of NF- κ B and JNK signaling, and M2 polarization. ATX promotes M2 polarization to suppress neuroinflammation *via* LRP-1 by inhibiting NF- κ B and JNK signaling. This novel mechanism may suppress neuroinflammation in diseases such as Alzheimer's disease.

KEYWORDS:

Gerotarget; M1/M2 phenotypes; astaxanthin; c-Jun N-terminal kinase; low-density lipoprotein receptor-related protein 1; nuclear factor- κ B

PMID: 29050210

PMCID: [PMC5642485](#)

DOI: [10.18632/oncotarget.20628](#)

[Free PMC Article](#)

Astaxanthin shows neuroprotective effect against hydrogen peroxide-induced neurotoxicity in-vitro and against cerebral ischemia in-vivo.

[Brain Res.](#) 2010 Sep 21. [Epub ahead of print]

Neuroprotective effect of astaxanthin on H₂O₂-induced neurotoxicity in vitro and on focal cerebral ischemia in vivo.

[Lu YP](#), [Liu SY](#), [Sun H](#), [Wu XM](#), [Li JJ](#), [Zhu L](#).

Institute of Nautical Medicine, Nantong University, Nantong 226001, China.

Abstract

Astaxanthin (AST) is a powerful antioxidant that occurs naturally in a wide variety of living organisms. Much experimental evidence has proved that AST has the function of eliminating oxygen free radicals and can protect organisms from oxidative damage. The present study was carried out to further investigate the neuroprotective effect of AST on oxidative stress induced toxicity in primary culture of cortical neurons and on focal cerebral ischemia-reperfusion induced brain damage in rats. AST, over a concentration range of 250-1000nM, attenuated 50μM H₂O₂-induced cell viability loss. 500nM AST pretreatment significantly inhibited H₂O₂-induced apoptosis measured by Hoechst 33342 staining and restored the mitochondrial membrane potential (MMP) measured by a fluorescent dye, Rhodamine 123. In vivo, AST prevented cerebral ischemic injury induced by 2h middle cerebral artery occlusion (MCAO) and 24h reperfusion in rats. Pretreatment of AST intragastrically twice at 5h and 1h prior to ischemia dramatically diminished infarct volume and improved neurological deficit in a dose-dependent manner. Nissl staining showed that the neuronal injury was significantly improved by pretreatment of AST at 80mg/kg. Taken together, these results suggest that pretreatment with AST exhibits noticeable neuroprotection against brain damage induced by ischemia-reperfusion and the antioxidant activity of AST maybe partly responsible for it.

PMID: 20846510 [PubMed - as supplied by publisher]

Astaxanthin inhibits cell death in mouse neural cells.

[J Microbiol Biotechnol.](#) 2009 Nov;19(11):1355-63.

Astaxanthin inhibits H₂O₂-mediated apoptotic cell death in mouse neural progenitor cells via modulation of P38 and MEK signaling pathways.

[Kim JH](#), [Choi W](#), [Lee JH](#), [Jeon SJ](#), [Choi YH](#), [Kim BW](#), [Chang HI](#), [Nam SW](#).

Source

Department of Biomaterial Control, Dong-Eui University, Busan 614-714, Korea.

Abstract

In the present study, neuroprotective effects of astaxanthin on H₂O₂-mediated apoptotic cell death using cultured mouse neural progenitor cells (mNPCs) were investigated. To cause apoptotic cell death, mNPCs were pretreated with astaxanthin for 8 h and followed by treatment of 0.3 mM H₂O₂. Pretreatment of mNPCs with astaxanthin significantly inhibited H₂O₂-mediated apoptosis and induced cell growth in a dose-dependent manner. In Western blot analysis, astaxanthin-pretreated cells showed the activation of p-Akt, p-MEK, p-ERK, and Bcl-2, and the reduction of p-P38, p-SAPK/JNK, Bax, p-GSK3beta, cytochrome c, caspase-3, and PARP. Because H₂O₂ triggers caspases activation, this study examined whether astaxanthin can inhibit caspases activation in H₂O₂-treated mNPCs. After H₂O₂ treatment, caspases activities were prominently increased but astaxanthin pretreatment significantly inhibited H₂O₂-mediated caspases activation. Astaxanthin pretreatment also significantly recovered ATP production ability of H₂O₂-treated cells. These findings indicate that astaxanthin inhibits H₂O₂-mediated apoptotic features in mNPCs. Inhibition assays with SB203580 (10 microM, a specific inhibitor of p38) and PD98059 (10 microM, a specific inhibitor of MEK) clearly showed that astaxanthin can inhibit H₂O₂-mediated apoptotic death via modulation of p38 and MEK signaling pathways.

PMID: 19996687 [PubMed – indexed for MEDLINE]

Astaxanthin limits oxidative insult in the forebrain of rats.

[Pharmacol Biochem Behav.](#) 2011 Sep;99(3):349-55. Epub 2011 May 17.

Astaxanthin limits fish oil-related oxidative insult in the anterior forebrain of Wistar rats: putative anxiolytic effects?

[Mattei R](#), [Polotow TG](#), [Vardaris CV](#), [Guerra BA](#), [Leite JR](#), [Otton R](#), [Barros MP](#).

Source

Department of Psychobiology, Universidade Federal de São Paulo (UNIFESP), ZIP 04023062, São Paulo, SP, Brazil.

Abstract

The habitual consumption of marine fish is largely associated to human mental health. Fish oil is particularly rich in n-3 polyunsaturated fatty acids that are known to play a role in several neuronal and cognitive functions. In parallel, the orange-pinkish carotenoid astaxanthin (ASTA) is found in salmon and displays important antioxidant and anti-inflammatory properties. Many neuronal dysfunctions and anomalous psychotic behavior (such as anxiety, depression, etc.) have been strongly related to the higher sensitivity of catecholaminergic brain regions to oxidative stress. Thus, the aim of this work was to study the combined effect of ASTA and fish oil on the redox status in plasma and in the monoaminergic-rich anterior forebrain region of Wistar rats with possible correlations with the anxiolytic behavior. Upon fish oil supplementation, the downregulation of superoxide dismutase and catalase activities combined to increased “free” iron content resulted in higher levels of lipid and protein oxidation in the anterior forebrain of animals. Such harmful oxidative modifications were hindered by concomitant supplementation with ASTA despite ASTA-related antioxidant protection was mainly observed in plasma. Although it is clear that ASTA properly crosses the brain-blood barrier, our data also address a possible indirect role of ASTA in restoring basal oxidative conditions in anterior forebrain of animals: by improving GSH-based antioxidant capacity of plasma. Preliminary anxiolytic tests performed in the elevated plus maze are in alignment with our biochemical observations.

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PMID: 21619892 [PubMed – in process]

Astaxanthin shows anti-anxiety effects in mice.

[Biofactors](#). 2011 Jan;37(1):25-30. Doi: 10.1002/biof.130. Epub 2010 Nov 11.

The antianxiety-like effect of astaxanthin extracted from *Paracoccus carotinifaciens*.

[Nishioka Y](#), [Oyagi A](#), [Tsuruma K](#), [Shimazawa M](#), [Ishibashi T](#), [Hara H](#).

Source

Molecular Pharmacology, Department of Biofunctional Evaluation, Gifu Pharmaceutical University, 1-25-4 Daigaku-nishi, Gifu, Japan.

Abstract

Astaxanthin is a red carotenoid pigment and is widely found in living organisms. Astaxanthin has a potent antioxidative ability and has been reported as having various biological effects on the central nerve system, such as a protective effect against ischemia/reperfusion injury and improvement in cognitive function. In this study, to investigate the effects of astaxanthin on anxiety and depression, we performed some behavioral trials including the elevated plus maze test, hole-board test, forced swim test, and tail suspension test. Astaxanthin (100 and 300 mg/kg/day for 10 days, p.o.) significantly increased the time spent in open arms in the elevated plus maze test and increased the head-dipping count and duration in the hole-board test. On the other hand, astaxanthin (10, 100, 300, and 500 mg/kg/day for 10 days, p.o.) did not change the immobility time in the forced swim test or the tail suspension test. In conclusion, in mice, astaxanthin exerted anxiolytic-like effects, but not antidepressant-like effects.

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PMID: 21328624 [PubMed – indexed for MEDLINE]

Astaxanthin protects against mitochondrial dysfunction and reactive oxygen species in-vitro and in-vivo in mouse model of Parkinson's disease and may provide a potential therapy for the treatment of progressive neurodegenerative diseases like Parkinson's.

[Food Chem Toxicol.](#) 2011 Jan;49(1):271-80. Epub 2010 Nov 5.

Astaxanthin protects against MPTP/MPP⁺-induced mitochondrial dysfunction and ROS production in vivo and in vitro.

[Lee DH](#), [Kim CS](#), [Lee YJ](#).

Source

Department of Surgery, School of Medicine, University of Pittsburgh, Pittsburgh, PA 15213, USA.

Abstract

Astaxanthin (AST) is a powerful antioxidant that occurs naturally in a wide variety of living organisms. We have investigated the role of AST in preventing 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)-induced apoptosis of the substantia nigra (SN) neurons in the mouse model of Parkinson's disease (PD) and 1-methyl-4-phenylpyridinium (MPP⁺)-induced cytotoxicity of SH-SY5Y human neuroblastoma cells. In in vitro study, AST inhibits MPP⁺-induced production of intracellular reactive oxygen species (ROS) and cytotoxicity in SH-SY5Y human neuroblastoma cells. Preincubation of AST (50 μM) significantly attenuates MPP⁺-induced oxidative damage. Furthermore, AST is able to enhance the expression of Bcl-2 protein but reduce the expression of α-synuclein and Bax, and suppress the cleavage of caspase-3. Our results suggest that the protective effects of AST on MPP⁺-induced apoptosis may be due to its anti-oxidative properties and anti-apoptotic activity via induction of expression of superoxide dismutase (SOD) and catalase and regulating the expression of Bcl-2 and Bax. Pretreatment with AST (30 mg/kg) markedly increases tyrosine hydroxylase (TH)-positive neurons and decreases the argyrophilic neurons compared with the MPTP model group. In summary, AST shows protection from MPP⁺/MPTP-induced apoptosis in the SH-SY5Y cells and PD model mouse SN neurons, and this effect may be attributable to upregulation of the expression of Bcl-2 protein, downregulation of the expression of Bax and α-synuclein, and inhibition of the activation of caspase-3. These data indicate that AST may provide a valuable therapeutic strategy for the treatment of progressive neurodegenerative disease such as Parkinson's disease.

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PMID: 21056612 [PubMed - indexed for MEDLINE]

PMCID: PMC3010303 [Available on 2012/1/1]

ASTAXANTHIN MAY HAVE THERAPEUTIC EFFECT AGAINST NEUROINFLAMMATION.

Life Sci. 2021 Feb 15;267:118943.

doi: 10.1016/j.lfs.2020.118943. Epub 2021 Jan 4.

Astaxanthin inhibits microglia M1 activation against inflammatory injury triggered by lipopolysaccharide through down-regulating miR-31-5p

[Xin Zhou](#)¹, [Junyu Zhang](#)², [Yuxin Li](#)², [Liao Cui](#)³, [Kefeng Wu](#)⁴, [Hui Luo](#)⁵

PMID: 33359248 DOI: [10.1016/j.lfs.2020.118943](https://doi.org/10.1016/j.lfs.2020.118943)

Abstract

Aims: Astaxanthin is a natural carotenoid, can readily cross the blood-brain barrier and exerts a powerful neuroprotective effect. In this study, experiments were performed to explore the underlying molecular mechanisms of which Astaxanthin inhibiting the microglia M1 activation.

Main Methods: BV2 cells and mice were pre-treated with Astaxanthin and treated by Lipopolysaccharide (LPS). The expressions of M1-related factors (pro-inflammatory cytokines and M1 markers) were measured by RT-qPCR and western blot. The target association between miR-31-5p and Numb was explored via luciferase activity assay. MiR-31-5p mimic was transfected into BV2 cells, then the cells were treated with Astaxanthin in combination with LPS. The expression of M1-related factors and Notch pathway-related molecules were measured via RT-qPCR, western blot and immunofluorescence assay.

Key findings: Precondition of BV2 cells with Astaxanthin inhibited the expression of M1-related factors triggered by LPS. In addition, Astaxanthin decreased the number of Iba1-positive microglia and downregulated the levels of M1-related factors in hippocampus in LPS-treated mice. Further investigation revealed that Astaxanthin-mediated suppression of M1-related factors levels was reversed by miR-31-5p mimic in BV2 cells stimulated by LPS. Subsequently, we verified that miR-31-5p repressed Numb expression by binding to the 3'-UTR of Numb mRNA. Also, Astaxanthin suppressed the expression of Notch1, Hes1 and Hes5 and improved the expression of Numb in BV2 cells challenged by LPS, but this alteration can be reversed by miR-31-5p mimic.

Significance: Our study demonstrated that down-regulating miR-31-5p by Astaxanthin could be a potential therapeutic approach to suppress neuroinflammation via regulating microglia M1 activation.

Astaxanthin improves stem cell potency by increasing the proliferation of neural progenitor cells.

[Int J Mol Sci.](#) 2010;11(12):5109-19. Epub 2010 Dec 9.

Astaxanthin Improves Stem Cell Potency via an Increase in the Proliferation of Neural Progenitor Cells.

[Kim JH](#), [Nam SW](#), [Kim BW](#), [Choi W](#), [Lee JH](#), [Kim WJ](#), [Choi YH](#).

Source

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Abstract

The present study was designed to investigate the question of whether or not astaxanthin improves stem cell potency via an increase in proliferation of neural progenitor cells (NPCs). Treatment with astaxanthin significantly increased proliferation and colony formation of NPCs. For identification of possible activated signaling molecules involved in active cell proliferation occurring after astaxanthin treatment, total protein levels of several proliferation-related proteins, and expression levels of proliferation-related transcription factors, were assessed in NPCs. In Western blot analysis, astaxanthin induced significant activation of phosphatidylinositol 3-kinase (PI3K) and its downstream mediators in a time-dependent manner. Results of RT-PCR analysis showed upregulation of proliferation-related transcription factors and stemness genes. To estimate the relevance of PI3K and mitogen-activated protein, or extracellular signal-regulated kinase kinase (MEK) signaling pathways in cell growth of astaxanthin-treated NPCs, inhibition assays were performed with LY294002, a specific inhibitor of PI3K, and PD98059, a specific inhibitor of MEK, respectively. These results clearly showed that astaxanthin induces proliferation of NPCs via activation of the PI3K and MEK signaling pathways and improves stem cell potency via stemness acting signals.

PMID: 21614195 [PubMed]

PMCID: PMC3100832

Astaxanthin improves memory in mice dose-dependently.

[Environ Geochem Health](#). 2007 Dec;29(6):483-9. Epub 2007 Aug 25.

Impact of astaxanthin-enriched algal powder of *Haematococcus pluvialis* on memory improvement in BALB/c mice.

[Zhang X¹](#), [Pan L](#), [Wei X](#), [Gao H](#), [Liu J](#).

Author information

Abstract

The impact of astaxanthin-enriched algal powder on auxiliary memory improvement was assessed in BALB/c mice pre-supplemented with different dosages of cracked green algal (*Haematococcus pluvialis*) powder daily for 30 days. The supplemented mice were first tested over 8 days to find a hidden platform by swimming in a Morris water maze. Then, for 5 days, the mice were used to search for a visible platform in a Morris water maze. After that, the mice practised finding a safe place--an insulated platform in a chamber--for 2 days. During these animal experimental periods, similar algal meals containing astaxanthin at 0, 0.26, 1.3 and 6.4 mg/kg body weight were continuously fed to each group of tested mice. Profiles of latency, distance, speed and the direction angle to the platforms as well as the diving frequency in each group were measured and analyzed. The process of mice jumping up onto the insulated platform and diving down to the copper-shuttered bottom with a 36 V electrical charge were also monitored by automatic video recording. The results of the Morris maze experiment showed that middle dosage of *H. pluvialis* meals (1.3 mg astaxanthin/kg body weight) significantly shortened the latency and distance required for mice to find a hidden platform. However, there was no obvious change in swim velocity in any of the supplemented groups. In contrast, the visible platform test showed a significant increase in latency and swim distance, and a significant decrease in swim speed for all groups of mice orally supplemented with *H. pluvialis* powder compared to the placebo group ($P < 0.05$ or $P < 0.01$). Mice supplemented with the algal meal hesitantly turned around the original hidden platform, in contrast to mice supplemented with placebo, who easily forgot the original location and accepted the visible platform as a new safe place. These results illustrate that astaxanthin-enriched *H. pluvialis* powder has the auxiliary property of memory improvement. The results from the platform diving test showed that the low and middle dosage of *H. pluvialis* powder, rather than the high dosage, increased the latency and reduced the frequency of diving from the safe insulated platform to the electrically stimulated copper shutter, especially in the low treatment group ($P < 0.05$). These results indicate that *H. pluvialis* powder is associated with dose-dependent memory improvement and that a low dosage of algal powder (\leq middle treatment group) is really good for improving the memory.

PMID:

17721823

[PubMed - indexed for MEDLINE]

Astaxanthin reduces neuropathic pain in rat and in-vitro models.

[Neurosci Lett](#). 2018 May 1;674:162-170. doi: 10.1016/j.neulet.2018.03.030. Epub 2018 Mar 17.

Astaxanthin ameliorates behavioral and biochemical alterations in in-vitro and in-vivo model of neuropathic pain.

[Sharma K¹](#), [Sharma D¹](#), [Sharma M¹](#), [Sharma N¹](#), [Bidve P¹](#), [Prajapati N¹](#), [Kalia K¹](#), [Tiwari V²](#).

Author information

Abstract

Despite considerable advances in understanding mechanisms involved in chronic pain, effective treatment remains limited. Astaxanthin, a marine natural drug, having potent anti-oxidant and anti-inflammatory activities is known to possess neuroprotective effects. However, effects of astaxanthin against nerve injury induce chronic pain remains unknown. Overactivity of glutamatergic NMDARs results in excitotoxicity which may participate in astrocytic and microglial activation during pathology which further contribute to the development of neuropathic pain. In this study, we investigate the effects of astaxanthin on oxido-inflammatory and NMDA receptor down-regulation pathway by using in-silico, in-vitro and in-vivo models of neuropathic pain. In-silico molecular docking study ascertained the binding affinity of astaxanthin to NMDA receptors and showed antagonistic effects. Data from in-vitro studies suggest that astaxanthin significantly reduces the oxidative stress induced by the lipopolysaccharides in C6 glial cells. In male Sprague dawley rats, a significant attenuation of neuropathic pain behavior was observed in Hargreaves test and von Frey hair test after astaxanthin treatment. Findings from the current study suggest that astaxanthin can be used as potential alternative in the treatment of chronic neuropathic pain. However, more detailed investigations are required to further probe the in-depth mechanism of action of astaxanthin.

KEYWORDS:

C6 glial cells; Mechanical allodynia; NMDA receptors; Neuropathic pain; Neuroprotection; Rats

PMID: 29559419

DOI: [10.1016/j.neulet.2018.03.030](https://doi.org/10.1016/j.neulet.2018.03.030)

Astaxanthin exerts significant anti-aging effects, prevents liver weight loss and improves locomotive muscular function in mouse model of jet lag.

[Endocr J.](#) 2018 May 28;65(5):569-578. doi: 10.1507/endocrj.EJ17-0500. Epub 2018 Mar 10.

Protective effects of astaxanthin on a combination of D-galactose and jet lag-induced aging model in mice.

[Ni Y¹](#), [Wu T¹](#), [Yang L¹](#), [Xu Y¹](#), [Ota T²](#), [Fu Z¹](#).

Author information

Abstract

Oxidative stress caused free radical and mitochondrial damage plays a critical role in the progression of aging and age-related damage at the cellular and tissue levels. Antioxidant supplementation has received growing attention and the effects of antioxidant on aging are increasingly assessed in both animal and human studies. However, additional and more promising treatments that contribute to the expansion of anti-aging therapies are needed. Astaxanthin, a super antioxidant carotenoid and free radical scavenger, inhibits lipid peroxidation more potently than vitamin E. In the present study, we investigated the preventative effects of astaxanthin on aging using an accelerated aging model: mice chronically treated with a combination of D-galactose and jet lag. After 6 weeks of treatment, astaxanthin administration tended to protect the liver weight loss in aged mice. It is probably by upregulating the mRNA expression of galactose-1-phosphate uridylyltransferase, which contribute to the enhancement of D-galactose metabolism. Astaxanthin supplementation also improved muscle endurance of aged mice in a swimming test. These results were associated with reduced oxidative stress in serum and increased anti-oxidative enzymes activities and mRNA expression in vivo. Moreover, astaxanthin reversed the dysregulation of aging-related gene expression caused by the combination of D-galactose and jet lag in the liver and kidney of mice. In conclusion, astaxanthin prevents liver weight loss, ameliorates locomotive muscular function, exerts significant anti-aging effects by reducing oxidative stress and improving the expression of age-related genes in D-galactose and jet lag-induced aging model.

KEYWORDS:

Aging; Antioxidant; Astaxanthin; D-galactose; Jet lag

PMID: 29526991

DOI: [10.1507/endocrj.EJ17-0500](https://doi.org/10.1507/endocrj.EJ17-0500)

[Indexed for MEDLINE]

Free full text

Astaxanthin combined with DHA prevents cognitive disorders in mouse model of Alzheimer's Disease.

[J Agric Food Chem.](#) 2018 May 16;66(19):4948-4957. doi: 10.1021/acs.jafc.8b00988. Epub 2018 May 7.

Effects of Astaxanthin and Docosahexaenoic-Acid-Acylated Astaxanthin on Alzheimer's Disease in APP/PS1 Double-Transgenic Mice.

[Che H¹](#), [Li Q¹](#), [Zhang T¹](#), [Wang D¹](#), [Yang L¹](#), [Xu J¹](#), [Yanagita T²](#), [Xue C^{1,3}](#), [Chang Y¹](#), [Wang Y^{1,3}](#).

Author information

Abstract

Alzheimer's disease (AD) is a progressive neurodegenerative disorder with the characteristics of senile plaques, neuroinflammation, neurofibrillary tangles, and destruction of synapse structure stability. Previous studies have verified the protective effects of astaxanthin (AST). However, whether synthesized docosahexaenoic-acid-acylated AST diesters (AST-DHA) could delay AD pathogenesis remains unclear. In the present study, APP/PSEN1 (APP/PS1) double-transgenic mice were administrated with AST and AST-DHA for 2 months. The results of radial 8-arm maze and Morris water maze tests showed that AST-DHA exerted more significant effects than AST in enhancing learning and memory levels of APP/PS1 mice. Further mechanical studies suggested that AST-DHA was superior to AST in regulating the parameters of oxidative stress, reducing tau hyperphosphorylation, suppressing neuroinflammation, and regulating inflammasome expression and activation in APP/PS1 mice. The findings suggested that AST-DHA attenuated cognitive disorders by reducing pathological features in APP/PS1 mice, suggesting that AST-DHA might be a potential therapeutic agent for AD.

KEYWORDS:

Alzheimer's disease; DHA-acylated AST esters; astaxanthin; cognitive disorder; neuroinflammation

PMID: 29695154

DOI: [10.1021/acs.jafc.8b00988](https://doi.org/10.1021/acs.jafc.8b00988)

[Indexed for MEDLINE]

ASTAXANTHIN AND FUcoxANTHIN DISPLAY MULTIPLE NEUROPROTECTIVE EFFECTS IN-VITRO.

Neurochem Int. 2019 Mar;124:215-224.

doi: 10.1016/j.neuint.2019.01.010. Epub 2019 Jan 9.

In vitro studies of the neuroprotective activities of astaxanthin and fucoxanthin against amyloid beta ($A\beta_{1-42}$) toxicity and aggregation

[Mousa Alghazwi](#)¹, [Scott Smid](#)², [Ian Musgrave](#)³, [Wei Zhang](#)⁴

- PMID: 30639263
- DOI: [10.1016/j.neuint.2019.01.010](https://doi.org/10.1016/j.neuint.2019.01.010)

Abstract

Amyloid beta ($A\beta$) can aggregate and form plaques, which are considered as one of the major hallmarks of Alzheimer's disease. This study aims to directly compare the neuroprotective activities in vitro of two marine-derived carotenoids astaxanthin and fucoxanthin that have shown a spectrum of biological activities, including neuroprotection. The in vitro neuroprotective activities were investigated against $A\beta_{1-42}$ -mediated toxicity in pheochromocytoma (PC-12) neuronal cells using the MTT cell viability assay, anti-apoptotic, antioxidant and neurite outgrowth activities; as well as inhibition against $A\beta_{1-42}$ fibrillization in the Thioflavin T (ThT) assay of fibril kinetics and via transmission electron microscopic (TEM) evaluation of fibril morphology. The results demonstrated that both astaxanthin and fucoxanthin exhibited multi-neuroprotective effects favouring fucoxanthin over astaxanthin supporting neuroprotective roles of marine-derived carotenoids as potential novel dementia prevention or therapeutic strategies.

Astaxanthin reduces spinal cord lesions, prevents cell death and inhibits lipid peroxidation in rats.

[Zhongguo Xiu Fu Chong Jian Wai Ke Za Zhi](#). 2018 May 1;32(5):548-553. doi: 10.7507/1002-1892.201712127.

[Effect of astaxanthin on the apoptosis after spinal cord injury in rats].

[Article in Chinese; Abstract available in Chinese from the publisher]

[Ren X¹](#), [Ding W²](#), [Yang X³](#).

Author information

Abstract

in [English](#), [Chinese](#)

OBJECTIVE:

To study the effects of astaxanthin on the apoptosis after spinal cord injury in rats.

METHODS:

One hundred and forty-four healthy adult Sprague Dawley rats were divided into experimental group, control group, and sham group according to the random number table ($n=48$). In the control group and the experimental group, the modified Allen's method was used to make the spinal cord injury model; in the sham group, only the lamina was cut without damaging the spinal cord. At immediate after operation, the rats in the experimental group were given intragastric administration of astaxanthin (75 mg/kg) twice a day; and the rats in the control group and the sham group were given equal amount of olive oil by gavage twice a day. BBB score was used to assess the motor function at 1 day and 1, 2, 3, and 4 weeks after operation. The malondialdehyde (MDA) content was determined by the thiobarbituric acid method at 24 hours after operation; and the activity of superoxide dismutase (SOD) was determined by the xanthine oxidase method. Apoptosis index (AI) was determined by TUNEL method at 6, 24, and 48 hours after operation. At 48 hours after operation, the water content of spinal cord was measured by dry-wet weight method, the lesion ratio of spinal cord was calculated, the ultrastructure of the spinal cord was observed by transmission electron microscopy, and ultrastructure scoring was performed using the Kaptanoglu score method.

RESULTS:

The BBB score in the control group and the experimental group was significantly lower than that in the sham group at each postoperative time point ($P<0.05$); and the BBB score in the experimental group were significantly higher than that in the control group at 1-4 weeks postoperatively ($P<0.05$). The MDA content in the control group and the experimental group was significantly higher than that in the sham group at 24 hours after operation, and in the experimental group was significantly lower than in the control group ($P<0.05$). The SOD activity in the control group and the experimental group was significantly lower than that in the sham group, and in the experimental group was significantly

higher than in the control group ($P<0.05$). At each time point postoperatively, the AI in the control group and the experimental group was significantly higher than that in the sham group, and in the experimental group was significantly lower than in the control group ($P<0.05$). At 48 hours after operation, the water content of spinal cord, the lesion ratio of spinal cord, and the ultrastructure score in the control group and the experimental group were significantly higher than those in the sham group, and in the experimental group were significantly lower than in the control group ($P<0.05$).

CONCLUSION:

Astaxanthin can inhibit the lipid peroxidation, reduce the apoptosis, reduce the spinal cord edema, reduce the spinal cord lesion, reduce the histopathological damage after spinal cord injury, and improve the motor function of rats with spinal cord injury, and protect the spinal cord tissue, showing an obvious neuroprotective effect.

KEYWORDS:

Astaxanthin; apoptosis; rat; spinal cord injury

PMID: 29806341

DOI: [10.7507/1002-1892.201712127](https://doi.org/10.7507/1002-1892.201712127)

[Indexed for MEDLINE]

Astaxanthin reviewed as a potential neuroprotective agent for neurological diseases.

[Mar Drugs](#). 2015 Sep 11;13(9):5750-66. doi: 10.3390/md13095750.

Astaxanthin as a Potential Neuroprotective Agent for Neurological Diseases.

[Wu H¹](#), [Niu H²](#), [Shao A³](#), [Wu C⁴](#), [Dixon BJ⁵](#), [Zhang J⁶](#), [Yang S⁷](#), [Wang Y⁸](#).

Author information

Abstract

Neurological diseases, which consist of acute injuries and chronic neurodegeneration, are the leading causes of human death and disability. However, the pathophysiology of these diseases have not been fully elucidated, and effective treatments are still lacking. Astaxanthin, a member of the xanthophyll group, is a red-orange carotenoid with unique cell membrane actions and diverse biological activities. More importantly, there is evidence demonstrating that astaxanthin confers neuroprotective effects in experimental models of acute injuries, chronic neurodegenerative disorders, and neurological diseases. The beneficial effects of astaxanthin are linked to its oxidative, anti-inflammatory, and anti-apoptotic characteristics. In this review, we will focus on the neuroprotective properties of astaxanthin and explore the underlying mechanisms in the setting of neurological diseases.

KEYWORDS:

apoptosis; astaxanthin; inflammation; neurological diseases; neuroprotection; oxidative stress

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[26378548](#)

PMCID:

[PMC4584352](#)

DOI:

[10.3390/md13095750](#)

Astaxanthin reviewed for its neuroprotective properties.

[Nutrients](#). 2014 Mar 24;6(3):1293-317. doi: 10.3390/nu6031293.

Neuroprotective properties of the marine carotenoid astaxanthin and omega-3 fatty acids, and perspectives for the natural combination of both in krill oil.

[Barros MP](#)¹, [Poppe SC](#)², [Bondan EF](#)³.

Author information

Abstract

The consumption of marine fishes and general seafood has long been recommended by several medical authorities as a long-term nutritional intervention to preserve mental health, hinder neurodegenerative processes, and sustain cognitive capacities in humans. Most of the neurological benefits provided by frequent seafood consumption comes from adequate uptake of omega-3 and omega-6 polyunsaturated fatty acids, n-3/n-6 PUFAs, and antioxidants. Optimal n-3/n-6 PUFAs ratios allow efficient inflammatory responses that prevent the initiation and progression of many neurological disorders. Moreover, interesting in vivo and clinical studies with the marine antioxidant carotenoid astaxanthin (present in salmon, shrimp, and lobster) have shown promising results against free radical-promoted neurodegenerative processes and cognition loss. This review presents the state-of-the-art applications of n-3/n-6 PUFAs and astaxanthin as nutraceuticals against neurodegenerative diseases associated with exacerbated oxidative stress in CNS. The fundamental "neurohormesis" principle is discussed throughout this paper. Finally, new perspectives for the application of a natural combination of the aforementioned anti-inflammatory and antioxidant agents (found in krill oil) are also presented herewith.

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24667135

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PMCID:

PMC3967194

Free PMC Article

Astaxanthin reviewed as a neuroprotective agent.

Marine Drugs 2015, 13, 1-x manuscripts; doi:10.3390/md130x000x ISSN 1660-3397

Astaxanthin as a Potential Neuroprotective Agent for Neurological Diseases

Haijian Wu ¹, **Huanjiang Niu** ¹, **Anwen Shao** ², **Cheng Wu** ¹, **Brandon J. Dixon** ³, **Jianmin Zhang** ², **Shuxu Yang** ^{1,*} and **Yirong Wang** ^{1,*}

Received: 6 June 2015 / Accepted: 7 September 2015 / Published:

Abstract: Neurological diseases, which consist of acute injuries and chronic neurodegeneration, are the leading causes of human death and disability. However, the pathophysiology of these diseases have not been fully elucidated, and effective treatments are still lacking. Astaxanthin, a member of the xanthophyll group, is a red-orange carotenoid with unique cell membrane actions and diverse biological activities. More importantly, there is evidence demonstrating that astaxanthin confers neuroprotective effects in experimental models of acute injuries, chronic neurodegenerative disorders, and neurological diseases. The beneficial effects of astaxanthin are linked to its oxidative, anti-inflammatory, and anti-apoptotic characteristics. In this review, we will focus on the neuroprotective properties of astaxanthin and explore the underlying mechanisms in the setting of neurological diseases.

Astaxanthin reviewed as a potential therapeutic aid in preserving cognitive function in neurodegeneration and aging.

[Geroscience](#). 2017 Feb;39(1):19-32. doi: 10.1007/s11357-017-9958-x. Epub 2017 Feb 13.

Neuroprotective mechanisms of astaxanthin: a potential therapeutic role in preserving cognitive function in age and neurodegeneration.

[Grimmig B¹](#), [Kim SH¹](#), [Nash K²](#), [Bickford PC^{3,4}](#), [Douglas Shytle R¹](#).

Author information

Abstract

Astaxanthin (AXT) is a carotenoid with multiple health benefits. It is currently marketed as a health supplement and is well known for its antioxidant capacity. Recent evidence has emerged to suggest a broad range of biological activities. The interest in this compound has increased dramatically over the last few years and many studies are now applying this molecule across many disease models. Results from the current research are beginning to come together to suggest neuroprotective properties including anti-inflammatory, anti-apoptotic, and antioxidant effects, as well as the potential to promote or maintain neural plasticity. These emergent mechanisms of actions implicate AXT as a promising therapeutic agent for neurodegenerative disease. This review will examine and extrapolate from the recent literature to build support for the use of AXT in mitigating neuropathy in normal aging and neurodegenerative disease.

KEYWORDS:

Aging; Astaxanthin; Microglial function; Neural plasticity; Neuroprotection

PMID: 28299644

PMCID: [PMC5352583](#)

DOI: [10.1007/s11357-017-9958-x](#)

[Indexed for MEDLINE]

[Free PMC Arti](#)

Astaxanthin reviewed as a potential therapeutic agent for Parkinson's Disease.

[Brain Sci.](#) 2016 Sep 23;6(4). pii: E41. doi: 10.3390/brainsci6040041.

Immunomodulators as Therapeutic Agents in Mitigating the Progression of Parkinson's Disease.

[Grimmig B](#)¹, [Morganti J](#)², [Nash K](#)³, [Bickford PC](#)^{4,5}.

[Author information](#)

Abstract

Parkinson's disease (PD) is a common neurodegenerative disorder that primarily afflicts the elderly. It is characterized by motor dysfunction due to extensive neuron loss in the substantia nigra pars compacta. There are multiple biological processes that are negatively impacted during the pathogenesis of PD, and are implicated in the cell death in this region. Neuroinflammation is evidently involved in PD pathology and mitigating the inflammatory cascade has been a therapeutic strategy. Age is the number one risk factor for PD and thus needs to be considered in the context of disease pathology. Here, we discuss the role of neuroinflammation within the context of aging as it applies to the development of PD, and the potential for two representative compounds, fractalkine and astaxanthin, to attenuate the pathophysiology that modulates neurodegeneration that occurs in Parkinson's disease.

KEYWORDS:

Parkinson's disease; astaxanthin; fractalkine; microglia; neuroinflammation

PMID: 27669315

PMCID: [PMC5187555](#)

DOI: [10.3390/brainsci6040041](#)

[Free PMC Article](#)

Astaxanthin reviewed for its mechanisms of action in brain health.

[Pharmacol Res.](#) 2018 Oct;136:1-20. doi: 10.1016/j.phrs.2018.08.012. Epub 2018 Aug 17.

Astaxanthin: A mechanistic review on its biological activities and health benefits.

[Fakhri S](#)¹, [Abbaszadeh F](#)², [Dargahi L](#)³, [Jorjani M](#)⁴.

Author information

Abstract

Astaxanthin (AST) is a potent lipid-soluble keto-carotenoid with auspicious effects on human health. It protects organisms against a wide range of diseases with excellent safety and tolerability. Various imperative biological activities in vitro and in vivo models have been suggested for AST. This review article is focused on the therapeutic potentials, biological activities and beneficial health effects of AST. The pharmacological mechanisms of action of AST in the treatment and prevention of the peripheral and central nervous system diseases was also reviewed to provide new insights to researchers. Finally, we suggested a novel hypothesis for the mechanism of action of AST in neuropathic pain following spinal cord injury.

KEYWORDS:

Alpha-Tocopherol (PubChem CID: 14985); Astaxanthin; Astaxanthin (PubChem CID: 5368397); Azoxymethane (PubChem CID: 33184); Beta-Carotene (PubChem CID: 5280489); Beta-Cryptoxanthin (PubChem CID: 5281235); Biological activities; Canthaxanthin (PubChem CID: 5281227); Health benefits; Lutein (PubChem CID: 5281243); Pharmacology; Zeaxanthin (PubChem CID: 5280899)

PMID: 30121358

DOI: [10.1016/j.phrs.2018.08.012](https://doi.org/10.1016/j.phrs.2018.08.012)

Astaxanthin reviewed as a neuroprotective with elucidation of its mechanisms.

[Mar Drugs](#). 2018 Jul 24;16(8). pii: E247. doi: 10.3390/md16080247.

On the Neuroprotective Role of Astaxanthin: New Perspectives?

[Galasso C](#)¹, [Orefice I](#)², [Pellone P](#)³, [Cirino P](#)⁴, [Miele R](#)⁵, [Iannora A](#)⁶, [Brunet C](#)⁷, [Sansone C](#)⁸.

Author information

Abstract

Astaxanthin is a carotenoid with powerful antioxidant and anti-inflammatory activity produced by several freshwater and marine microorganisms, including bacteria, yeast, fungi, and microalgae. Due to its deep red-orange color it confers a reddish hue to the flesh of salmon, shrimps, lobsters, and crayfish that feed on astaxanthin-producing organisms, which helps protect their immune system and increase their fertility. From the nutritional point of view, astaxanthin is considered one of the strongest antioxidants in nature, due to its high scavenging potential of free radicals in the human body. Recently, astaxanthin is also receiving attention for its effect on the prevention or co-treatment of neurological pathologies, including Alzheimer and Parkinson diseases. In this review, we focus on the neuroprotective properties of astaxanthin and explore the underlying mechanisms to counteract neurological diseases, mainly based on its capability to cross the blood-brain barrier and its oxidative, anti-inflammatory, and anti-apoptotic properties.

KEYWORDS:

astaxanthin; neuroactive carotenoids; neurodegenerative diseases; neuroinflammation; neuroprotective effect

PMID: 30042358

PMCID: [PMC6117702](#)

DOI: [10.3390/md16080247](#)

[Indexed for MEDLINE]

[Free PMC Article](#)

Astaxanthin reviewed for possible neuroprotective effects against various neurodegenerative disorders with a particular emphasis on Parkinson's disease.

[Neuromolecular Med.](#) 2014 Jun;16(2):217-30. doi: 10.1007/s12017-014-8294-x. Epub 2014 Feb 13.

Oxidative stress-induced signaling pathways implicated in the pathogenesis of Parkinson's disease.

[Gaki GS¹](#), [Papavassiliou AG](#).

Author information

Abstract

Parkinson's disease is the second most common neurodegenerative movement disorder; however, its etiology remains elusive. Nevertheless, in vivo observations have concluded that oxidative stress is one of the most common causes in the pathogenesis of Parkinson's disease. It is known that mitochondria play a crucial role in reactive oxygen species-mediated pathways, and several gene products that associate with mitochondrial function are the subject of Parkinson's disease research. The PTEN-induced kinase 1 (PINK1) protects cells from mitochondrial dysfunction and is linked to the autosomal recessive familial form of the disease. PINK1 is a key player in many signaling pathways engaged in mitophagy, apoptosis, or microglial inflammatory response and is induced by oxidative stress. Several proteins participate in mitochondrial networks, and they are associated with PINK1. The E3 ubiquitin ligase Parkin, the protease presenilin-associated rhomboid-like serine protease, the tyrosine kinase c-Abl, the protein kinase MARK2, the protease HtrA2, and the tumor necrosis factor receptor-associated protein 1 (TRAP1) provide different steps of control in protection against oxidative stress. Furthermore, environmental toxins, such as 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine, have been identified as contributors to parkinsonism by increasing oxidative stress in dopaminergic neurons. The present review discusses the mechanisms and effects of oxidative stress, the emerging concept of the impact of environmental toxins, and a possible neuroprotective role of the antioxidant astaxanthin in various neurodegenerative disorders with particular emphasis in Parkinson's disease.

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24522549

[PubMed - indexed for MEDLINE]

Molecules. 2019 Jul 20;24(14):2640.

doi: 10.3390/molecules24142640.

The Neuroprotective Effects of Astaxanthin: Therapeutic Targets and Clinical Perspective

[Sajad Fakhri](#)¹, [Ina Yosifova Aneva](#)², [Mohammad Hosein Farzaei](#)³, [Eduardo Sobarzo-Sánchez](#)^{4,5}

- PMID: **31330843**
- PMCID: [PMC6680436](#)
- DOI: [10.3390/molecules24142640](#)

Free PMC article

Abstract

As the leading causes of human disability and mortality, neurological diseases affect millions of people worldwide and are on the rise. Although the general roles of several signaling pathways in the pathogenesis of neurodegenerative disorders have so far been identified, the exact pathophysiology of neuronal disorders and their effective treatments have not yet been precisely elucidated. This requires multi-target treatments, which should simultaneously attenuate neuronal inflammation, oxidative stress, and apoptosis. In this regard, astaxanthin (AST) has gained growing interest as a multi-target pharmacological agent against neurological disorders including Parkinson's disease (PD), Alzheimer's disease (AD), brain and spinal cord injuries, neuropathic pain (NP), aging, depression, and autism. The present review highlights the neuroprotective effects of AST mainly based on its anti-inflammatory, antioxidative, and anti-apoptotic properties that underlies its pharmacological mechanisms of action to tackle neurodegeneration. The need to develop novel AST delivery systems, including nanoformulations, targeted therapy, and beyond, is also considered.

Mar Drugs. 2020 Jul 5;18(7):351.

doi: 10.3390/md18070351.

Astaxanthin as a Putative Geroprotector: Molecular Basis and Focus on Brain Aging

[Vincenzo Sorrenti](#)^{1,2}, [Sergio Davinelli](#)³, [Giovanni Scapagnini](#)³, [Bradley J Willcox](#)^{4,5}, [Richard C Allsopp](#)⁶, [Donald C Willcox](#)^{4,5,7}

- PMID: **32635607**
- PMCID: [PMC7401246](#)
- DOI: [10.3390/md18070351](#)

Free PMC article

Abstract

In recent years, the scientific interest in natural compounds with geroprotective activities has grown exponentially. Among the various naturally derived molecules, astaxanthin (ASX) represents a highly promising candidate geroprotector. By virtue of the central polyene chain, ASX acts as a scavenger of free radicals in the internal membrane layer and simultaneously controls oxidation on the membrane surface. Moreover, several studies have highlighted ASX's ability to modulate numerous biological mechanisms at the cellular level, including the modulation of transcription factors and genes directly linked to longevity-related pathways. One of the main relevant evolutionarily-conserved transcription factors modulated by astaxanthin is the forkhead box O3 gene (FOXO3), which has been recognized as a critical controller of cell fate and function. Moreover, FOXO3 is one of only two genes shown to robustly affect human longevity. Due to its tropism in the brain, ASX has recently been studied as a putative neuroprotective molecule capable of delaying or preventing brain aging in different experimental models of brain damage or neurodegenerative diseases. Astaxanthin has been observed to slow down brain aging by increasing brain-derived neurotrophic factor (BDNF) levels in the brain, attenuating oxidative damage to lipids, protein, and DNA and protecting mitochondrial functions. Emerging data now suggest that ASX can modulate Nrf2, FOXO3, Sirt1, and Klotho proteins that are linked to longevity. Together, these mechanisms provide support for a role of ASX as a potential geroneuroprotector.

ASTAXANTHIN REVIEWED FOR ITS POTENTIAL THERAPEUTIC EFFECT FOR ALZHEIMER'S RESULTING IN SLOWER MEMORY DECLINE IN ANIMAL AND HUMAN STUDIES.

Open Biol. 2021 Jun;11(6):210013.

doi: 10.1098/rsob.210013. Epub 2021 Jun 30.

Therapeutic potential of astaxanthin and superoxide dismutase in Alzheimer's disease

[Vyshnavy Balendra](#)¹, [Sandeep Kumar Singh](#)²

- PMID: [34186009](#)
- PMCID: [PMC8241491](#)
- DOI: [10.1098/rsob.210013](#)

Free PMC article

Abstract

Oxidative stress, the imbalance of the antioxidant system, results in an accumulation of neurotoxic proteins in Alzheimer's disease (AD). The antioxidant system is composed of exogenous and endogenous antioxidants to maintain homeostasis. Superoxide dismutase (SOD) is an endogenous enzymatic antioxidant that converts superoxide ions to hydrogen peroxide in cells. SOD supplementation in mice prevented cognitive decline in stress-induced cells by reducing lipid peroxidation and maintaining neurogenesis in the hippocampus. Furthermore, SOD decreased expression of BACE1 while reducing plaque burden in the brain. Additionally, Astaxanthin (AST), a potent exogenous carotenoid, scavenges superoxide anion radicals. Mice treated with AST showed slower memory decline and decreased depositions of amyloid-beta ($A\beta$) and tau protein. Currently, the neuroprotective potential of these supplements has only been examined separately in studies. However, a single antioxidant cannot sufficiently resist oxidative damage to the brain, therefore, a combinatory approach is proposed as a relevant therapy for ameliorating pathological changes in AD.

Cardiovascular Health

Astaxanthin inhibits LDL oxidation in human clinical study and may contribute to the prevention of atherosclerosis. Results were best at 14.4mg per day as compared to 3.6mg per day and 21.6mg per day.

[J Atheroscler Thromb.](#) 2000;7(4):216-22.

Inhibition of low-density lipoprotein oxidation by astaxanthin.

[Iwamoto T¹](#), [Hosoda K](#), [Hirano R](#), [Kurata H](#), [Matsumoto A](#), [Miki W](#), [Kamiyama M](#), [Itakura H](#), [Yamamoto S](#), [Kondo K](#).

Author information

Abstract

Marine animals produce astaxanthin which is a carotenoid and antioxidant. In this study we determined the in vitro and ex vivo effects of astaxanthin on LDL oxidation. The oxidation of LDL was measured in a 1 ml reaction system consisting of increasing concentrations of astaxanthin (12.5, 25.0, 50.0 microg/ml), 400 microM V-70 (2, 2'-azobis(4-methoxy-2, 4-dimethylvaleronitrile)), and LDL (70 microg/ml protein). Astaxanthin dose, dependently significantly prolonged the oxidation lag time (31.5, 45.4, 65.0 min) compared with the control (19.9 min). For the ex vivo study 24 volunteers (mean age 28.2 [SD 7.8] years) consumed astaxanthin at doses of 1.8, 3.6, 14.4 and 21.6 mg per day for 14 days. No other changes were made in the diet. Fasting venous blood samples were taken at days 0, +14. LDL lag time was longer (5.0, 26.2, 42.3 and 30.7% respectively) compared with day 0 after consuming astaxanthin at doses of 1.8, 3.6, 14.4 and 21.6 mg for 14 days compared with day 0, but there was no difference in oxidation of LDL between day 0 (lag time 59.9+/-7.2 min) and day 14 (57.2+/-6.0 min) in the control group. Our results provide evidence that consumption of marine animals producing astaxanthin inhibits LDL oxidation and possibly therefore contributes to the prevention of atherosclerosis.

PMID:

11521685

[PubMed - indexed for MEDLINE]

Astaxanthin reduces blood pressure, improves glucose metabolism and reduces visceral body fat mass in placebo-controlled randomized study on patients with Type-2 diabetes.

[Asia Pac J Clin Nutr.](#) 2018;27(2):341-346. doi: 10.6133/apjcn.052017.11.

Astaxanthin improves glucose metabolism and reduces blood pressure in patients with type 2 diabetes mellitus.

[Mashhadi NS¹](#), [Zakerkish M²](#), [Mohammadiasl J³](#), [Zarei M⁴](#), [Mohammadshahi M⁵](#), [Haghighizadeh MH⁶](#).

Author information

Abstract

BACKGROUND AND OBJECTIVES:

This randomized, placebo-controlled trial was performed for 8 weeks to investigate the potential effects of astaxanthin (AST) supplementation on the adiponectin concentration, lipid peroxidation, glycemic control, insulin sensitivity, and anthropometric indices in participants with type 2 diabetes mellitus.

METHODS AND STUDY DESIGN:

We enrolled 44 participants with type 2 diabetes who met our inclusion criteria. Eight milligrams of AST supplementation or a placebo were randomly administered once daily for 8 weeks to these participants.

RESULTS:

The 8-week administration of AST supplementation increased the serum adiponectin concentration and reduced visceral body fat mass ($p < 0.01$), serum triglyceride and very-low-density lipoprotein cholesterol concentrations, and systolic blood pressure ($p < 0.05$). Furthermore, AST significantly reduced the fructosamine concentration ($p < 0.05$) and marginally reduced the plasma glucose concentration ($p = 0.057$).

CONCLUSIONS:

We demonstrated that because participants with type 2 diabetes often have hypertriglycemia and uncontrolled glucose metabolism; our findings of dual beneficial effects are clinically valuable. Our results may provide a novel complementary treatment with potential impacts on diabetic complications without adverse effects.

PMID: 29384321

DOI: [10.6133/apjcn.052017.11](#)

Free full text

Astaxanthin decreases blood pressure and improves oxidative stress in human clinical trial.

Anti-Aging Med

Anti-Aging Med 6(4), 15-21, 2009

Japanese Society of Anti-Aging Medicine

Efficacy and safety of eight-week treatment with astaxanthin in individuals screened for increased oxidative stress burden

- **Iwabayashi Masaaki, Fujioka Noriko, Nomoto Keitaro, Miyazaki Ryo, Takahashi Hozumi, Hibino Sawako, Takahashi Yoko, Nishikawa Koji, Nishida Mitsunori, Yonei Yoshikazu,**
- **Abstract**

Objective: An open-label noncontrolled study was conducted in subjects with increased oxidative stress burden to evaluate the mental and physical effects of antioxidant astaxanthin. **Methods:** Of 35 healthy postmenopausal women, 21 with high oxidative stress (diacron-reactive oxygen metabolites; d-ROM) were selected, and 20 (55.7±4.8 years old, BMI 22.1±3.9) were included in the study, after excluding 1 dropout. In subjects orally treated with astaxanthin (Fuji Chemical Industry) at a daily dose of 12 mg for eight weeks, Anti-Aging QOL Common Questionnaire, somatometry, hematological examination/urinalysis, oxidative stress test, and vascular function tests (cardio ankle vascular index, CAVI; ankle brachial pressure index, ABI; fingertip acceleration pulse wave; flow-mediated dilation FMD) were performed before and four and eight weeks after the start of the study. **Results:** After eight-week treatment with astaxanthin, significant improvement was observed in 5 of 34 physical symptoms listed in the common questionnaire, including "tired eyes", "stiff shoulders", "constipation", "gray hair", and "cold skin", and in 3 of 21 mental symptoms, including "daily life is not enjoyable", "difficulty in falling asleep", and "a sense of tension". In addition, systolic (118.0±16.4 mmHg at baseline, -4.6%, p=0.021) and diastolic blood pressure (74.1±11.7 mmHg at baseline, -6.9%, p<0.001) significantly decreased. In the vascular function test, CAVI, fingertip acceleration pulse wave, and FMD did not change, but ABI significantly increased from 1.06±0.10 at baseline to 1.10±0.06 at Week 8 (+3.7%, p=0.030). In the oxidative stress test, d-ROM did not change, but BAP significantly increased (+4.6%, p=0.030). In biochemical examination, AST (-19.2%, p=0.044), LDH (-6.4%, p=0.006), and HbA1c (-3.2%, p<0.001) significantly improved. Although IGF-I and insulin did not change, DHEA-s (-15.1%, p<0.001), cortisol (-22.8%, p=0.002), and adiponectin (-14.1%, p=0.003) decreased. No serious adverse event occurred during or after the study. **Conclusion:** Results show that astaxanthin may enhance antioxidant capacity (increase BAP), reduce lower limb vascular resistance (increase ABI), decrease blood pressure, and improve physical symptoms in women with high oxidative stress.

ASTAXANTHIN IMPROVED EXERCISE TOLERANCE; REDUCED OXIDATIVE STRESS; AND IMPROVED CARDIAC CONTRACTILITY IN HEART FAILURE PATIENTS IN HUMAN CLINICAL STUDY.

Nutrients. 2020 Jun 26;12(6):1896.

doi: 10.3390/nu12061896.

Effects of 3-Month Astaxanthin Supplementation on Cardiac Function in Heart Failure Patients with Left Ventricular Systolic Dysfunction-A Pilot Study

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PMID: [32604721](#) PMCID: [PMC7353230](#) DOI: [10.3390/nu12061896](#)

Abstract

Astaxanthin has strong antioxidant properties. We conducted a prospective pilot study on heart failure (HF) patients with left ventricular (LV) systolic dysfunction to investigate improvements in cardiac function and exercise tolerance in relation to suppression of oxidative stress by 3-month astaxanthin supplementation. Oxidative stress markers-serum Diacron reactive oxygen metabolite (dROM), biological antioxidant potential (BAP), and urinary 8-hydroxy-2'-deoxyguanosine (8-OHdG) concentrations, LV ejection fraction (LVEF), and 6-min walk distance (6MWD) were assessed before and after 3-month astaxanthin supplementation. Finally, the data of 16 HF patients were analyzed. Following 3-month astaxanthin supplementation, dROM level decreased from 385.6 ± 82.6 U.CARR to 346.5 ± 56.9 U.CARR ($p = 0.041$) despite no changes in BAP and urinary 8-OHdG levels. LVEF increased from $34.1 \pm 8.6\%$ to $38.0 \pm 10.0\%$ ($p = 0.031$) and 6MWD increased from 393.4 ± 95.9 m to 432.8 ± 93.3 m ($p = 0.023$). Significant relationships were observed between percent changes in dROM level and those in LVEF. In this study, following 3-month astaxanthin supplementation, suppressed oxidative stress and improved cardiac contractility and exercise tolerance were observed in HF patients with LV systolic dysfunction. Correlation between suppression of oxidative stress and improvement of cardiac contractility suggests that suppression of oxidative stress by astaxanthin supplementation had therapeutic potential to improve cardiac functioning.

Astaxanthin increases HDL (good) cholesterol and adiponectin in patients with mild hyperlipidemia in randomized placebo-controlled human clinical study.

[Atherosclerosis](#). 2010 Apr;209(2):520-3. Epub 2009 Oct 14.

Administration of natural astaxanthin increases serum HDL-cholesterol and adiponectin in subjects with mild hyperlipidemia.

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Abstract

BACKGROUND: Astaxanthin has been reported to improve dyslipidemia and metabolic syndrome in animals, but such effects in humans are not well known.

METHODS: Placebo-controlled astaxanthin administration at doses of 0, 6, 12, 18 mg/day for 12 weeks was randomly allocated to 61 non-obese subjects with fasting serum triglyceride of 120-200mg/dl and without diabetes and hypertension, aged 25-60 years.

RESULTS: In before and after tests, body mass index (BMI) and LDL-cholesterol were unaffected at all doses, however, triglyceride decreased, while HDL-cholesterol increased significantly. Multiple comparison tests showed that 12 and 18 mg/day doses significantly reduced triglyceride, and 6 and 12 mg doses significantly increased HDL-cholesterol. Serum adiponectin was increased by astaxanthin (12 and 18 mg/day), and changes of adiponectin correlated positively with HDL-cholesterol changes independent of age and BMI.

CONCLUSIONS: This first-ever randomized, placebo-controlled human study suggests that astaxanthin consumption ameliorates triglyceride and HDL-cholesterol in correlation with increased adiponectin in humans.

PMID: 19892350 [PubMed - indexed for MEDLINE]

Astaxanthin decreases blood lipid peroxidation in double-blind, placebo controlled human clinical trial.

[Int J Vitam Nutr Res.](#) 2007 Jan;77(1):3-11.

Effects of astaxanthin supplementation on lipid peroxidation.

[Karppi J¹](#), [Rissanen TH](#), [Nyssönen K](#), [Kaikkonen J](#), [Olsson AG](#), [Voutilainen S](#), [Salonen JT](#).

Author information

Abstract

Astaxanthin, the main carotenoid pigment in aquatic animals, has greater antioxidant activity in vitro (protecting against lipid peroxidation) and a more polar configuration than other carotenoids. We investigated the effect of three-month astaxanthin supplementation on lipid peroxidation in healthy non-smoking Finnish men, aged 19-33 years by using a randomized double-blind study design. Also absorption of astaxanthin from capsules into bloodstream and its safety were evaluated. The intervention group received two 4-mg astaxanthin (Astaxin) capsules daily, and the control group two identical-looking placebo capsules. Astaxanthin supplementation elevated plasma astaxanthin levels to 0.032 pmol/L ($p < 0.001$ for the change compared with the placebo group). We observed that levels of plasma 12- and 15-hydroxy fatty acids were reduced statistically significantly in the astaxanthin group ($p = 0.048$ and $p = 0.047$ respectively) during supplementation, but not in the placebo group and the change of 15-hydroxy fatty acid was almost significantly greater ($p = 0.056$) in the astaxanthin group, as compared with the placebo group. The present study suggests that intestinal absorption of astaxanthin delivered as capsules is adequate, and well tolerated. Supplementation with astaxanthin may decrease in vivo oxidation of fatty acids in healthy men.

PMID:

17685090

[PubMed - indexed for MEDLINE]

ASTAXANTHIN IMPROVES PERFORMANCE; ENHANCES WHOLE-BODY FAT OXIDATION RATES; AND REDUCES RESPIRATORY EXCHANGE RATIO IN RECREATIONAL CYCLISTS IN ONLY SEVEN DAYS OF SUPPLEMENTATION IN HUMAN CLINICAL TRIAL.

J Sci Med Sport. 2021 Jan;24(1):92-97.

doi: 10.1016/j.jsams.2020.06.017. Epub 2020 Jul 3.

The effect of astaxanthin supplementation on performance and fat oxidation during a 40 km cycling time trial

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PMID: 32660833 DOI: [10.1016/j.jsams.2020.06.017](https://doi.org/10.1016/j.jsams.2020.06.017)

Abstract

Objectives: This study aimed to investigate whether supplementation with 12 mg·day⁻¹ astaxanthin for 7 days can improve exercise performance and metabolism during a 40 km cycling time trial.

Design: A randomised, double-blind, crossover design was employed.

Methods: Twelve recreationally trained male cyclists (VO_{2peak} : 56.5 ± 5.5 mL·kg⁻¹·min⁻¹, W_{max} : 346.8 ± 38.4 W) were recruited. Prior to each experimental trial, participants were supplemented with either 12 mg·day⁻¹ astaxanthin or an appearance-matched placebo for 7 days (separated by 14 days of washout). On day 7 of supplementation, participants completed a 40 km cycling time trial on a cycle ergometer, with indices of exercise metabolism measured throughout.

Results: Time to complete the 40 km cycling time trial was improved by $1.2 \pm 1.7\%$ following astaxanthin supplementation, from 70.76 ± 3.93 min in the placebo condition to 69.90 ± 3.78 min in the astaxanthin condition (mean improvement = 51 ± 71 s, $p = 0.029$, $g = 0.21$). Whole-body fat oxidation rates were also greater ($+0.09 \pm 0.13$ g·min⁻¹, $p = 0.044$, $g = 0.52$), and the respiratory exchange ratio lower (-0.03 ± 0.04 , $p = 0.024$, $g = 0.60$) between 39-40 km in the astaxanthin condition.

Conclusions: Supplementation with 12 mg·day⁻¹ astaxanthin for 7 days provided an ergogenic benefit to 40 km cycling time trial performance in recreationally trained male cyclists and enhanced whole-body fat oxidation rates in the final stages of this endurance-type performance event.

ASTAXANTHIN-CONTAINING FORMULA INCREASES RESTING OXYGEN CONSUMPTION; DECREASES OXIDATION MARKER AFTER EXERCISE; AND INCREASES MAXIMAL VOLUNTARY CONTRACTION, LEADING TO CONCLUSION THAT THE FORMULA SUPPORTS RESISTANCE TRAINING-INDUCED STRENGTH AND METABOLIC APPLICATIONS IN HUMAN CLINICAL TRIAL.

Antioxidants (Basel). 2021 Jan 14;10(1):113.
doi: 10.3390/antiox10010113.

Astaxanthin-, β -Carotene-, and Resveratrol-Rich Foods Support Resistance Training-Induced Adaptation

[Aki Kawamura](#)^{1,2}, [Wataru Aoi](#)¹, [Ryo Abe](#)^{1,3}, [Yukiko Kobayashi](#)¹, [Masashi Kuwahata](#)¹, [Akane Higashi](#)¹

PMID: [33466842](#) PMCID: [PMC7830030](#) DOI: [10.3390/antiox10010113](#) [Free PMC article](#)

Abstract

Resistance training adaptively increases the muscle strength associated with protein anabolism. Previously, we showed that the combined intake of astaxanthin, β -carotene, and resveratrol can accelerate protein anabolism in the skeletal muscle of mice. The purpose of this study was to investigate the effect of anabolic nutrient-rich foods on muscle adaptation induced by resistance training. Twenty-six healthy men were divided into control and intervention groups. All participants underwent a resistance training program twice a week for 10 weeks. Astaxanthin-, β -carotene-, and resveratrol-rich foods were provided to the intervention group. Body composition, nutrient intake, maximal voluntary contraction of leg extension, oxygen consumption, and serum carbonylated protein level were measured before and after training. The skeletal muscle mass was higher after training than before training in both groups ($p < 0.05$). Maximal voluntary contraction was increased after training in the intervention group ($p < 0.05$), but not significantly increased in the control group. Resting oxygen consumption was higher after training in the intervention group only ($p < 0.05$). As an oxidative stress marker, serum carbonylated protein level tended to be lower immediately after exercise than before exercise in the intervention group only ($p = 0.056$). Intake of astaxanthin-, β -carotene-, and resveratrol-rich foods supported resistance training-induced strength and metabolic adaptations.

Astaxanthin improves blood flow rate at 6mg per day in placebo-controlled human clinical trial.

[J Clin Biochem Nutr.](#) 2008 Sep;43(2):69-74. doi: 10.3164/jcbn.2008048.

Effects of astaxanthin on human blood rheology.

[Miyawaki H¹](#), [Takahashi J](#), [Tsukahara H](#), [Takehara I](#).

Author information

Abstract

Effects of astaxanthin (AX) derived from *H. pluvialis* on human blood rheology were investigated in 20 adult men with a single-blind method. The experimental group was 57.5 +/- 9.8 years of age and the placebo group was 50.8 +/- 13.1 years of age. A blood rheology test that measures whole blood transit time was conducted using heparinized blood of the volunteers by a MC-FAN apparatus (microchannel array flow analyzer). After administration of AX 6 mg/day for 10 days, the values of the experimental group were decreased from 52.8 +/- 4.9 s to 47.6 +/- 4.2 s ($p < 0.01$) and a comparison of the values between the experimental (47.6 +/- 4.2 s) and the placebo (54.2 +/- 6.7 s) groups showed a significant difference ($p < 0.05$). There were no adverse effects resulting from the administration of AX 6 mg/day for 10 days. Informed consent was obtained from each subject.

KEYWORDS:

astaxanthin; blood rheology; blood transit time; male volunteers; microchannel array flow analyzer

PMID:

18818755

[PubMed]

PMCID:

PMC2533721

[Free PMC Article](#)

ASTAXANTHIN INCREASES PHYSICAL ACTIVITY AND IMPROVES BOTH PHYSICAL AND MENTAL QUALITY-OF-LIFE SELF-ASSESSMENT IN PATIENTS WITH HEART FAILURE IN HUMAN CLINICAL TRIAL.

Ann Palliat Med. 2020 Nov 10;apm-20-1378.

doi: 10.21037/apm-20-1378. Online ahead of print.

Changes in self-reported physical activity and health-related quality of life following 3-month astaxanthin supplementation in patients with heart failure: results from a pilot study

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- PMID: [33183036](#)
- DOI: [10.21037/apm-20-1378](#)

Free article

Abstract

Background: Astaxanthin has a strong antioxidant effect. We recently demonstrated that following 3-month astaxanthin supplementation, cardiac contractility and exercise tolerance improved, possibly through the suppression of oxidative stress in a small pilot study involving patients with heart failure with left ventricular systolic dysfunction. This is a sub-study of our pilot study to investigate whether improvements of self-reported physical activity and health-related quality of life were observed following 3-month astaxanthin supplementation.

Methods: We investigated the changes in physical activity by the Specific Activity Scale score and health-related quality of life by physical and mental component summary scores in Short Form-8 at baseline and after 3-month astaxanthin supplementation.

Results: Data from 17 patients with heart failure were assessed. Following 3-month astaxanthin supplementation, the Specific Activity Scale score increased from the median of 4.5 (interquartile range, 2.0) to 6.5 (interquartile range, 1.1) metabolic equivalent ($P=0.001$), and the physical and mental component summary scores increased from 46.1 ± 9.2 to 50.8 ± 6.8 ($P=0.015$) and from 48.9 ± 9.1 to 53.8 ± 4.8 ($P=0.022$), respectively. There was a linear relationship of the baseline heart rate, or mental component summary score with the percent change in the Specific Activity Scale score ($r=0.523$, $P=0.031$ and $r=-0.505$, $P=0.039$, respectively). In addition, there was a direct relationship of ischemic etiology with the percent change in the physical component summary score ($r=0.483$, $P=0.049$, respectively). Finally, there was a linear relationship between the percent change in the Specific Activity Scale score and that in the mental component summary score ($r=0.595$, $P=0.012$).

Conclusions: Following 3-month astaxanthin supplementation, improvements of the self-reported physical activity level and health-related quality of life in both mental and physical components were observed. In patients with heart failure, those with higher baseline heart rate, ischemic etiology, and poorer baseline health-related quality of life have potentials to have greater improvement of physical activity and/or health-related quality of life.

Astaxanthin dose-dependently inhibits LDL oxidation and may prevent atherosclerosis in human clinical trial.

Prog Med F0664B 0287-3648 VOL.24;NO.6;PAGE.1437-1442(2004)

Multivitamin and Carotenoid Supplements

[ITAKURA HIROSHIGE](#) (Dep. Life Sci., Ibaraki Christian Univ., JPN)

Abstract; Vitamins are regarded as essential nutrients for health and maintain stable tissue environments. Vitamins and carotenoids have multiple roles both as participants in many important metabolic processes throughout the body and to counter the oxidative stress resulting from normal metabolism and daily exposure to environmental agents.

Epidemiological studies have consistently indicated that the consumption of vegetables and fruits is inversely related to the incidence of cardiovascular and cerebrovascular diseases and cancer. Although the majority of vitamins and carotenoids are derived from these foods, foods of animal origin also contribute supplementation of these nutrients. Marine animals supply astaxanthin which is a carotenoid and antioxidant. We studied the effects of astaxanthin on in vitro and ex vivo LDL oxidation. Astaxanthin prolonged dose-dependently the oxidation lag time compared with the control. For the ex vivo study 24 volunteers consumed astaxanthin at doses of 1.8, 3.6, 14.4, 21.6 mg per day for 14 days. LDL lag time was longer in the groups who intaked astaxanthin compared with day 0, but there was no difference in oxidation of LDL in the control group. Our results provide evidence that consumption of marine animals producing astaxanthin inhibits LDL oxidation and possibly therefore contributes to the prevention of atherosclerosis.

Astaxanthin decreases heart rate in endurance athletes in double-blind, placebo-controlled human clinical trial.

[EC Nutr](#) 11.6 (2016) 253-259.

Effect of Astaxanthin Supplementation on Cardiorespiratory Function in Runners

Talbott, S., Hantla, D., Capelli, B., Ding, L., Li, Y., Artaria, C.

Abstract

Purpose: Marine microalgae is the predominant source of natural astaxanthin (NAX), a red-orange carotenoid with powerful antioxidant and anti-inflammatory properties. Studies in both rodents and humans suggest that NAX supplementation improves antioxidant capacity and reduces oxidative stress, while also improving fat utilization and exercise endurance. The purpose of this study was to assess the effects of a moderate dose of NAX supplementation (12mg/day for 8 weeks) on cardiorespiratory function during both higher and lower intensity exercise in recreational runners.

Patients and Methods: Using a double-blind parallel design, 28 recreational runners (male = 14, female = 14, age = 42) were supplemented with NAX (*Haematococcus pluvialis* algal extract) or a placebo. Before and after the supplementation period, subjects performed a maximal running test (VO₂max on treadmill) and a maximal cycling test (watts on cycle ergometer).

Results: There was no improvement in maximal oxygen uptake (running VO₂ max) or maximal power output (cycling watts) with NAX supplementation. However, subjects in the NAX group showed a significant ~10% lower average heart rate at submaximal running intensities compared to placebo (aerobic threshold, AeT; NAX 130+17 v. PL 145+14; and anaerobic threshold, AT; NAX 139+20 v. PL 154+11, $p < 0.05$).

Conclusion: Supplementation with 12 mg/day of NAX for 8 weeks reduced average heart rate at submaximal endurance intensities (AeT and AT), but not at higher “peak” intensities. These results suggest that NAX may be a beneficial ergogenic aid for long/ultradistance endurance athletes, but not necessarily for athletes competing in shorter higher intensity efforts. In addition, these data are also suggestive of a general “cardiotonic” effect of NAX, that should be investigated in non-athletic populations including elderly subjects and those with cardiac complications including post-myocardial infarction, heart failure, statin usage, mitochondrial dysfunction, chronic fatigue, and related conditions.

ASTAXANTHIN IMPROVES METABOLIC ADAPTATION AND IMPROVES MUSCLE ENDURANCE IN ELDERLY SUBJECTS DURING AEROBIC TRAINING IN RANDOMIZED, PLACEBO-CONTROLLED HUMAN CLINICAL STUDY.

Physiol Rep. 2021 Jun;9(11):e14887.

doi: 10.14814/phy2.14887.

Astaxanthin supplementation enhances metabolic adaptation with aerobic training in the elderly

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- PMID: 34110707 PMCID: [PMC8191397](#) DOI: [10.14814/phy2.14887](#) [Free PMC article](#)

Abstract

Endurance training (ET) is recommended for the elderly to improve metabolic health and aerobic capacity. However, ET-induced adaptations may be suboptimal due to oxidative stress and exaggerated inflammatory response to ET. The natural antioxidant and anti-inflammatory dietary supplement astaxanthin (AX) has been found to increase endurance performance among young athletes, but limited investigations have focused on the elderly. We tested a formulation of AX in combination with ET in healthy older adults (65-82 years) to determine if AX improves metabolic adaptations with ET, and if AX effects are sex-dependent. Forty-two subjects were randomized to either placebo (PL) or AX during 3 months of ET. Specific muscle endurance was measured in ankle dorsiflexors. Whole body exercise endurance and fat oxidation (FATox) was assessed with a graded exercise test (GXT) in conjunction with indirect calorimetry. Results: ET led to improved specific muscle endurance only in the AX group (Pre 353 ± 26 vs. Post 472 ± 41 contractions), and submaximal GXT duration improved in both groups (PL $40.8 \pm 9.1\%$ and AX $41.1 \pm 6.3\%$). The increase in FATox at lower intensity after ET was greater in AX (PL 0.23 ± 0.15 g vs. AX 0.76 ± 0.18 g) and was associated with reduced carbohydrate oxidation and increased exercise efficiency in males but not in females.

ASTAXANTHIN IMPROVES AEROBIC EXERCISE RECOVERY IN HUMAN CLINICAL TRIAL.

Front Sports Act Living. 2019 Sep 4;1:17.
doi: 10.3389/fspor.2019.00017. eCollection 2019.

Astaxanthin Improves Aerobic Exercise Recovery Without Affecting Heat Tolerance in Humans

[Chen Fleischmann](#)^{1,2,3}, [Michal Horowitz](#)², [Ran Yanovich](#)^{1,2,4}, [Hany Raz](#)⁵, [Yuval Heled](#)²

PMID: 33344941 PMCID: [PMC7739736](#) DOI: [10.3389/fspor.2019.00017](#) [Free PMC article](#)

Abstract

Objectives: To examine the supplementation effects of the xanthophyll carotenoid Astaxanthin on physical performance and exertional heat strain in humans. **Design:** A randomized double blind placebo controlled trial. **Methods:** Twenty two male participants (Age: 23.14 ± 3.5 y, height: 175 ± 6 cm, body mass: 69.6 ± 8.7 kg, % body fat: 16.8 ± 3.8) received placebo (PLA, $n = 10$) or Astaxanthin (ATX, $n = 12$) 12 mg/day Per os (P.O), for 30 days, and were tested pre and post-supplementation with a maximal oxygen uptake (VO_2 Max) test and the heat tolerance test (HTT) (2 h walk at 40°C , 40% relative humidity (RH), 5 kph, 2% incline). NIH database registration no. [NCT02088242](#). Gas exchange, Heart rate (HR), Relative perceived exertion (RPE), and blood lactate were measured during the VO_2 Max test. Heart rate (HR), rectal (T_{rec}), and skin (T_{skin}) temperatures, RPE, and sweat rate (SR) were monitored in the HTT. Serum heat shock protein 72 (HSP72), Creatine phospho-kinase (CPK), C-reactive protein (CRP), and lipid profile were measured before and after the test. **Results:** The rise in blood lactate caused by the VO_2 Max test was significantly diminished in the ATX group (9.4 ± 3.1 and 13.0 ± 3.1 $\text{mmole}\cdot\text{l}^{-1}$ in the ATX and PLA groups, respectively $P < 0.02$), as was the change in oxygen uptake during recovery (-2.02 ± 0.64 and $0.83 \pm 0.79\%$ of VO_2 Max in the ATX and PLA group, respectively, $p = 0.001$). No significant differences were observed in the anaerobic threshold or VO_2 Max. In the HTT, no significant physiological or biochemical differences were observed (HR < 120 bpm, T_{rec} rose by $\sim 1^\circ\text{C}$ to $< 38^\circ\text{C}$, no difference in SR). **Conclusions:** Astaxanthin supplementation improved exercise recovery. No benefit was observed for ATX over PLA in response to heat stress. Further examination of Astaxanthin in higher exertional heat strain is required.

Astaxanthin formula reduces LDL and total cholesterol similar to statin drug pravastatin in patients with high blood lipids in double-blind, placebo-controlled randomized crossover human clinical trial.

J Clin Lipidol. 2014 Jan-Feb;8(1):61-8. doi: 10.1016/j.jacl.2013.11.003. Epub 2013 Nov 11.

Nutraceutical approach to moderate cardiometabolic risk: results of a randomized, double-blind and crossover study with Armolipid Plus.

Ruscica M¹, Gomaschi M¹, Mombelli G², Macchi C³, Bosisio R², Pazzucconi F¹, Pavanello C², Calabresi L¹, Arnoldi A⁴, Sirtori CR⁵, Magni P¹.

Author information

Abstract

BACKGROUND: Primary cardiovascular prevention may be achieved by lifestyle/nutrition improvements and specific drugs, although a relevant role is now emerging for specific functional foods and nutraceuticals.

OBJECTIVES: The aim of this study was to evaluate the usefulness of a nutraceutical multitarget approach in subjects with moderate cardiovascular risk and to compare it with pravastatin treatment.

SUBJECTS: Thirty patients with moderate dyslipidemia and metabolic syndrome (according to the Third Report of the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults) were included in an 8-week randomized, double-blind crossover study and took either placebo or a nutraceutical combination that contained red yeast rice extract, berberine, policosanol, astaxanthin, coenzyme Q10, and folic acid (Armolipid Plus). Subsequently, they were subjected to another 8-week treatment with pravastatin 10 mg/d. This dosage was selected on the basis of its expected -20% efficacy in reducing low-density lipoprotein-cholesterol.

RESULTS: Treatment with Armolipid Plus led to a significant reduction of total cholesterol (-12.8%) and low-density lipoprotein-cholesterol (-21.1%), similar to pravastatin (-16% and -22.6%, respectively), and an increase of high-density lipoprotein-cholesterol (4.8%). Armolipid Plus improved the leptin-to-adiponectin ratio, whereas adiponectin levels were unchanged.

CONCLUSIONS: These results indicate that this nutraceutical approach shows a lipid-lowering activity comparable to pravastatin treatment. Hence, it may be a safe and useful option, especially in conditions of moderate cardiovascular risk, in which a pharmacologic intervention may not be appropriate.

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KEYWORDS: Berberine; Cardiovascular risk; HDL-cholesterol; LDL-cholesterol; Monacolin K

PMID: 24528686 DOI: [10.1016/j.jacl.2013.11.003](https://doi.org/10.1016/j.jacl.2013.11.003) [Indexed for MEDLINE]

Astaxanthin formula reduces blood lipids in patients with heart disease in human clinical trial.

[Am J Cardiol.](#) 2015 Dec 15;116(12):1798-801. doi: 10.1016/j.amjcard.2015.09.023. Epub 2015 Oct 3.

Usefulness of Nutraceuticals (Armolid Plus) Versus Ezetimibe and Combination in Statin-Intolerant Patients With Dyslipidemia With Coronary Heart Disease.

[Marazzi G](#)¹, [Pelliccia F](#)², [Campolongo G](#)³, [Quattrino S](#)³, [Cacciotti L](#)⁴, [Volterrani M](#)³, [Gaudio C](#)², [Rosano G](#)³.

Author information

Abstract

Statins are extensively used to treat dyslipidemia, but, because of their low tolerability profile, they are discontinued in a significant proportion of patients. Ezetimibe and nutraceuticals have been introduced as alternative therapies and have proved to be effective and well tolerated. A single-blind, single-center, randomized, prospective, and parallel group trial comparing a combination of nutraceuticals (red yeast rice, policosanol, berberine, folic acid, coenzyme Q10 and astaxanthin), called Armolid Plus, and ezetimibe for 3 months in terms of efficacy and tolerability. Patients who did not achieve their therapeutic target (low-density lipoprotein cholesterol <100 mg/dl) could add the alternative treatment on top of randomized treatment for another 12 months: 100 patients who are dyslipidemic with ischemic heart disease treated with percutaneous coronary intervention were enrolled (ezetimibe n = 50, nutraceutical n = 50). Efficacy (lipid profile) and tolerability (adverse events, transaminases, and creatine kinase) were assessed after 3 and 12 months. After 3 months, 14 patients in the nutraceutical group achieved their therapeutic target, whereas none of the patients in the ezetimibe group did. At 1-year follow-up, 58 patients (72.5%) of the combined therapy group (n = 86) and 14 (100%) of the nutraceutical group reached the therapeutic goal. No patients experienced important undesirable effects. In conclusion, nutraceuticals alone or in combination with ezetimibe are well tolerated and improve the lipid profile in statin-intolerant patients with coronary heart disease. Further studies are needed to assess long-term effects of nutraceuticals on mortality.

PMID: 26611120

DOI: [10.1016/j.amjcard.2015.09.023](https://doi.org/10.1016/j.amjcard.2015.09.023)

[Indexed for MEDLINE]

Astaxanthin combined with berberine is effective in reducing cholesterol in human clinical trial.

[Arzneimittelforschung](#). 2007;57(1):26-30.

Eulipidemic effects of berberine administered alone or in combination with other natural cholesterol-lowering agents. A single-blind clinical investigation.

[Cicero AF](#), [Rovati LC](#), [Setnikar I](#).

"G. Descovich" Atherosclerosis and Dysmetabolic Disease Research Center, "D. Campanacci" Clinical Medicine and Applied Biotechnology Department, University of Bologna, Bologna, Italy.

Berberine (BERB) and a combination (COMB) of berberine (CAS 2086-83-1) with policosanol (CAS 557-61-9), red yeast extract (containing monacolin, CAS 557-61-9), folic acid and astaxanthin were orally administered daily for 4 weeks to 40 subjects with moderate dyslipidemias divided in two parallel groups each of 20 subjects. Total cholesterol (TC), LDL, HDL, Non HDL, ApoB, ApoA, Lp(a) and triglycerides (TG) were measured before and at the end of treatments. BERB and COMB significantly reduced TC (respectively by 16% and 20%), LDL (by 20% and 25%), ApoB (by 15% and 29%) and TG (by 22% and 26%), and increased HDL (by 6.6% and 5.1%). Adverse events or impairments of liver transaminases or of CPK were not observed. In conclusion, food supplements containing natural products such as berberine, policosanol, red yeast extracts, folic acid and astaxanthin could be a useful support to diet and life style changes to correct dyslipidemias and to reduce cardiovascular risk in subjects with moderate mixed dyslipidemias.

Publication Types:

PMID: 17341006 [PubMed - indexed for MEDLINE]

Astaxanthin formula decreases LDL and total cholesterol in patients with dyslipidemia and may be suitable as an alternative to statin drugs: Review of human clinical research.

[Atheroscler Suppl.](#) 2017 Feb;24:1-15. doi: 10.1016/j.atherosclerosissup.2016.10.003. Epub 2016 Dec 18.

A nutraceutical approach (Armolid Plus) to reduce total and LDL cholesterol in individuals with mild to moderate dyslipidemia: Review of the clinical evidence.

[Barrios V](#)¹, [Escobar C](#)², [Cicero AF](#)³, [Burke D](#)⁴, [Fasching P](#)⁵, [Banach M](#)⁶, [Bruckert E](#)⁷.

Author information

Abstract

Compelling evidence supports the effectiveness of the reduction of total and LDL cholesterol (TC and LDL-C) in primarily preventing cardiovascular events, within the framework of life-long prevention programs mainly consisting in lifestyle changes. Pharmacological treatment should be introduced when lifestyle changes, including use of nutraceuticals, have failed. ESC/EAS guidelines list a number of nutraceutical compounds and functional foods which have been individually studied in randomized, controlled clinical trials (RCTs). To date only a proprietary formulation of three naturally occurring substances with putative complementary lipid-lowering properties - red yeast rice, policosanol and berberine - combined with folic acid, astaxanthin, and coenzyme Q10 (Armolid Plus[®]) has been extensively investigated in several RCTs, 7 of which were placebo-controlled, 2 were ezetimibe comparators and 4 were "real life" studies comparing diet and Armolid Plus to diet alone. The trials included mostly patients with mild to moderate dyslipidemia, treated for 6-48 weeks. The trials also included special populations and patients in whom statins were contraindicated or who could not tolerate them. Armolid Plus has proved to be able to achieve significant reductions in TC (11-21%) and in LDL-C (15-31%) levels, which is equivalent to expectations from low dose statins. In patients intolerant to statins, who do not achieve their therapeutic target with ezetimibe, Armolid Plus can achieve a further 10% improvement in TC and LDL-C. The safety and tolerability of Armolid Plus were excellent, thought likely due to the intentional combination of low doses of its active ingredients: low enough not to be associated with untoward effects, but high enough to exert therapeutic effects in combination with other complementary substances. Consequently, in the event of intolerance to statins, Armolid Plus offers an effective alternative, which is devoid of the safety risks associated with synthetic pharmacological therapy. In conclusion Armolid Plus, in addition to dietary measures, could be a rational choice for individuals with mild to moderate hyperlipidemia and for all dyslipidemic patients in whom statins are not indicated or who cannot tolerate them.

KEYWORDS: Armolid plus; Functional foods; Hypercholesterolemia; Lifestyle change; Nutraceuticals

PMID: 27998714 DOI: [10.1016/j.atherosclerosissup.2016.10.003](https://doi.org/10.1016/j.atherosclerosissup.2016.10.003) [Indexed for MEDLINE] **Free full text**

ASTAXANTHIN-CONTAINING FORMULA REDUCES SYSTOLIC BLOOD PRESSURE; REDUCES HIGH-SENSITIVITY C-REACTIVE PROTEIN AND INTERLEUKIN-6 INFLAMMATORY MARKERS; AND IMPROVES ENDOTHELIAL FUNCTION IN HUMAN CLINICAL STUDY.

Clin Nutr ESPEN. 2020 Feb;35:174-179.

doi: 10.1016/j.clnesp.2019.09.011. Epub 2019 Oct 24.

A combined effect of Cavacurcumin, Eicosapentaenoic acid (Omega-3s), Astaxanthin and Gamma -linoleic acid (Omega-6) (CEAG) in healthy volunteers- a randomized, double-blind, placebo-controlled study

[Divya Birudaraju¹](#), [Lavanya Cherukuri¹](#), [April Kinninger¹](#), [Bhanu T Chaganti¹](#), [Kashif Shaikh¹](#), [Sajad Hamal¹](#), [Ferdinand Flores¹](#), [Sion K Roy¹](#), [Matthew J Budoff²](#)

- PMID: 31987113
- DOI: [10.1016/j.clnesp.2019.09.011](https://doi.org/10.1016/j.clnesp.2019.09.011)

Abstract

Background: Inflammation plays a key role and is one of the early steps in the pathogenesis of endothelial function, thereby increasing the risk of hypertension (HTN), coronary artery disease (CAD), stroke and several other risk factors of cardiovascular disease (CVD). We assessed the efficacy for improving cardiovascular health (blood pressure, inflammation and endothelial reactivity) over a 4-week intervention period in healthy individuals.

Methods: We performed a randomized, double-blinded, placebo-controlled, randomized clinical trial to investigate Curcumin, Eicosapentaenoic acid (EPA), Astaxanthin and Gamma -linoleic acid (GLA) (CEAG) supplements with 80 individuals (30 men and 50 women). The mean age of participants was 48.8 ± 16.0 years. Participants were enrolled and randomized to active or placebo and followed for 4 weeks. Paired

and Independent T-tests were used to analyze the mean differences between and within groups.

Results: The primary endpoints of the study were the effect on inflammatory markers (IL-6, CRP), endothelial function and blood pressure at 4 weeks. There was a significant reduction in mean SBP at 4 weeks in the CEAG group compared to placebo [mean \pm SD 4.7 ± 6.8 ($p = 0.002$)]. Relative to placebo, active group showed a significant decrease in High sensitivity C Reactive Protein (hsCRP) (-0.49 ± 1.9 vs $+ 0.51 \pm 2.5$, $p = 0.059$) and blunted increase in IL-6 ($+0.2$ vs $+ 0.4$ in placebo, $p = 0.60$).

Conclusion: Inflammatory markers were reduced or blunted by CEAG, with a robust increase in both EPA levels and the fatty acid index. Furthermore, systolic BP was reduced over 4 weeks with concurrent improvement in endothelial function.

Gov id: [NCT03906825](https://clinicaltrials.gov/ct2/show/study/NCT03906825).

ASTAXANTHIN FORMULA MODULATES TRAINING-INDUCED AEROBIC METABOLISM OF CARBS AND FAT DURING REST AND EXERCISE IN HEALTHY YOUNG MEN IN HUMAN CLINICAL TRIAL.

J Clin Biochem Nutr. 2019 Jan;64(1):79-85.

doi: 10.3164/jcbn.18-40. Epub 2018 Aug 8.

Effect of dietary antioxidant-rich foods combined with aerobic training on energy metabolism in healthy young men

[Maki Takami](#)¹, [Wataru Aoi](#)¹, [Hitomi Terajima](#)¹, [Yuko Tanimura](#)², [Sayori Wada](#)¹, [Akane Higashi](#)¹

PMID: 30705516 PMCID: [PMC6348409](#) DOI: [10.3164/jcbn.18-40](#) [Free PMC article](#)

Abstract

Although supplementation with several antioxidants has been suggested to improve aerobic metabolism during exercise, whether dietary foods containing such antioxidants can exert the metabolic modulation is unclear. This study aimed to investigate the effect of intake of the specific antioxidant-rich foods coupled with exercise training on energy metabolism. Twenty young healthy, untrained men were assigned to antioxidant and control groups: participants in the antioxidant group were encouraged to consume foods containing catechin, astaxanthin, quercetin, glutathione, and anthocyanin. All participants performed cycle training at 60% maximum oxygen consumption for 30 min, 3 days per week for 4 weeks. Maximum work load was significantly increased by training in both groups, while oxygen consumption during exercise was significantly increased in the antioxidant group only. There were positive correlations between maximum work load and fat/carbohydrate oxidations in the antioxidant group. Carbohydrate oxidation during rest was significantly higher in the post-training than that in the pre-training only in the antioxidant group. More decreased levels of serum insulin and HOMA-IR after training were observed in the antioxidant group than in the control group. This study suggests that specific antioxidant-rich foods could modulate training-induced aerobic metabolism of carbohydrate and fat during rest and exercise.

Astaxanthin Ameliorates Blood Pressure in Salt-Induced Prehypertensive Rats Through ROS/MAPK/NF- κ B Pathways in the Hypothalamic Paraventricular Nucleus

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- PMID: 34537923 DOI: [10.1007/s12012-021-09695-6](https://doi.org/10.1007/s12012-021-09695-6)

Abstract

Astaxanthin (AST) has a variety of biochemical effects, including anti-inflammatory, antioxidative, and antihypertensive functions. The aim of the present study was to determine whether AST ameliorates blood pressure in salt-induced prehypertensive rats by ROS/MAPK/NF- κ B pathways in hypothalamic paraventricular nucleus. To explore the central effects of AST on the development of blood pressure, prehypertensive rats were induced by a high-salt diet (HS, 8% NaCl) and its control groups were treated with normal-salt diet (NS, 0.3% NaCl). The Dahl salt-sensitive (S) rats with HS diet for 6 weeks received AST or vehicle by gastric perfusion for 6 weeks. Compared to those with NS diet, rats with HS diet exhibited increased mean arterial pressure (MAP) and heart rate (HR). These increases were associated with higher plasma level of norepinephrine (NE), interleukin 1 β (IL-1 β), and interleukin 6 (IL-6); elevated PVN level of reactive oxygen species (ROS), NOX2, and NOX4, that of IL-1 β , IL-6, monocyte chemoattractant protein 1 (MCP-1), tyrosine hydroxylase (TH), phosphorylation extracellular-signal-regulated kinase (p-ERK1/2), phosphorylation Jun N-terminal kinases (p-JNK), nuclear factor-kappa B (NF- κ B) activity; and lower levels of IL-10, superoxide dismutase (SOD), and catalase (CAT) in the PVN. In addition, our data demonstrated that chronic AST treatment ameliorated these changes in the HS but not NS diet rats. These data suggested that AST could alleviate prehypertensive response in HS-induced prehypertension through ROS/MAPK/NF- κ B pathways in the PVN.

Astaxanthin is the best of all carotenoids tested during cholesterol oxidation in-vitro.

[Mol Cell Biochem](#). 2008 Feb;309(1-2):61-8. Epub 2007 Nov 16.

The protective role of carotenoids against 7-keto-cholesterol formation in solution.

[Palozza P](#), [Barone E](#), [Mancuso C](#), [Picci N](#).

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The antioxidant activity of beta-carotene and oxygenated carotenoids lutein, canthaxanthin, and astaxanthin was investigated during spontaneous and peroxy-radical-induced cholesterol oxidation. Cholesterol oxidation, measured as generation of 7-keto-cholesterol (7-KC), was evaluated in a heterogeneous solution with cholesterol, AAPH, and carotenoids solubilized in tetrahydrofuran and in water, and in a homogeneous solution of chlorobenzene, with AIBN as a prooxidant. The formation of 7-KC was dependent on temperature and on cholesterol and prooxidant concentrations. All the carotenoids tested, exhibited significant antioxidant activity by inhibiting spontaneous, AAPH- and AIBN-induced formation of 7-KC, although the overall order of efficacy of these compounds was astaxanthin > canthaxanthin > lutein = beta-carotene. The finding that carotenoids exert protective effects on spontaneous and free radical-induced cholesterol oxidation may have important beneficial effects on human health, by limiting the formation of atheroma and by inhibiting cholesterol oxidation in food processing or storage.

Publication Types:

PMID: 18008144 [PubMed - indexed for MEDLINE]

ASTAXANTHIN IN ESTERIFIED FORM (FOUND IN ALGAE) IS SUPERIOR TO FREE FORM (FOUND IN YEAST AND IN SYNTHESIZED ASTAXANTHIN) IN PREVENTING SYNTHESIS OF INTRACELLULAR FATTY ACIDS AND TRIGLYCERIDES.

Curr Pharm Biotechnol. 2020 Jun 26.

doi: 10.2174/1389201021666200626162301. Online ahead of print.

Comparison of different molecular forms of astaxanthin in inhibiting lipogenesis and its mechanism

[Yanqi Li¹](#), [Yaxuan Liu¹](#), [Yingying Tian²](#), [Yao Guo¹](#), [Changhu Xue¹](#), [Jingfeng Wang¹](#)

PMID: 32589556 DOI: [10.2174/1389201021666200626162301](https://doi.org/10.2174/1389201021666200626162301)

Abstract

Background: Astaxanthin is a natural active substance with a plurality of biological activities, such as antioxidation, anti-inflammatory and anti-cardio-cerebrovascular diseases. However, there is less research on the effects of astaxanthin on obesity. Astaxanthin with different structural forms affect corresponding biological activity.

Objective: Comparing Astaxanthin-octanoic acid diester (C8-AST) and Free astaxanthin (F-AST) to explore the effect on lipogenesis in vitro.

Methods: 3T3-L1 preadipocytes were cultured under astaxanthin treatment. Cell proliferation and differentiation were evaluated by MTT assay and oil red O staining, respectively. The synthesis metabolic mechanism of intracellular fatty acids and triglycerides were examined by qRT-PCR and Western blotting.

Results: C8-AST and F-AST had no effect on adipocyte proliferation at low concentration, but inhibited adipocyte differentiation. The treatment of astaxanthin could inhibit the expression of PPAR γ , C/EBP α and SREBP-1c in adipocytes, upregulate the expression of Wnt10b, LRP6, FZ in Wnt/ β -catenin signaling pathway and increase the β -catenin entry into nucleus, suggesting that activation of Wnt/ β -catenin signaling was involved in astaxanthin-regulated lipogenesis. Notably, inhibition effect of lipogenesis on C8-AST was better than F-AST overall.

Conclusion: At the cellular level, both two kinds of astaxanthins inhibit the synthesis of intracellular fatty acids and triglycerides. Notably, the inhibition effect of C8-AST is better than F-AST overall.

ASTAXANTHIN SHOWS BOTH PREVENTIVE AND THERAPEUTIC POTENTIAL FOR ISCHEMIC-REPERFUSION DAMAGE IN RAT MODEL.

J Orthop Sci 2021 Aug 9;S0949-2658(21)00201-3. doi: 10.1016/j.jos.2021.05.014. Online ahead of print.

The effect of astaxanthine on ischemia-reperfusion injury in a rat model

[Yasin Durukan](#)¹, [Mehmet Murat Bala](#)², [Abdullah Alper Şahin](#)³, [Tülin Fırat](#)⁴, [Güler Buğdaycı](#)⁵, [Kutay Engin Özturan](#)⁶

- PMID: 34384658 DOI: [10.1016/j.jos.2021.05.014](https://doi.org/10.1016/j.jos.2021.05.014)

Abstract

Background: We aimed to compare biochemical and histopathological findings of astaxanthin's potential effects on oxidative stress in ischemia/reperfusion damage (I/R).

Methods: Thirty-two rats were randomly divided into four groups: control group; I/R group; I/R + treatment group; drug group. Astaxanthin was orally administered to groups C and D for 14 days. In groups B and C, the femoral artery was clamped for 2 h to form ischemia. The clamp was opened, and reperfusion was performed for 1 h. In all groups, 4 ml of blood sample through intracardiac puncture and gastrocnemius muscle tissue samples were collected. Serum and tissue samples were analyzed by measuring malondialdehyde (MDA), superoxide dismutase (SOD), total antioxidant capacity (TAC), and total oxidative level (TOL). Necrosis, inflammation, and caspase-3 in muscle tissue collected for histopathological examination were evaluated.

Results: Tissue MDA, SOD and TOL values significantly differed between groups. Serum MDA, SOD, TOL and TAC values significantly differed between groups. On necrosis examination, there was a significant difference between groups B and C. Although signs of inflammation significantly differed between groups, there was no significant difference between groups A and C and groups A and D. Although there was a significant difference in caspase-3 results between groups, there was no significant difference between groups A and C.

Conclusions: The use of astaxanthin before and after surgery showed preventive or therapeutic effects against I/R damage.

ASTAXANTHIN REDUCED WEIGHT GAIN IN RATS FED A HIGH-FAT DIET WHICH RESULTED IN IMPROVEMENTS IN INSULIN SENSITIVITY, BLOOD LIPID PROFILES, AND INFLAMMATION LEVELS.

Curr Pharm Biotechnol 2021 Aug 9. doi: 10.2174/1389201022666210810105804. Online ahead of print.

Astaxanthin Attenuates Adiponectin, Calprotectin, miRNA222 and miRNA378 in Obesity induced by High-Fat Diet in Rats

[Sylvia A Boshra](#)¹

- PMID: 34375188 DOI: [10.2174/1389201022666210810105804](https://doi.org/10.2174/1389201022666210810105804)

Abstract

Background: Astaxanthin suppressed obesity in rats fed with high-fat diet(HFD) via the restriction of adipose tissue build-out, therefore, improving insulin sensitivity and inflammation. Metformin reduces insulin resistance and may reduce weight.

Aim: Investigation of the effects of astaxanthin and metformin in obesity prompted by a high-fat diet.

Objective: The present article investigates the effects of astaxanthin and metformin in obesity prompted by a high-fat diet in rats through measuring miRNA222 and 378.

Materials: The rats were classified into four classes containing ten albino rats each: Group I(Normal group): nourished with ordinary diet for 8weeks. Group II(Control positive): nourished with a high-fat diet for 8 weeks. Group III: nourished with astaxanthin(50mg/kg)(1/40 LD50) orally plus a high-fat diet for 8weeks. Group IV: nourished with metformin (500mg/kg) orally plus a high-fat diet for 8 weeks.

Methods: Leptin, adiponectin, calprotectin and interleukin 6 (IL-6) were assessed by rat-specific ELISA kits. Tumor necrosis factor-alpha (TNF- α), miRNA222 and miRNA378 expressions were quantified by quantitative real-time PCR.

Results: Astaxanthin and metformin have anti-obesity and antioxidant actions and significantly decreased the weight of the body, glucose, insulin, triglycerides, total cholesterol, triglycerides and leptin, as well as plasma calprotectin & IL-6 and increased HDL-C and adiponectin. The liver TNF- α gene expression, adipose tissue miRNA222 and miRNA378 expression were decreased compared to HFD control rats.

Discussion and conclusion: Astaxanthin has regulated the aberrant expression of miRNA222 and 378 that may be related to hyperlipidemia and insulin resistance. Accordingly, astaxanthin deserves a clinical trial in the future due to its effects on miRNAs involved in obesity.

Astaxanthin prevents clogging of cerebral blood vessels in rats with high blood pressure.

[Nutr Res.](#) 2011 Oct;31(10):784-9. doi: 10.1016/j.nutres.2011.09.010.

Astaxanthin inhibits thrombosis in cerebral vessels of stroke-prone spontaneously hypertensive rats.

[Sasaki Y¹](#), [Kobara N](#), [Higashino S](#), [Giddings JC](#), [Yamamoto J](#).

Author information

Abstract

It is known that vitamin E and some carotenoids have antioxidant activities that alleviate endothelial dysfunction and play a protective role against cardiovascular disease. The current study was designed to examine the hypothesis that astaxanthin, a red pigment carotenoid found in salmonid and crustacean aquaculture, protects stroke-prone spontaneously hypertensive rats (SHRSP) from vascular oxidative damage, hypertension, and cerebral thrombosis. Male 6-week-old SHRSP were classified into 4 groups: a control group, 2 astaxanthin groups, and a vitamin E group. The treated animals were given either astaxanthin or vitamin E for 3 weeks. Body weights in each group were not significantly different from control group during the treatment period, but the usual increase in systolic blood pressure in SHRSP observed with age was significantly suppressed by treatment. Thrombogenesis, assessed using a helium-neon (He-Ne) laser technique in pial blood vessels, together with antioxidant activity, assessed by measuring urinary 8-OHdG levels, were significantly moderated. Urinary nitric oxide (NO) metabolites were increased after treatment. These results supported our hypothesis and strongly suggested that the antithrombotic and antihypertensive effects of astaxanthin or vitamin E may be related to an increase in bioavailable NO, possibly mediated by decreased inactivation of NO by reactive oxygen species.

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PMID:

22074803

[PubMed - indexed for MEDLINE]

Astaxanthin reduces blood pressure and improves cardiovascular parameters in rats with high blood pressure.

[Pharmacol Res.](#) 2011 Jan;63(1):44-50. doi: 10.1016/j.phrs.2010.09.003. Epub 2010 Sep 22.

Astaxanthin-enriched-diet reduces blood pressure and improves cardiovascular parameters in spontaneously hypertensive rats.

[Monroy-Ruiz J¹](#), [Sevilla M^Á](#), [Carrón R](#), [Montero MJ](#).

Author information

Abstract

The aim of this study was to investigate the effects of astaxanthin-enriched diet on blood pressure, cardiac hypertrophy, both vascular structure and function and superoxide ($\text{O}_2^{\cdot-}$) production in spontaneously hypertensive rats (SHR). Twelve-week-old SHR were treated for 8 weeks with anastaxanthin-enriched diet (75 or 200mg/kg body weight per day). Systolic blood pressure was monitorized periodically during the study by the tail cuff method. At the end of the study animals were sacrificed and heart, kidneys and aorta were removed. Left ventricular weight/body weight ratio was used as left ventricular hypertrophy index (LVH). Vascular function and structure were studied in conductance (aortic rings) and resistance (renal vascular bed) arteries. Also $\text{O}_2^{\cdot-}$ production was evaluated by lucigenin-enhanced chemiluminescence. Systolic blood pressure was lower inastaxanthin-treated groups than the control group from the first week of treatment, and LVH was significantly reduced. Astaxanthin improved endothelial function on resistance arteries, but had no effect on aorta. These effects were accompanied by a decrease in oxidative stress and improvements in NO bioavailability. Taken together, these results show that diet supplemented with astaxanthin has beneficial effects on hypertension, by decreasing blood pressure values, improving cardiovascular remodeling and oxidative stress.

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PMID:

20868751

[PubMed - indexed for MEDLINE]

Astaxanthin demonstrates cardioprotective properties in rabbits with high cholesterol levels.

[Nutrition](#). 2012 Jun;28(6):605-10. doi: 10.1016/j.nut.2011.11.028. Epub 2012 Apr 4.

Novel phytonutrient contributors to antioxidant protection against cardiovascular disease.

[Riccioni G¹](#), [Speranza L](#), [Pesce M](#), [Cusenza S](#), [D'Orazio N](#), [Glade MJ](#).

Author information

Abstract

The associations linking endothelial inflammation, endothelial oxidative stress, and atherogenesis and the potential for dietary phytonutrients to decrease the impact of these associations were assessed. A detailed literature review was conducted and summarized. A large body of scientific evidence describes the interactions among endothelial inflammation, endothelial oxidative stress, and atherogenesis. A growing body of research indicates that several dietary phytonutrients (astaxanthin, lycopene, lutein, and glabridin) can decrease the risk for atherosclerosis by decreasing endothelial inflammation and oxidative stress. The consumption of foods or dietary supplements that provide astaxanthin, lycopene, lutein, and glabridin can ameliorate endothelial inflammation and oxidative stress, retard atherogenesis, and decrease the risk for atherogenic cardiovascular disease.

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PMID:

22480801

[PubMed - indexed for MEDLINE]

Astaxanthin lowers cholesterol and reduces atherosclerosis in mice.

[Atherosclerosis](#). 2012 May;222(1):99-105. doi: 10.1016/j.atherosclerosis.2012.02.002. Epub 2012 Feb 8.

Effect of an oral astaxanthin prodrug (CDX-085) on lipoprotein levels and progression of atherosclerosis in LDLR(-/-) and ApoE(-/-) mice.

[Ryu SK¹](#), [King TJ](#), [Fujioka K](#), [Pattison J](#), [Pashkow FJ](#), [Tsimikas S](#).

Author information

Abstract

Oxidative stress and inflammation are key promoters of atherosclerosis and myocardial damage. When orally administered, the novel astaxanthin prodrug CDX-085 delivers high levels of the xanthophyll antioxidant astaxanthin that protects LDL from oxidation and reduces primary thrombosis. In this study, we analyzed whether delivery of astaxanthin from administration of the CDX-085 prodrug reduces plasma lipoprotein levels and the progression of atherosclerosis in low-density lipoprotein receptor negative (LDLR(-/-)) and apolipoprotein E deficient (ApoE(-/-)) mice.

METHODS:

Relative circulating levels of astaxanthin derived from CDX-085 administration compared to administration of pure astaxanthin was initially evaluated in a canine model. In mouse Study #1, 16 wild-type and 16 LDLR(-/-) mice on 0.5% cholesterol diet supplemented with either 0.0%, 0.08%, 0.2% and 0.4% CDX-085 were used to assess plasma levels and lipoprotein biodistribution measured by FPLC after 4 weeks treatment. In Study #2, 36 male LDLR(-/-) mice were randomized to a 0.5% cholesterol chow diet (CHOW group, n=12) or 0.5% cholesterol chow fortified with 0.08% CDX-085 (n=12) or 0.5% cholesterol chow with 0.4% CDX-085 (n=12) for 12 weeks. In Study #3, 34 male ApoE(-/-) mice were randomized in the same fashion as the Study #2 and fed similar diets for 9 weeks.

RESULTS:

CDX-085 administration was shown to result in significantly higher levels of circulating astaxanthin ($p < 0.001$ ANOVA) over a 72 h period compared to pure, non-esterified astaxanthin in a single-dose pharmacokinetic study in beagles. In Study #1, plasma astaxanthin levels were 5-9-fold higher in LDLR(-/-) mice compared to wild-type mice. Astaxanthin was highly distributed among all lipoprotein fractions, generally reflecting cholesterol content of lipoproteins. In Study #2, administration of CDX-085 resulted in significantly lower total cholesterol levels (528 ± 68 mg/dL vs. 550 ± 67 mg/dL vs. 602 ± 80 mg/dL, $p = 0.047$) and aortic arch atherosclerosis ($9.0 \pm 4.2\%$ vs. $9.8 \pm 3.5\%$ vs. $13.2 \pm 3.6\%$, $p = 0.023$) in the 0.4% CDX-085 group compared to the 0.08% CDX-085 and CHOW groups, respectively. In ApoE(-/-) mice, a 72% reduction in triglycerides in the 0.4% CDX-085 group and 50% reduction in the 0.08% CDX-085 groups was noted compared to CHOW group (final levels 17 ± 11 mg/dL vs. 30 ± 15 mg/dL vs. 60 ± 32 mg/dL, respectively, $p = 0.001$).

CONCLUSION:

Oral administration of the novel astaxanthin prodrug CDX-085 shows that it distributes among lipoproteins. CDX-085 lowers total cholesterol and aortic arch atherosclerosis in LDLR(-/-) mice and triglyceride levels in ApoE(-/-) mice and shows promise for further evaluation in human studies.

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PMID: 2406426

Astaxanthin reduces the risk of clogged arteries in dogs.

[Pharmacology](#). 2008;82(1):67-73. Epub 2008 May 14.

Disodium disuccinate astaxanthin prevents carotid artery rethrombosis and ex vivo platelet activation.

[Lauver DA](#), [Driscoll EM](#), [Lucchesi BR](#).

Department of Pharmacology, University of Michigan Medical School, Ann Arbor, Mich 48109, USA.

BACKGROUND/AIMS:The disodium disuccinate derivative of astaxanthin (DDA) is a carotenoid antioxidant under development for the treatment of ischemic cardiovascular events. Recent evidence suggests that reactive oxygen species (ROS) play an important role in platelet activation. This study seeks to investigate the effects of a reactive oxygen species quencher, DDA, in a canine model of carotid artery thrombosis. **METHODS:** After formation of an occlusive carotid thrombus, dogs were administered recombinant tissue plasminogen activator intra-arterially to achieve thrombolysis in the presence of either 0.9% NaCl solution or DDA (10-50 mg/kg i.v. infusion). Ex vivo platelet aggregation and tongue bleeding times were measured before and after drug administration. Residual thrombus mass was analyzed at the end of each experiment. **RESULTS:**The data indicated a dose- dependent reduction in the incidence of carotid artery rethrombosis. In addition, platelet aggregation and thrombus weights were dose-dependently inhibited by DDA. No change was recorded in tongue bleeding time among the treatment groups. **CONCLUSIONS:**The data demonstrate that at the doses used in this study, DDA significantly reduced the incidence of secondary thrombosis while maintaining normal hemostasis. The results suggest that upon further study, DDA may one day find utility in revascularization procedures. Copyright 2008 S. Karger AG, Basel.

PMID: 18477858 [PubMed - indexed for MEDLINE]

Astaxanthin as a novel approach to cardioprotection.

[Cardiovasc Hematol Agents Med Chem](#). 2006 Oct;4(4):335-49.

Retrometabolic syntheses of astaxanthin (3,3'-dihydroxy-beta,beta-carotene-4,4'-dione) conjugates: a novel approach to oral and parenteral cardio-protection.

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Disodium disuccinate astaxanthin has potent cardioprotective effects in animals, with demonstrated preclinical efficacy in the rat, rabbit, and canine models of experimental infarction. It has been effective in subchronic and acute dosing regimens after parenteral administration, and recently published data in rats demonstrate that oral cardioprotection is also readily achieved. Myocardial salvage in the canine can reach 100% with a 4-day subchronic dosing regimen; single-dose I.V. cardioprotection, when given 2 hours before experimental coronary occlusion, is on average two-thirds of that achieved with the subchronic regimen in dogs. In conscious animals, no effects on hemodynamic parameters have been observed. Recently, the beneficial properties of this prototypical astaxanthin conjugate have been extended to include second- and third-generation compounds with improved pharmacokinetic and/or potency profiles. The primary mechanism of cardioprotection appears to be antioxidant activity: potent direct scavenging of the lynchpin radical in ischemia-reperfusion injury, superoxide anion, has been documented in appropriate model systems. In addition, modulation of serum complement activity, reduction of the levels of deposition of C-reactive protein (CRP) and the membrane attack complex (MAC) in infarcted tissue, and reduction in oxidative stress markers from the arachidonic acid and linoleic acid pathways also suggest a significant anti-inflammatory component to the mechanism of cardioprotection. Favorable plasma protein binding has been demonstrated in vitro for several astaxanthin conjugates; this binding capacity overcomes the supramolecular assembly of the compounds that occurs in aqueous solution, which in itself improves the stability and shelf-life of aqueous formulations. Astaxanthin readily populates cardiac tissue after metabolic hydrolysis of both oral and parenteral administration of the astaxanthin ester derivatives, providing a reservoir of cardioprotective agent with a significant half-life due to favorable ADME in mammals. Due to the well-documented safety profile of astaxanthin in humans, disodium disuccinate astaxanthin may well find clinical utility in cardiovascular applications in humans following successful completion of preclinical and clinical pharmacology and toxicology studies in animals and humans, respectively.

Publication Types:

PMID: 17073610 [PubMed - indexed for MEDLINE]

Astaxanthin completely negates the pro-oxidant effect of Vioxx and may have prevented heart attacks had it been combined with Vioxx and given to cholesterol patients.

[J Cardiovasc Pharmacol.](#) 2006;47 Suppl 1:S7-14.

Rofecoxib increases susceptibility of human LDL and membrane lipids to oxidative damage: a mechanism of cardiotoxicity.

[Mason RP](#), [Walter MF](#), [McNulty HP](#), [Lockwood SF](#), [Byun J](#), [Day CA](#), [Jacob RF](#).

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Clinical investigations have demonstrated a relationship between the extended use of rofecoxib and the increased risk for atherothrombotic events. This has led to the removal of rofecoxib from the market and concern over the cardiovascular safety of other cyclooxygenase (COX)-2 selective agents. Experimental findings from independent laboratories now indicate that the cardiotoxicity of rofecoxib may not be a class effect but because of its intrinsic chemical properties. Specifically, rofecoxib has been shown to increase the susceptibility of human low-density lipoprotein and cellular membrane lipids to oxidative modification, a contributing factor to plaque instability and thrombus formation. Independently of COX-2 inhibition, rofecoxib also promoted the nonenzymatic formation of isoprostanes and reactive aldehydes from biologic lipids. The basis for these observations is that rofecoxib alters lipid structure and readily forms a reactive maleic anhydride in the presence of oxygen. By contrast, other selective (celecoxib, valdecoxib) and nonselective (naproxen, diclofenac) inhibitors did not influence rates of low-density lipoprotein and membrane lipid oxidation. We have now further confirmed these findings by demonstrating that the prooxidant activity of rofecoxib can be blocked by the potent antioxidant astaxanthin in homochiral form (all-trans 3S, 3'S). These findings provide a mechanistic rationale for differences in cardiovascular risk among COX-selective inhibitors because of their intrinsic physicochemical properties.

PMID: 16785833 [PubMed - indexed for MEDLINE]

Astaxanthin shows potential for treatment of hypertension in rat study.

[Biol Pharm Bull.](#) 2006 Apr;29(4):684-8.

Antihypertensive potential and mechanism of action of astaxanthin: III. Antioxidant and histopathological effects in spontaneously hypertensive rats.

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We investigated the effects of a dietary astaxanthin (ASX-O) on oxidative parameters in spontaneously hypertensive rats (SHR), by determination of the level of nitric oxide (NO) end products nitrite/nitrate (NO₂-/NO₃-) and lipid peroxidation in ASX-O-treated SHR. Oral administration of the ASX-O significantly reduced the plasma level of NO₂-/NO₃- compared to the control vehicle (p<0.05). The lipid peroxidation level, however, was reduced in both ASX-O- and olive oil-treated groups. We also analyzed the post-treatment effects of ASX-O on the vascular tissues by examining the changes in the aorta and coronary arteries and arterioles. The dietary ASX-O showed significant reduction in the elastin bands in the rat aorta (p<0.05). It also significantly decreased the [wall : lumen] aerial ratio of the coronary arteries. These results suggest that ASX-O can modulate the oxidative condition and may improve vascular elastin and arterial wall thickness in hypertension.

Publication Types:

PMID: 16595899 [PubMed - indexed for MEDLINE]

Astaxanthin shows promise in mice and in-vitro for diseases including atherosclerosis.

[Life Sci.](#) 2006 Jun 6;79(2):162-74. Epub 2006 Feb 8.

The effects of oral Cardax (disodium disuccinate astaxanthin) on multiple independent oxidative stress markers in a mouse peritoneal inflammation model: influence on 5-lipoxygenase in vitro and in vivo.

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Disodium disuccinate astaxanthin ('rac'-dAST; Cardax) is a water-dispersible C40 carotenoid derivative under development for oral and parenteral administration for cardioprotection of the at-risk ischemic cardiovascular patient. In experimental infarction models in animals (rats, rabbits, and dogs), significant myocardial salvage has been obtained, up to 100% at the appropriate dose in dogs. The documented mechanism of action in vitro includes direct scavenging of biologically produced superoxide anion; in vivo in rabbits, modulation of the complement activity of serum has also been shown. A direct correlation between administration of the test compound in animals and reductions of multiple, independent markers of oxidative stress in serum was recently obtained in a rat experimental infarction model. For the current study, it was hypothesized that oral Cardax administration would inhibit oxidative damage of multiple relevant biological targets in a representative, well-characterized murine peritoneal inflammation model. A previously developed mass spectrometry-based (LC/ESI/MS/MS) approach was used to interrogate multiple distinct pathways of oxidation in a black mouse (C57/BL6) model system. In vivo markers of oxidant stress from peritoneal lavage samples (supernatants) were evaluated in mice on day eight (8) after treatment with either Cardax or vehicle (lipophilic emulsion without drug) orally by gavage at 500 mg/kg once per day for seven (7) days at five (5) time points: (1) baseline prior to treatment (t=0); (2) 16 h following intraperitoneal (i.p.) injection with thioglycollate to elicit a neutrophilic infiltrate; (3) 4 h following i.p. injection of yeast cell wall (zymosan; t=16 h/4 h thioglycollate+zymosan); (4) 72 h following i.p. injection with thioglycollate to elicit monocyte/macrophage infiltration; and (5) 72 h/4 h thioglycollate+zymosan. A statistically significant sparing effect on the arachidonic acid (AA) and linoleic acid (LA) substrates was observed at time points two and five. When normalized to the concentration of the oxidative substrates, statistically significant reductions of 8-isoprostane-F(2alpha) (8-iso-F(2alpha)) at time point three (maximal neutrophil recruitment/activation), and 5-HETE, 5-oxo-EET, 11-HETE, 9-HODE, and PGF(2alpha) at time point five (maximal monocyte/macrophage recruitment/activation) were observed. Subsequently, the direct interaction of the optically inactive stereoisomer of Cardax (meso-dAST) with human 5-lipoxygenase (5-LOX) was evaluated in vitro with circular dichroism (CD) and electronic absorption (UV/Vis) spectroscopy, and subsequent molecular docking calculations were made using mammalian 15-LOX as a surrogate (for which XRC data has been reported). The results suggested that the meso-compound was capable of interaction with, and binding to, the solvent-exposed surface of the enzyme. These preliminary studies provide the foundation for more detailed evaluation of the therapeutic effects of this compound on the 5-LOX enzyme, important in chronic diseases such as atherosclerosis, asthma, and prostate cancer in humans.

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ASTAXANTHIN SUPPORTS HEART FUNCTION AFTER HEART ATTACK BY SUPPRESSING INFLAMMATION IN RAT MODEL.

Chin Med J (Engl). 2020 Aug 5;133(15):1786-1797.
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Astaxanthin promotes M2 macrophages and attenuates cardiac remodeling after myocardial infarction by suppression inflammation in rats

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- PMID: 32701588
- PMCID: [PMC7470000](#)
- DOI: [10.1097/CM9.0000000000000814](#)

Abstract

Background: Cardiac remodeling after acute myocardial infarction (AMI) is an important process. The present study aimed to assess the protective effects of astaxanthin (ASX) on cardiac remodeling after AMI.

Methods: The study was conducted between April and September 2018. To create a rat AMI model, rats were anesthetized, and the left anterior descending coronary artery was ligated. The rats in the ASX group received 10 mg·kg·day ASX by gavage for 28 days. On the 1st day after AMI, but before ASX administration, six rats from each group were sacrificed to evaluate changes in the heart function and peripheral blood (PB) levels of inflammatory factors. On the 7th day after AMI, eight rats from each group were sacrificed to evaluate the PB levels of inflammatory factors and the M2 macrophage count using both immunofluorescence (IF) and flow cytometry (FC). The remaining rats were observed for 28 days. Cardiac function was examined using echocardiography. The inflammatory factors, namely, tumor necrosis factor- α (TNF- α), interleukin-1 β (IL-1 β), and IL-10, were assessed using enzyme-linked immunosorbent assay. The heart weight/body weight (BW), and lung weight (LW)/BW ratios were calculated, and

myocardial fibrosis in the form of collagen volume fraction was measured using Masson trichrome staining. Hematoxylin and eosin (H&E) staining was used to determine the myocardial infarct size (MIS), and TdT-mediated dUTP nick-end labeling staining was used to analyze the myocardial apoptosis index. The levels of apoptosis-related protein, type I/III collagen, transforming growth factor β 1 (TGF- β 1), metalloproteinase 9 (MMP9), and caspase 3 were assessed by Western blotting. Unpaired t-test, one-way analysis of variance, and non-parametric Mann-Whitney test were used to analyze the data.

Results: On day 1, cardiac function was worse in the ASX group than in the sham group (left ventricular end-systolic diameter [LVIDs]: 0.72 ± 0.08 vs. 0.22 ± 0.06 cm, $t = -11.38$; left ventricular end-diastolic diameter [LVIDd]: 0.89 ± 0.09 vs. 0.48 ± 0.05 cm, $t = -9.42$; end-systolic volume [ESV]: 0.80 [0.62, 0.94] vs. 0.04 [0.03, 0.05] mL, $Z = -2.89$; end-diastolic volume [EDV]: 1.39 [1.03, 1.49] vs. 0.28 [0.22, 0.32] mL, $Z = -2.88$; ejection fraction [EF]: 0.40 ± 0.04 vs. 0.86 ± 0.05 , $t = 10.00$; left ventricular fractional shortening [FS] rate: 0.19 [0.18, 0.20] %FS vs. 0.51 [0.44, 0.58] %FS, $Z = -2.88$, all $P < 0.01$; $n = 6$). The levels of inflammatory factors significantly increased (TNF- α : 197.60 [133.89, 237.94] vs. 50.48 [47.21, 57.10] pg/mL, $Z = -2.88$; IL-1 β : 175.23 [160.74, 215.09] vs. 17.78 [16.83, 19.56] pg/mL, $Z = -2.88$; IL-10: 67.64 [58.90, 71.46] vs. 12.33 [11.64, 13.98] pg/mL, $Z = -2.88$, all $P < 0.01$; $n = 6$). On day 7, the levels of TNF- α and IL-1 β were markedly lower in the ASX group than in the AMI group (TNF- α : 71.70 [68.60, 76.00] vs. 118.07 [106.92, 169.08] pg/mL, $F = 42.64$; IL-1 β : 59.90 [50.83, 73.78] vs. 151.60 [108.4, 198.36] pg/mL, $F = 44.35$, all $P < 0.01$, $n = 8$). Conversely, IL-10 levels significantly increased (141.84 [118.98, 158.36] vs. 52.96 [42.68, 74.52] pg/mL, $F = 126.67$, $P < 0.01$, $n = 8$). The M2 macrophage count significantly increased (2891.42 ± 211.29 vs. 1583.38 ± 162.22 , $F = 274.35$, $P < 0.01$ by immunofluorescence test; 0.96 ± 0.18 vs. 0.36 ± 0.05 , $F = 46.24$, $P < 0.05$ by flowcytometry test). On day 28, cardiac function was better in the ASX group than in the AMI group (LVIDs: 0.50 [0.41, 0.56] vs. 0.64 [0.56, 0.74] cm, $Z = -3.60$; LVIDd: 0.70 [0.60, 0.76] vs. 0.80 [0.74, 0.88] cm, $Z = -2.96$; ESV: 0.24 [0.18, 0.45] vs. 0.58 [0.44, 0.89] mL, $Z = -3.62$; EDV: 0.76 [0.44, 1.04] vs. 1.25 [0.82, 1.46] mL, $Z = -2.54$; EF: 0.60 ± 0.08 vs. 0.50 ± 0.12 , $F = 160.48$; %FS: 0.29 [0.24, 0.31] vs. 0.20 [0.17, 0.21], $Z = -4.43$, all $P < 0.01$; $n = 16$). The MIS and LW/BW ratio were markedly lower in the ASX group than in the AMI group (myocardial infarct size: 32.50 ± 1.37 vs. 50.90 ± 1.73 , $t = 23.63$, $P < 0.01$, $n = 8$; LW/BW: 1.81 ± 0.15 vs. 2.17 ± 0.37 , $t = 3.66$, $P = 0.01$, $n = 16$). The CVF was significantly lower in the ASX group than in the AMI group: 12.88 ± 2.53 vs. 28.92 ± 3.31 , $t = 10.89$, $P < 0.01$, $n = 8$. The expression of caspase 3, TGF- β 1, MMP9, and type I/III collagen was lower in the ASX group than in the AMI group (caspase 3: 0.38 ± 0.06 vs. 0.66 ± 0.04 , $t = 8.28$; TGF- β 1: 0.37 ± 0.04 vs. 0.62 ± 0.07 , $t = 6.39$; MMP9: 0.20 ± 0.06 vs. 0.40 ± 0.06 , $t = 4.62$; type I collagen: 0.42 ± 0.09 vs. 0.74 ± 0.07 , $t = 5.73$; type III collagen: 0.13 ± 0.02 vs. 0.74 ± 0.07 , $t = 4.32$, all $P < 0.01$; $n = 4$).

Conclusions: ASX treatment after AMI may promote M2 macrophages and effectively attenuate cardiac remodeling by inhibiting inflammation and reducing myocardial fibrosis.

ASTAXANTHIN PREVENTS HEART MITOCHONDRIAL IMPAIRMENT IN RATS AND MAY HAVE A ROLE IN PREVENTION OF CARDIOVASCULAR DISEASES.

Antioxidants (Basel). 2020 Mar 23;9(3):262.

doi: [10.3390/antiox9030262](https://doi.org/10.3390/antiox9030262).

Astaxanthin Prevents Mitochondrial Impairment Induced by Isoproterenol in Isolated Rat Heart Mitochondria

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- PMID: **32210012**
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Abstract

Mitochondria are considered to be a power station of the cell. It is known that they play a major role in both normal and pathological heart function. Alterations in mitochondrial bioenergetics are one of the main causes of the origin and progression of heart failure since they have an inhibitory effect on the activity of respiratory complexes in the inner mitochondrial membrane. Astaxanthin (AST) is a xanthophyll carotenoid of mainly marine origin. It has both lipophilic and hydrophilic properties and may prevent mitochondrial dysfunction by permeating the cell membrane and co-localizing within mitochondria. The carotenoid suppresses oxidative stress-induced mitochondrial dysfunction and the development of diseases. In the present study, it was found that the preliminary oral administration of AST upregulated the activity of respiratory chain complexes and ATP synthase and the level of their main subunits, thereby improving the respiration of rat heart mitochondria (RHM) in the heart injured by isoproterenol (ISO). AST decreased the level of cyclophilin D (CyP-D) and increased the level of adenine nucleotide translocase (ANT) in this condition. It was concluded that AST could be considered as a potential mitochondrial-targeted agent in the therapy of pathological conditions associated with oxidative damage and mitochondrial dysfunction. AST, as a dietary supplement, has a potential in the prevention of cardiovascular diseases.

ASTAXANTHIN SUPPORTS IMPROVED METABOLIC FUNCTION; REDUCES BLOOD LIPIDS; IMPROVES GLUCOSE METABOLISM; AND STIMULATES MITOCHONDRIAL BIOGENESIS IN MICE.

J Cachexia Sarcopenia Muscle. 2020 Feb;11(1):241-258.
doi: 10.1002/jcsm.12530. Epub 2020 Jan 31.

Astaxanthin stimulates mitochondrial biogenesis in insulin resistant muscle via activation of AMPK pathway

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Abstract

Background: Skeletal muscle is mainly responsible for insulin-stimulated glucose disposal. Dysfunction in skeletal muscle metabolism especially during obesity contributes to the insulin resistance. Astaxanthin (AX), a natural antioxidant, has been shown to ameliorate hepatic insulin resistance in obese mice. However, its effects in skeletal muscle are poorly understood. The current study aimed to investigate the molecular target of AX in ameliorating skeletal muscle insulin resistance.

Methods: We fed 6-week-old male C57BL/6J mice with normal chow (NC) or NC supplemented with AX (NC+AX) and high-fat-diet (HFD) or HFD supplemented with AX for 24 weeks. We determined the effect of AX on various parameters including insulin sensitivity, glucose uptake, inflammation, kinase signaling, gene expression, and mitochondrial function in muscle. We also determined energy metabolism in intact

C2C12 cells treated with AX using the Seahorse XFe96 Extracellular Flux Analyzer and assessed the effect of AX on mitochondrial oxidative phosphorylation and mitochondrial biogenesis.

Results: AX-treated HFD mice showed improved metabolic status with significant reduction in blood glucose, serum total triglycerides, and cholesterol ($p < 0.05$). AX-treated HFD mice also showed improved glucose metabolism by enhancing glucose incorporation into peripheral target tissues, such as the skeletal muscle, rather than by suppressing gluconeogenesis in the liver as shown by hyperinsulinemic-euglycemic clamp study. AX activated AMPK in the skeletal muscle of the HFD mice and upregulated the expressions of transcriptional factors and coactivator, thereby inducing mitochondrial remodeling, including increased mitochondrial oxidative phosphorylation component and free fatty acid metabolism. We also assessed the effects of AX on mitochondrial biogenesis in the siRNA-mediated AMPK-depleted C2C12 cells and showed that the effect of AX was lost in the genetically AMPK-depleted C2C12 cells. Collectively, AX treatment (i) significantly ameliorated insulin resistance and glucose intolerance through regulation of AMPK activation in the muscle, (ii) stimulated mitochondrial biogenesis in the muscle, (iii) enhanced exercise tolerance and exercise-induced fatty acid metabolism, and (iv) exerted antiinflammatory effects via its antioxidant activity in adipose tissue.

Conclusions: We concluded that AX treatment stimulated mitochondrial biogenesis and significantly ameliorated insulin resistance through activation of AMPK pathway in the skeletal muscle.

Astaxanthin supplementation provides significant cardioprotection in rats.

[Mol Cell Biochem](#). 2006 Feb;283(1-2):23-30.

Seven day oral supplementation with Cardax (disodium disuccinate astaxanthin) provides significant cardioprotection and reduces oxidative stress in rats.

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In the current study, the improved oral bioavailability of a synthetic astaxanthin derivative (Cardax; disodium disuccinate astaxanthin) was utilized to evaluate its potential effects as a cardioprotective agent after 7-day subchronic oral administration as a feed supplement to Sprague-Dawley rats. Animals received one of two concentrations of Cardax in feed (0.1 and 0.4%; approximately 125 and 500 mg/kg/day, respectively) or control feed without drug for 7 days prior to the infarct study carried out on day 8. Thirty minutes of occlusion of the left anterior descending (LAD) coronary artery was followed by 2 h of reperfusion prior to sacrifice, a regimen which resulted in a mean infarct size (IS) as a percentage (%) of the area at risk (AAR; IS/AAR,%) of 61 +/- 1.8%. The AAR was quantified by Patent blue dye injection, and IS was determined by triphenyltetrazolium chloride (TTC) staining. Cardax at 0.1 and 0.4% in feed for 7 days resulted in a significant mean reduction in IS/AAR,% to 45 +/- 2.0% (26% salvage) and 39 +/- 1.5% (36% salvage), respectively. Myocardial levels of free astaxanthin achieved after 7-day supplementation at each of the two concentrations (400 +/- 65 nM and 1634 +/- 90 nM, respectively) demonstrated excellent solid-tissue target organ loading after oral supplementation. Parallel trends in reduction of plasma levels of multiple lipid peroxidation products with disodium disuccinate astaxanthin supplementation were observed, consistent with the documented in vitro antioxidant mechanism of action. These results extend the potential utility of this compound for cardioprotection to the elective human cardiovascular patient population, for which 7-day oral pre-treatment (as with statins) provides significant reductions in induced periprocedural infarct size.

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Astaxanthin improves cardiac dysfunction and oxidative status in rats.

[Naunyn-Schmiedeberg's Arch Pharmacol.](#) 2018 Nov 30. doi: 10.1007/s00210-018-1595-0. [Epub ahead of print]

Astaxanthin ameliorates cardiomyocyte apoptosis after coronary microembolization by inhibiting oxidative stress via Nrf2/HO-1 pathway in rats.

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Author information

Abstract

Coronary microembolization (CME) caused by physical obstruction in coronary microcirculation induces myocardial apoptosis and cardiac dysfunction, and it was reported that the inactivation of the Nrf2/HO-1 signaling was involved in this process. Astaxanthin (AST) is a reddish pigment that belongs to keto-carotenoids. It is also a potent antioxidant and has been reported to activate Nrf2/HO-1 signaling in vein endothelial cells. However, it is still unknown whether AST is able to activate Nrf2/HO-1 signaling pathway to protect cardiac functions from CME in vivo. To address this question, rats were orally administrated with AST or AST plus Zinc protoporphyrin IX (ZnPP, a HO-1 inhibitor), followed by CME modeling operation. Then, cardiac function was evaluated by echocardiographic measurement. Myocardial infarction was measured by HBFP staining, and apoptosis was assessed by TUNEL staining. The protein levels and mRNA expressions of Bax and Bcl-2 were measured by Western blot and qRT-PCR, respectively. ELISA was performed to measure the activity of enzymes related to oxidative stress. AST pretreatment dramatically attenuated CME-induced cardiac dysfunction, myocardial infarction, and cardiomyocyte apoptosis. Mechanistically, AST suppressed CME-induced oxidative stress by re-activating Nrf2/HO-1 signaling. HO-1 inhibitor ZnPP completely eliminated the benefits of AST in CEM, supporting the critical role of Nrf2/HO-1 signaling in mediating the cardioprotective function of AST in CME. Conclusion: AST suppresses oxidative stress via activating Nrf2/HO-1 pathway and thus prevents CME-induced cardiomyocyte apoptosis and ameliorates cardiac dysfunction in rats.

KEYWORDS:

Astaxanthin; Cardiomyocyte apoptosis; Coronary microembolization; Nrf2/HO-1 signaling; Oxidative stress

PMID: 30506291

DOI: [10.1007/s00210-018-1595-0](https://doi.org/10.1007/s00210-018-1595-0)

Astaxanthin provides cardio-protective properties in mice after heart attack.

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Sphingomyelin phosphodiesterase 1 (SMPD1) mediates the attenuation of myocardial infarction-induced cardiac fibrosis by astaxanthin.

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Author information

Abstract

Uncontrolled cardiac fibrosis following myocardial infarction (MI) is a critical pathological change leading to heart failure. Current pharmacotherapies are limited by unsatisfactory efficacy and undesired systemic side effects. Astaxanthin (ASX) is a natural carotenoid with strong antioxidant and anti-inflammatory activities. The effects of ASX on MI-induced cardiac fibrosis and the underlying mechanisms remain largely unknown. In this study, after the establishment of MI model, mice were administrated with ASX (200 mg/kg·d) for 4 weeks. We found that ASX treatment attenuated cardiac fibrosis and improved heart function following MI, as evidenced by reduced collagen I/III ratio, hydroxyproline content and left ventricular end diastolic pressure (LVEDP). Lipidomic analysis revealed the overaccumulation of myocardial ceramides in mice with cardiac fibrosis, which was normalized by ASX treatment. Molecular docking analysis showed that ASX produced a tight fit in the pocket of sphingomyelin phosphodiesterase 1 (SMPD1), a key enzyme in the production of ceramides. Western blot analysis confirmed the significant inhibition of SMPD1 expression by ASX. Furthermore, MI-induced overexpression of transforming growth factor β 1 (TGF- β 1) and phosphorylated SMAD2/3 were attenuated by ASX administration. SMPD1 knockout (KO) abrogated the beneficial effect of ASX. Taken together, our results suggest that the cardioprotective effects of ASX are mediated by SMPD1 through the indirect inhibition of TGF- β 1/SMAD signaling cascade.

KEYWORDS:

Astaxanthin; Cardiac fibrosis; Lipidomics; Myocardial infarction; SMPD1

PMID: 29906461

DOI: [10.1016/j.bbrc.2018.06.054](https://doi.org/10.1016/j.bbrc.2018.06.054)

[Indexed for MEDLINE]

Astaxanthin shows cardioprotective properties by reducing homocysteine-induced toxicity in rodents and in-vitro.

[Front Physiol.](#) 2017 Dec 12;8:1041. doi: 10.3389/fphys.2017.01041. eCollection 2017.

Astaxanthin Attenuates Homocysteine-Induced Cardiotoxicity *in Vitro* and *in Vivo* by Inhibiting Mitochondrial Dysfunction and Oxidative Damage.

[Fan CD](#)¹, [Sun JY](#)², [Fu XT](#)¹, [Hou YJ](#)¹, [Li Y](#)¹, [Yang MF](#)¹, [Fu XY](#)¹, [Sun BL](#)^{1,3}.

Author information

Abstract

Homocysteine (Hcy) as an independent risk factor contributes to the occurrence and development of human cardiovascular diseases (CVD). Induction of oxidative stress and apoptosis was commonly accepted as the major mechanism in Hcy-induced cardiotoxicity. Astaxanthin(ATX) as one of the most powerful antioxidants exhibits novel cardioprotective potential against Hcy-induced endothelial dysfunction. However, the protective effect and mechanism of ATX against Hcy-induced cardiotoxicity in cardiomyocytes have not been elucidated yet. Herein, H9c2 rat cardiomyocytes and Hcy-injured animal model were employed in the present study. The MTT, flow cytometry analysis (FCM), TUNEL-DAPI and western blotting results all demonstrated that ATX significantly alleviated Hcy-induced cytotoxicity in H9c2 cells through inhibition of mitochondria-mediated apoptosis. The JC-1 and Mito-tracker staining both revealed that ATX pre-treatment blocked Hcy-induced mitochondrial dysfunction by regulating Bcl-2 family expression. Moreover, DCFH-DA and Mito-SOX staining showed that ATX effectively attenuated Hcy-induced oxidative damage via scavenging intracellular reactive oxygen species (ROS). Importantly, the ELISA and immunohistochemical results indicated that Hcy-induced cardiotoxicity *in vivo* was also significantly inhibited by ATX through inhibition of oxidative damage and apoptosis, and improvement of the angiogenesis. Taken together, our results demonstrated that ATX suppressed Hcy-induced cardiotoxicity *in vitro* and *in vivo* by inhibiting mitochondrial dysfunction and oxidative damage. Our findings validated the strategy of using ATX may be a highly efficient way to combat Hcy-mediated human CVD.

KEYWORDS:

astaxanthin; cardiovascular diseases; homocysteine; mitochondrial dysfunction; oxidative damage

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DOI: [10.3389/fphys.2017.01041](#)

[Free PMC Article](#)

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Exposure to Oxadiazon-Butachlor causes cardiac toxicity in zebrafish embryos

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Abstract

Oxadiazon-Butachlor (OB) is a widely used herbicide for controlling most annual weeds in rice fields. However, its potential toxicity in aquatic organisms has not been evaluated so far. We used the zebrafish embryo model to assess the toxicity of OB, and found that it affected early cardiac development and caused extensive cardiac damage.

Mechanistically, OB significantly increased oxidative stress in the embryos by inhibiting antioxidant enzymes that resulted in excessive production of reactive oxygen species (ROS), eventually leading to cardiomyocyte apoptosis. In addition, OB also inhibited the WNT signaling pathway and downregulated its target genes including *lcf1*, *axin2* and β -catenin. Reactivation of this pathway by the Wnt activator BML-284 and the antioxidant astaxanthin rescued the embryos from the cardiotoxic effects of OB, indicating that oxidative stress, and inhibition of WNT target genes are the mechanistic basis of OB-induced damage in zebrafish. Our study shows that OB exposure causes cardiotoxicity in zebrafish embryos and may be potentially toxic to other aquatic life and even humans.

Astaxanthin prevents the development of atherosclerosis in mice.

[Biomed Res Int](#). 2017;2017:4625932. doi: 10.1155/2017/4625932. Epub 2017 Nov 1.

Effects of Astaxanthin on Reverse Cholesterol Transport and Atherosclerosis in Mice.

[Zou TB](#)¹, [Zhu SS](#)¹, [Luo F](#)¹, [Li WQ](#)¹, [Sun XR](#)², [Wu HF](#)³.

Author information

Abstract

High plasma level of HDL-cholesterol (HDL-C) has been consistently associated with a decreased risk of atherosclerosis (AS); thus, HDL-C is considered to be an antiatherogenic lipoprotein. The development of novel therapies to enhance the atheroprotective properties of HDL may have the possibility of further reducing the residual AS risk. Reverse cholesterol transport (RCT) is believed to be a primary atheroprotective activity of HDL, which has been shown to promote the efflux of excess cholesterol from macrophage-derived foam cells via ATP-binding cassette transporter A1 (ABCA1), ATP-binding cassette transporter G1 (ABCG1), and scavenger receptor class B type I (SR-BI) and then transport it back to the liver for excretion into bile and eventually into the feces. In the current study, we investigated the effects of astaxanthin on RCT and AS progression in mice. The results showed that short- and long-term supplementation of astaxanthin promote RCT in C57BL/6J and ApoE^{-/-} mice, respectively. Moreover, astaxanthin can relieve the plaque area of the aortic sinus and aortic cholesterol in mice. These findings suggest that astaxanthin is beneficial for boosting RCT and preventing the development of AS.

PMID: 29226138

PMCID: [PMC5687128](#)

DOI: [10.1155/201](#)

Astaxanthin protects from cerebral infarction in rats.

[Hum Exp Toxicol](#). 2018 Sep;37(9):929-936. doi: 10.1177/0960327117745693. Epub 2017 Dec 8.

Protective effect of astaxanthin on acute cerebral infarction in rats.

[Nai Y¹](#), [Liu H¹](#), [Bi X¹](#), [Gao H²](#), [Ren C¹](#).

Author information

Abstract

The aim of the study was to investigate the effect of astaxanthin and its possible mechanisms on acute cerebral infarction (ACI) in rat model. Male Sprague Dawley rats were randomly divided into sham group, model group, and astaxanthin-treated groups (20, 40, and 80 mg/kg). Neurological examination, the ratio of cerebral edema, and histopathology changes were assessed. Moreover, some oxidative stress markers were obtained for biochemical analysis, and the expression of neurotrophic factors gene was detected by real-time polymerase chain reaction (RT-PCR) method. The results showed that treatment with astaxanthin notably reduced neurological deficit scores and the ratio of cerebral edema compared with the model group. Meanwhile, astaxanthin increased the activity of catalase, superoxide dismutase, and glutathioneperoxidase as well as decreased the content of malondialdehyde in brain tissue. RT-PCR results showed that the expression of brain-derived neurotrophic factor (BDNF) and nerve growth factor (NGF) mRNA were increased with astaxanthin treatment. The results indicated that astaxanthin could ameliorate ACI followed by suppressing oxidative stress and upregulating the expression of BDNF and NGF mRNA.

KEYWORDS:

Astaxanthin; acute cerebral infarction; neurological factors; oxidative stress

PMID: 29216762

DOI: [10.1177/0960327117745693](https://doi.org/10.1177/0960327117745693)

[Indexed for MEDLINE]

Astaxanthin provides marked cardioprotection in dog hearts.

[Mol Cell Biochem](#). 2005 Apr;272(1-2):221-7.

Acute and chronic administration of disodium disuccinate astaxanthin (Cardax) produces marked cardioprotection in dog hearts.

Gross GJ, Lockwood SF.

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Previous results from our laboratory have shown that a novel carotenoid derivative (disodium disuccinate astaxanthin; Cardax) produced dose-related reductions in myocardial infarct size (IS) in Sprague-Dawley rats when it was administered at any of three doses (25, 50 and 75 mg/kg, iv) on four consecutive days, followed by the acute infarct size study on day 5. Maximum salvage occurred at the highest dose (75 mg/kg) tested, and was shown as a 56% reduction in IS. In the present follow-up study, we used a more relevant large animal model, the dog, and looked at the effect of administering Cardax iv either acutely 2 h prior to occlusion (N = 8) or for 4 days at 50 mg/kg iv as previously done in the rat model (N = 6). The results were compared to a saline vehicle-treated group (N = 10). In all groups, dogs were subjected to 60 min of left anterior descending (LAD) coronary artery occlusion and 3 h of reperfusion. IS was determined using a triphenyltetrazolium chloride (TTZ) histochemical stain and was expressed as a percent of the area at risk (IS/AAR). IS/AAR was 20.9 +/- 1.6 % (mean +/- S.E.M.) in controls and was reduced to 11.0 +/- 1.7% (47.3% salvage; $p < 0.01$) in dogs treated only once iv at 2 h prior to occlusion, and 6.6 +/- 2.8% (68.4% salvage; $p < 0.001$) in dogs treated for 4 days. In the chronic treatment group, two of the three dogs with plasma concentrations of non-esterified astaxanthin above 1 microM had 0% IS/AAR (100% cardioprotection). These results suggest that Cardax has marked cardioprotective properties in both rodents and canines. Thus, Cardax may be a novel and powerful new means to prevent myocardial injury and/or necrosis associated with elective and/or urgent cardiac surgical interventions such as coronary angioplasty and stenting, as well as coronary artery bypass surgery (CABG).

PMID: 16010990 [PubMed - indexed for MEDLINE]

Astaxanthin effective in treating hypertension in rats, possibly through modulation of blood fluidity.

[Biol Pharm Bull.](#) 2005 Jun;28(6):967-71.

**Antihypertensive potential and mechanism of action of astaxanthin: II.
Vascular reactivity and hemorheology in spontaneously hypertensive rats.**

[Hussein G](#), [Goto H](#), [Oda S](#), [Iguchi T](#), [Sankawa U](#), [Matsumoto K](#), [Watanabe H](#).

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The current study was designed to determine the effects of a dietary astaxanthin (ASX-O) on vascular reactivity in spontaneously hypertensive rats (SHR), in order to verify its antihypertensive action mechanism. We evaluated contractions induced by phenylephrine (Phe), angiotensin II (Ang II) and the xanthine/xanthine oxidase (Xan/XOD) system, and relaxations induced by sodium nitroprusside (SNP) as well as endothelium-dependent relaxations mediated by acetylcholine (ACh) in thoracic aorta of the SHR, with and without ASX-O intervention. We also investigated the effects of ASX-O on blood rheology using a microchannel array system. In this study, ASX-O showed a significant modulatory effect on nitric oxide (NO)-induced vasorelaxation by the NO-donor SNP ($p < 0.05$). However, it did not show significant effects in restoring the impaired endothelium-dependent relaxation to ACh in the SHR. On the other hand, the constrictive effects by Phe, Ang II and Xan/XOD were ameliorated by ASX-O ($p < 0.05$). ASX-O also demonstrated significant hemorheological effect by decreasing the microchannel transit time of whole blood. In conclusion, the results suggest that ASX-O may act in modulating the blood fluidity in hypertension, and that the antihypertensive effects of ASX-O may be exerted through mechanisms including normalization of the sensitivity of the adrenoceptor sympathetic pathway, particularly $[\alpha]$ -adrenoceptors, and by restoration of the vascular tone through attenuation of the Ang II- and reactive oxygen species (ROS)-induced vasoconstriction.

Publication Types:

PMID: 15930728 [PubMed - indexed for MEDLINE]

Astaxanthin prevents damage from stroke in rabbits.

[J Pharmacol Exp Ther.](#) 2005 Aug;314(2):686-92. Epub 2005 May 4.

Disodium Disuccinate Astaxanthin (Cardax) attenuates complement activation and reduces myocardial injury following ischemia/reperfusion.

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Carotenoids are a naturally occurring group of compounds that possess antioxidant properties. Most natural carotenoids display poor aqueous solubility and tend to form aggregates in solution. Disodium disuccinate astaxanthin (DDA; Cardax) is a water-dispersible synthetic carotenoid that rapidly and preferentially associates with serum albumin, thereby preventing the formation of supramolecular complexes and facilitating its efficacy after parenteral administration. This study investigated the ability of DDA to reduce inflammation and myocardial injury in a rabbit model of ischemia/reperfusion. DDA (50 mg/kg/day) or saline was administered i.v. for 4 consecutive days before the initiation of the protocol for induction of myocardial ischemia/reperfusion. On the 5th day, rabbits underwent 30 min of coronary artery occlusion, followed by a 3-h reperfusion period. Myocardial infarct size, as a percentage of the area at risk, was calculated for both groups. Infarct size was 52.5 +/- 7.5% in the vehicle-treated (n = 9) and 25.8 +/- 4.7% in the DDA-treated (n = 9) animals (p < 0.01 versus vehicle; mean myocardial salvage = 51%). To evaluate the anti-inflammatory effects of DDA, complement activity was assessed at the end of reperfusion using a red blood cell lysis assay. DDA administration significantly reduced (p < 0.01) the activation of the complement system in the serum. The current results, coupled with the well established antioxidant ability of carotenoids, suggest that the mechanism(s) of action by which DDA reduces the tissue damage associated with reperfusion injury may include both antioxidant and anticomplement components.

Publication Types:

PMID: 15872041 [PubMed - indexed for MEDLINE]

Astaxanthin works as an anti-hypertensive and a neuroprotective agent in rats.

[Biol Pharm Bull.](#) 2005 Jan;28(1):47-52.

Antihypertensive and neuroprotective effects of astaxanthin in experimental animals.

[Hussein G](#), [Nakamura M](#), [Zhao Q](#), [Iguchi T](#), [Goto H](#), [Sankawa U](#), [Watanabe H](#).

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Astaxanthin is a natural antioxidant carotenoid that occurs in a wide variety of living organisms. We investigated, for the first time, antihypertensive effects of astaxanthin (ASX-O) in spontaneously hypertensive rats (SHR). Oral administration of ASX-O for 14 d induced a significant reduction in the arterial blood pressure (BP) in SHR but not in normotensive Wistar Kyoto (WKY) strain. The long-term administration of ASX-O (50 mg/kg) for 5 weeks in stroke prone SHR (SHR-SP) induced a significant reduction in the BP. It also delayed the incidence of stroke in the SHR-SP. To investigate the action mechanism of ASX-O, the effects on PGF(2alpha)-induced contractions of rat aorta treated with NG-nitro-L-arginine methyl ester (L-NAME) were studied in vitro. ASX-O (1 to 10 microM) induced vasorelaxation mediated by nitric oxide (NO). The results suggest that the antihypertensive effect of ASX-O may be due to a NO-related mechanism. ASX-O also showed significant neuroprotective effects in ischemic mice, presumably due to its antioxidant potential. Pretreatment of the mice with ASX-O significantly shortened the latency of escaping onto the platform in the Morris water maze learning performance test. In conclusion, these results indicate that astaxanthin can exert beneficial effects in protection against hypertension and stroke and in improving memory in vascular dementia.

Publication Types:

PMID: 15635162 [PubMed - indexed for MEDLINE]

Astaxanthin more effective than alpha tocopherol at preventing plaque buildup in the arteries of rabbits with high cholesterol.

[J Mol Cell Cardiol.](#) 2004 Nov;37(5):969-78.

Alpha-tocopherol and astaxanthin decrease macrophage infiltration, apoptosis and vulnerability in atheroma of hyperlipidaemic rabbits.

[Li W](#), [Hellsten A](#), [Jacobsson LS](#), [Blomqvist HM](#), [Olsson AG](#), [Yuan XM](#).

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The composition of atherosclerotic plaques, not just macroscopical lesion size, has been implicated in their susceptibility to rupture and the risk of thrombus formation. By focusing on the quality of lipids, macrophages, apoptosis, collagen, metalloproteinase expression and plaque integrity, we evaluated the possible anti-atherosclerotic effect of the antioxidants alpha-tocopherol and astaxanthin in Watanabe heritable hyperlipidemic (WHHL) rabbits. Thirty-one WHHL rabbits were divided into three groups and were fed a standard diet, as controls (N =10), or a standard diet with the addition of 500 mg alpha-tocopherol per kg feed (N =11) or 100 mg astaxanthin per kg feed (N =10) for 24 weeks. We found that both antioxidants, particularly astaxanthin, significantly decreased macrophage infiltration in the plaques although they did not affect lipid accumulation. All lesions in the astaxanthin-treated rabbits were classified as early plaques according to the distribution of collagen and smooth muscle cells. Both antioxidants also improved plaque stability and significantly diminished apoptosis, which mainly occurred in macrophages, matrix metalloproteinase three expressions and plaque ruptures. Although neither antioxidant altered the positive correlations between the lesion size and lipid accumulation, the lesion size and apoptosis were only positively correlated in the control group. Astaxanthin and alpha-tocopherol may improve plaque stability by decreasing macrophage infiltration and apoptosis in this atherosclerotic setting. Apoptosis reduction by alpha-tocopherol and astaxanthin may be a new anti-atherogenic property of these antioxidants.

Publication Types:

PMID: 15522274 [PubMed - indexed for MEDLINE]

Astaxanthin provides cardioprotection and reduces damage from heart attacks in rats.

[Life Sci.](#) 2004 May 28;75(2):215-24.

Cardioprotection and myocardial salvage by a disodium disuccinate astaxanthin derivative (Cardax).

[Gross GJ](#), [Lockwood SF](#).

Department of Pharmacology and Toxicology, Medical College of Wisconsin, 8701 Watertown Plank Road, Milwaukee, WI 53226, USA.

Cardioprotection in humans by carotenoids has been inferred from observational and epidemiologic studies, however, direct studies of cardioprotection and myocardial salvage by carotenoids are lacking. In the current study, intravenous (I.V.) pre-treatment with a novel carotenoid derivative (disodium disuccinate astaxanthin; Cardax) was evaluated as a myocardial salvage agent in a Sprague-Dawley rat infarct model. Animals were dosed once per day I.V. by tail vein injection for 4 days at one of 3 doses (25, 50, and 75 mg/kg) prior to the infarct study carried out on day 5. The results were compared with control animals treated with saline vehicle. Thirty (30) minutes of occlusion of the left anterior descending (LAD) coronary artery was followed by 2 hours of reperfusion prior to sacrifice, a regimen which resulted in a mean infarct size (IS) as a percent (%) of the area at risk (AAR) of 59 +/- 3%. Area at risk was quantified by Patent blue dye injection, and infarct size (IS) was determined by triphenyltetrazolium chloride (TTC) staining. Cardax at 50 and 75 mg/kg for 4 days resulted in a significant mean reduction in IS/AAR to 35 +/- 3% (41% salvage) and 26 +/- 2% (56% salvage), respectively. Infarct size and myocardial salvage were significantly, and linearly, correlated with plasma levels of non-esterified, free astaxanthin at the end of reperfusion. These results suggest that parenteral Cardax may find utility in those clinical applications where pre-treatment of patients at risk for myocardial infarction is performed.

Publication Types:

PMID: 15120573 [PubMed - indexed for MEDLINE]

Astaxanthin inhibits oxidation of lipoproteins in human blood.

[Biull Eksp Biol Med.](#) 1997 Mar;123(3):285-8.

[Astaxanthine-induced inhibition of oxidation of apolipoprotein B-containing lipoproteins in human blood]

[Article in Russian]

[Kukharchuk VV](#), [Shumaev KB](#), [Dmitrovskii AA](#), [Cherniad'eva IF](#), [Bykhovskii VIa](#).

PMID: 9162235 [PubMed - indexed for MEDLINE]

Astaxanthin preserves membrane structure and exhibits significant antioxidant activity as compared to other carotenoids such as lycopene and beta-carotene which exhibit pro-oxidant activity.

Biochimica et Biophysica Acta 1768 (2007) 167–174

Differential effects of carotenoids on lipid peroxidation due to membrane interactions: X-ray diffraction analysis

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Robert F. Jacob a, R. Preston Mason a,c

Abstract

The biological benefits of certain carotenoids may be due to their potent antioxidant properties attributed to specific physico-chemical interactions with membranes. To test this hypothesis, we measured the effects of various carotenoids on rates of lipid peroxidation and correlated these findings with their membrane interactions, as determined by small angle X-ray diffraction approaches. The effects of the homochiral carotenoids (astaxanthin, zeaxanthin, lutein, β -carotene, lycopene) on lipid hydroperoxide (LOOH) generation were evaluated in membranes enriched with polyunsaturated fatty acids. Apolar carotenoids, such as lycopene and β -carotene, disordered the membrane bilayer and showed a potent pro-oxidant effect (>85% increase in LOOH levels) while astaxanthin preserved membrane structure and exhibited significant antioxidant activity (40% decrease in LOOH levels). These findings indicate distinct effects of carotenoids on lipid peroxidation due to membrane structure changes. These contrasting effects of carotenoids on lipid peroxidation may explain differences in their biological activity.

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Astaxanthin reduces cardiac muscle damage in mouse study.

Antioxid Redox Signal. 2003 Feb;5(1):139-44.

Astaxanthin limits exercise-induced skeletal and cardiac muscle damage in mice.

Aoi, et al, 2003

Dietary antioxidants may attenuate oxidative damage from strenuous exercise in various tissues. Beneficial effects of the antioxidant astaxanthin have been demonstrated in vitro, but not yet in vivo. We investigated the effect of dietary supplementation with astaxanthin on oxidative damage induced by strenuous exercise in mouse gastrocnemius and heart. C57BL/6 mice (7 weeks old) were divided into groups: rested control, intense exercise, and exercise with astaxanthin supplementation. After 3 weeks of exercise acclimation, both exercise groups ran on a treadmill at 28 m/min until exhaustion. Exercise-increased 4-hydroxy-2-nonenal-modified protein and 8-hydroxy-2'-deoxyguanosine in gastrocnemius and heart were blunted in the astaxanthin group. Increases in plasma creatine kinase activity, and in myeloperoxidase activity in gastrocnemius and heart, also were lessened by astaxanthin. Astaxanthin showed accumulation in gastrocnemius and heart from the 3 week supplementation. Astaxanthin can attenuate exercise-induced damage in mouse skeletal muscle and heart, including an associated neutrophil infiltration that induces further damage.

ASTAXANTHIN REDUCES CARDIOVASCULAR CELL DEATH AND OXIDATIVE STRESS AFTER CORONARY MICROEMBOLIZATION IN RATS.

Naunyn Schmiedebergs Arch Pharmacol. 2019 Mar;392(3):341-348.

doi: 10.1007/s00210-018-1595-0. Epub 2018 Nov 30.

Astaxanthin ameliorates cardiomyocyte apoptosis after coronary microembolization by inhibiting oxidative stress via Nrf2/HO-1 pathway in rats

[Yugang Xue](#)¹, [Chuang Sun](#)¹, [Qimeng Hao](#)¹, [Jin Cheng](#)²

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- DOI: [10.1007/s00210-018-1595-0](https://doi.org/10.1007/s00210-018-1595-0)

Abstract

Coronary microembolization (CME) caused by physical obstruction in coronary microcirculation induces myocardial apoptosis and cardiac dysfunction, and it was reported that the inactivation of the Nrf2/HO-1 signaling was involved in this process. Astaxanthin (AST) is a reddish pigment that belongs to keto-carotenoids. It is also a potent antioxidant and has been reported to activate Nrf2/HO-1 signaling in vein endothelial cells. However, it is still unknown whether AST is able to activate Nrf2/HO-1 signaling pathway to protect cardiac functions from CME in vivo. To address this question, rats were orally administrated with AST or AST plus Zinc protoporphyrin IX (ZnPP, a HO-1 inhibitor), followed by CME modeling operation. Then, cardiac function was evaluated by echocardiographic measurement. Myocardial infarction was measured by H&E staining, and apoptosis was assessed by TUNEL staining. The protein levels and mRNA expressions of Bax and Bcl-2 were measured by Western blot and qRT-PCR, respectively. ELISA was performed to measure the activity of enzymes related to oxidative stress. AST pretreatment dramatically attenuated CME-induced cardiac dysfunction, myocardial infarction, and cardiomyocyte apoptosis. Mechanistically, AST suppressed CME-induced oxidative stress by re-activating Nrf2/HO-1 signaling. HO-1 inhibitor ZnPP completely eliminated the benefits of AST in CEM, supporting the critical role of Nrf2/HO-1 signaling in mediating the cardioprotective function of AST in CME.

Conclusion: AST suppresses oxidative stress via activating Nrf2/HO-1 pathway and thus

prevents CME-induced cardiomyocyte apoptosis and ameliorates cardiac dysfunction in rats.

ASTAXANTHIN PREVENTS THE DEVELOPMENT OF HIGH BLOOD PRESSURE AND IMPROVES ENDOTHELIAL FUNCTION IN RATS.

Biol Pharm Bull. 2020;43(3):404-408.
doi: 10.1248/bpb.b19-01013.

Daily Meal Supplemented with Astaxanthin-Enriched Yolk Has Mitigative Effects against Hypertension in Spontaneously Hypertensive Rats

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- PMID: [32115501](#)
- DOI: [10.1248/bpb.b19-01013](#)

Free article

Abstract

The aim of this study was to investigate the effects of egg yolk powder enriched with astaxanthin (ASX-E) on blood pressure in spontaneously hypertensive rats (SHR) and to verify the benefits of ASX-E as a functional food. To investigate the antihypertensive effect, SHR were fed with an ASX-E mixed diet before hypertension development. Blood pressures were determined periodically during the study by the tail-cuff method. At the end of the study, animals were euthanized, and their thoracic aortas were collected to determine vascular conductance. The thoracic aorta tension was measured with a force displacement transducer. Concentration-dependent response relationships were determined by cumulative addition of 10^{-9} - 10^{-4} M Carbamoylcholine (Cch). Blood pressures of the SHR in the ASX-E mixed diet group were ASX-dose-dependently lower than that of those in the control group. In SHR fed with an ASX-E mixed diet, Cch induced vasorelaxation in the thoracic aorta with endothelium lining but not without endothelium. However, the antihypertensive effect of ASX-E was not observed on blood pressures in SHR that were fed with ASX-E only after the development of hypertension. Results suggest that ASX-E protects endothelial function and thereby prevents the development of hypertension. Hence, the results of our research indicate that daily consumption of ASX-E has a potential benefit on human health.

ASTAXANTHIN PROTECTS AGAINST HYPERTENSION AND PLAYS A ROLE IN THE BRAIN OF SPONTANEOUSLY HYPERTENSIVE RATS.

J Cardiovasc Pharmacol. 2021 Feb 1;77(2):170-181.

doi: 10.1097/FJC.0000000000000953.

Chronic Infusion of Astaxanthin Into Hypothalamic Paraventricular Nucleus Modulates Cytokines and Attenuates the Renin-Angiotensin System in Spontaneously Hypertensive Rats

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- PMID: **33538532**
- DOI: [10.1097/FJC.0000000000000953](https://doi.org/10.1097/FJC.0000000000000953)

Abstract

Oxidative stress, the renin-angiotensin system (RAS), and inflammation are some of the mechanisms involved in the pathogenesis of hypertension. The aim of this study is to examine the protective effect of the chronic administration of astaxanthin, which is extracted from the shell of crabs and shrimps, into hypothalamic paraventricular nucleus (PVN) in spontaneously hypertensive rats. Animals were randomly assigned to 2 groups and treated with bilateral PVN infusion of astaxanthin or vehicle (artificial cerebrospinal fluid) through osmotic minipumps (Alzet Osmotic Pumps, Model 2004, 0.25 μ L/h) for 4 weeks. Spontaneously hypertensive rats had higher mean arterial pressure and plasma level of norepinephrine and proinflammatory cytokine; higher PVN levels of reactive oxygen species, NOX2, NOX4, IL-1 β , IL-6, ACE, and AT1-R; and lower PVN levels of IL-10 and Cu/Zn SOD, Mn SOD, ACE2, and Mas receptors than Wistar-Kyoto rats. Our data showed that chronic administration of astaxanthin into PVN attenuated the overexpression of reactive oxygen species, NOX2, NOX4, inflammatory cytokines, and components of RAS within the PVN and suppressed hypertension. The present results revealed that astaxanthin played a role in the brain. Our findings demonstrated that astaxanthin had protective effect on hypertension by improving the balance between inflammatory cytokines and components of RAS.

ASTAXANTHIN PROTECTS AGAINST MITOCHONDRIAL PERMEABILITY IN RAT HEARTS WHICH SHOULD LEAD TO IMPROVEMENT OF HEART MUSCLE FUNCTION.

Antioxidants (Basel). 2019 Nov 21;8(12):576.

doi: [10.3390/antiox8120576](https://doi.org/10.3390/antiox8120576).

Astaxanthin Inhibits Mitochondrial Permeability Transition Pore Opening in Rat Heart Mitochondria

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- PMCID: [PMC6943429](https://pubmed.ncbi.nlm.nih.gov/PMC6943429/)
- DOI: [10.3390/antiox8120576](https://doi.org/10.3390/antiox8120576)

[Free PMC article](#)

Abstract

The mitochondrion is the main organelle of oxidative stress in cells. Increased permeability of the inner mitochondrial membrane is a key phenomenon in cell death. Changes in membrane permeability result from the opening of the mitochondrial permeability transition pore (mPTP), a large-conductance channel that forms after the overload of mitochondria with Ca²⁺ or in response to oxidative stress. The ketocarotenoid astaxanthin (AST) is a potent antioxidant that is capable of maintaining the integrity of mitochondria by preventing oxidative stress. In the present work, the effect of AST on the functioning of mPTP was studied. It was found that AST was able to inhibit the opening of mPTP, slowing down the swelling of mitochondria by both direct addition to mitochondria and administration. AST treatment changed the level of mPTP regulatory proteins in isolated rat heart mitochondria. Consequently, AST can protect mitochondria from changes in the induced permeability of the inner membrane. AST inhibited serine/threonine protein kinase B (Akt)/cAMP-responsive element-binding protein (CREB) signaling pathways in mitochondria, which led to the prevention of mPTP opening. Since AST improves the resistance of rat heart mitochondria to Ca²⁺-dependent stress, it can be assumed that after further studies, this antioxidant will be considered an

effective tool for improving the functioning of the heart muscle in general under normal and medical conditions.

ASTAXANTHIN PROTECTS AGAINST HEART CELL DEATH AND OXIDATIVE STRESS IN MOUSE MODEL.

Oxid Med Cell Longev. 2020 Mar 4;2020:7639109.
doi: 10.1155/2020/7639109. eCollection 2020.

Astaxanthin Protects Ochratoxin A-Induced Oxidative Stress and Apoptosis in the Heart via the Nrf2 Pathway

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PMID: 32190177 PMCID: [PMC7073479](#) DOI: [10.1155/2020/7639109](#) [Free PMC article](#)

Abstract

This study assessed the protective mechanism of astaxanthin (ASX) against ochratoxin A- (OTA-) induced cardiac injury in mice. Four groups of mice were established: control group (0.1 mL olive oil + 0.1 mL NaHCO₂), OTA group (0.1 mL OTA 5 mg/kg body weight), ASX group (0.1 mL ASX 100 mg/kg body weight), and ASX + OTA group (0.1 mL ASX 100 mg/kg body weight, 2 h later, 0.1 mL OTA 5 mg/kg body weight). The test period lasted for 27 days (7 days of dosing, 2 days of rest). Electrocardiogram, body weight, heart weight, tissue pathology, oxidative markers (malondialdehyde (MDA), superoxide dismutase (SOD), catalase (CAT), and glutathione (GSH)), biochemical markers (creatinine kinase (CK), creatine kinase isoenzyme (CK-MB), and lactate dehydrogenase (LDH)), electron microscopy, TUNEL, and Western blot tests were used to examine the effects of OTA on myocardial injury and ASX detoxification. The results showed that OTA exposure significantly decreased both body weight and heart weight. OTA induced a decrease in heart rate in mice and decreased tissue concentrations of SOD, CAT, and GSH, while increasing serum concentrations of cardiac enzymes (CK, CK-MB, and LDH) and tissue MDA. ASX improved heart rate, cardiac enzymes, and antioxidant levels in mice. The results of tissue pathology and TUNEL assay showed that ASX protects against OTA-induced myocardial injury. In addition, Western blot results showed that the OTA group upregulated Keap1, Bax, Caspase3, and Caspase9, while it downregulated Nrf2, HO-1, and Bcl-2 protein expression. ASX played a protective role by changing the expression of Keap1, Nrf2, HO-1, Bax, Bcl-2, Caspase3, and Caspase9 proteins. These results indicate that the protective mechanism of ASX on the myocardium works through the Keap1-Nrf2 signaling pathway and mitochondria-mediated apoptosis pathway. This study provides a molecular rationale for the mechanism underlying OTA-induced myocardial injury and the protective effect of ASX on the myocardium.

ASTAXANTHIN REDUCES MYOCARDIAL INJURY; PREVENTS CARDIAC DYSFUNCTION; AND REDUCES INFLAMMATORY MARKERS IN MICE.

Mol Med Rep. 2020 Oct;22(4):3338-3346.

doi: 10.3892/mmr.2020.11443. Epub 2020 Aug 19.

Astaxanthin suppresses lipopolysaccharide-induced myocardial injury by regulating MAPK and PI3K/AKT/mTOR/GSK3 β signaling

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PMID: [32945516](#) PMCID: [PMC7453592](#) DOI: [10.3892/mmr.2020.11443](#) [Free PMC article](#)

Abstract

Cardiac dysfunction is a significant manifestation of sepsis and it is associated with the prognosis of the disease. Astaxanthin (ATX) has been discovered to serve a variety of pharmacological effects, including anti-inflammatory, antioxidant and antiapoptotic properties. The present study aimed to investigate the role and mechanisms of ATX in sepsis-induced myocardial injury. Male C57BL/6 mice were divided into three groups (15 mice per group): Control group, lipopolysaccharide (LPS) group and LPS + ATX group. The cardiac dysfunction model was induced through an intraperitoneal injection of LPS (10 mg/kg) and ATX (40 mg/kg) was administered to the LPS + ATX group by intraperitoneal injection 30 min following the administration of LPS. All animals were sacrificed after 24 h. Inflammatory cytokine levels in the serum were detected using ELISAs, and cardiac B-type natriuretic peptide (BNP) levels were analyzed using western blot analysis and reverse transcription-quantitative PCR. Furthermore, the extent of myocardial injury was evaluated using pathological analysis, and cardiomyocyte apoptosis was analyzed using a TUNEL assay, in addition to determining the expression levels of Bcl-2 and Bax. The expression levels of proteins involved in the mitogen activated protein kinase (MAPK) and PI3K/AKT signaling pathways were also analyzed using western blot analysis. ATX significantly suppressed the LPS-induced increased production of TNF- α and IL-6 and suppressed the protein expression levels of BNP, Bax and Bcl-2 to normal levels. ATX also prevented the histopathological changes to the myocardial tissue and reduced the extent of necrosis. Furthermore, the treatment with ATX suppressed the LPS-activated MAPK and PI3K/AKT signaling. ATX additionally exerted a protective effect on cardiac dysfunction caused by sepsis by inhibiting MAPK and PI3K/AKT signaling.

ASTAXANTHIN DEMONSTRATES A PROTECTIVE EFFECT IN RAT HEART MITOCHONDRIA.

Biomedicines. 2020 Oct 20;8(10):437.

doi: 10.3390/biomedicines8100437.

Isoproterenol-Induced Permeability Transition Pore-Related Dysfunction of Heart Mitochondria Is Attenuated by Astaxanthin

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- PMID: [33092172](#)
- PMCID: [PMC7589423](#)
- DOI: [10.3390/biomedicines8100437](#)

Free PMC article

Abstract

Mitochondria are key organelles of the cell because their main function is the capture of energy-rich substrates from the cytoplasm and oxidative cleavage with the generation of carbon dioxide and water, processes that are coupled with the synthesis of ATP. Mitochondria are subject to oxidative stress through the formation of the mitochondrial permeability transition pore (mPTP). Various antioxidants are used to reduce damage caused by oxidative stress and to improve the protection of the antioxidant system. Astaxanthin (AST) is considered to be a dietary antioxidant, which is able to reduce oxidative stress and enhance the antioxidant defense system. In the present investigation, the effect of AST on the functional state of rat heart mitochondria impaired by isoproterenol (ISO) under mPTP functioning was examined. It was found that AST raised mitochondrial respiration, the Ca²⁺ retention capacity (CRC), and the rate of TPP⁺ influx in rat heart mitochondria (RHM) isolated from ISO-injected rats. However, the level of reactive oxygen species (ROS) production increased. In addition, the concentrations of cardiolipin (CL), Mn-SOD2, and the proteins regulating mPTP rose after the injection of ISO in RHM pretreated with AST. Based on the data obtained, we suggest that AST has a protective effect in rat heart mitochondria.

ASTAXANTHIN PROTECTS AGAINST ALCOHOL-INDUCED CARDIOMYOPATHY IN MICE.

Toxicol Appl Pharmacol. 2021 Feb 1;412:115378.

doi: 10.1016/j.taap.2020.115378. Epub 2021 Jan 2.

Astaxanthin attenuates alcoholic cardiomyopathy via inhibition of endoplasmic reticulum stress-mediated cardiac apoptosis

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PMID: 33352188 DOI: [10.1016/j.taap.2020.115378](https://doi.org/10.1016/j.taap.2020.115378) Free article

Abstract

Chronic excessive ethanol consumption is associated with a high incidence of mortality due to ethanol-induced dilated cardiomyopathy, known as alcoholic cardiomyopathy (ACM). Mechanistic studies have demonstrated that apoptosis is key to the pathogenesis of ACM, and endoplasmic reticulum (ER) stress-associated apoptosis contributes to various ethanol-related diseases. Astaxanthin (AST) is a natural carotenoid that exerts an anti-ER stress effect. Importantly, strong evidence has shown that AST induces beneficial effects in various cardiovascular diseases. The present study aimed to investigate whether AST induces beneficial effects on ACM by suppressing cardiac apoptosis mediated by ER stress. We showed that after 2 months of chronic excessive ethanol consumption, mice displayed obvious cardiac dysfunction and morphological changes associated with increased fibrosis, oxidative stress, ER stress and apoptosis. However, cardiac damage above was attenuated in response to AST treatment. The cardioprotective effect of AST against ethanol toxicity was also confirmed in both H9c2 cells and primary cardiomyocytes, indicating that AST-induced protection directly targets cardiomyocytes. Both in vivo and in vitro studies showed that AST inhibited all three ER stress signaling pathways activated by ethanol. Furthermore, administration of the ER stress inhibitor sodium 4-phenylbutyrate (4-PBA) strongly suppressed ethanol-induced cardiomyocyte damage. Interestingly, AST induced further anti-apoptotic effects once co-treated with 4-PBA, indicating that AST protects the heart from ACM partially by attenuating ER stress, but other mechanisms still exist. This study highlights that administration of AST ablated chronic excessive ethanol consumption-induced cardiomyopathy by suppressing cardiac ER stress and subsequent apoptosis.

ASTAXANTHIN IMPROVES LIPID METABOLISM; REDUCES HEAT STRESS; AND INHIBITS INFLAMMATION IN CHICKENS.

Poult Sci. 2020 Oct;99(10):4853-4860.

doi: 10.1016/j.psj.2020.05.022. Epub 2020 Jul 18.

Dietary supplemental microalgal astaxanthin modulates molecular profiles of stress, inflammation, and lipid metabolism in broiler chickens and laying hens under high ambient temperatures

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- PMID: 32988522
- PMCID: [PMC7810900](#)
- DOI: [10.1016/j.psj.2020.05.022](#)

[Free PMC article](#)

Abstract

This research was to determine effects of supplemental dietary microalgal astaxanthin (AST) on hepatic gene expression and protein production of redox enzymes, heat shock proteins (HSPs), cytokines, and lipid metabolism in broilers (BR) and laying hens (LH) under high ambient temperatures. A total of 240 (day old) Cornish male BR and 50 (19 wk old) White Leghorn Shavers LH were allotted in 5 dietary treatments with 6 and 10 cages/treatment (8 BR or 1 LH/cage), respectively. The birds were fed corn-soybean meal basal diets supplemented with microalgal (*Haematococcus pluvialis*) AST at 0, 10, 20, 40, and 80 mg/kg diet for 6 wk. Supplemental AST to the BR diet linearly decreased ($P < 0.10$, $R^2 = 0.18-0.36$) hepatic mRNA levels of several redox status-controlling genes, heat shock protein 70 (HSP70), heat shock transcription factor 1 (HSTF1), c-Jun N-terminal kinase 1 (JNK1), tumor necrosis factor- α , and sterol regulatory element-binding protein 1 (SREBP1). The supplementation linearly elevated ($P = 0.04$, $R^2 = 0.20$) diacylglycerol acyltransferase 2 (DGAT2) mRNA level and produced quadratic changes (P

< 0.10, $R^2 = 0.15-0.47$) in mRNA levels of glutathione S-transferase (GST), serine/threonine kinase (AKT1), P38 mitogen-activated protein kinase (P38MAKP), lipid metabolism-controlling genes, and the protein production of HSP90 and P38MAPK in the liver. Supplementing AST to the LH diets linearly decreased ($P < 0.10$, $R^2 = 0.18-0.56$) mRNA levels of GST, HSF1, JNK1, and interleukin 10; lipogenesis genes; and JNK1 protein production. However, supplemental dietary AST produced quadratic changes ($P < 0.10$, $R^2 = 0.26-0.72$) in mRNA levels of most antioxidant-, stress-responsive, and lipid metabolism-related genes in the liver of LH. In conclusion, supplemental dietary AST affected the hepatic gene expression and protein production related to redox status, heat stress and inflammation, and lipid metabolism in both BR and LH. The impacts varied with the chicken type and demonstrated linear and quadratic regressions with the inclusion levels of AST.

ASTAXANTHIN SHOWS POTENTIAL AS AN ANTI-CLOTTING FACTOR IN RAT STUDY AND MAY SERVE AS A NATURAL ANTI-COAGULANT WITH LESS SIDE EFFECTS THAN DRUGS CURRENTLY USED.

J Food Biochem. 2020 Jul 28;e13407.

doi: [10.1111/jfbc.13407](https://doi.org/10.1111/jfbc.13407). Online ahead of print.

Subacute administration of Astaxanthin inhibits vitamin K-dependent clotting factors in rats

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- PMID: [32725659](https://pubmed.ncbi.nlm.nih.gov/32725659/)
- DOI: [10.1111/jfbc.13407](https://doi.org/10.1111/jfbc.13407)

Abstract

This study investigated the effect of Astaxanthin (ASTX) on levels and activities of the clotting factors in control rats. Untreated or ASTX-treated rats (10 mg/kg, dissolved in DMSO) were used in this study. ASTX treatment was conducted for 10 days daily. ASTX significantly decreased the platelet count and prolonged values of prothrombin and activated partial thromboplastin time (PT and aPTT, respectively). Besides, it significantly reduced serum levels of vitamin K and the plasma activities and hepatic expression of vitamin K-dependent factors (FII, FVII, FIX, and FX) without altering the activities or levels of all other clotting factors nor plasma levels of fibrinogen or von Willebrand Factor. These effects were associated with a reduction in serum and fecal levels of cholesterol and triglycerides and lower serum levels of LDL-c. In conclusion, ASTX exerts an in vivo hypocoagulant effects mediated by the inhibition of vitamin K-dependent factors. PRACTICAL APPLICATIONS: The findings presented here are the first that show the ability of Astaxanthin (ASTX) to inhibit coagulation in rats by suppressing the circulatory levels of Vitamin K and decrease the synthesis and release of all Vitamin-K dependent factor (FII, FVII, FIX, and FX). Since some synthetic anti-coagulants had side effects, these findings may illustrate ASTX as a natural anti-coagulant with fewer side effects that require further investigation in more clinical trials. Besides, awareness should be established for those individuals with some bleeding disorders who are being treated with ASTX for other beneficial effects.

ASTAXANTHIN IMPROVES VASCULAR REMODELING IN RATS WITH HIGH BLOOD PRESSURE.

Oxid Med Cell Longev. 2020 Apr 14;2020:4629189.
doi: 10.1155/2020/4629189. eCollection 2020.

Astaxanthin Attenuates Hypertensive Vascular Remodeling by Protecting Vascular Smooth Muscle Cells from Oxidative Stress-Induced Mitochondrial Dysfunction

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PMID: 32351673 PMCID: [PMC7178508](#) DOI: [10.1155/2020/4629189](#) [Free PMC article](#)

Abstract

Oxidative stress aggravates mitochondrial injuries and accelerates the proliferation of vascular smooth muscle cells (VSMCs), which are important mechanisms contributing to vascular remodeling in hypertension. We put forward the hypothesis that Astaxanthin (ATX), known to possess strong features of antioxidant, could attenuate vascular remodeling by inhibiting VSMC proliferation and improving mitochondrial function. The potential effects of ATX were tested on spontaneously hypertensive rats (SHRs) and cultured VSMCs that injured by angiotensin II (Ang II). The results showed that ATX lowered blood pressure, reduced aortic wall thickness and fibrosis, and decreased the level of reactive oxygen species (ROS) and H₂O₂ in tunica media. Moreover, ATX decreased the expression of proliferating cell nuclear antigen (PCNA) and ki67 in aortic VSMCs. *In vitro*, ATX mitigated VSMC proliferation and migration, decreased the level of cellular ROS, and balanced the activities of ROS-related enzymes including NADPH oxidase, xanthine oxidase, and superoxide dismutase (SOD). Besides, ATX mitigated Ca²⁺ overload, the overproduction of mitochondrial ROS (mtROS), mitochondrial dysfunction, mitochondrial fission, and Drp1 phosphorylation at Ser616. In addition, ATX enhanced mitophagy and mitochondrial biosynthesis by increasing the expression of PINK, parkin, mtDNA, mitochondrial transcription factor A (Tfam), and PGC-1 α . The present study indicated that ATX could efficiently treat vascular remodeling through restraining VSMC proliferation and restoring mitochondrial function. Inhibiting mitochondrial fission by decreasing the phosphorylation of Drp1 and stimulating mitochondrial autophagy and biosynthesis via increasing the expression of PINK, parkin, Tfam, and PGC-1 α may be part of its underlying mechanisms.

ASTAXANTHIN SHOWS CARDIOVASCULAR BENEFITS IN RATS BY POSITIVELY AFFECTING ALL BIOMEDICAL AND MOLECULAR PARAMETERS TESTED IN RATS WITH MYOCARDIAL INFARCTION.

Eur Rev Med Pharmacol Sci. 2021 Jun;25(11):4099-4105.

doi: 10.26355/eurrev_202106_26052.

The cardioprotective effect of astaxanthin against isoprenaline-induced myocardial injury in rats: involvement of TLR4/NF- κ B signaling pathway

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- PMID: 34156689 DOI: [10.26355/eurrev_202106_26052](https://doi.org/10.26355/eurrev_202106_26052)

Abstract

Objective: Cardiovascular diseases (CVDs) are a major cause of morbidity and mortality around the world. Nuclear transcription factor kappa B (NF- κ B) represents a factor that plays a major role in the pathogenesis of CVDs. The current study aims to investigate the modulatory effects of astaxanthin and its molecular mechanisms in rats with isoprenaline-induced myocardial infarction.

Materials and methods: Rats were pretreated with astaxanthin daily for 14 days prior to inducing myocardial infarction with isoprenaline in the final two days. Blood and heart tissue samples were collected 24 hours after the last dose of isoprenaline was injected for biochemical and histological analysis.

Results: Isoprenaline-induced myocardial injury was demonstrated with histopathological examination of heart tissue and the significantly elevated serum troponin-I. Isoprenaline caused an increase in oxidative stress and a decrease in antioxidants. Toll-like receptor-4 (TLR4), NF- κ B and tumor necrosis factor- α (TNF- α) expression levels were significantly higher in infarcted rats. Astaxanthin pretreatment had a significant preventive effect on all of the biochemical and molecular parameters tested in myocardial infarcted rats.

Conclusions: Astaxanthin's cardioprotective effect has been linked to the inhibition of the TLR4/NF- κ B signaling pathway. This inhibits the release of inflammatory cytokines, which can cause myocardial cell death. Because of its antioxidant and anti-inflammatory properties, astaxanthin is a promising cardioprotective agent.

Astaxanthin demonstrates potential against obesity and metabolic syndrome through results of trial on obese mice fed a high-fat diet.

[Biosci Biotechnol Biochem.](#) 2007 Apr;71(4):893-9. Epub 2007 Apr 7.

Effects of astaxanthin in obese mice fed a high-fat diet.

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Astaxanthin is a natural antioxidant carotenoid that occurs in a wide variety of living organisms. We investigated the effects of astaxanthin supplementation in obese mice fed a high-fat diet. Astaxanthin inhibited the increases in body weight and weight of adipose tissue that result from feeding a high-fat diet. In addition, astaxanthin reduced liver weight, liver triglyceride, plasma triglyceride, and total cholesterol. These results suggest that astaxanthin might be of value in reducing the likelihood of obesity and metabolic syndrome in affluent societies.

Astaxanthin with flaxseed oil reduces risk of atherosclerosis in rats fed a high fat diet.

[Lipids Health Dis.](#) 2014 Apr 4;13:63. doi: 10.1186/1476-511X-13-63.

A combination of flaxseed oil and astaxanthin alleviates atherosclerosis risk factors in high fat diet fed rats.

[Xu J](#), [Gao H](#), [Zhang L](#), [Chen C](#), [Yang W](#), [Deng Q](#), [Huang Q](#), [Huang F](#)¹.

Author information

Abstract

BACKGROUND:

Atherosclerosis is the most common pathologic process underlying cardiovascular disease. Both flaxseed oil (FO) and astaxanthin(ASX) are believed to benefit cardiovascular system. The combined effect of FO and ASX on the atherosclerosis risk factors in rats fed a high-fat diet was investigated.

METHODS:

Astaxanthin was dissolved in flaxseed oil to a final concentration of 1g/kg (FO + ASX). Male Sprague-Dawley rats were fed a rodent diet contained 20% fat whose source was lard (HFD) or 75% lard and 25% FO + ASX (50 mg ASX/kg diet) or 50% lard and 50% FO + ASX (100 mg ASX/kg diet) or FO + ASX (200 mg ASX/kg diet) for 10 weeks.

RESULTS:

The combination of FO and ASX significantly increased the antioxidant defense capacity and decreased lipid peroxidation in plasma. Evident decreases in the levels TG, TC and LDL-C contents, as well as IL-6 and CRP were also observed in plasma of FO and ASX fed rats.

CONCLUSION:

The combination of FO and ASX can improve oxidative stress, lipid abnormalities and inflammation, providing evidence that the combination of FO and ASX could be a promising functional food in cardiovascular health promotion.

PMID:

24708887

[PubMed - indexed for MEDLINE]

PMCID:

PMC3994197

[Free PMC Article](#)

Astaxanthin lowers blood pressure in rats.

JOURNAL OF FUNCTIONAL FOODS 1 (2009) 13–22

Astaxanthin lowers blood pressure and lessens the activity of the renin-angiotensin system in Zucker Fatty Rats

Harry G. Preussa,* , Bobby Echarda, Debasis Bagchib, Nicholas V. Perriconec, Eiji Yamashita

The ability of astaxanthin to favorably influence the renin-angiotensin system (RAS), blood pressure (BP), and metabolic parameters in Zucker Fatty Rats (ZFR) was examined. In separate experiments, 96 ZFR were equally divided into four groups: control, captopril (30 mg/kg), low astaxanthin (5 mg/kg) and high astaxanthin (25 mg/kg). RAS and insulin systems were examined following recovery from heat stress. RAS was lower in test groups; however, there was no evidence of enhanced insulin sensitivity. Test groups decreased SBP (systolic blood pressure) significantly compared to the control. The tests carried out suggested that RAS was involved in the ability of astaxanthin to lower BP. Astaxanthin at high dosage influenced circulating TNF- α and MCP-1 and lessened fat oxidation in liver and kidneys. Thus, astaxanthin may be considered as a good stress reducer with regards to heat stress. Astaxanthin's effects on RAS indicate it might overcome perturbations associated with increased activity, especially those related to the cardiovascular system.

Astaxanthin shows various cardioprotective properties in rats such as inhibition of stroke; anti-hypertensive; and inhibition of vascular contraction.

J of the Pharmaceutical Society of Japan VOL.126;NO.Suppl.3;PAGE.16-19(2006)

**PREVENTION BY ASTAXANTHIN OF LIFE STYLE DISEASES:
EXPERIMENTAL EVIDENCES**

[WATANABE HIROSHI](#); [HUSSEIN GHAZI](#); [GOTO HIROZO](#); [NAKAGAWA TAKAKO](#); [MATSUMOTO KINZO](#); [SANKAWA USHIO](#)

Astaxanthin (ASX), a red-orange carotenoid pigment, is a powerful antioxidant that occurs naturally in a wide variety of living organisms. We investigated the effect of ASX on the incidence of stroke, hypertension, and hyperglycemia in rats. Repeated ASX (50 mg/kg/day, p.o.) inhibited the incidence of stroke in SHR-stroke prone (SP). Pretreatment with 50 mg/kg/day of ASX for a week produced anti-hypertensive effect in awaked SHR. In the isolated aorta, ASX inhibited the vascular contraction induced by PGF₂.ALPHA.. Pretreatment with L-NAME (10⁻⁴M) ameliorated the inhibitory effect of ASX. ASX produced a significant reduction in the elastin bands and diminished the wall thickness in the SHR aorta. Fifty mg/kg of ASX for 18 weeks caused a significant decrease in the blood glucose in SHR/ND mcr-cp (cp/cp). ASX (50 mg/kg) produced a tendency to improve the learning behavior deficit induced by the brain ischemia in mice. These results suggest that ASX may exert beneficial effects for the protection against lifestyle related diseases.

Astaxanthin reduces blood pressure and improves cardiovascular parameters in rats with high blood pressure.

[Future Cardiol.](#) 2009 Jul;5(4):333-42.

Astaxanthin, oxidative stress, inflammation and cardiovascular disease.

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Abstract

It is accepted that oxidative stress and inflammation play an integral role in the pathophysiology of many chronic diseases including atherosclerotic cardiovascular disease. The xanthophyll carotenoid dietary supplement astaxanthin has demonstrated potential as an antioxidant and anti-inflammatory therapeutic agent in models of cardiovascular disease. There have been at least eight clinical studies conducted in over 180 humans using astaxanthin to assess its safety, bioavailability and clinical aspects relevant to oxidative stress, inflammation or the cardiovascular system. There have been no adverse outcomes reported. Studies have demonstrated reduced markers of oxidative stress and inflammation and improved blood rheology. A larger number of experimental studies have been performed using astaxanthin. In particular, studies in a variety of animals using a model of myocardial ischemia and reperfusion have demonstrated protective effects from prior administration of astaxanthin both intravenously and orally. Future clinical studies and trials will help determine the efficacy of antioxidants such as astaxanthin on vascular structure, function, oxidative stress and inflammation in a variety of patients at risk of, or with, established cardiovascular disease. These may lead to large intervention trials assessing cardiovascular morbidity and mortality.

PMID: 19656058 [PubMed - indexed for MEDLINE]

Astaxanthin more effective than other carotenoids at preserving membrane structure and antioxidant activity during lipid peroxidation.

[Am J Cardiol.](#) 2008 May 22;101(10A):20D-29D.

Biologic activity of carotenoids related to distinct membrane physicochemical interactions.

[McNulty H](#), [Jacob RE](#), [Mason RP](#).

Elucida Research, Beverly, MA 01915, USA.

Carotenoids are naturally occurring organic pigments that are believed to have therapeutic benefit in treating cardiovascular disease (CVD) because of their antioxidant properties. However, prospective randomized trials have failed to demonstrate a consistent benefit for the carotenoid beta-carotene in patients at risk for CVD. The basis for this apparent paradox is not well understood but may be attributed to the distinct antioxidant properties of various carotenoids resulting from their structure-dependent physicochemical interactions with biologic membranes. To test this hypothesis, we measured the effects of astaxanthin, zeaxanthin, lutein, beta-carotene, and lycopene on lipid peroxidation using model membranes enriched with polyunsaturated fatty acids. The correlative effects of these compounds on membrane structure were determined using small-angle x-ray diffraction approaches. The nonpolar carotenoids, lycopene and beta-carotene, disordered the membrane bilayer and stimulated membrane lipid peroxidation (>85% increase in lipid hydroperoxide levels), whereas astaxanthin (a polar carotenoid) preserved membrane structure and exhibited significant antioxidant activity (>40% decrease in lipid hydroperoxide levels). These results suggest that the antioxidant potential of carotenoids is dependent on their distinct membrane lipid interactions. This relation of structure and function may explain the differences in biologic activity reported for various carotenoids, with important therapeutic implications.

Publication Types:

PMID: 18474269 [PubMed - indexed for MEDLINE]

Astaxanthin prevents protein oxidation and prevents other changes that may be helpful in cardiovascular diseases.

[AcJ Clin Biochem Nutr.](#) 2012 Jul;51(1):42-9. doi: 10.3164/jcbn.11-74. Epub 2012 Jun 8.

Astaxanthin prevents changes in the activities of thioredoxin reductase and paraoxonase in hypercholesterolemic rabbits.

[Augusti PR¹](#), [Quatrin A](#), [Somacal S](#), [Conterato GM](#), [Sobieski R](#), [Ruviaro AR](#), [Maurer LH](#), [Duarte MM](#), [Roehrs M](#), [Emanuelli T](#).

Author information

Abstract

This study explored the effects of the antioxidant astaxanthin on paraoxonase and thioredoxin reductase activities as well as on other oxidative stress parameters and on the lipid profile in hypercholesterolemic rabbits. Rabbits were fed a standard or a hypercholesterolemic diet alone or supplemented with 50, 100 and 500 mg/100 g of astaxanthin for 60 days. Antioxidant enzymes activities, lipid profile and oxidative stress markers were evaluated in the serum. The hypercholesterolemic diet increased lipids, including unsaturated fatty acids level, whereas it decreased saturated fatty acids level. These changes were accompanied by increased levels of oxidized low-density lipoprotein and oxidized low-density lipoprotein antibodies, as well as lipid and protein oxidation. Astaxanthin (100 and 500 mg/100 g) prevented hypercholesterolemia-induced protein oxidation, whereas 500 mg/100 g of astaxanthin decreased protein oxidation per se. The activities of superoxide dismutase and thioredoxin reductase were enhanced, whereas paraoxonase activity was inhibited in hypercholesterolemic rabbits. All astaxanthin doses prevented changes in thioredoxin reductase and paraoxonase activities. This effect was not related to a direct effect of astaxanthin on these enzymes, because in vitro astaxanthin enhanced thioredoxin reductase and had no effect on paraoxonase activity. Astaxanthin could be helpful in cardiovascular diseases by restoring thioredoxin reductase and paraoxonase activities.

KEYWORDS:

atherosclerosis; fatty acids; oxidative stress

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22798712

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PMC3391862

[Free PMC Article](#)

Astaxanthin may have positive benefits in the formation of new blood vessels in rat study.

[ta Physiol \(Oxf\)](#). 2013 Feb;207(2):405-15. doi: 10.1111/apha.12018. Epub 2012 Oct 22.

Protective effects of astaxanthin on capillary regression in atrophied soleus muscle of rats.

[Kanazashi M¹](#), [Okumura Y](#), [Al-Nassan S](#), [Murakami S](#), [Kondo H](#), [Nagatomo F](#), [Fujita N](#), [Ishihara A](#), [Roy RR](#), [Fujino H](#).

Author information

Abstract

AIM:

The capillary regression in skeletal muscles associated with a chronic decrease in activity is related to a dysfunction of endocapillary cells induced by over-expression of oxidative stress. We hypothesized that treatment with astaxanthin, an antioxidant, would attenuate the oxidative stress induced by decreased skeletal muscle use, and that this attenuation would prevent the associated capillary regression. The purpose of the present study was to investigate the antioxidant and preventive effects of astaxanthin on capillary regression in the soleus muscle during hindlimb unloading.

METHODS:

Twenty-four adult male Wistar rats were assigned randomly either to a control, control plus astaxanthin treatment, hindlimb unloaded or hindlimb unloaded plus astaxanthin treatment group for 7 days.

RESULTS:

Hindlimb unloading resulted in a decrease in mean soleus absolute weight, capillary number, volume and luminal diameter. The accumulation of reactive oxygen species and the over-expression of superoxide dismutase (SOD-1), a decrease in the levels of vascular endothelial growth factor (VEGF) and its receptors, an inhibition of the angiotensin pathway and an increase of thrombospondin-1 (TSP-1), as an anti-angiogenic factor were showed. Administration of astaxanthin attenuated the changes in SOD-1 and VEGF, up-regulated the angiogenic factors and reduced the capillary regression in the soleus of hindlimb unloaded rats. In addition, the VEGF-to-TSP1 ratio was higher in the astaxanthin treated groups than in the control and HU groups.

CONCLUSION:

These results suggest that astaxanthin may be an effective treatment to counter the detrimental effects of a chronic decrease in skeletal muscle use on the capillary network and associated angiogenic pathways.

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PMID:

23088455

[PubMed - indexed for MEDLINE]

Astaxanthin provides protection from stroke in mouse model.

[Thromb Res.](#) 2010 Oct;126(4):299-305. Epub 2010 Aug 21.

Novel astaxanthin prodrug (CDX-085) attenuates thrombosis in a mouse model.

[Khan SK](#), [Malinski T](#), [Mason RP](#), [Kubant R](#), [Jacob RF](#), [Fujioka K](#), [Denstaedt SJ](#), [King TJ](#), [Jackson HL](#), [Hieber AD](#), [Lockwood SF](#), [Goodin TH](#), [Pashkow FJ](#), [Bodary PF](#).

School of Kinesiology, University of Michigan, Ann Arbor, MI, USA.

Abstract

BACKGROUND: Cardiovascular disease remains the leading cause of morbidity and premature mortality in most industrialized countries as well as in developing nations. A pro-oxidative state appears to promote and/or exacerbate vascular disease complications. Furthermore, a state of low-grade chronic inflammation can promote increased oxidative stress and lead to endothelial cell and platelet dysfunction ultimately contributing to thrombogenesis.

OBJECTIVES: In this study, the effect of a proprietary astaxanthin prodrug (CDX-085) on thrombus formation was investigated using a mouse model of arterial thrombosis. The influence of free astaxanthin, the active drug of CDX-085, on human endothelial cells and rat platelets was evaluated to investigate potential mechanisms of action.

METHODS AND RESULTS: Oral administration of CDX-085 (0.4% in chow, approximately 500 mg/kg/day) to 6-8 week old C57BL/6 male mice for 14 days resulted in significant levels of free astaxanthin in the plasma, liver, heart and platelets. When compared to control mice, the CDX-085 fed group exhibited significant increases in basal arterial blood flow and significant delays in occlusive thrombus formation following the onset of vascular endothelial injury. Primary human umbilical vein endothelial cells (HUVECs) and platelets isolated from Wistar-Kyoto rats treated with free astaxanthin demonstrated significantly increased levels of released nitric oxide (NO) and significantly decreased peroxynitrite (ONOO-) levels.

CONCLUSION: Observations of increased NO and decreased ONOO- levels in endothelial cells and platelets support a potential mechanism of action for astaxanthin (CDX-085 active drug). These studies support the potential of CDX-085 and its metabolite astaxanthin in the treatment or prevention of thrombotic cardiovascular complications.

PMID: 20728920 [PubMed - in process]

Astaxanthin decreases inflammation in mouse model and may be suitable for cardioprotection.

[Anticancer Res.](#) 2010 Jul;30(7):2721-5.

Effect of astaxanthin supplementation on inflammation and cardiac function in BALB/c mice.

[Nakao R](#), [Nelson OL](#), [Park JS](#), [Mathison BD](#), [Thompson PA](#), [Chew BP](#).

School of Food Science, Washington State University, Pullman, WA 99164, USA.

Abstract

Astaxanthin is an antioxidant with immunomodulatory, anti-inflammatory and anticancer properties. This study evaluated the use of dietary astaxanthin to decrease oxidative stress and improve cardiac function, thereby providing a potential cardioprotective supplement. Female BALB/c mice (8 weeks of age) were fed a semi-synthetic diet containing 0, 0.02 or 0.08% astaxanthin for 8 weeks. Cardiac function was assessed by echocardiography bi-weekly, and blood and tissue samples were collected at 8 weeks. Plasma astaxanthin concentrations increased ($p < 0.05$) dose-dependently to 0.5 and 4 $\mu\text{mol/l}$ in the astaxanthin-supplemented mice. Blood glutathione concentrations and lymphocyte mitochondrial membrane potential were not significantly affected by astaxanthin treatment. However, mice fed 0.08% astaxanthin had higher ($p < 0.05$) heart mitochondrial membrane potential and contractility index compared to the control group. These results support the possible use of dietary astaxanthin for cardiac protection.

PMID: 20683004 [PubMed - indexed for MEDLINE]

Astaxanthin improves blood lipid profiles in atherosclerotic rats.

[Pharmacognosy Res.](#) 2017 Apr-Jun;9(2):161-167. doi: 10.4103/0974-8490.204654.

Evaluation of Antioxidant, Hypolipidemic, and Antiatherogenic Property of Lycopene and Astaxanthin in Atherosclerosis-induced Rats.

[Kumar R](#)¹, [Salwe KJ](#)², [Kumarappan M](#)².

Author information

Abstract

BACKGROUND: Atherosclerosis is one of the major causes of morbidity and mortality in the world. Antioxidants play a major role in prophylaxis and prevention of progression and complications of atherosclerosis.

OBJECTIVE: In this study, we are evaluating the antiatherosclerotic effect of two antioxidants such as astaxanthin and lycopene.

MATERIALS AND METHODS: After acclimatization, 24 male SD rats, 8-10 weeks old, 150 ± 10 g, maintained as per CPCSEA guidelines were divided into four groups of six rats each. Baseline values of weight lipid profile and 2-Thiobarbituric Acid Reactive Substances (TBARS) assay were taken. All the rats were fed with high cholesterol diet (HCD). HCD only, HCD + atorvastatin (50 mg/kg), HCD + lycopene (50 mg/kg), and HCD + astaxanthin (50 mg/kg) were given to control, standard, lycopene, and astaxanthin groups, respectively, through oral gavage for 45 days. The rats were sacrificed at the end of the study, blood sample collected from aorta, and then aorta was dissected for histopathology.

RESULTS: The lipid profile showed lycopene and astaxanthin decreased total cholesterol, low-density lipoprotein-cholesterol (LDL-C), very LDL-C, and triglycerides and increased high-density lipoprotein-cholesterol level significantly ($P < 0.05$) compared to the control but less than atorvastatin. The TBARS value of lycopene was significantly lower compared to HCD and atorvastatin groups, whereas astaxanthin was significantly less than HCD group only. The histopathology showed only Type I lesions, no naked fatty streaks, few foam cells in lycopene, and astaxanthin groups compared to control where we observed Type II and III lesions, visible fatty streaks and many foam cells with intimal thickening in HCD group.

CONCLUSION: In this study, lycopene and astaxanthin showed antioxidant, antihyperlipidemic, and antiatherosclerotic property. This warrants further study for including them in the treatment of atherosclerosis.

SUMMARY: Antioxidants play a major role in prophylaxis and prevention of progression and complications of atherosclerosis. Lycopene and Astaxanthin are suitable candidates for further

research in cardiovascular disease and there is paucity of studies evaluating their role in prevention of atherosclerosis. The effect of lycopene and Astaxanthin for anti-atherosclerotic property was evaluated in high cholesterol diet fed rats. The lipid profile showed lycopene and Astaxanthin decreased TC, LDL-C, VLDL-C and triglycerides and increased HDL-C level significantly ($P < 0.05$) compared to the control but less than atorvastatin. The TBARS value of Lycopene was significantly lower compared to HCD and atorvastatin groups while Astaxanthin was significantly less than HCD group only. The histopathology showed only type I lesions, no naked fatty streaks, few foam cells in lycopene and Astaxanthin groups compared to control. The study proves Lycopene and Astaxanthin have hypolipidemic and anti-atherogenic potential can be included in the treatment of hypercholesterolemia and atherosclerosis. **Abbreviations Used:** TC: total cholesterol, HDL-C: high density lipoprotein cholesterol, LDL-C: low density lipoprotein cholesterol, VLDL-C: very Low density lipoprotein cholesterol, TG: triglycerides, and TBARS: thiobarbituric acid reactive substances, HCD: high cholesterol diet.

KEYWORDS: Antioxidant; astaxanthin; atherosclerosis; hypercholesterolemia; lycopene

PMID: 28539740

PMCID: [PMC5424557](#)

DOI: [10.4103/0974-8490.204654](#)

[Free PMC Article](#)

Astaxanthin improves blood fluidity in hyperlipidemic rats.

[Pharm Biol.](#) 2017 Dec;55(1):663-672.

Effects of astaxanthin on blood coagulation, fibrinolysis and platelet aggregation in hyperlipidemic rats.

[Deng ZY](#)^{1,2}, [Shan WG](#)¹, [Wang SF](#)¹, [Hu MM](#)¹, [Chen Y](#)¹.

Author information

Abstract

CONTEXT: Astaxanthin (ASTX) is a xanthophyll carotenoid that reduces hemostasis in hyperlipidemic organisms. Its antihemostatic mechanisms remain unclear.

OBJECTIVE: The effects of ASTX on coagulation, the fibrinolytic system and platelet aggregation were investigated in hyperlipidemic rats.

MATERIALS AND METHODS: Different doses of ASTX (5, 10 and 30 mg/kg/day, p.o.) were administered for four weeks to high-fat diet-induced hyperlipidemic rats. Serum lipid and lipoprotein levels were measured with an automatic biochemical analyzer. The prothrombin time (PT), activated partial thromboplastin time (APTT) and maximum platelet aggregation rate (MAR) were determined by a coagulation analyzer. The activities of the tissue-type plasminogen activator (t-PA), type-1 plasminogen activator inhibitor (PAI-1) and endothelial nitric oxide synthase (eNOS), as well as the levels of thromboxane B(2) [TXB(2)], 6-keto prostaglandin F(1 α) [6-keto-PGF(1 α)] and platelet granule membrane protein (GMP-140), were measured with enzyme-linked immunosorbent assay kits. Gene and protein expression levels were analyzed by reverse transcriptase polymerase chain reaction and Western blot, respectively.

RESULTS: ASTX (30 mg/kg) treatment in hyperlipidemic rats reduced serum TG (0.58 ± 0.14 versus 1.12 ± 0.24 mmol/L), serum TC (1.77 ± 0.22 versus 2.24 ± 0.21 mmol/L), serum LDL-C (1.13 ± 0.32 versus 2.04 ± 0.48 mmol/L), serum MDA (69%), plasma MAR (55%), serum TXB2/6-keto-PGF1 α (34%) and serum GMP-140 levels (25%), plasma PAI-1 activity (48%) and downregulated the mRNA (33%) and protein (23%) expression of aorta eNOS, the mRNA (79%) and protein (72%) expression levels of aorta PAI-1. However, ASTX (30 mg/kg/d) treatment increased serum SOD activity (2.1 fold), serum GPx activity (1.8 fold), plasma PT (1.3 fold), plasma APTT (1.7 fold), serum NO (1.4-fold), serum 6-keto-PGF1 α (1.3 fold).

CONCLUSIONS: ASTX reduced blood coagulation and platelet aggregation and promoted fibrinolytic activity in hyperlipidemic rats. These activities were closely correlated with ASTX, maintaining the balance of t-PA/PAI-1, NO/ROS and TXA2/PGI2 in vivo.

KEYWORDS: Carotenoid; NO/ROS balance; TXA2/PGI2 balance; antioxidant activity; t-PA/PAI-1 balance

PMID: 27951728 PMCID: [PMC6130668](#) DOI: [10.1080/13880209.2016.1261905](#) [Indexed for MEDLINE]

Free PMC Article

Astaxanthin prevents oxidative stress in heart and kidneys of aged rats after inducement of heart attack.

[J Diet Suppl.](#) 2018 Jan 2;15(1):42-54. doi: 10.1080/19390211.2017.1321078. Epub 2017 May 10.

Astaxanthin Prevented Oxidative Stress in Heart and Kidneys of Isoproterenol-Administered Aged Rats.

[Alam MN¹](#), [Hossain MM¹](#), [Rahman MM¹](#), [Subhan N¹](#), [Mamun MAA¹](#), [Ulla A¹](#), [Reza HM¹](#), [Alam MA¹](#).

Author information

Abstract

The objective of this study was to investigate the effect of astaxanthin on isoproterenol (ISO)-induced myocardial infarction and cardiac hypertrophy in rats. To evaluate the effect of astaxanthin on ISO-induced cardiac dysfunction, 18 aged Long Evans male rats were evenly divided into three groups. Group I (Control group) was given only the laboratory-ground food and normal water. Group II (ISO group) was administered ISO at a dose of 50 mg/kg subcutaneously (SC) twice a week for two weeks. Group III (Astaxanthin + ISO group) was treated with astaxanthin (25 mg/kg) orally every day and ISO 50 mg/kg SC twice a week for two weeks. ISO administration in rats increased the heart and left ventricular wet weights and increased inflammatory cell infiltration and fibrosis. Moreover, ISO administration increased the lipid peroxidation and decreased antioxidant enzyme activities in heart tissues. Astaxanthin treatment prevented the increased wet weight of heart and decreased inflammatory cell infiltration and fibrosis. The protective effect of astaxanthin was associated with reduction of free radicals by improving antioxidant enzyme function, as well as normalization and/or suppression of elevated oxidative stress markers, such as malondialdehyde (MDA), nitric oxide (NO), and advanced protein oxidation product (APOP) in ISO-administered rats. Furthermore, astaxanthin decreased the elevated activities of aspartate transaminase (AST), alanine transaminase (ALT), and creatinin kinase muscle/brain (CK-MB) in ISO-administered rats. In conclusion, astaxanthin may protect cardiac tissues in ISO-administered rats through suppression of oxidative stress and enhancement of antioxidant enzyme functions.

KEYWORDS:

antioxidant enzymes; astaxanthin; free radicals; heart, fibrosis; oxidative stress

PMID: 28489954 DOI: [10.1080/19390211.2017.1321078](https://doi.org/10.1080/19390211.2017.1321078)

[Indexed for MEDLINE]

Astaxanthin shows potential to improve cardiac function in-vitro and in rodent trial.

[Biochim Biophys Acta Gen Subj](#). 2017 Jul;1861(7):1715-1728. doi: 10.1016/j.bbagen.2017.03.007. Epub 2017 Mar 12.

Astaxanthin attenuated pressure overload-induced cardiac dysfunction and myocardial fibrosis: Partially by activating SIRT1.

[Zhang J¹](#), [Wang QZ¹](#), [Zhao SH²](#), [Ji X¹](#), [Qiu J¹](#), [Wang J³](#), [Zhou Y⁴](#), [Cai Q³](#), [Zhang J⁵](#), [Gao HQ⁶](#).

Author information

Abstract

BACKGROUND: Myocardial fibrosis contributes to cardiac dysfunction. Astaxanthin (AST), a member of the carotenoid family, is a well-known antioxidant, but its effect on and underlying mechanisms in myocardial fibrosis are poorly understood.

METHODS: In vivo, myocardial fibrosis and cardiac dysfunction were induced using transverse aortic constriction (TAC). AST was administered to mice for 12weeks post-surgery. In vitro, transforming growth factor β 1 (TGF- β 1) was used to stimulate human cardiac fibroblasts (HCFs). EX-527 (6-chloro-2, 3, 4, 9-tetrahydro-1H-carbazole-1-carboxamide) and SIRT1 siRNA were used to inhibit SIRT1 in vivo and in vitro, respectively. The effects of AST on cardiac function and fibrosis were determined. SIRT1 expression and activity were measured to explore the mechanisms underlying its effects.

RESULTS: AST improved cardiac function and attenuated fibrosis. Receptor activated-SMADs (R-SMADs), including SMAD2 and SMAD3, played important roles in these processes. The TAC surgery-induced increases in the expression of phosphorylated and acetylated R-SMADs were attenuated by treatment with AST, the translocation and transcriptional activity of R-SMADs were also restrained. These effects were accompanied by an increase in the expression and activity of SIRT1. Inhibiting SIRT1 attenuated the acetylation and transcriptional activity of R-SMADs, but not their phosphorylation and translocation.

CONCLUSIONS: Our data demonstrate that AST improves cardiac function and attenuates fibrosis by decreasing phosphorylation and deacetylation of R-SMADs. SIRT1 contributes to AST's protective function by reducing acetylation of R-SMADs.

GENERAL SIGNIFICANCE: These data suggest that AST may be useful as a preventive/therapeutic agent for cardiac dysfunction and myocardial fibrosis.

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KEYWORDS: Astaxanthin; Cardiac function; Fibrosis; R-SMADs; SIRT1

PMID: 28300638 DOI: [10.1016/j.bbagen.2017.03.007](#) [Indexed for MEDLINE]

ASTAXANTHIN EXHIBITS CARDIOPROTECTIVE EFFECT AGAINST OXIDATIVE STRESS IN-VITRO.

Mol Med Rep. 2020 Dec;22(6):5125-5134.

doi: 10.3892/mmr.2020.11613. Epub 2020 Oct 19.

Attenuation of the Na/K-ATPase/Src/ROS amplification signaling pathway by astaxanthin ameliorates myocardial cell oxidative stress injury

[Xuefeng Qu¹](#), [Zhouyi Zhang¹](#), [Wenli Hu¹](#), [Minhan Lou¹](#), [Bingzhong Zhai¹](#), [Song Mei¹](#), [Zhihang Hu¹](#), [Lijing Zhang¹](#), [Dongying Liu¹](#), [Zhen Liu¹](#), [Jianguo Chen¹](#), [Yin Wang¹](#)

PMID: 33173978 PMCID: [PMC7646965](#) DOI: [10.3892/mmr.2020.11613](#) [Free PMC article](#)

Abstract

The 3S, 3'S-ASTaxanthin (3S, 3'S-AST) isomer has strong antioxidant activity; however, its protective roles and potential mechanisms against oxidative stress damage in cardiomyocytes have not been investigated. Na⁺/K⁺-ATPase (NKA)/Src signal activation has an important role in increasing reactive oxygen species (ROS) production. The aim of the present study was to investigate the protective effects and mechanism of 3S, 3'S-AST on hydrogen peroxide (H₂O₂)-induced oxidative stress injury in H9c2 myocardial cells. The protective effects of 3S, 3'S-AST on H₂O₂-induced H9c2 cell injury was observed by measuring lactate dehydrogenase and creatine kinase myocardial band content, cell viability and nuclear morphology. The antioxidant effect was investigated by analyzing ROS accumulation and malondialdehyde, glutathione (GSH) peroxidase, GSH and glutathione reductase activity levels. The protein expression levels of Bax, Bcl-2, caspase-3 and cleaved caspase-3 were analyzed using western blotting to determine cardiomyocyte apoptosis. Western blot analysis of the phosphorylation levels of Src and Erk1/2 were also performed to elucidate the molecular mechanism involved. The results showed that 3S, 3'S-AST reduced the release of LDH and promoted cell viability, and attenuated ROS accumulation and cell apoptosis induced by H₂O₂. Furthermore, 3S, 3'S-AST also restored apoptosis-related Bax and Bcl-2 protein expression levels in H₂O₂-treated H9c2 cells. The phosphorylation levels of Src and Erk1/2 were significantly higher in the H₂O₂ treatment group, whereas 3S, 3'S-AST pretreatment significantly decreased the levels of phosphorylated (p)-Src and p-ERK1/2. The results provided evidence that 3S, 3'S-AST exhibited a cardioprotective effect against oxidative stress injury by attenuating NKA/Src/Erk1/2-modulated ROS amplification.

ASTAXANTHIN MAY BE A CANDIDATE FOR TREATMENT OF VASCULAR CALCIFICATION BASED ON *IN-VITRO* RESULTS.

Int J Mol Sci. 2020 Nov 12;21(22):8530.

doi: 10.3390/ijms21228530.

Astaxanthin Counteracts Vascular Calcification In Vitro Through an Early Up-Regulation of SOD2 Based on a Transcriptomic Approach

[Chia-Ter Chao](#)^{1,2,3}, [Hsiang-Yuan Yeh](#)⁴, [You-Tien Tsai](#)³, [Tzu-Hang Yuan](#)⁵, [Min-Tser Liao](#)⁶, [Jenq-Wen Huang](#)⁷, [Huei-Wen Chen](#)³

PMID: 33198315 PMCID: [PMC7698184](#) DOI: [10.3390/ijms21228530](#) [Free PMC article](#)

Abstract

Vascular calcification (VC) is a critical contributor to the rising cardiovascular risk among at-risk populations such as those with diabetes or renal failure. The pathogenesis of VC involves an uprising of oxidative stress, for which antioxidants can be theoretically effective. However, astaxanthin, a potent antioxidant, has not been tested before for the purpose of managing VC. To answer this question, we tested the efficacy of astaxanthin against VC using the high phosphate (HP)-induced vascular smooth muscle cell (VSMC) calcification model. RNAs from treated groups underwent Affymetrix microarray screening, with intra-group consistency and inter-group differential expressions identified. Candidate hub genes were selected, followed by validation in experimental models and functional characterization. We showed that HP induced progressive calcification among treated VSMCs, while astaxanthin dose-responsively and time-dependently ameliorated calcification severities. Transcriptomic profiling revealed that 3491 genes exhibited significant early changes during VC progression, among which 26 potential hub genes were selected based on closeness ranking and biologic plausibility. SOD2 was validated in the VSMC model, shown to drive the deactivation of cellular senescence and enhance antioxidative defenses. Astaxanthin did not alter intracellular reactive oxygen species (ROS) levels without HP, but significantly lowered ROS production in HP-treated VSMCs. SOD2 knockdown prominently abolished the anti-calcification effect of astaxanthin on HP-treated VSMCs, lending support to our findings. In conclusion, we demonstrated for the first time that astaxanthin could be a potential candidate treatment for VC, through inducing the up-regulation of SOD2 early during calcification progression and potentially suppressing vascular senescence.

ASTAXANTHIN PROTECTS HEART MUSCLE CELLS IN-VITRO.

Eur Rev Med Pharmacol Sci. 2020 Jul;24(14):7722-7731.

doi: 10.26355/eurrev_202007_22276.

Astaxanthin protecting myocardial cells from hypoxia/reoxygenation injury by regulating miR-138/HIF-1 α axis

[Y-S Gai](#)¹, [Y-H Ren](#), [Y Gao](#), [H-N Liu](#)

PMID: 32744699 DOI: [10.26355/eurrev_202007_22276](https://doi.org/10.26355/eurrev_202007_22276) **Free article**

Abstract

Objective: To investigate astaxanthin (AST) protecting myocardial cells from hypoxia/reoxygenation (H/R) injury by regulating miR-138/HIF-1 α axis.

Materials and Methods: Myocardial cells were collected and divided into a control group, a H/R group, and a H/R+AST group. The H/R injury model was established, and cells in the H/R+AST group were given AST before modeling. The cell survival rate, contents of myocardial enzymes, and apoptosis were detected.

Results: The survival rate in the H/R group reduced and was lower than that in the H/R+AST group ($p < 0.05$). Compared with the control group, activities of myocardial enzymes significantly increased in the H/R group but those were inhibited in the H/R+AST group ($p < 0.05$). The apoptotic rate in the H/R group significantly increased compared with the control group but that significantly decreased compared with the H/R+AST group ($p < 0.05$). The expression of cleaved caspase-9 and caspase-3 increased in the H/R group ($p < 0.05$), and was higher than that in the H/R+AST group ($p < 0.05$). The expression levels of miR-138 and HIF-1 α were detected. MiR-138 level significantly decreased in the H/R group but increased in the H/R+AST group ($p < 0.05$). Compared with the control group, HIF-1 α content significantly increased in the H/R group but that was significantly inhibited in the H/R+AST group ($p < 0.05$). The Luciferase reporter gene assay confirmed that HIF-1 α was the target gene of miR-138. After miR-138 mimics and HIF-1 α siRNA were transfected into myocardial cells, the cell survival rate significantly increased, and activities of myocardial enzymes were significantly inhibited in the H/R+AST+miR-138 mimics and H/R+AST+HIF-1 α siRNA groups ($p < 0.05$). The apoptotic rate significantly decreased, and contents of cleaved caspase-9 and caspase-3 were significantly inhibited in the miR-138 mimics and HIF-1 α siRNA groups ($p < 0.05$).

Conclusions: AST can exert a protective function in myocardial cells via regulating the expression of miR-138/HIF-1 α axis.

ASTAXANTHIN PROTECTS HEART MUSCLE CELLS IN-VITRO.

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[Y-S Gai](#)¹, [Y-H Ren](#), [Y Gao](#), [H-N Liu](#)

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Materials and Methods: Myocardial cells were collected and divided into a control group, a H/R group, and a H/R+AST group. The H/R injury model was established, and cells in the H/R+AST group were given AST before modeling. The cell survival rate, contents of myocardial enzymes, and apoptosis were detected.

Results: The survival rate in the H/R group reduced and was lower than that in the H/R+AST group ($p < 0.05$). Compared with the control group, activities of myocardial enzymes significantly increased in the H/R group but those were inhibited in the H/R+AST group ($p < 0.05$). The apoptotic rate in the H/R group significantly increased compared with the control group but that significantly decreased compared with the H/R+AST group ($p < 0.05$). The expression of cleaved caspase-9 and caspase-3 increased in the H/R group ($p < 0.05$), and was higher than that in the H/R+AST group ($p < 0.05$). The expression levels of miR-138 and HIF-1 α were detected. MiR-138 level significantly decreased in the H/R group but increased in the H/R+AST group ($p < 0.05$). Compared with the control group, HIF-1 α content significantly increased in the H/R group but that was significantly inhibited in the H/R+AST group ($p < 0.05$). The Luciferase reporter gene assay confirmed that HIF-1 α was the target gene of miR-138. After miR-138 mimics and HIF-1 α siRNA were transfected into myocardial cells, the cell survival rate significantly increased, and activities of myocardial enzymes were significantly inhibited in the H/R+AST+miR-138 mimics and H/R+AST+HIF-1 α siRNA groups ($p < 0.05$). The apoptotic rate significantly decreased, and contents of cleaved caspase-9 and caspase-3 were significantly inhibited in the miR-138 mimics and HIF-1 α siRNA groups ($p < 0.05$).

Conclusions: AST can exert a protective function in myocardial cells via regulating the expression of miR-138/HIF-1 α axis.

Astaxanthin administered in a hydrogel patch shows promise in preventing damage from heart attack.

[Biomed Mater.](#) 2017 Dec 28;13(1):015020. doi: 10.1088/1748-605X/aa8a86.

PVA/Dextran hydrogel patches as delivery system of antioxidant astaxanthin: a cardiovascular approach.

[Zuluaga M¹](#), [Gregnanin G](#), [Cencetti C](#), [Di Meo C](#), [Gueguen V](#), [Letourneur D](#), [Meddahi-Pellé A](#), [Pavon-Djavid G](#), [Matricardi P](#).

Author information

Abstract

After myocardial infarction, the heart's mechanical properties and its intrinsic capability to recover are compromised. To improve this recovery, several groups have developed cardiac patches based on different biomaterials strategies. Here, we developed polyvinylalcohol/dextran (PVA/Dex) elastic hydrogel patches, obtained through the freeze thawing (FT) process, with the aim to deliver locally a potent natural antioxidant molecule, astaxanthin, and to assist the heart's response against the generated myofibril stress. Extensive rheological and dynamo-mechanical characterization of the effect of the PVA molecular weight, number of freeze-thawing cycles and Dex addition on the mechanical properties of the resulting hydrogels, were carried out. Hydrogel systems based on PVA 145 kDa and PVA 47 kDa blended with Dex 40 kDa, were chosen as the most promising candidates for this application. In order to improve astaxanthin solubility, an inclusion system using hydroxypropyl- β -cyclodextrin was prepared. This system was posteriorly loaded within the PVA/Dex hydrogels. PVA145/Dex 1FT and PVA47/Dex 3FT showed the best rheological and mechanical properties when compared to the other studied systems; environmental scanning electron microscope and confocal imaging evidenced a porous structure of the hydrogels allowing astaxanthin release. In vitro cellular behavior was analyzed after 24 h of contact with astaxanthin-loaded hydrogels. In vivo subcutaneous biocompatibility was performed in rats using PVA145/Dex 1FT, as the best compromise between mechanical support and astaxanthin delivery. Finally, ex vivo and in vivo experiments showed good mechanical and compatibility properties of this hydrogel. The obtained results showed that the studied materials have a potential to be used as myocardial patches to assist infarcted heart mechanical function and to reduce oxidative stress by the in situ release of astaxanthin.

PMID: 28875946

DOI: [10.1088/1748-605X/aa8a86](https://doi.org/10.1088/1748-605X/aa8a86)

Astaxanthin protects against high blood pressure during pregnancy by reducing inflammation and oxidative stress in rats.

[Mol Med Rep.](#) 2016 Sep;14(3):2697-704. doi: 10.3892/mmr.2016.5569. Epub 2016 Jul 28.

Astaxanthin blocks preeclampsia progression by suppressing oxidative stress and inflammation.

[Xuan RR¹](#), [Niu TT²](#), [Chen HM²](#).

Author information

Abstract

To investigate the antioxidative effect of astaxanthin on Nw-nitro-L-arginine methyl ester (L-NAME)-induced preeclamptic rats. Cell survival, the level of reactive oxygen species (ROS) and the changes in mitochondrial membrane potential (MMP) were examined in astaxanthin and H₂O₂-treated human umbilical vein endothelial cells (HUVECs). The preeclamptic Sprague-Dawley (SD) rat model was established by injection of L-NAME and treatment with astaxanthin. The activities of malondialdehyde (MDA), superoxide dismutase (SOD) and nitric oxide synthase (NOS) in serum were analyzed. Pathological changes were examined by hematoxylin and eosin (H&E) staining. The expression of nuclear factor (NF)- κ B, Rho-associated protein kinase II (ROCK II), heme oxygenase-1 (HO-1) and caspase 3 in preeclamptic placentas were examined by immunohistochemistry. Astaxanthin significantly reduced H₂O₂-induced HUVEC cell death, decreased ROS and increased MMP. Astaxanthin significantly reduced blood pressure and the content of MDA, but significantly increased the activity of SOD in preeclamptic rats. The urinary protein and the level of NO and NOS were also decreased. H&E staining revealed that the thickness of the basilar membrane was increased, while the content of trophoblast cells and spiral arteries were reduced following astaxanthin treatment. Immunohistochemistry results showed that the expression of NF- κ B, ROCK II and caspase 3 in preeclamptic placentas was significantly decreased after astaxanthin treatment, while HO-1 expression was increased. In conclusion, astaxanthin inhibited H₂O₂-induced oxidative stress in HUVECs. Astaxanthin treatment significantly improved L-NAME-induced preeclamptic symptoms and reduced the oxidative stress and inflammatory damages in preeclamptic placentas. Astaxanthin treatment may effectively prevent and treat preeclampsia.

PMID: 27484589

DOI: [10.3892/mmr.2016.5569](https://doi.org/10.3892/mmr.2016.5569)

[Indexed for MEDLINE]

Astaxanthin reduces oxidative stress and lipid peroxidation in rabbits with atherosclerosis.

[J Cardiovasc Pharmacol Ther.](#) 2009 Dec;14(4):314-22. Epub 2009 Oct 21.

Astaxanthin reduces oxidative stress, but not aortic damage in atherosclerotic rabbits.

[Augusti PR](#), [Conterato GM](#), [Somacal S](#), [Sobieski R](#), [Quatrin A](#), [Maurer L](#), [Rocha MP](#), [Denardin IT](#), [Emanuelli T](#).

Department of Biochemistry, Institute of Health Basic Sciences, Federal University of Rio Grande do Sul, Porto Alegre, RS, Brazil.

Abstract

We evaluated whether carotenoid astaxanthin (ASX) could prevent oxidative and atherosclerotic damage in rabbits. Rabbits received regular chow (control) or an atherogenic diet (1% cholesterol) alone or supplemented with 50, 100, and 500 mg% ASX for 60 days (n = 5-9 per group). The atherogenic diet increased the serum cholesterol levels and the ratio of the intima/media area in the aortic arch. These changes were not prevented by ASX. Atherosclerotic rabbits showed increased aortic lipid peroxidation and nonprotein thiol group (NPSH) levels along with inhibition of glutathione peroxidase (GSH-Px). All ASX doses attenuated lipid peroxidation and the increase in NPSH but not the inhibition of GSH-Px. Aortic superoxide dismutase (SOD), catalase (CAT), and thioredoxin reductase (TrxR) activities were enhanced in atherosclerotic rabbits. Although all ASX doses prevented the increase in SOD activity, only 100 and 500 mg% ASX prevented the increase in CAT activity. Furthermore, these same doses partially prevented the increase in TrxR activity, while 50 mg% ASX completely prevented the effects of the atherogenic diet on this enzyme. However, ASX did not attenuate the hypercholesterolemia or the atherosclerotic lesions caused by the atherogenic diet at any of the doses evaluated. Our results indicate that although ASX did not prevent hypercholesterolemia or atherosclerotic lesions, it could play a beneficial role by preventing lipid peroxidation and changes in antioxidant enzyme activities.

PMID: 19846890 [PubMed - indexed for MEDLINE]

Astaxanthin induces the development of new blood vessels in rats.

[Phytomedicine](#). 2015 Jul 15;22(7-8):744-51. doi: 10.1016/j.phymed.2015.05.054. Epub 2015 Jun 3.

Astaxanthin induces angiogenesis through Wnt/ β -catenin signaling pathway.

[Xu Y¹](#), [Zhang J¹](#), [Jiang W²](#), [Zhang S³](#).

Author information

Abstract

OBJECTIVE: In the present study, we sought to elucidate whether astaxanthin contributes to induce angiogenesis and its mechanisms.

MATERIALS AND METHODS: To this end, we examined the role of astaxanthin on human brain microvascular endothelial cell line (HBMEC) and rat aortic smooth muscle cell (RASMC) proliferation, invasion and tube formation in vitro. For study of mechanism, the Wnt/ β -catenin signaling pathway inhibitor IWR-1-endo was used. HBMECs and RASMCs proliferation were tested by cell counting. Scratch adhesion test was used to assess the ability of invasion. A matrigel tube formation assay was performed to test capillary tube formation ability. The Wnt/ β -catenin pathway activation in HBMECs and RASMCs were tested by Western blot.

RESULTS: Our data suggested that astaxanthin induces angiogenesis by increasing proliferation, invasion and tube formation in vitro. Wnt and β -catenin expression were increased by astaxanthin and counteracted by IWR-1-endo in HBMECs and RASMCs. Tube formation was increased by astaxanthin and counteracted by IWR-1-endo.

CONCLUSIONS: It may be suggested that astaxanthin induces angiogenesis in vitro via a programmed Wnt/ β -catenin signaling pathway.

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KEYWORDS: Angiogenesis; Astaxanthin; HBMEC; RASMC; Wnt; β -catenin

PMID: 26141761

DOI: [10.1016/j.phymed.2015.05.054](https://doi.org/10.1016/j.phymed.2015.05.054)

[Indexed for MEDLINE]

The cardioprotective effect of astaxanthin against isoprenaline-induced myocardial injury in rats: involvement of TLR4/NF- κ B signaling pathway

[M A Zaafan](#)¹, [A M Abdelhamid](#)

- PMID: 34156689 DOI: [10.26355/eurrev_202106_26052](https://doi.org/10.26355/eurrev_202106_26052)

Abstract

Objective: Cardiovascular diseases (CVDs) are a major cause of morbidity and mortality around the world. Nuclear transcription factor kappa B (NF- κ B) represents a factor that plays a major role in the pathogenesis of CVDs. The current study aims to investigate the modulatory effects of astaxanthin and its molecular mechanisms in rats with isoprenaline-induced myocardial infarction.

Materials and methods: Rats were pretreated with astaxanthin daily for 14 days prior to inducing myocardial infarction with isoprenaline in the final two days. Blood and heart tissue samples were collected 24 hours after the last dose of isoprenaline was injected for biochemical and histological analysis.

Results: Isoprenaline-induced myocardial injury was demonstrated with histopathological examination of heart tissue and the significantly elevated serum troponin-I. Isoprenaline caused an increase in oxidative stress and a decrease in antioxidants. Toll-like receptor-4 (TLR4), NF- κ B and tumor necrosis factor- α (TNF- α) expression levels were significantly higher in infarcted rats. Astaxanthin pretreatment had a significant preventive effect on all of the biochemical and molecular parameters tested in myocardial infarcted rats.

Conclusions: Astaxanthin's cardioprotective effect has been linked to the inhibition of the TLR4/NF- κ B signaling pathway. This inhibits the release of inflammatory cytokines, which can cause myocardial cell death. Because of its antioxidant and anti-inflammatory properties, astaxanthin is a promising cardioprotective agent.

Astaxanthin provides intense protection from lipid infiltration of the aortic wall when combined with red yeast rice extract and policosanol.

[Arzneimittelforschung](#). 2005;55(6):312-7.

Antiatherosclerotic efficacy of policosanol, red yeast rice extract and astaxanthin in the rabbit.

[Setnikar I](#), [Senin P](#), [Rovati LC](#).

Rotta Research Laboratorium, Division of Rottapharm SPA, Monza, Italy.
ivo.setnikar@rotta.com

The effects of policosanol (P), of extract of red yeast rice (rice fermented with *Monascus purpureus*) (RYE) and of astaxanthin (A) (constituents of Armolipid) were investigated in a model of experimental atherosclerosis provoked in the rabbit by atherogenic cholesterol-enriched feed (ACEF). P and RYE and their combination were able to lower the increase of serum total cholesterol and of LDL cholesterol elicited by 3-month feeding with ACEF. They also were able to reduce the increase of blood malondialdehyde (MDA), a tracer of lipid peroxidation by the free radicals released by ACEF. When combined, the substances developed either additive or potentiated effects, supporting the rationale of their combination. Remarkable was the protective effect on lipid infiltration in the aortic wall provoked by ACEF, which was reduced by P and by RYE and almost completely prevented by the addition of A to the P-RYE combination. The results support the rationale of a combination of P, RYE and A as a useful food supplement in hyperlipemic patients.

PMID: 16032970 [PubMed - indexed for MEDLINE]

ASTAXANTHIN REVIEWED FOR ITS THERAPEUTIC MITOCHONDRIAL SUPPORT DURING HEART FAILURE.

Int J Mol Sci 2021 Jul 26;22(15):7964. doi: 10.3390/ijms22157964.

Mitochondrion as a Target of Astaxanthin Therapy in Heart Failure

[Olga Krestinina](#)[‡], [Yulia Baburina](#)[‡], [Roman Krestinin](#)[‡]

- PMID: 34360729 PMCID: [PMC8347622](#) DOI: [10.3390/ijms22157964](#)

Free PMC article

Abstract

Mitochondria are considered to be important organelles in the cell and play a key role in the physiological function of the heart, as well as in the pathogenesis and development of various heart diseases. Under certain pathological conditions, such as cardiovascular diseases, stroke, traumatic brain injury, neurodegenerative diseases, muscular dystrophy, etc., mitochondrial permeability transition pore (mPTP) is formed and opened, which can lead to dysfunction of mitochondria and subsequently to cell death. This review summarizes the results of studies carried out by our group of the effect of astaxanthin (AST) on the functional state of rat heart mitochondria upon direct addition of AST to isolated mitochondria and upon chronic administration of AST under conditions of mPTP opening. It was shown that AST exerted a protective effect under all conditions. In addition, AST treatment was found to prevent isoproterenol-induced oxidative damage to mitochondria and increase mitochondrial efficiency. AST, a ketocarotenoid, may be a potential mitochondrial target in therapy for pathological conditions associated with oxidative damage and mitochondrial dysfunction, and may be a potential mitochondrial target in therapy for pathological conditions.

Astaxanthin reviewed for its potential against high blood pressure.

[Integr Blood Press Control](#). 2008;1:1-3. Epub 2008 Oct 27.

Antihypertensive effects of astaxanthin.

[Yanai H](#), [Ito K](#), [Yoshida H](#), [Tada N](#).

Source

Department of Internal Medicine;

Abstract

Astaxanthin is a biological antioxidant naturally found in a wide variety of aquatic living organisms, and has shown various pharmacological activities, such as anti-inflammatory and antidiabetic activities. A recent study reported that the administration of astaxanthin induced a significant reduction in blood pressure and delayed the incidence of stroke in stroke-prone spontaneously hypertensive rats, suggesting that astaxanthin also has antihypertensive effect. In a study using aortic rings of spontaneously hypertensive rats, astaxanthin induced a significant reduction of the contractile responses of the aorta to α -adrenergic receptor agonist and angiotensin II, which may contribute to the antihypertensive effect of astaxanthin. In a histopathological study, astaxanthin decreased coronary artery wall thickness compared with the control, indicating the possibility that astaxanthin ameliorates hypertension-induced vascular remodeling. Astaxanthin has anti-inflammatory, antidiabetic, antihypertensive, and antioxidative activities; therefore, we should perform further studies to elucidate an antiatherogenic effect of astaxanthin.

PMID: 21949609 [PubMed - in process]

PMCID: PMC3172056

Astaxanthin reviewed for its potential to treat cardiovascular disease.

[Am J Cardiol.](#) 2008 May 22;101(10A):58D-68D.

Astaxanthin: a novel potential treatment for oxidative stress and inflammation in cardiovascular disease.

[Pashkow FJ](#), [Watumull DG](#), [Campbell CL](#).

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Oxidative stress and inflammation are implicated in several different manifestations of cardiovascular disease (CVD). They are generated, in part, from the overproduction of reactive oxygen species (ROS) and reactive nitrogen species (RNS) that activate transcriptional messengers, such as nuclear factor-kappaB, tangibly contributing to endothelial dysfunction, the initiation and progression of atherosclerosis, irreversible damage after ischemic reperfusion, and even arrhythmia, such as atrial fibrillation. Despite this connection between oxidative stress and CVD, there are currently no recognized therapeutic interventions to address this important unmet need. Antioxidants that provide a broad, "upstream" approach via ROS/RNS quenching or free radical chain breaking seem an appropriate therapeutic option based on epidemiologic, dietary, and in vivo animal model data. However, human clinical trials with several different well-known agents, such as vitamin E and beta-carotene, have been disappointing. Does this mean antioxidants as a class are ineffective, or rather that the "right" compound(s) have yet to be found, their mechanisms of action understood, and their appropriate targeting and dosages determined? A large class of potent naturally-occurring antioxidants exploited by nature-the oxygenated carotenoids (xanthophylls)-have demonstrated utility in their natural form but have eluded development as successful targeted therapeutic agents up to the present time. This article characterizes the mechanism by which this novel group of antioxidants function and reviews their preclinical development. Results from multiple species support the antioxidant/anti-inflammatory properties of the prototype compound, astaxanthin, establishing it as an appropriate candidate for development as a therapeutic agent for cardiovascular oxidative stress and inflammation.

Publication Types:

- [Review](#)
PMID: 18474276 [PubMed - indexed for MEDLINE]

Astaxanthin reviewed for its effects on cardiovascular health and in cardiovascular disease.

[Molecules](#). 2012 Feb 20;17(2):2030-48. doi: 10.3390/molecules17022030.

Astaxanthin in cardiovascular health and disease.

[Fassett RG](#)¹, [Coombes JS](#).

Author information

- ¹School of Medicine, The University of Queensland, Brisbane, Queensland 4000, Australia. r.fassett@uq.edu.au

Abstract

Oxidative stress and inflammation are established processes contributing to cardiovascular disease caused by atherosclerosis. However, antioxidant therapies tested in cardiovascular disease such as vitamin E, C and β -carotene have proved unsuccessful at reducing cardiovascular events and mortality. Although these outcomes may reflect limitations in trial design, new, more potent antioxidant therapies are being pursued. Astaxanthin, a carotenoid found in microalgae, fungi, complex plants, seafood, flamingos and quail is one such agent. It has antioxidant and anti-inflammatory effects. Limited, short duration and small sample size studies have assessed the effects of astaxanthin on oxidative stress and inflammation biomarkers and have investigated bioavailability and safety. So far no significant adverse events have been observed and biomarkers of oxidative stress and inflammation are attenuated with astaxanthin supplementation. Experimental investigations in a range of species using a cardiac ischaemia-reperfusion model demonstrated cardiac muscle preservation when astaxanthin is administered either orally or intravenously prior to the induction of ischaemia. Human clinical cardiovascular studies using astaxanthin therapy have not yet been reported. On the basis of the promising results of experimental cardiovascular studies and the physicochemical and antioxidant properties and safety profile of astaxanthin, clinical trials should be undertaken.

PMID:

22349894

[PubMed - indexed for MEDLINE]

Free full text

Astaxanthin reviewed for its commercial applications including the area of cardiovascular diseases.

[Mar Drugs](#). 2014 Jan 7;12(1):128-52. doi: 10.3390/md12010128.

Astaxanthin: sources, extraction, stability, biological activities and its commercial applications--a review.

[Ambati RR¹](#), [Phang SM²](#), [Ravi S³](#), [Aswathanarayana RG⁴](#).

Author information

Abstract

There is currently much interest in biological active compounds derived from natural resources, especially compounds that can efficiently act on molecular targets, which are involved in various diseases. Astaxanthin (3,3'-dihydroxy- β , β '-carotene-4,4'-dione) is a xanthophyll carotenoid, contained in *Haematococcus pluvialis*, *Chlorella zofingiensis*, *Chlorococcum*, and *Phaffia rhodozyma*. It accumulates up to 3.8% on the dry weight basis in *H. pluvialis*. Our recent published data on astaxanthin extraction, analysis, stability studies, and its biological activities results were added to this review paper. Based on our results and current literature, astaxanthin showed potential biological activity in in vitro and in vivo models. These studies emphasize the influence of astaxanthin and its beneficial effects on the metabolism in animals and humans. Bioavailability of astaxanthin in animals was enhanced after feeding *Haematococcus* biomass as a source of astaxanthin. Astaxanthin, used as a nutritional supplement, antioxidant and anticancer agent, prevents diabetes, cardiovascular diseases, and neurodegenerative disorders, and also stimulates immunization. Astaxanthin products are used for commercial applications in the dosage forms as tablets, capsules, syrups, oils, soft gels, creams, biomass and granulated powders. Astaxanthin patent applications are available in food, feed and nutraceutical applications. The current review provides up-to-date information on astaxanthin sources, extraction, analysis, stability, biological activities, health benefits and special attention paid to its commercial applications.

PMID:

24402174

[PubMed - indexed for MEDLINE]

PMCID:

PMC3917265

[Free PMC Article](#)

Astaxanthin reviewed for its potential for human health including cardiovascular health.

[J Nat Prod.](#) 2006 Mar;69(3):443-9.

Astaxanthin, a carotenoid with potential in human health and nutrition.

[Hussein G](#), [Sankawa U](#), [Goto H](#), [Matsumoto K](#), [Watanabe H](#).

International Research Center for Traditional Medicine, Toyama Prefecture, Japan.
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Astaxanthin (1), a red-orange carotenoid pigment, is a powerful biological antioxidant that occurs naturally in a wide variety of living organisms. The potent antioxidant property of 1 has been implicated in its various biological activities demonstrated in both experimental animals and clinical studies. Compound 1 has considerable potential and promising applications in human health and nutrition. In this review, the recent scientific literature (from 2002 to 2005) is covered on the most significant activities of 1, including its antioxidative and anti-inflammatory properties, its effects on cancer, diabetes, the immune system, and ocular health, and other related aspects. We also discuss the green microalga *Haematococcus pluvialis*, the richest source of natural 1, and its utilization in the promotion of human health, including the antihypertensive and neuroprotective potentials of 1, emphasizing our experimental data on the effects of dietary astaxanthin on blood pressure, stroke, and vascular dementia in animal models, is described.

Publication Types:

PMID: 16562856 [PubMed - indexed for MEDLINE]

Astaxanthin reviewed for its cardioprotective properties.

[Cardiovasc Drug Rev.](#) 2005 Fall;23(3):199-216.

Disodium disuccinate astaxanthin (Cardax): antioxidant and antiinflammatory cardioprotection.

[Lockwood SE](#), [Gross GJ](#).

Hawaii Biotech, Inc., 99-193 Aiea Heights Drive, Suite 200, Aiea, HI 96701, USA.
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Disodium disuccinate astaxanthin (Cardax), DDA) has cardioprotective effects in the rat, rabbit, and canine models of experimental infarction. It is highly effective by parenteral administration in subchronic and acute dosing regimens. Unpublished data in rats suggest that oral cardioprotection is also readily achievable. DDA-induced myocardial salvage in the canine can reach 100% with a 4-day subchronic dosing regimen. At a single i.v. dose DDA is cardioprotective, when given 2 h before experimental coronary occlusion, but the protection is on the average two-thirds of that achieved with the subchronic regimen in dogs. In conscious animals DDA has no effects on hemodynamic parameters. The primary mechanism of cardioprotection appears to be antioxidant activity involving direct scavenging of superoxide anion, the lynchpin radical in ischemia-reperfusion injury. In addition, modulation of serum complement activity, as well as the reduction in the levels of C-reactive protein (CRP) and the membrane attack complex (MAC) in infarcted tissue suggest a significant antiinflammatory component in the mechanism of cardioprotective action of DDA. Stoichiometric binding of the meso-form of the compound to human serum albumin (HSA) has been demonstrated in vitro. This binding capacity overcomes the supramolecular assembly of the compound in aqueous solution, which by itself improves the stability and shelf life of aqueous formulations. Non-esterified astaxanthin readily enters cardiac tissue after either oral or parenteral administration, providing a reservoir of a cardioprotective agent with a significant half-life due to favorable ADME in mammals. Due to the well-documented safety profile of non-esterified astaxanthin in humans, disodium disuccinate astaxanthin may well find clinical utility in cardiovascular indications in humans following successful completion of preclinical and clinical pharmacology and toxicology studies.

Publication Types:

PMID: 16252014 [PubMed - indexed for MEDLINE]

Astaxanthin reviewed for cardiovascular pathologies.

[Chem Biol Interact](#). 2018 Jan 5;279:145-158. doi: 10.1016/j.cbi.2017.11.012. Epub 2017 Nov 24.

Astaxanthin-antioxidant impact on excessive Reactive Oxygen Species generation induced by ischemia and reperfusion injury.

[Zuluaga M](#)¹, [Gueguen V](#)¹, [Letourneur D](#)¹, [Pavon-Djavid G](#)².

Author information

Abstract

Oxidative stress induced by Reactive Oxygen Species (ROS) was shown to be involved in the pathogenesis of chronic diseases such as cardiovascular pathologies. Particularly, oxidative stress has proved to mediate abnormal platelet function and dysfunctional endothelium-dependent vasodilatation representing a key factor in the progression of ischemic injuries. Antioxidants like carotenoids have been suggested to contribute in their prevention and treatment. Astaxanthin, a xanthophyll carotenoid produced naturally and synthetically, shows interesting antioxidant and anti-inflammatory properties. In vivo studies applying different models of induced ischemia and reperfusion (I/R) injury confirm astaxanthin's protective action after oral or intravenous administration. However, some studies have shown some limitations after oral administration such as low stability, bioavailability and bioefficacy, revealing a need for the implementation of new biomaterials to act as astaxanthin vehicles in vivo. Here, a brief overview of the chemical characteristics of astaxanthin, the carrier systems developed for overcoming its delivery drawbacks and the animal studies showing its potential effect to treat I/R injury are presented.

KEYWORDS:

Astaxanthin; Drug delivery; Ischemia and reperfusion; Oxidative stress; ROS

PMID: 29179950

DOI: [10.1016/j.cbi.2017.11.012](https://doi.org/10.1016/j.cbi.2017.11.012)

[Indexed for MEDLINE]

Astaxanthin reviewed for its potential against cardiovascular disease.

Review Future Cardiology www.futuremedicine.com

Astaxanthin, oxidative stress, inflammation and cardiovascular disease

Robert G Fassett & Jeff S Coombes

It is accepted that oxidative stress and inflammation play an integral role in the pathophysiology of many chronic diseases including atherosclerotic cardiovascular disease. The xanthophyll carotenoid dietary supplement astaxanthin has demonstrated potential as an antioxidant and anti-inflammatory therapeutic agent in models of cardiovascular disease. There have been at least eight clinical studies conducted in over 180 humans using astaxanthin stress, inflammation or the cardiovascular system. There have been no adverse outcomes reported. Studies have demonstrated reduced markers of oxidative stress and inflammation and improved blood rheology. A larger number of experimental studies have been performed using astaxanthin. In particular, studies in a variety of animals using a model of myocardial ischemia and reperfusion have demonstrated protective effects from prior administration of astaxanthin both intravenously and orally. Future clinical studies and trials will help determine the efficacy of antioxidants such as astaxanthin on vascular structure, function oxidative stress and inflammation in a variety of patients at risk of , or with, established cardiovascular disease. These may lead to large intervention trials assessing cardiovascular morbidity and mortality.

Astaxanthin reviewed for its anti-atherosclerotic properties.

[Mar Drugs](#). 2016 Feb 5;14(2). pii: E35. doi: 10.3390/md14020035.

Potential Anti-Atherosclerotic Properties of Astaxanthin.

[Kishimoto Y](#)¹, [Yoshida H](#)², [Kondo K](#)^{3,4}.

Author information

Abstract

Astaxanthin is a naturally occurring red carotenoid pigment classified as a xanthophyll, found in microalgae and seafood such as salmon, trout, and shrimp. This review focuses on astaxanthin as a bioactive compound and outlines the evidence associated with its potential role in the prevention of atherosclerosis. Astaxanthin has a unique molecular structure that is responsible for its powerful antioxidant activities by quenching singlet oxygen and scavenging free radicals. Astaxanthin has been reported to inhibit low-density lipoprotein (LDL) oxidation and to increase high-density lipoprotein (HDL)-cholesterol and adiponectin levels in clinical studies. Accumulating evidence suggests that astaxanthin could exert preventive actions against atherosclerotic cardiovascular disease (CVD) via its potential to improve oxidative stress, inflammation, lipid metabolism, and glucose metabolism. In addition to identifying mechanisms of astaxanthin bioactivity by basic research, much more epidemiological and clinical evidence linking reduced CVD risk with dietary astaxanthin intake is needed.

KEYWORDS:

astaxanthin; atherosclerosis; cardiovascular disease; glucose metabolism; inflammation; lipid metabolism; oxidative stress

PMID: 26861359

PMCID: [PMC4771988](#)

DOI: [10.3390/md14020035](#)

[Indexed for MEDLINE]

[Free PMC Article](#)

ASTAXANTHIN REVIEWED FOR ITS POTENTIAL IN CARDIOVASCULAR DISEASE.

Int J Mol Med. 2021 Jan;47(1):37-48.

doi: 10.3892/ijmm.2020.4783. Epub 2020 Nov 4.

Antioxidant and anti-inflammatory mechanisms of action of astaxanthin in cardiovascular diseases (Review)

[Carolina Parga Martins Pereira¹](#), [Ana Carolina Remondi Souza¹](#), [Andrea Rodrigues Vasconcelos²](#), [Pietra Sacramento Prado¹](#), [José João Name¹](#)

- PMID: **33155666**
- PMCID: [PMC7723678](#)
- DOI: [10.3892/ijmm.2020.4783](#)

Free PMC article

Abstract

Cardiovascular diseases are the most common cause of mortality worldwide. Oxidative stress and inflammation are pathophysiological processes involved in the development of cardiovascular diseases; thus, anti-inflammatory and antioxidant agents that modulate redox balance have become research targets so as to evaluate their molecular mechanisms of action and therapeutic properties. Astaxanthin, a carotenoid of the xanthophyll group, has potent antioxidant properties due to its molecular structure and its arrangement in the plasma membrane, factors that favor the neutralization of reactive oxygen and nitrogen species. This carotenoid also has prominent anti-inflammatory activity, possibly interrelated with its antioxidant effect, and is also involved in the modulation of lipid and glucose metabolism. Considering the potential beneficial effects of astaxanthin on cardiovascular health evidenced by preclinical and clinical studies, the aim of the present review was to describe the molecular and cellular mechanisms associated with the antioxidant and anti-inflammatory properties of this carotenoid in cardiovascular diseases, particularly atherosclerosis. The beneficial properties and safety profile of astaxanthin indicate that this compound may be used for preventing progression or as an adjuvant in the treatment of cardiovascular diseases.

ASTAXANTHIN REVIEWED FOR EFFECTS ON OBESITY-ASSOCIATED DISEASES IN ANIMALS.

Free Radic Biol Med. 2021 Aug 1;171:156-168.

doi: 10.1016/j.freeradbiomed.2021.05.008. Epub 2021 May 8.

Effects of astaxanthin in animal models of obesity-associated diseases: A systematic review and meta-analysis

[Rosa Paola Radice](#)¹, [Antonina Rita Limongi](#)¹, [Emanuele Viviano](#)², [Maria Carmela Padula](#)³, [Giuseppe Martelli](#)², [Giovanna Bermano](#)⁴

- PMID: 33974978
- DOI: [10.1016/j.freeradbiomed.2021.05.008](https://doi.org/10.1016/j.freeradbiomed.2021.05.008)

Abstract

Background and aim: Obesity is a major risk factor for several diseases, including metabolic syndrome (MetS), non-alcoholic fatty liver disease (NAFLD) and type 2 diabetes (T2D). The use of natural products, such as astaxanthin (ASX), a potent antioxidant compound produced by the freshwater green microalga *Haematococcus pluvialis*, has gained particular interest to reduce oxidative stress and inflammation, and to improve redox status, often associated with obesity. A systematic review and meta-analysis was performed to comprehensively examine the effects of ASX in animal models of diet induced obesity-associated diseases in order to inform the design of future human clinical studies for ASX use as supplement or nutraceutical.

Methods: Cinahl, Cochrane, MEDLINE, Scopus and Web of Science were searched for English-language manuscripts published between January 2000 and April 2020 using the following key words: astaxanthin, obesity, non-alcoholic fatty liver disease, diabetes mellitus type 2, NAFLD and metabolic.

Results: Seventeen eligible articles, corresponding to 21 animal studies, were included in the final quantitative analysis. ASX, at different concentrations and administered for different length of time, induced a significant reduction in adipose tissue weight (P =

0.05) and systolic blood pressure ($P < 0.0001$) in control animals. In animal models of T2D, ASX significantly reduced serum glucose levels ($P = 0.04$); whereas it improved several disease biomarkers in the blood (e.g. cholesterol, triglycerides, ALT and AST, $P < 0.10$), and reduced liver ($P = 0.0002$) and body weight ($P = 0.11$), in animal models of NAFLD.

Conclusions: Supplementation of ASX in the diet has positive effects on symptoms associated with obesity related diseases in animals, by having lipid-lowering, hypo-insulin and hypoglycaemic capacity, protecting organs from oxidative stress and mitigating the immune system, as suggested in this review.

Astaxanthin reviewed for cardiovascular health.

[Food Funct.](#) 2017 Jan 25;8(1):39-63. doi: 10.1039/c6fo01721e.

Astaxanthin in cardiovascular health and disease: mechanisms of action, therapeutic merits, and knowledge gaps.

[Visioli F](#)¹, [Artaria C](#)².

[Author information](#)

Abstract

Cardiovascular disease is the main contributor to morbidity and mortality worldwide. Based on its unique chemical features, the xanthophyll carotenoid astaxanthin is being proposed as a suitable preventive and therapeutic agent in cardiovascular disease. This review focuses on recent advances in astaxanthin research relevant to cardiovascular health and disease, i.e. its direct antioxidant, indirect antioxidant, anti-inflammatory, anti-hypertensive, anti-diabetic, renoprotective, lipid-lowering and anti-atherosclerotic activities in vitro and in vivo. Disparities in the biological activities and health benefits of astaxanthin observed in vitro (strong evidence), in animals (moderate evidence), and in humans (weak evidence) and the variety of astaxanthin sources hamper efforts to establish areas of astaxanthin application in human health care. A list of knowledge gaps and experimental pitfalls is proposed to overcome some of the short-comings in astaxanthin research.

PMID: 27924978

DOI: [10.1039/c6fo01721e](https://doi.org/10.1039/c6fo01721e)

[Indexed for MEDLINE]

Astaxanthin and Lycopene reviewed for their potential with cardiovascular disease.

[Curr Atheroscler Rep.](#) 2009 Nov;11(6):434-9.

Carotenoids and cardiovascular disease.

[Riccioni G.](#)

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griccioni@hotmail.com

Abstract

Carotenoids are a class of natural fat-soluble pigments found principally in plants. They have potential antioxidant biological properties due to their chemical structure and interaction with biological membranes. The most abundant carotenoids in the diet are beta-carotene, lycopene, lutein, beta-cryptoxanthin, zeaxanthin, and astaxanthin. Numerous epidemiologic studies have supported the hypothesis that antioxidants could be used as an inexpensive means of prevention, and possibly treatment, of cardiovascular diseases, even though findings from interventional trials have been mixed, with some positive findings, many null findings, and some suggestion of harm in certain high-risk populations. Recent smaller interventional studies with carefully chosen populations, such as those under high levels of oxidative stress, have yielded largely positive results. This suggests that we need more hypothesis-driven and rigorous clinical trial designs. The aim of this review is to examine the published studies about the use of carotenoids, especially lycopene and astaxanthin, in the treatment of cardiovascular diseases.

PMID: 19852884 [PubMed - indexed for MEDLINE]

Skin Health: Internal Beauty and UV Protection

Internal beauty effects of Natural Astaxanthin in placebo-controlled human clinical trial.

Carotenoid Science Vol 10, p 91-5 (2006)

The Effects of a Dietary Supplement Containing Astaxanthin on Skin Condition
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Kamiichi, Toyama 930-0397, Japan

The cosmetic effects on human skin by 4mg per day astaxanthin supplementation were demonstrated in a single blind placebo controlled study using forty-nine US healthy middle-aged women. There were significant improvements in fine lines/wrinkles and elasticity by dermatologist's assessment and in the moisture content by instrumental assessment at week 6 compared to base-line initial values.

Astaxanthin, widely and naturally distributed in marine organisms, including Crustacea such as shrimps and crabs and such fish as salmon and sea bream exhibits a strong anti-oxidative effect, and its action is reported to 1,000 times stronger than alpha-tocopherol and approximately 40 times stronger than beta-carotene. It has also been reported that astaxanthin doesn't have any pro-oxidative nature like beta-carotene and lycopene and its potent anti-oxidant property is exhibited at the cell membrane. Although used only as a coloring in the past (either as a food additive or a dye-up agent for cultured fish), astaxanthin has become one of the major materials eagerly anticipated by industries for dietary supplements and personal care products.

Furthermore its other various important benefits to date have suggested for human health such as anti-inflammation, LDL cholesterol oxidation suppression, immunomodulation, anti-stress, limiting diabetic nephropathy, improved semen quality, attenuating eye fatigue, sport performance and endurance, limiting exercised induced muscle damage and improving hypertension.

In terms of dermatological actions, suppression of hyper-pigmentation, inhibitions of melanin synthesis and photo-aging have been reported. We have also reported visual wrinkled reduction by topical astaxanthin. However, only one study for internal use about cosmetic benefit of a dietary supplement including astaxanthin and tocotrienol on human skin has been reported.

Here we report the effects of a dietary supplement containing astaxanthin on skin condition performed in the United States of America.

Astaxanthin taken internally improves the beauty of the skin in human clinical trial.

[Acta Biochim Pol.](#) 2012;59(1):43-7. Epub 2012 Mar 17.

Cosmetic benefits of astaxanthin on humans subjects.

[Tominaga K¹](#), [Hongo N](#), [Karato M](#), [Yamashita E](#).

Author information

Abstract

Two human clinical studies were performed. One was an open-label non-controlled study involving 30 healthy female subjects for 8 weeks. Significant improvements were observed by combining 6 mg per day oral supplementation and 2 ml (78.9 μ M solution) per day topical application of astaxanthin. Astaxanthin derived from the microalgae, *Haematococcus pluvialis* showed improvements in skin wrinkle (crow's feet at week-8), age spot size (cheek at week-8), elasticity (crow's feet at week-8), skin texture (cheek at week-4), moisture content of corneocyte layer (cheek in 10 dryskin subjects at week-8) and corneocyte condition (cheek at week-8). It may suggest that astaxanthin derived from *H. pluvialis* can improve skin condition in all layers such as corneocyte layer, epidermis, basal layer and dermis by combining oral supplementation and topical treatment. Another was a randomized double-blind placebo controlled study involving 36 healthy male subjects for 6 weeks. Crow's feet wrinkle and elasticity; and transepidermal water loss (TEWL) were improved after 6 mg of astaxanthin (the same as former study) daily supplementation. Moisture content and sebum oil level at the cheek zone showed strong tendencies for improvement. These results suggest that astaxanthin derived from *Haematococcus pluvialis* may improve the skin condition in not only in women but also in men.

PMID:

22428137

[PubMed - indexed for MEDLINE]

Free full text

Astaxanthin prevents skin deterioration due to environmental factors such as UV and dehydration in placebo-controlled human clinical study.

[J Clin Biochem Nutr.](#) 2017 Jul;61(1):33-39. doi: 10.3164/jcbn.17-35. Epub 2017 Jun 20.

Protective effects of astaxanthin on skin deterioration.

[Tominaga K¹](#), [Hongo N¹](#), [Fujishita M¹](#), [Takahashi Y¹](#), [Adachi Y¹](#).

Author information

Abstract

Astaxanthin is a carotenoid with potent antioxidant and anti-inflammatory activity. To evaluate the anti-inflammatory effect of astaxanthin on skin deterioration, we confirmed its role in epidermal-dermal interactions *in vitro*. Astaxanthin treatment suppressed ultraviolet B (UVB)-induced inflammatory cytokine secretion in keratinocytes, and matrix metalloproteinase-1 secretion by fibroblasts cultured in UVB-irradiated keratinocyte medium. To verify these findings, we conducted a 16-week clinical study with 65 healthy female participants. Participants were orally administered either a 6 mg or 12 mg dose of astaxanthin or a placebo. Wrinkle parameters and skin moisture content significantly worsened in the placebo group after 16 weeks. However, significant changes did not occur in the astaxanthin groups. Interleukin-1 α levels in the stratum corneum significantly increased in the placebo and low-dose groups but not in the high-dose group between weeks 0 and 16. This study was performed in Japan from August to December, when changing environmental factors, such as UV and dryness, exacerbate skin deterioration. In conclusion, our study suggests that long-term prophylactic astaxanthin supplementation may inhibit age-related skin deterioration and maintain skin conditions associated with environmentally induced damage via its anti-inflammatory effect. (UMIN Clinical Trials Registry ID: UMIN000018550).

KEYWORDS:

astaxanthin; inflammatory cytokines; interleukin-1 α ; skin elasticity; wrinkle formation

PMID: 28751807

PMCID: [PMC5525019](#)

DOI: [10.3164/jcbn.17-35](#)

[Free PMC Article](#)

Astaxanthin reduces wrinkles and improves skin moisture and elasticity in double-blind, randomized study.

[Clin Interv Aging](#). 2015 Nov 19;10:1849-56. doi: 10.2147/CIA.S90092. eCollection 2015.

The effectiveness of a standardized rose hip powder, containing seeds and shells of *Rosa canina*, on cell longevity, skin wrinkles, moisture, and elasticity.

[Phetcharat L](#)¹, [Wongsuphasawat K](#)¹, [Winther K](#)².

Author information

Abstract

OBJECTIVE: To evaluate the effects of a rose hip powder (Hyben Vital(®)) made from seeds and shells on cell senescence, skin wrinkling, and aging.

METHODS: A total of 34 healthy subjects, aged 35-65 years, with wrinkles on the face (crow's-feet) were subjected to a randomized and double-blinded clinical study of the effects of the rose hip powder, as compared to astaxanthin, a well-known remedy against wrinkles. During the 8-week study, half of the participants ingested the standardized rose hip product, while the other half ingested astaxanthin. Objective measurements of facial wrinkles, skin moisture, and elasticity were made by using Visioscan, Corneometer, and Cutometer at the beginning of the study, after 4 weeks, and after 8 weeks. Evaluation of participant satisfaction of both supplements was assessed using questionnaires. In addition, the effect of the rose hip preparation on cell longevity was measured in terms of leakage of hemoglobin through red cell membranes (hemolytic index) in blood samples kept in a blood bank for 5 weeks. Significance of all values was attained with $P \leq 0.05$.

RESULTS: In the double-blinded study, the rose hip group showed statistically significant improvements in crow's-feet wrinkles ($P < 0.05$), skin moisture ($P < 0.05$), and elasticity ($P < 0.05$) after 8 weeks of treatment. A similar improvement was observed for astaxanthin, with P -values 0.05, 0.001, and 0.05. Likewise, both groups expressed equal satisfaction with the results obtained in their self-assessment. The rose hip powder further resulted in increased cell longevity of erythrocyte cells during storage for 5 weeks in a blood bank.

CONCLUSION: Results suggest that intake of the standardized rose hip powder (Hyben Vital(®)) improves aging-induced skin conditions. The apparent stabilizing effects of the rose hip product on cell membranes of stored erythrocyte cells observed in this study may contribute to improve the cell longevity and obstructing skin aging.

PMID: 26604725 PMCID: [PMC4655903](#) DOI: [10.2147/CIA.S90092](#) [Indexed for MEDLINE] [Free PMC Article](#)

Astaxanthin is effective against UV-induced skin deterioration in double-blind, placebo-controlled human clinical study.

Nutrients **2018**, *10*(7), 817; doi:[10.3390/nu10070817](https://doi.org/10.3390/nu10070817)

Article

The Protective Role of Astaxanthin for UV-Induced Skin Deterioration in Healthy People—A Randomized, Double-Blind, Placebo-Controlled Trial

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Received: 7 June 2018 / Accepted: 21 June 2018 / Published: 25 June 2018

Abstract

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Skin is a major safeguard tissue in humans. Because biological barrier function is deteriorated by several kinds of stresses including exposure to ultra-violet (UV) rays, the protection and treatment of skin conditions by dietary supplements are important. We therefore evaluated the effects of dietary supplementation with an algal food-derived antioxidant, astaxanthin, on UV-induced skin deterioration. Twenty-three healthy Japanese participants were recruited to a 10-week double-blind placebo-controlled study. They were assigned to the astaxanthin group supplemented with a capsule containing 4 mg of astaxanthin or the placebo group. To assess the protective role of astaxanthin for UV-induced skin deterioration, we determined the minimal erythema dose (MED) and analyzed UV-induced changes of moisture and transepidermal water loss (TEWL) at baseline and after 9 weeks of supplementation. Subjective skin conditions were assessed by the visual analog scale. The astaxanthin group showed increased MED compared with placebo. In addition, the astaxanthin group had a reduced loss of skin moisture in the irradiated area compared with placebo. Subjective skin conditions for “improvement of rough skin” and “texture” in non-irradiated areas were significantly improved by astaxanthin. Astaxanthin seems protective against UV-induced skin deterioration and helps maintain healthy skin in healthy people.

Keywords:

astaxanthin; antioxidant; skin; ultra-violet; UV; MED; moisture

Astaxanthin rejuvenates facial skin and reduces oxidative stress in skin in human clinical study.

[Nutr Res.](#) 2017 Dec;48:40-48. doi: 10.1016/j.nutres.2017.10.006. Epub 2017 Oct 10.

Continuous astaxanthin intake reduces oxidative stress and reverses age-related morphological changes of residual skin surface components in middle-aged volunteers.

[Chalyk NE](#)¹, [Klochkov VA](#)¹, [Bandaletova TY](#)², [Kyle NH](#)³, [Petyaev IM](#)⁴.

Author information

Abstract

Oxidative stress accelerates skin aging, and dietary supplementation with antioxidants may alleviate it. Morphological analysis of the residual skin surface components (RSSCs) allows detecting age-related changes in corneocyte desquamation, microbial presence, and lipid droplet size. We hypothesized that continuous ingestion of carotenoid antioxidant astaxanthin (4 mg/d) for 4 weeks could influence RSCC morphology and evaluated RSCC samples taken from middle-aged subjects before and after this dietary intervention. The study included 31 volunteers (17 men and 14 women) over the age of 40. RSCC samples were collected from the surface of the facial skin at the beginning (day 0) and end (day 29) of the study. In addition, blood samples were taken on days 0, 15, and 29 for measuring plasma levels of malondialdehyde that allowed assessing systemic oxidative stress. The results demonstrated that plasma malondialdehyde consistently decreased during astaxanthin consumption (by 11.2% on day 15 and by 21.7% on day 29). The analysis of RSCC samples has revealed significantly decreased levels of corneocyte desquamation ($P=.0075$) and microbial presence ($P=.0367$) at the end of the study. These phenomena as well as a significant ($P=.0214$) increase in lipid droplet size were more strongly manifested among obese (body mass index >30 kg/m²) subjects. All described RSCC changes correspond to a shift toward characteristics of skin associated with a younger age. The results confirm our hypothesis by demonstrating that continuous astaxanthin consumption produces a strong antioxidant effect resulting in facial skin rejuvenation which is especially pronounced in obese subjects.

KEYWORDS:

Antiaging effect; Antioxidant; Astaxanthin; Corneocyte desquamation; Malondialdehyde; Skin surface

PMID: 29246280

DOI: [10.1016/j.nutres.2017.10.006](https://doi.org/10.1016/j.nutres.2017.10.006)

[Indexed for MEDLINE]

Astaxanthin combined with Tocotrienols show excellent “Beauty from Within” benefits.

Beauty From Within: A Synergistic Combination Of Astaxanthin And Tocotrienol For Beauty Supplements

Eiji Yamashita, Life Science Division, Fuji Chemical Industry Co., Ltd., 55 Yokohoonji, Kamiichi, Toyama 930-0397, Japan

(2002) Cosmetic Benefit of Dietary Supplements Containing Astaxanthin and Tocotrienol on Human Skin. *Food Style* 21 6(6):112-17.

Previously reported dermatological benefits of natural astaxanthin included anti-hyperpigmentation, melanin synthesis inhibition, and reduced photo-skin aging. Hence, the potency of astaxanthin for cosmetic effect is “clearly visible”. Another class of natural compounds called tocotrienols also offer cosmetic benefits. A member of the vitamin E family, its isomeric form (chemically identical, but structurally different) imparts greater protection against free radicals than its popular cousin, alpha-tocopherol. Tocotrienols are generally 40-60 times more powerful than alpha-tocopherols in terms of free radical protection. Both astaxanthin and tocotrienols are found naturally in daily foods we consume. By concentrating these into an oral beauty supplement, it can provide an excellent source of protection in addition to the daily skincare regime. Results in 4 weeks supplementation indicated reduction in fine wrinkles, increased skin moisture and increased skin elasticity compared to placebo.

Astaxanthin combined with collagen improves skin elasticity and barrier integrity in human facial skin in placebo-controlled human clinical study.

[J Med Food](#). 2014 Jul;17(7):810-6. doi: 10.1089/jmf.2013.3060. Epub 2014 Jun 23.

Supplementating with dietary astaxanthin combined with collagen hydrolysate improves facial elasticity and decreases matrix metalloproteinase-1 and -12 expression: a comparative study with placebo.

[Yoon HS¹](#), [Cho HH](#), [Cho S](#), [Lee SR](#), [Shin MH](#), [Chung JH](#).

Author information

Abstract

Photoaging accounts for most age-related changes in skin appearance. It has been suggested that both astaxanthin, a potent antioxidant, and collagen hydrolysate can be used as antiaging modalities in photoaged skin. However, there is no clinical study using astaxanthin combined with collagen hydrolysate. We investigated the effects of using a combination of dietary astaxanthin and collagen hydrolysate supplementation on moderately photoaged skin in humans. A total of 44 healthy subjects were recruited and treated with astaxanthin (2 mg/day) combined with collagen hydrolysate (3 g/day) or placebos, which were identical in appearance and taste to the active supplementation for 12 weeks. The elasticity and hydration properties of facial skin were evaluated using noninvasive objective devices. In addition, we also evaluated the expression of procollagen type I, fibrillin-1, matrix metalloproteinase-1 (MMP-1) and -12, and ultraviolet (UV)-induced DNA damage in artificially UV-irradiated buttock skin before and after treatment. The supplement group showed significant improvements in skin elasticity and transepidermal water loss in photoaged facial skin after 12 weeks compared with the placebo group. In the supplement group, expression of procollagen type I mRNA increased and expression of MMP-1 and -12 mRNA decreased compared with those in the placebo group. In contrast, there was no significant difference in UV-induced DNA damage between groups. These results demonstrate that dietary astaxanthin combined with collagen hydrolysate can improve elasticity and barrier integrity in photoaged human facial skin, and such treatment is well tolerated.

KEYWORDS:

anti-aging; astaxanthin; collagen hydrolysate; photoaging

PMID: 24955642 DOI: [10.1089/jmf.2013.3060](#)

[PubMed - indexed for MEDLINE]

Natural Astaxanthin shows more effective results than Synthetic in inhibiting skin cancer in rats due to increased bioavailability.

[J Agric Food Chem.](#) 2013 Apr 24;61(16):3842-51. doi: 10.1021/jf304609j. Epub 2013 Apr 16.

Effective inhibition of skin cancer, tyrosinase, and antioxidative properties by astaxanthin and astaxanthin esters from the green alga *Haematococcus pluvialis*.

[Rao AR¹](#), [Sindhuja HN](#), [Dharmesh SM](#), [Sankar KU](#), [Sarada R](#), [Ravishankar GA](#).

Author information

Abstract

Astaxanthin mono- (AXME) and diesters (AXDE) were characterized and examined for anticancer potency with total carotenoids (TC) and astaxanthin (AX) against UV-7,12-dimethylbenz(a)anthracene (DMBA)-induced skin cancer model in rat. At 200 µg/kg bw, AXDE and AXME reduced UV-DMBA-induced tumor incidences up to 96 and 88%, respectively, when compared to AX (66%) and TC (85%). UV-DMBA has been known to generate high levels of free radicals and tyrosinase enzyme, leading to characteristic symptoms of skin pigmentation and tumor initiation. Intriguingly, ~7-fold increase in tyrosinase and 10-fold decrease in antioxidant levels were normalized by AXDE and AXME as opposed to only ~1.4-2.2-fold by AX and TC, respectively. This result together with the appearance of 72 and 58 ng/mL of retinol in the serum of respective AXE-treated (AXDE + AXME) and AX-treated animals suggested that better anticancer potency of AXEs could be due to increased bioavailability.

PMID:

23473626

[PubMed - indexed for MEDLINE]

Astaxanthin has superior photo-aging preventive properties than other carotenoids.

[Exp Dermatol.](#) 2009 Mar;18(3):222-31. doi: 10.1111/j.1600-0625.2008.00790.x. Epub 2008 Sep 18.

Astaxanthin, canthaxanthin and beta-carotene differently affect UVA-induced oxidative damage and expression of oxidative stress-responsive enzymes.

[Camera E¹](#), [Mastrofrancesco A](#), [Fabbri C](#), [Daubrawa F](#), [Picardo M](#), [Sies H](#), [Stahl W](#).

Author information

Abstract

Carotenoids are used for systemic photoprotection in humans. Regarding mechanisms underlying photoprotective effects of carotenoids, here we compared the modulation of UVA-related injury by carotenoids. Human dermal fibroblasts (HDF) were exposed to moderate doses of UVA, which stimulated apoptosis, increased levels of reactive oxygen species and thiobarbituric acid reactive substances, decreased antioxidant enzymes activities, promoted membrane perturbation, and induced the expression of heme oxygenase-1 (HO-1). The carotenoids astaxanthin (AX), canthaxanthin (CX) and beta-carotene (betaC) were delivered to HDF 24 h before exposure to UVA. Astaxanthin exhibited a pronounced photoprotective effect and counteracted all of the above-mentioned UVA-induced alterations to a significant extent. beta-Carotene only partially prevented the UVA-induced decline of catalase and superoxide dismutase activities, but it increased membrane damage and stimulated HO-1 expression. Moreover, betaC dose-dependently induced caspase-3 activity following UVA exposure. In contrast, CX had no effect on oxidative damage, except for HO-1 expression, which was augmented. Uptake of AX by fibroblasts was higher than that of the other two carotenoids. The photostability of the three compounds in fibroblasts was AX > CX >> betaC. The data indicate that the oxo-carotenoid AX has a superior preventive effect towards photo-oxidative changes in cell culture.

PMID:

18803658

[PubMed - indexed for MEDLINE]

Astaxanthin may have protective effect against photo-aging, wrinkles and sagging.

[J Dermatol Sci](#). 2010 May;58(2):136-42. doi: 10.1016/j.jdermsci.2010.02.009. Epub 2010 Feb 18.

Astaxanthin attenuates the UVA-induced up-regulation of matrix-metalloproteinase-1 and skin fibroblast elastase in human dermal fibroblasts.

[Suganuma K](#)¹, [Nakajima H](#), [Ohtsuki M](#), [Imokawa G](#).

Author information

Abstract

BACKGROUND:

Repetitive exposure of the skin to UVA radiation elicits sagging more frequently than wrinkling, which is mainly attributed to its biochemical mechanism to up-regulate the expression of matrix-metalloproteinase (MMP)-1 and skin fibroblast elastase (SFE)/neutral endopeptidase (NEP), respectively.

OBJECTIVE:

In this study, we examined the effects of a potent antioxidant, astaxanthin (AX), on the induction of MMP-1 and SFE by UVA treatment of cultured human dermal fibroblasts.

METHODS:

Those effects were assessed by real-time RT-PCR, Western blotting and enzymic activity assays.

RESULTS:

UVA radiation elicited a significant increase in the gene expression of MMP-1 as well as SFE/NEP (to a lesser extent) which was followed by distinct increases in their protein and enzymatic activity levels. The addition of AX at concentrations of 4-8 microM immediately after UVA exposure significantly attenuated the induction of MMP-1 and SFE/NEP expression elicited by UVA at the gene, protein and activity levels although both the UVA stimulation and the subsequent AX inhibition were greater for MMP-1 than for SFE/NEP. Analysis of the UVA-induced release of cytokines revealed that UVA significantly stimulated only the secretion of IL-6 among the cytokines tested and that AX significantly diminished only the IL-6 secretion.

CONCLUSION:

These findings indicate that, based on different effective concentrations of AX, a major mode of action leading to the inhibition elicited by AX depends on inhibition of UVA effects of the reactive oxygen species-directed signaling cascade, but not on interruption of the IL-6-mediated signaling cascade. We hypothesize that AX would have a significant benefit on protecting against UVA-induced skin photo-aging such as sagging and wrinkles.

2010 Japanese Society for Investigative Dermatology. Published by Elsevier Ireland Ltd. All rights reserved.

PMID:

20219323

[PubMed - indexed for MEDLINE]

Astaxanthin inhibits secretion of wrinkle-inducing cytokines.

[PLoS One](#). 2016 Sep 20;11(9):e0161580. doi: 10.1371/journal.pone.0161580. eCollection 2016.

The Inhibitory Effects of Anti-Oxidants on Ultraviolet-Induced Up-Regulation of the Wrinkling-Inducing Enzyme Neutral Endopeptidase in Human Fibroblasts.

[Nakajima H](#)^{1,2}, [Terazawa S](#)³, [Niwano T](#)², [Yamamoto Y](#)², [Imokawa G](#)³.

Author information

Abstract

We recently reported that the over-expression of skin fibroblast-derived neutral endopeptidase (NEP) plays a pivotal role in impairing the three-dimensional architecture of dermal elastic fibers during the biological mechanism of ultraviolet (UV)-induced skin wrinkling. In that process, a UVB-associated epithelial-mesenchymal cytokine interaction as well as a direct UVA-induced cellular stimulation are associated with the up-regulation of NEP in human fibroblasts. In this study, we characterized the mode of action of ubiquinol10 which may abrogate the up-regulation of NEP by dermal fibroblasts, resulting in a reported in vivo anti-wrinkling action, and compared that with 3 other anti-oxidants, astaxanthin (AX), riboflavin (RF) and flavin mononucleotide (FMN). Post-irradiation treatment with all 4 of those anti-oxidants elicited an interrupting effect on the UVB-associated epithelial-mesenchymal cytokine interaction leading to the up-regulation of NEP in human fibroblasts but with different modes of action. While AX mainly served as an inhibitor of the secretion of wrinkle-inducing cytokines, such as interleukin-1 α (IL-1 α) and granulocyte macrophage colony stimulatory factor (GM-CSF) in UVB-exposed epidermal keratinocytes, ubiquinol10, RF and FMN predominantly interrupted the IL-1 α and GM-CSF-stimulated expression of NEP in dermal fibroblasts. On the other hand, as for the UVA-associated mechanism, similar to the abrogating effects reported for AX and FMN, ubiquinol10 but not RF had the potential to abrogate the increased expression of NEP and matrix-metalloproteinase-1 in UVA-exposed human fibroblasts. Our findings strongly support the in vivo anti-wrinkling effects of ubiquinol10 and AX on human and animal skin and provide convincing proof of the UV-induced wrinkling mechanism that essentially focuses on the over-expression of NEP by dermal fibroblasts as an intrinsic causative factor.

PMID: 27648570 PMID: [PMC5029912](#)

DOI: [10.1371/journal.pone.0161580](#) PubMed - in process]

[Free PMC Article](#)

ASTAXANTHIN REDUCED CELL DEATH INDUCED BY BPA IN HUMAN SKIN CELLS.

Antioxidants (Basel) 2021 Aug 11;10(8):1273. doi: 10.3390/antiox10081273.

Astaxanthin Inhibits Autophagic Cell Death Induced by Bisphenol A in Human Dermal Fibroblasts

[Seong-Ryeong Lim](#)¹, [Do-Wan Kim](#)¹, [Junghee Sung](#)², [Tae Hoon Kim](#)³, [Chang-Hyung Choi](#)⁴, [Sei-Jung Lee](#)¹

Affiliations expand

- PMID: 34439521 PMCID: [PMC8389241](#) DOI: [10.3390/antiox10081273](#)

Free PMC article

Abstract

Astaxanthin, a natural antioxidant carotenoid, is a nutrient with diverse health benefits, given that it decreases the risk of oxidative stress-related diseases. In the present study, we investigate the functional role of astaxanthin during autophagic cell death induced by the estrogenic endocrine-disrupting chemical bisphenol A (BPA) in normal human dermal fibroblasts (NHDF). BPA significantly induced apoptotic cell death and autophagy in NHDF. Autophagic cell death evoked by BPA was significantly restored upon a treatment with astaxanthin (10 μ M) via the inhibition of intracellular reactive oxygen species (ROS) production. Astaxanthin inhibited the phosphorylation of extracellular signal-regulated kinases (ERK) stimulated by ROS production, but it did not influence the activation of c-Jun N-terminal kinase (JNK) and p38 mitogen-activated protein kinase (MAPK) in BPA-treated NHDF. Astaxanthin abrogated the ERK-mediated activation of nuclear factor-kappa B (NF- κ B), which is responsible for the mRNA expression of LC3-II, Beclin-1, Atg12, and Atg14 during apoptotic cell death induced by BPA. These results indicate that astaxanthin is a pharmacological and nutritional agent that blocks the skin fibroblastic autophagic cell death induced by BPA in human dermal fibroblasts.

Astaxanthin protects against UV-induced inflammation.

[Exp Dermatol](#). 2014 Mar;23(3):178-83. doi: 10.1111/exd.12347.

Astaxanthin, a xanthophyll carotenoid, inhibits ultraviolet-induced apoptosis in keratinocytes.

[Yoshihisa Y](#)¹, [Rehman MU](#), [Shimizu T](#).

Author information

Abstract

Intra-cellular reactive nitrogen/oxygen species and apoptosis play important roles in ultraviolet (UV)-induced inflammatory responses in the skin. Astaxanthin (AST), a xanthophyll carotenoid, exhibits diverse clinical benefits. The protective effects of AST against UV-induced apoptosis were investigated in the present study. Astaxanthin (5 μ m) caused a significant decrease in the protein content and the mRNA levels of inducible nitric oxide (iNOS) and cyclooxygenase (COX)-2, and decreased the release of prostaglandin E2 from HaCaT keratinocytes after UVB (20 mJ/cm²) or UVC (5 mJ/cm²) irradiation. No significant protective effects against UV-induced reactive oxygen species (ROS) were observed in AST-pretreated cells. Astaxanthin caused a significant inhibition of UV-irradiation-induced apoptosis, as evidence by a DNA fragmentation assay. Furthermore, we found that the treatment with AST caused a reduction in the UVB- or UVC-induced protein and mRNA expression of macrophage migration inhibitory factor (MIF), IL-1 β and TNF- α in HaCaT keratinocytes. These results suggest that AST effectively protects against UV-induced inflammation by decreasing iNOS and COX-2, and thereby inhibiting the apoptosis of keratinocytes.

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KEYWORDS:

apoptosis; astaxanthin; keratinocyte; reactive oxygen species; ultraviolet

PMID:

24521161

[PubMed - indexed for MEDLINE]

Astaxanthin superior to lutein and beta-carotene in protecting against UV-induced oxidative stress.

[J Dermatol Sci.](#) 1998 Mar;16(3):226-30.

Modulation of UVA light-induced oxidative stress by beta-carotene, lutein and astaxanthin in cultured fibroblasts.

[O'Connor I, O'Brien N.](#)

Department of Nutrition, University College, Cork, Ireland.

The ability of beta-carotene, lutein or astaxanthin to protect against UVA-induced oxidative stress in rat kidney fibroblasts (NRK) was assessed. Activities of the antioxidant enzymes catalase (CAT) and superoxide dismutase (SOD), and changes in thiobarbituric acid reactive substances (TBARS) were measured as indices of oxidative stress. Exposure to UVA light at a dose intensity of 5.6 mW/cm² for 4 h resulted in a significant decrease in CAT and SOD activities and a significant increase in TBARS. No cytotoxicity, as indicated by lactate dehydrogenase (LDH) release, was observed. beta-Carotene (1 microM), lutein (1 microM) and astaxanthin (10 nM) protect against UVA light-induced oxidative stress in vitro with astaxanthin exhibiting superior protective properties.

Publication Types:

PMID: 9651820 [PubMed - indexed for MEDLINE]

Astaxanthin enhances collagen production in human dermal fibroblasts.

[Int J Mol Sci](#). 2016 Jun 16;17(6). pii: E955. doi: 10.3390/ijms17060955.

Enriched Astaxanthin Extract from *Haematococcus pluvialis* Augments Growth Factor Secretions to Increase Cell Proliferation and Induces MMP1 Degradation to Enhance Collagen Production in Human Dermal Fibroblasts.

[Chou HY](#)^{1,2}, [Lee C](#)³, [Pan JL](#)^{4,5}, [Wen ZH](#)⁶, [Huang SH](#)^{7,8,9,10}, [Lan CW](#)¹¹, [Liu WT](#)¹², [Hour TC](#)^{13,14}, [Hseu YC](#)^{15,16}, [Hwang BH](#)¹⁷, [Cheng KC](#)^{18,19,20}, [Wang HM](#)^{21,22,23,24,25}.

Author information

Abstract

Among many antioxidants that are used for the repairing of oxidative stress induced skin damages, we identified the enriched astaxanthin extract (EAE) from *Haematococcus pluvialis* as a viable ingredient. EAE was extracted from the red microalgae through supercritical fluid carbon dioxide extraction. To compare the effectiveness, EAE was treated on human dermal fibroblasts with other components, phorbol 12-myristate 13-acetate (PMA), and doxycycline. With sirius red staining and quantitative real-time polymerase chain reaction (qRT-PCR), we found that PMA decreased the collagen concentration and production while overall the addition of doxycycline and EAE increased the collagen concentration in a trial experiments. EAE increased collagen contents through inhibited MMP1 and MMP3 mRNA expression and induced TIMP1, the antagonists of MMPs protein, gene expression. As for when tested for various proteins through western blotting, it was seen that the addition of EAE increased the expression of certain proteins that promote cell proliferation. Testing those previous solutions using growth factor assay, it was noticeable that EAE had a positive impact on cell proliferation and vascular endothelial growth factor (VEGF) than doxycycline, indicating that it was a better alternative treatment for collagen production. To sum up, the data confirmed the possible applications as medical cosmetology agents and food supplements.

KEYWORDS:

Haematococcus pluvialis; doxycycline; enriched astaxanthin extract (EAE); phorbol 12-myristate 13-acetate (PMA)

PMID: 27322248 PMCID: [PMC4926488](#)

DOI: [10.3390/ijms17060955](#)

[PubMed - in process]

[Free PMC Article](#)

Astaxanthin prevents skin photoaging from chronic UVA exposure in hairless mice.

[PLoS One](#). 2017 Feb 7;12(2):e0171178. doi: 10.1371/journal.pone.0171178. eCollection 2017.

Preventive effect of dietary astaxanthin on UVA-induced skin photoaging in hairless mice.

[Komatsu T¹](#), [Sasaki S¹](#), [Manabe Y¹](#), [Hirata T¹](#), [Sugawara T¹](#).

Author information

Abstract

Astaxanthin, a carotenoid found mainly in seafood, has potential clinical applications due to its antioxidant activity. In this study, we evaluated the effect of dietary astaxanthin derived from *Haematococcus pluvialis* on skin photoaging in UVA-irradiated hairless mice by assessing various parameters of photoaging. After chronic ultraviolet A (UVA) exposure, a significant increase in transepidermal water loss (TEWL) and wrinkle formation in the dorsal skin caused by UVA was observed, and dietary astaxanthin significantly suppressed these photoaging features. We found that the mRNA expression of lympho-epithelial Kazal-type-related inhibitor, steroid sulfatase, and aquaporin 3 in the epidermis was significantly increased by UVA irradiation for 70 days, and dietary astaxanthin significantly suppressed these increases in mRNA expression to be comparable to control levels. In the dermis, the mRNA expression of matrix metalloproteinase 13 was increased by UVA irradiation and significantly suppressed by dietary astaxanthin. In addition, HPLC-PDA analysis confirmed that dietary astaxanthin reached not only the dermis but also the epidermis. Our results indicate that dietary astaxanthin accumulates in the skin and appears to prevent the effects of UVA irradiation on filaggrin metabolism and desquamation in the epidermis and the extracellular matrix in the dermis.

PMID: 28170435

PMCID: [PMC5295690](#)

DOI: [10.1371/journal.pone.0171178](#)

[Indexed for MEDLINE]

[Free PMC Article](#)

ASTAXANTHIN PROTECTS SKIN FROM UV-INDUCED PHOTOAGING IN HAIRLESS MICE.

Biomedicines. 2020 Jan 21;8(2):18.
doi: 10.3390/biomedicines8020018.

Protective Effects of Astaxanthin Supplementation against Ultraviolet-Induced Photoaging in Hairless Mice

[Xing Li](#)¹, [Tomohiro Matsumoto](#)¹, [Miho Takuwa](#)¹, [Mahmood Saeed Ebrahim Shaiku Ali](#)¹, [Takumi Hirabashi](#)¹, [Hiroyo Kondo](#)¹, [Hidemi Fujino](#)¹

- PMID: **31973028**
- PMCID: [PMC7168265](#)
- DOI: [10.3390/biomedicines8020018](#)

Free PMC article

Abstract

Ultraviolet (UV) light induces skin photoaging, which is characterized by thickening, wrinkling, pigmentation, and dryness. Astaxanthin (AST), a ketocarotenoid isolated from *Haematococcus pluvialis*, has been extensively studied owing to its possible effects on skin health as well as UV protection. In addition, AST attenuates the increased generation of reactive oxygen species (ROS) and capillary regression of the skeletal muscle. In this study, we investigated whether AST could protect against UV-induced photoaging and reduce capillary regression in the skin of HR-1 hairless mice. UV light induces wrinkle formation, epidermal thickening, and capillary regression in the dermis of HR-1 hairless mice. The administration of AST reduced the UV-induced wrinkle formation and skin thickening, and increased collagen fibers in the skin. AST supplementation also inhibited the generation of ROS, decreased wrinkle formation, reduced epidermal thickening, and increased the density of capillaries in the skin. We also found an inverse correlation between wrinkle formation and the density of capillaries. An association between photoaging and capillary regression in the skin was also observed. These results suggest that AST can protect against photoaging caused by UV irradiation and the inhibitory effects of AST on photoaging may be associated with the reduction of capillary regression in the skin.

ASTAXANTHIN PROMOTES TISSUE REGENERATION BY REDUCING OXIDATIVE STRESS AND THE SECRETION OF COLLAGEN IN-VITRO AND IN-VIVO.

Oxid Med Cell Longev. 2020 Aug 3;2020:4946902.
doi: 10.1155/2020/4946902. eCollection 2020.

Purified Astaxanthin from *Haematococcus pluvialis* Promotes Tissue Regeneration by Reducing Oxidative Stress and the Secretion of Collagen *In Vitro* and *In Vivo*

[Hsin-Yu Chou](#)^{1,2}, [Dik-Lung Ma](#)³, [Chung-Hang Leung](#)⁴, [Chien-Chih Chiu](#)⁵, [Tzyh-Chyuan Hour](#)^{2,6}, [Hui-Min David Wang](#)^{1,7,8,9,10}

PMID: 32832000 PMCID: [PMC7424503](#) DOI: [10.1155/2020/4946902](#) [Free PMC article](#)

Abstract

Intracellular reactive apoptosis and reactive oxygen species (ROS) play a crucial role in ultraviolet- (UV-) induced inflammation and aging reaction in human dermal tissues. This study determines the mechanism by which *Haematococcus pluvialis* extracts (HPE) and purified astaxanthin (HPA) to promote skin regeneration in the injured tissue *in vitro* and *in vivo*. The results show that HPE and HPA decrease the DNA damage and promote the secretion of collagen from the human normal fibroblast cell line (Hs68) in a dose-dependent manner. UV irradiation and HPA reduce oxidative stress damage due to phorbol-12-myristate-13-acetate (PMA). When skin cells are injured by free radicals, cells undergo a programmed cellular death. Cellular apoptotic death is determined using annexin V-fluorescein isothiocyanate (FITC)/propidium iodide (PI) double staining to verify that there is no cell membrane asymmetry and that the nuclear membrane is broken. Inflammatory symptoms and apoptotic injuries to experimental rats in a group that is treated with HPA treated are decreased in a dose-dependent manner after UVB exposure (300 mJ/cm²) for 15 min *in vivo*, compared to the vehicle control group. These positive results show that HPA repairs UVB-triggered skin tissue injury and aging by conducting electrons out of cells to maintain a low level of oxidative stress so that collagen is synthesized *in vitro* and *in vivo*.

Astaxanthin improves dermatitis in a mouse model of atopic dermatitis (a common chronic inflammatory skin disease).

[PLoS One](#). 2016 Mar 29;11(3):e0152288. doi: 10.1371/journal.pone.0152288. eCollection 2016.

Efficacy of Astaxanthin for the Treatment of Atopic Dermatitis in a Murine Model.

[Yoshihisa Y](#)¹, [Andoh T](#)², [Matsunaga K](#)¹, [Rehman MU](#)^{1,3}, [Maoka T](#)⁴, [Shimizu T](#)¹.

Author information

Abstract

Atopic dermatitis (AD) is a common chronic inflammatory skin disease associated with various factors, including immunological abnormalities and exposure to allergens. Astaxanthin (AST) is a xanthophyll carotenoid that has recently been demonstrated to have anti-inflammatory effects and to regulate the expression of inflammatory cytokines. Thus, we investigated whether AST could improve the dermatitis and pruritus in a murine model of AD using NC/Nga mice. In addition to a behavioral evaluation, the effects of AST on the AD were determined by the clinical skin severity score, serum IgE level, histological analyses of skin, and by reverse transcription-PCR and Western blotting analyses for the expression of inflammation-related factors. AST (100 mg/kg) or vehicle (olive oil) was orally administered once day and three times a week for 26 days. When compared with vehicle-treated group, the administration of AST significantly reduced the clinical skin severity score. In addition, the spontaneous scratching in AD model mice was reduced by AST administration. Moreover, the serum IgE level was markedly decreased by the oral administration of AST compared to that in vehicle-treated mice. The number of eosinophils, total and degranulated mast cells all significantly decreased in the skin of AST-treated mice compared with vehicle-treated mice. The mRNA and protein levels of eotaxin, MIF, IL-4, IL-5 and L-histidine decarboxylase were significantly decreased in the skin of AST-treated mice compared with vehicle-treated mice. These results suggest that AST improves the dermatitis and pruritus in AD via the regulation of the inflammatory effects and the expression of inflammatory cytokines.

PMID: 27023003 PMCID: [PMC4811408](#)

DOI: [10.1371/journal.pone.0152288](#)

[PubMed - indexed for MEDLINE]

[Free PMC Article](#)

Astaxanthin and beta-carotene but not lycopene prevent against UV-mediated carcinogenesis in mice.

[Nutr Cancer](#). 1998;31(3):212-7.

Radical interception by carotenoids and effects on UV carcinogenesis.

[Black HS](#)¹.

Author information

Abstract

Studies employing time-resolved techniques have shown that beta-carotene, astaxanthin, and lycopene behave quite distinctly with respect to radical quenching and stability, lycopene being the least stable. These results are compatible with the relative effects of the various carotenoids on ultraviolet (UV)-mediated carcinogenesis in mice in which a statistically significant exacerbation by beta-carotene and astaxanthin, but not by lycopene, was observed. Interactions between these carotenoids and vitamin C and E radicals not only provide a chemical basis to explain the failure of beta-carotene to provide benefit in recent clinical trials but suggest that future carotenoid supplementation studies should proceed with caution until carotenoid interactions and radical repair mechanism(s) are elucidated.

PMID:

9795974

[PubMed - indexed for MEDLINE]

Astaxanthin shows additional benefits compared to other carotenoids in hairless mice after UV irradiation.

[Int J Vitam Nutr Res.](#) 1995;65(2):79-86.

Vitamin A status and metabolism of cutaneous polyamines in the hairless mouse after UV irradiation: action of beta-carotene and astaxanthin.

[Savouré N](#), [Briand G](#), [Amory-Touz MC](#), [Combre A](#), [Maudet M](#), [Nicol M](#).

Biochimie Médicale A - Faculté de Médecine de Rennes, France.

Solar radiations (UV A and B) can cause epidermis photoaging and skin cancers. These frequently irreversible effects result from the in situ generation of free radicals. However, it has been noted that nutritional factors can modulate photochemical damage, in particular the common carotenoids present in food, which can be considered as potential prophylactic agents against carcinogenesis. We investigated the effect of UV A and B radiations on the skin of the SKH1 hairless mouse fed a diet either lacking in vitamin A or supplemented with retinol, beta-carotene or astaxanthin. The latter is an oxygenated carotenoid (like canthaxanthin) without provitamin A activity and with strong singlet oxygen quenching ability. After analysing of vitamin status of each group (plasma retinol concentrations and hepatic reserves), we searched for UV-induced modifications of polyamine metabolism by measuring epidermal ornithine decarboxylase (ODC) activity and free polyamines concentration (putrescine, spermidine and spermine). In the basal state without irradiation, differences in ODC activity between groups were nonsignificant; but after UV stimulation, ODC increased markedly in the skin of vitamin A-deficient animals, much more than in other groups. Curiously, the addition of astaxanthin or beta-carotene to the regimen containing retinol reduced the protective effect of retinol alone. Regarding polyamines after irradiation, putrescine was significantly increased in the skin of deficient animals, in parallel with ODC activity. However, astaxanthin had a stronger inhibitory effect on putrescine accumulation than retinol, and decreased spermidine and spermine concentrations: this suggests a specific action on transglutaminases.

Publication Types:

PMID: 7591536 [PubMed - indexed for MEDLINE]

Astaxanthin dose-dependently reduces skin pigmentation.

[Arch Dermatol Res.](#) 2012 Dec;304(10):803-16. doi: 10.1007/s00403-012-1248-y. Epub 2012 May 26.

Abrogating effect of a xanthophyll carotenoid astaxanthin on the stem cell factor-induced stimulation of human epidermal pigmentation.

[Nakajima H¹](#), [Fukazawa K](#), [Wakabayashi Y](#), [Wakamatsu K](#), [Senda K](#), [Imokawa G](#).

Author information

Abstract

We established a model for the stem cell factor (SCF)-associated stimulation of human epidermal equivalent (HEE) pigmentation. The addition of SCF (at 5 nM) gradually stimulated the visible pigmentation of HEEs over 14 days of treatment. A time course study using real-time RT-PCR and western blotting analysis demonstrated that the expression of all melanocyte-specific genes and proteins examined was gradually up-regulated over 7-10 days of treatment with SCF. The addition of astaxanthin (Ax) at concentrations of 1, 4, or 8 μ M markedly abolished the SCF- but not the endothelin (EDN)1-elicited increase in visible pigmentation over 14 days in a dose-dependent manner, with almost complete inhibition at 8 μ M. While no degeneration of the epidermal tissue was visible at day 14 by HE staining, melanin deposition throughout the epidermis was markedly reduced in the Ax-treated HEEs at day 14 compared to untreated controls. Ax significantly reduced the eumelanin content of HEEs to the non-SCF-stimulated level at concentrations of 4 or 8 μ M compared with untreated controls. Real-time RT-PCR and western blotting of Ax-treated HEEs revealed that the SCF-stimulated expression of tyrosinase (TYR), TYR-related protein-1 (TYRP1), and Pmel17, as well as microphthalmia-associated transcription factor (MITF), is significantly suppressed by Ax at the transcriptional and translational levels. Studies using cultured normal human melanocytes revealed that pre-treatment with Ax interrupts the SCF- but not the EDN1-induced stimulation of TYR activity, and there was no direct inhibitory effect of Ax on TYR activity in vitro. These findings indicate that Ax attenuates SCF-stimulated pigmentation by directly interrupting SCF-associated intracellular signaling linkages through increased expression of MITF, which leads to the stimulated expression of melanogenic genes and proteins in a reactive oxygen species depletion-independent mechanism.

PMID:

22639095

[PubMed - indexed for MEDLINE]

Astaxanthin's ability in preventing wrinkles from UV exposure.

Journal of Japanese Cosmetic Science Society VOL.27;NO.4;PAGE.298-303(2003)

Effect of Antioxidant to Inhibit UV-Induced Wrinkles

ARAKANE KUMI

Living organisms are protected from harmful ultraviolet (UV) rays by the ozone layer surrounding the earth. However, depletion of the ozone layer and an increase in the amount of UV rays in sunlight reaching the earth's surface have been recently reported. As a result, social concerns over the effects of UV on living organisms have been increasing year by year. The skin covers the outer surface of the body, and so it is most vulnerable to UV. Because UV-induced wrinkles are prominently observed only in sun-exposed areas, they are apparently caused by chronic damage due to accumulated UV exposure. In addition to a change in appearance (large deep wrinkles), histological changes including thickening of the epidermis and dermis, elastin fiber deposition and decreased collagen fibers are observed as a result of continuous UV irradiation. Many reports indicate the involvement of action of reactive oxygen species in UV-induced wrinkles formation. Reactive oxygen species are known to damage essential elements including collagen and elastin which maintain elasticity and firmness of the skin, and also damage the function of fibroblasts producing these elements. It goes without saying that application of UV-absorbing agents is effective in preventing changes associated with photoaging. It is also reported that antioxidants such as vitamins C, E and iron chelators are effective for photoaging. We demonstrate that reactive oxygen species quenchers play an important role in reduction of UV-induced wrinkles formation using a carotenoid, astaxanthin, which has no pro-vitamin A activity unlike .BETA.-carotene, and a new iron chelator, N-(4-pyridoxylmethylene)-L-serine (PYSer), which consists of biomimetic molecules and effectively suppresses production of hydroxyl radical by chelating iron in skin. The demonstrable and potential roles of antioxidants for suppression of UV-induced wrinkles formation effectively are summarized here.

Astaxanthin shows promise against hyperpigmentation of the skin.

[Int J Mol Sci](#). 2014 May 12;15(5):8293-315. doi: 10.3390/ijms15058293.

Inhibitors of intracellular signaling pathways that lead to stimulated epidermal pigmentation: perspective of anti-pigmenting agents.

[Imokawa G](#)¹, [Ishida K](#)².

Author information

Abstract

Few anti-pigmenting agents have been designed and developed according to their known hyperpigmentation mechanisms and corresponding intracellular signaling cascades. Most anti-pigmenting agents developed so far are mechanistically involved in the interruption of constitutional melanogenic mechanisms by which skin color is maintained at a normal and unstimulated level. Thus, owing to the difficulty of confining topical application to a specific hyperpigmented skin area, potent anti-pigmenting agents capable of attenuating the natural unstimulated pigmentation process have the risk of leading to hypopigmentation. Since intracellular signaling pathways within melanocytes do not function substantially in maintaining normal skin color and are activated only by environmental stimuli such as UV radiation, specifically down-regulating the activation of melanogenesis to the constitutive level would be an appropriate strategy to develop new potent anti-pigmenting agents with a low risk of hypopigmentation. In this article, we review the hyperpigmentation mechanisms and intracellular signaling pathways that lead to the stimulation of melanogenesis. We also discuss a screening and evaluation system to select candidates for new anti-melanogenic substances by focusing on inhibitors of endothelin-1 or stem cell factor-triggered intracellular signaling cascades. From this viewpoint, we show that extracts of the herbs *Withania somnifera* and *Melia toosendan* and the natural chemicals Withaferin A and Astaxanthin are new candidates for potent anti-pigmenting substances that avoid the risk of hypopigmentation.

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24823877

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PMC4057732

Free PMC Article

Astaxanthin taken internally in combination with two other ingredients shows improvements in skin quality in human clinical trial.

Journal of Cosmetic Dermatology Volume 4 Page 277 - December 2005

A novel micronutrient supplement in skin aging: a randomized placebo-controlled double-blind study

Alain Béguin

Summary

Background: Skin aging, a combination of intrinsic and environmentally induced processes, predominantly ultraviolet (UV) light from the sun, results in characteristic tissue alterations, such as the degradation of collagen and the formation of visible fine lines and wrinkles.

Objective To test the efficacy and safety of a novel micronutrient supplement (Estime® containing Natural Astaxanthin and two other ingredients) in skin aging.

Methods A 4-month randomized double-blind controlled study including 40 subjects where the supplement was tested against placebo for 3 months followed by a 1-month supplement-free period for both groups to assess lasting effects. Efficacy measurements included skin surface evaluation, ultrasound measurement of sun-exposed and protected areas of the skin (back of the hand and ventral forearms, respectively), and photographic assessment.

Results All investigated parameters showed a continuous and significant improvement in the active group during the 3 months of supplementation as compared to placebo.

Photographs showed visible improvement of the overall skin appearance and reduction of fine lines. Ultrasound measurements showed an increase in dermis density of up to 78% in the active group ($P < 0.0001$). The final assessment after 1 month without supplementation showed no further improvements, but a slight decrease was observed in most improved parameters. No treatment-related side effects were reported.

Conclusion The study demonstrated that the supplement appears to be effective and safe as an oral supplement to protect the skin and support its repair process.

Recommendations are made for further evaluations.

Astaxanthin combined with two other ingredients and used both internally and topically shows improvements in skin quality in human clinical trial.

(Excerpt from Nutrition Business Journal, December 2004)

Beauty clinical: Astaxanthin with Omega 3 and Marine Glycosaminoglycans

Alain Thibodeau, Director of Scientific Affairs for Atrium Biotechnologies Inc. in Quebec, Canada published results of a blinded parallel group clinical trial on topical and supplemental forms of a product they call MRT2 (Matrix Rejuvenation Technology 2). The trial was done using both a topical product containing marine glycosaminoglycans and a supplement containing marine glycosaminoglycans, astaxanthin and omega-3 fatty acids. The trial involved 100 subjects.

Significant improvements were measured in skin hydration and elasticity. Skin appearance (including skin tone, fine lines and sallowness) also showed benefits, with the strongest improvements made in subjects using both the supplement and the topical products.

“We can demonstrate a synergistic activity between the topical product and the dietary supplement...The topical product works. The supplement works as well, but you get much better results from using both” said Thibodeau.

Astaxanthin protects against UV-induced inflammation and inhibits the apoptosis of keratinocytes.

[Exp Dermatol](#). 2014 Mar;23(3):178-83. doi: 10.1111/exd.12347.

Astaxanthin, a xanthophyll carotenoid, inhibits ultraviolet-induced apoptosis in keratinocytes.

[Yoshihisa Y¹](#), [Rehman MU](#), [Shimizu T](#).

Author information

Abstract

Intra-cellular reactive nitrogen/oxygen species and apoptosis play important roles in ultraviolet (UV)-induced inflammatory responses in the skin. Astaxanthin (AST), a xanthophyll carotenoid, exhibits diverse clinical benefits. The protective effects of AST against UV-induced apoptosis were investigated in the present study. Astaxanthin (5 μm) caused a significant decrease in the protein content and the mRNA levels of inducible nitric oxide (iNOS) and cyclooxygenase (COX)-2, and decreased the release of prostaglandin E2 from HaCaT keratinocytes after UVB (20 mJ/cm^2) or UVC (5 mJ/cm^2) irradiation. No significant protective effects against UV-induced reactive oxygen species (ROS) were observed in AST-pretreated cells. Astaxanthin caused a significant inhibition of UV-irradiation-induced apoptosis, as evidence by a DNA fragmentation assay. Furthermore, we found that the treatment with AST caused a reduction in the UVB- or UVC-induced protein and mRNA expression of macrophage migration inhibitory factor (MIF), IL-1 β and TNF- α in HaCaT keratinocytes. These results suggest that AST effectively protects against UV-induced inflammation by decreasing iNOS and COX-2, and thereby inhibiting the apoptosis of keratinocytes.

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KEYWORDS:

apoptosis; astaxanthin; keratinocyte; reactive oxygen species; ultraviolet

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[PubMed - indexed for MEDLINE]

Astaxanthin potentially offers greater antioxidant protection against premature signs of aging than other commonly used cosmetic ingredients.

Photoprotective Effect of Astaxanthin Applied to the Skin

Arakane, K. 2002. KOSE Corporation

Reactive oxygen species generated by exposing the skin to sunlight are responsible for sunburn, lipid peroxidation and degenerative changes in dermal connective tissues. This causes premature aging of the skin.

A researcher from a Japanese company called KOSE Corporation compared astaxanthin to other commonly used ingredients in cosmetics that are thought to protect the skin from the damaging effects of sunlight. He found that astaxanthin potentially offers greater antioxidant protection against premature signs of aging.

Astaxanthin is a superior carotenoid to prevent photo-aging in topical applications.

Journal of Japanese Cosmetic Science Society VOL.29;NO.1;PAGE.9-19(2005)

[Preventive Effects of Carotenoids on Photoaging and Its Application for Cosmetics](#)

[MIZUTANI YUKI](#); [SAKATA OSAMU](#); [HOSHINO TAKU](#); [HONDA YOSHIKO](#);
[YAMASHITA MIKA](#); [ARAKANE KUMI](#); [SUZUKI TADASHI](#)

Carotenoids are functional materials and more than 650 kinds of carotenoids are isolated from nature. They have been applied for foods, but most of these carotenoids have not been studied in terms of their effects on skin functions, and because of their instability under light exposure they were hardly used in the cosmetics field until now. Using hairless mice irradiated with UVB to produce photoaged skin, we investigated the inhibitory effect of astaxanthin on wrinkle formation, decrease of skin elasticity, ultrastructural change of dermal collagen fiber bundles and elastic fibers and the level of matrix metalloproteinase-1 (MMP-1) activity. These results indicated that the astaxanthin had the superior protection effect on photoaging as a ROS scavenger. It is well known that carotenoids are easy to decompose during storage by UV light and oxygen. We found that the incorporation of dl- α -tocopherol and α -glucosyl rutin was able to maintain long-term stability of astaxanthin in preparation. This research demonstrated the superior anti-aging effects by carotenoids and this is the first time for carotenoids to be practically applicable to cosmetic formulation.

ASTAXANTHIN IN LIPOSOME SHOWS INCREASED ANTI-INFLAMMATORY EFFECT COMPARED TO FREE ASTAXANTHIN IN ANIMAL DERMATITIS MODEL.

Front Immunol. 2020 Dec 1;11:565285.
doi: 10.3389/fimmu.2020.565285. eCollection 2020.

Improved Anti-Inflammatory Effects of Liposomal Astaxanthin on a Phthalic Anhydride-Induced Atopic Dermatitis Model

[Yong Sun Lee](#)¹, [Seong Hee Jeon](#)¹, [Hyeon Joo Ham](#)¹, [Hee Pom Lee](#)¹, [Min Jong Song](#)², [Jin Tae Hong](#)¹

- PMID: 33335525
- PMCID: [PMC7736086](#)
- DOI: [10.3389/fimmu.2020.565285](#)

Abstract

Previously, we found that astaxanthin (AST) elicited an anti-inflammatory response in an experimental atopic dermatitis (AD) model. However, the use of AST was limited because of low bioavailability and solubility. We hypothesized that liposome formulation of AST could improve this. In this study, we compared the anti-inflammatory and anti-dermatotic effects of liposomal AST (L-AST) and free AST. We evaluated the effect of L-AST on a phthalic anhydride (PA)-induced animal model of AD by analyzing morphological and histopathological changes. We measured the mRNA levels of AD-related cytokines in skin tissue and immunoglobulin E concentrations in the serum. Oxidative stress and transcriptional activities of signal transducer and activator of transcription 3 (STAT3) and nuclear factor (NF)- κ B were analyzed *via* western blotting and enzyme-linked immunosorbent assay. PA-induced dermatitis severity, epidermal thickening, and infiltration of mast cells in skin tissues were ameliorated by L-AST treatment. L-AST suppressed AD-related inflammatory mediators and the inflammation markers, inducible nitric oxide synthase (iNOS) and cyclooxygenase (COX)-2 in PA-induced skin conditions. Oxidative stress and expression of antioxidant proteins, glutathione peroxidase-1 (GPx-1) and heme oxygenase-1 (HO-1), were recovered by L-AST treatment in skin tissues from PA-induced mice. L-AST treatment reduced transcriptional activity of STAT3 and NF- κ B in PA-induced skin tissues. Our results indicate that L-AST could be more effective than free AST for AD therapy.

Astaxanthin topical liposome protects against photo-aging in mice skin.

[Sichuan Da Xue Xue Bao Yi Xue Ban](#). 2018 Sep;49(5):712-715.

[The Preliminary Study on Anti-photodamaged Effect of Astaxanthin Liposomes in Mice Skin].

[Article in Chinese]

[Li FM](#)¹, [Liu Y](#)², [Liao JF](#)¹, [Duan XL](#)¹.

Author information

Abstract

OBJECTIVE: To study the protective effects of astaxanthin liposome (Asx-lipo) on photodamage by UVB in mice skin.

METHODS: 40 C57BL/6J mice were randomly divided into four groups: The blank group (no irradiation, no drug use), model group (UVB light injury group, no drug use), control group (irradiation + astaxanthin), experimental group (irradiation + astaxanthin liposome), each group with 10 mice. Each group was given the corresponding light (the radiation intensity was 2 mW·cm², the time of irradiation was 60 s, 1 times a day for the first 5 days, and 1 times every other day for the next 9 days, 10 times in a total of 2 weeks.) and drug intervention (topically treated with 4 mL 0.2‰ astaxanthin or 4 mL 0.2‰ Asx-lipo 10 min before the irradiation) for two weeks. After that, samples were examined by the following indicators: the histological changes of skin, Ki-67, 8-hydroxy-2'-deoxyguanosine(8-OHdG), superoxide dismutase(SOD) activities and serum matrix metalloproteinase-13 (MMP-13).

RESULTS: HE staining the model group and the control group showed that the dermis became thin, the dermal collagen fibers were long and thin, and the arrangement was loose and disordered. Compared with the blank group, the expression of Ki-67, MMP-13 and 8-OHdG increased and SOD activity decreased, and the differences were statistically significant ($P<0.05$). Compared with the model group, the pathological changes of skin tissues in the experimental group were significantly improved, with decreased expressions of Ki-67, MMP-13 and 8-OHdG and increased SOD activity, and the differences were statistically significant ($P<0.05$).

CONCLUSION: The photodamage of mice skin can be improved by topical Asx-lipo. The mechanism may be related to the strong antioxidation of Asx-lipo.

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KEYWORDS: Astaxanthin liposome ; MMP-13 ; Photodamage ; SOD

PMID: 30378331

Astaxanthin used topically in mice and in-vitro exhibits properties indicating that it may be effective in treating patients with allergic skin conditions.

[Mol Med Rep](#). 2015 Sep;12(3):3632-8. doi: 10.3892/mmr.2015.3892. Epub 2015 Jun 4.

Effects of astaxanthin on dinitrofluorobenzene-induced contact dermatitis in mice.

[Kim H¹](#), [Ahn YT²](#), [Lee GS³](#), [Cho SI¹](#), [Kim JM⁴](#), [Lee C⁵](#), [Lim BK⁶](#), [Ju SA⁷](#), [An WG¹](#).

Author information

Abstract

Astaxanthin (AST) is known to exhibit antioxidative and antitumor properties, therefore, the present study investigated its other potential medical applications. AST was observed to exhibit anti-allergic and anti-inflammatory effects in a dinitrofluorobenzene (DNFB)-induced contact dermatitis (CD) mouse model and RBL-2H3 cell lines. The topical application of AST effectively inhibited the enlargement of ear thickness and increase in weight, which occurred following repeated application of DNFB. Furthermore, topical application of different concentrations of AST inhibited inflammatory hyperplasia, edema, spongiosis, and the infiltration of mononuclear cells and mast cells in the ear tissue. In addition, the levels of TNF- α and IFN- γ produced were decreased by application of AST in vivo, and treatment of RBL-2H3 cells with AST inhibited the release of histamine and β -hexosaminidase in vitro. Taken together, these data suggested that AST may be used to treat patients with allergic skin diseases through a mechanism, which may be associated with that involved in anti-inflammatory or anti-allergic activities.

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26044209

DOI:

[10.3892/mmr.2015.3892](https://doi.org/10.3892/mmr.2015.3892)

[PubMed - indexed for MEDLINE]

Astaxanthin applied topically prevents UV-induced skin damage.

[J Pharm Sci](#). 2012 Aug;101(8):2909-16. doi: 10.1002/jps.23216. Epub 2012 May 24.

Protective effects of topical application of a poorly soluble antioxidant astaxanthin liposomal formulation on ultraviolet-induced skin damage.

[Hama S](#)¹, [Takahashi K](#), [Inai Y](#), [Shiota K](#), [Sakamoto R](#), [Yamada A](#), [Tsuchiya H](#), [Kanamura K](#), [Yamashita E](#), [Kogure K](#).

Author information

Abstract

Astaxanthin (Asx) would be expected to prevent ultraviolet (UV)-induced skin damage, as it is regarded as a potent antioxidative carotenoid in biological membranes. However, it is difficult to administer Asx topically to skin because of its poor water solubility. In this study, we attempted to solve this problem by preparing liposomes containing Asx (Asx-lipo), which were dispersible in the water phase, and therefore, suitable for topical application to the skin. Asx-lipo was shown to have potent scavenging ability against chemiluminescence-dependent singlet oxygen production in the water phase. When Asx-lipo was applied to skin before UV exposure, UV-induced skin thickening was prevented. Interestingly, collagen reduction induced by UV exposure was also prevented by preadministration of Asx-lipo. In addition, topical administration of Asx-lipo containing cationic lipid inhibited melanin production in skin exposed to UV. Consequently, we succeeded in preventing UV-induced skin damage using a topical application of a liposomal formulation containing Asx.

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Astaxanthin applied topically shows wrinkle-reducing effect.

Fragr J VOL.29;NO.12;PAGE.98-103(2001)

[Effects of astaxanthin from Haematococcus pluvialis on human skin. Patch testing Skin repeated application test Effect on wrinkle reduction.](#)

[SEKI TAISUKE; SUEKI HIROHIKO; KONO HIROMI; SUGANUMA KAORU; YAMASHITA EIJI](#)

Astaxanthin is a natural color carotenoid found in salmon, salmon eggs, krill, and crab. Therefore, astaxanthin has been contained in the human diet for a long time. Astaxanthin from krill has been used for cosmetics to suppress post-UVB hyperpigmentation in human skin and food color additives. Recently, astaxanthin from Haematococcus pluvialis is available using new fermentation technology of H. pluvialis and it is used for dietary supplements, food color additives and cosmetics. Effects of astaxanthin from Haematococcus pluvialis on human subjects were tested. No serious adverse effects were observed by patch testing and sequencing applied test on human skin. In a pilot study, the skin repeated application test of cream containing astaxanthin on human skin showed the visual wrinkle reduction. The present paper described about patch testing, skin repeated application test, and a pilot study evaluating the wrinkle reduction effect on human skin.

Astaxanthin as a cosmetic ingredient.

Carotenoid Science, Vol. 5, p21-4 April 2002 Toyama, Japan

Superior Skin Protection via Astaxanthin

Kumi Arakane

It has been believed for a long time that the skin exists only for the purpose of merely protecting our body by physically shielding it from outside factors. But in recent years, along with the radical progress in the field of dermatological science studies, it is known that the skin does actually indicate various responses and accept acute and chronic damages under UV irradiation. According to the enthusiastic studies to clarify the mechanism leading to the skin damages, nowadays the reactive oxygen species generated by UV irradiation is considered to be an important factor mediating photo-induced skin damages. Accumulation skin damages by reactive oxygen species such' as lipid peroxidation, sunburn and degenerative changes in dermal connective tissues induce the skin aging. To protect skin from reactive oxygen species, many cosmetics contain nowadays both naturally occurring molecules and synthetic compounds as antioxidant. However, B-carotene was the only carotenoid for cosmetics among more than 600 carotenoids which had been isolated from nature, until astaxanthin from Antarctic krill was approved for cosmetics in 1997. In this paper, I would like to show the possibility of astaxanthin as a cosmetic ingredient and the useful formula for maintaining the stability of astaxanthin in the preparation.

TOPICAL ASTAXANTHIN FORMULATIONS SHOW ANTIOXIDANT PROPERTIES AND HAVE POTENTIAL FOR ANTI-AGING PRODUCTS.

J Cosmet Dermatol. 2019 Feb;18(1):242-250.

doi: 10.1111/jocd.12665. Epub 2018 May 10.

Antioxidant properties evaluation of topical astaxanthin formulations as anti-aging products

[Bilge Eren¹](#), [Sakine Tuncay Tanrıverdi¹](#), [Fadime Aydın Köse²](#), [Özgen Özer¹](#)

PMID: 29745467 DOI: [10.1111/jocd.12665](https://doi.org/10.1111/jocd.12665)

Abstract

Background: The reactive oxygen species lead to skin aging via oxidative damage that are induced by UV radiation. Therefore, topical formulations which have antioxidant effect could reduce aging level. Astaxanthin is an antioxidant substance.

Aims: The aim of this study was to investigate antioxidant activity and cytotoxicity potential of the astaxanthin-loaded gel formulations.

Methods: Astaxanthin-loaded oleoresin and algae extract were used as natural active materials. The lipogel and hydrogel of these natural materials were prepared as anti-aging formulations. The formulations were characterized via parameters such as, pH, rheological analysis, mechanical properties, and stability. And also in vitro release experiments of the formulations were carried out. The antioxidant activity and cytotoxicity test were performed.

Results: The results of characterization studies confirmed the formulations suitable for topical application. After 24 hours, 99 µg, 88.3 µg, 403 µg, and 234.8 µg of astaxanthin released through oleoresin lipogel, oleoresin hydrogel, algae extract lipogel, and algae extract hydrogel, respectively. It was found by the cytotoxicity tests that astaxanthin is more proliferative in lipogel formulations compared to hydrogel formulations. And finally, the highest antioxidant activity was found in the algae extract hydrogel and algae extract lipogel formulation, respectively (P < .05).

Conclusions: Topical formulations of astaxanthin-loaded oleoresin and algae extract were prepared successfully. At the same time, according to antioxidant activity and release studies, algae extract loaded could be suggested as topical anti-aging formulations.

Astaxanthin applied topically shows promise against allergic skin diseases.

[Mol Med Rep](#). 2015 Jun 4. doi: 10.3892/mmr.2015.3892. [Epub ahead of print]

Effects of astaxanthin on dinitrofluorobenzene-induced contact dermatitis in mice.

[Kim H¹](#), [Ahn YT²](#), [Lee GS³](#), [Cho SI¹](#), [Kim JM⁴](#), [Lee C⁵](#), [Lim BK⁶](#), [Ju SA⁷](#), [An WG¹](#).

Author information

Abstract

Astaxanthin (AST) is known to exhibit antioxidative and antitumor properties, therefore, the present study investigated its other potential medical applications. AST was observed to exhibit anti-allergic and anti-inflammatory effects in a dinitrofluorobenzene (DNFB)-induced contact dermatitis (CD) mouse model and RBL-2H3 cell lines. The topical application of AST effectively inhibited the enlargement of ear thickness and increase in weight, which occurred following repeated application of DNFB. Furthermore, topical application of different concentrations of AST inhibited inflammatory hyperplasia, edema, spongiosis, and the infiltration of mononuclear cells and mast cells in the ear tissue. In addition, the levels of TNF- α and IFN- γ produced were decreased by application of AST *in vivo*, and treatment of RBL-2H3 cells with AST inhibited the release of histamine and β -hexosaminidase *in vitro*. Taken together, these data suggested that AST may be used to treat patients with allergic skin diseases through a mechanism, which may be associated with that involved in anti-inflammatory or anti-allergic activities.

PMID:

26044209

[PubMed - as supplied by publisher]

Astaxanthin combined with soy oil shows UV photo-aging protective and anti-wrinkle potential in mice.

[Int J Mol Sci](#). 2017 Mar 22;18(3). pii: E682. doi: 10.3390/ijms18030682.

A Combination of Soybean and Haematococcus Extract Alleviates Ultraviolet B-Induced Photoaging.

[Shin J](#)¹, [Kim JE](#)², [Pak KJ](#)³, [Kang JI](#)⁴, [Kim TS](#)⁵, [Lee SY](#)⁶, [Yeo IH](#)⁷, [Park JH](#)⁸, [Kim JH](#)⁹, [Kang NJ](#)¹⁰, [Lee KW](#)^{11,12}.

Author information

Abstract

Soybean-derived isoflavones have been investigated for their preventative effects against UV-induced symptoms of skin damage including wrinkle formation and inflammation. Haematococcus pluvialis is a freshwater species of Chlorophyta that contains high concentrations of the natural carotenoid pigment astaxanthin. Astaxanthin is known to be involved in retinoic acid receptor (RAR) signaling and previously been associated with the inhibition of activator protein (AP)-1 dependent transcription. Based on previous studies, we hypothesized that a combination of soy extract (SE) and Haematococcus extract (HE) may prevent UVB-induced photoaging through specific signaling pathways, as measured by UVB-induced wrinkling on hairless mice skin and expression changes in human dermal fibroblasts (HDFs). The 1:2 ratio of SE and HE mixture (SHM) showed the optimal benefit in vivo. SHM was found to inhibit wrinkle formation via the downregulation of matrix metalloproteinase (MMP)-1 mRNA and protein expression. SHM also inhibited mitogen-activated protein kinase (MAPK) phosphorylation and the transactivation of AP-1 which plays an important role in regulating MMP expression. These results highlight the potential for SHM to be developed as a therapeutic agent to prevent UVB-induced skin wrinkling.

KEYWORDS:

Haematococcus; photoaging; soybean; ultraviolet B

PMID: 28327532

PMCID: [PMC5372692](#)

DOI: [10.3390/ijms18030682](#)

[Indexed for MEDLINE]

[Free PMC Article](#)

Astaxanthin combined with Panax ginseng extract reduces DNA damage induced by UV exposure in vitro.

[Anim Cells Syst \(Seoul\)](#). 2018 Oct 9;22(6):400-406. doi: 10.1080/19768354.2018.1523806. eCollection 2018.

Protective effects of ginsenoside Rg2 and astaxanthin mixture against UVB-induced DNA damage.

[Chung YH¹](#), [Jeong SA¹](#), [Choi HS¹](#), [Ro S²](#), [Lee JS³](#), [Park JK¹](#).

Author information

Abstract

Ultraviolet B (UVB) radiation induces skin damage, skin matrix degradation, and wrinkle formation through photochemical reaction and oxidative stress. Therefore, protecting the skin from UVB can prevent skin aging. In this study, we investigated the effects of a mixture (RA) of Rg2, a ginsenoside, and astaxanthin, an antioxidant, on the responses of HaCaT cells exposed to UVB (700 J/m²). The cells were incubated for 24 h after UVB exposure and cell viability was determined by MTT assay. UVB decreased cell viability by 60% compared to that of untreated control cells, whereas RA increased cell viability in a concentration-dependent manner, and this increase was significantly higher than that in the single treatment groups. Further, UVB increased the levels of DNA lesions such as cyclobutane pyrimidine dimer (CPD) and 8-hydroxyguanine (8-OHdG). Conversely, RA decreased both CPD and 8-OHdG levels in a concentration-dependent manner. UVB exposure also increased phosphorylation of ataxia-telangiectasia mutated (ATM) protein kinase and p53 and subsequently increased the levels of GADD45 α , p21, and matrix metalloproteinases (MMPs)-3, -9, and -13. Additionally, UVB exposure decreased the level of COL1A1. However, RA treatment decreased the levels of p-ATM, p-p53, GADD45 α , p21, MMP-3, -9, and -13 and increased the level of COL1A1 in a concentration-dependent manner. These results suggest that RA reduces UVB-induced cytotoxicity and genotoxicity through up-regulation of DNA repair via the combined effects of Rg2 and astaxanthin.

KEYWORDS:

Astaxanthin; Ginsenoside Rg2; HaCaT cells; Ultraviolet B

PMID: 30533262

PMCID: [PMC6282468](#)

DOI: [10.1080/19768354.2018.1523806](#)

[Free PMC Article](#)

Astaxanthin exerts anti-inflammatory activity in eczema model in rodents and in-vitro.

[Exp Dermatol](#). 2018 Apr;27(4):378-385. doi: 10.1111/exd.13437.

Anti-inflammatory effect of astaxanthin in phthalic anhydride-induced atopic dermatitis animal model.

[Park JH](#)^{1,2}, [Yeo IJ](#)¹, [Han JH](#)¹, [Suh JW](#)³, [Lee HP](#)¹, [Hong JT](#)¹.

Author information

Abstract

In this study, we investigated anti-dermatitic effects of astaxanthin (AST) in phthalic anhydride (PA)-induced atopic dermatitis (AD) animal model as well as in vitro model. AD-like lesion was induced by the topical application of 5% PA to the dorsal skin or ear of Hos:HR-1 mouse. After AD induction, 100 μ L of 1 mg/mL and 2 mg/mL of AST (10 μ g or 20 μ g/cm²) was spread on the dorsum of ear or back skin three times a week for four weeks. We evaluated dermatitis severity, histopathological changes and changes in protein expression by Western blotting for inducible nitric oxide synthase (iNOS), cyclooxygenase-2 (COX-2) and nuclear factor- κ B (NF- κ B) activity. We also measured tumor necrosis factor- α (TNF- α), interleukin-1 β (IL-1 β), interleukin-6 (IL-6) and immunoglobulin E (IgE) concentration in the blood of AD mice by enzyme-linked immunosorbent assay (ELISA). AST treatment attenuated the development of PA-induced AD. Histological analysis showed that AST inhibited hyperkeratosis, mast cells and infiltration of inflammatory cells. AST treatment inhibited expression of iNOS and COX-2, and NF- κ B activity as well as release of TNF- α , IL-1 β , IL-6 and IgE. In addition, AST (5, 10 and 20 μ M) potently inhibited lipopolysaccharide (LPS) (1 μ g/mL)-induced nitric oxide (NO) production, expression of iNOS and COX-2 and NF- κ B DNA binding activities in RAW 264.7 macrophage cells. Our data demonstrated that AST could be a promising agent for AD by inhibition of NF- κ B signalling.

KEYWORDS:

IgE; NF- κ B; astaxanthin; atopic dermatitis; cytokine; skin inflammation

PMID: 28887839

DOI: [10.1111/exd.13437](https://doi.org/10.1111/exd.13437)

ASTAXANTHIN SHOWS PROPENSITY TO ALLEVIATE DRY SKIN AND INCREASE SKIN MOISTURE IN THIS IN-VITRO STUDY.

Life (Basel). 2020 Sep 11;10(9):193.
doi: 10.3390/life10090193.

Effect of Astaxanthin on the Expression and Activity of Aquaporin-3 in Skin in an In-Vitro Study

[Nobutomo Ikarashi](#)¹, [Risako Kon](#)¹, [Chika Nagoya](#)², [Airi Ishikura](#)², [Yuri Sugiyama](#)², [Jiro Takahashi](#)³, [Kiyoshi Sugiyama](#)⁴

PMID: 32932769 PMCID: [PMC7554991](#) DOI: [10.3390/life10090193](#) [Free PMC article](#)

Abstract

Astaxanthin (3,3'-dihydroxy- β,β -carotene-4,4'-dione) is a red lipophilic pigment with strong antioxidant action. Oral or topical administration of astaxanthin has been reported to improve skin function, including increasing skin moisture. In this study, we examined the mechanism by which astaxanthin improves skin function by focusing on the water channel aquaporin-3 (AQP3), which plays important roles in maintaining skin moisture and function. When astaxanthin was added to PHK16-0b or HaCaT cells, the mRNA expression level of AQP3 increased significantly in a concentration-dependent manner in both cell lines. The AQP3 protein expression level was also confirmed to increase when astaxanthin was added to HaCaT cells. Similarly, when astaxanthin was added to 3D human epidermis model EpiSkin, AQP3 expression increased. Furthermore, when glycerol and astaxanthin were simultaneously added to EpiSkin, glycerol permeability increased significantly compared with that observed for the addition of glycerol alone. We demonstrated that astaxanthin increases AQP3 expression in the skin and enhances AQP3 activity. This result suggests that the increased AQP3 expression in the skin is associated with the increase in skin moisture by astaxanthin. Thus, we consider astaxanthin useful for treating dry skin caused by decreased AQP3 due to factors such as diabetes mellitus and aging.

Astaxanthin shows potential in skin wound healing in-vitro.

[Nutr Res Pract](#). 2017 Aug;11(4):275-280. doi: 10.4162/nrp.2017.11.4.275. Epub 2017 Jul 21.

Astaxanthin induces migration in human skin keratinocytes via Rac1 activation and RhoA inhibition.

[Ritto D](#)¹, [Tanasawet S](#)², [Singhorn S](#)¹, [Klaypradit W](#)³, [Hutamekalin P](#)⁴, [Tipmanee V](#)⁵, [Sukketsiri W](#)¹.

Author information

Abstract

BACKGROUND/OBJECTIVES: Re-epithelialization has an important role in skin wound healing. Astaxanthin (ASX), a carotenoid found in crustaceans including shrimp, crab, and salmon, has been widely used for skin protection. Therefore, we investigated the effects of ASX on proliferation and migration of human skin keratinocyte cells and explored the mechanism associated with that migration.

MATERIAL/METHOD: HaCaT keratinocyte cells were exposed to 0.25-1 µg/mL of ASX. Proliferation of keratinocytes was analyzed by using MTT assays and flow cytometry. Keratinocyte migration was determined by using a scratch wound-healing assay. A mechanism for regulation of migration was explored via immunocytochemistry and western blot analysis.

RESULTS: Our results suggest that ASX produces no significant toxicity in human keratinocyte cells. Cell-cycle analysis on ASX-treated keratinocytes demonstrated a significant increase in keratinocyte cell proliferation at the S phase. In addition, ASX increased keratinocyte motility across the wound space in a time-dependent manner. The mechanism by which ASX increased keratinocyte migration was associated with induction of filopodia and formation of lamellipodia, as well as with increased Cdc42 and Rac1 activation and decreased RhoA activation.

CONCLUSIONS: ASX stimulates the migration of keratinocytes through Cdc42, Rac1 activation and RhoA inhibition. ASX has a positive role in the re-epithelialization of wounds. Our results may encourage further *in vivo* and clinical study into the development of ASX as a potential agent for wound repair.

KEYWORDS: Carotenoids; cell movement; re-epithelialization; wound healing

PMID: 28765773

PMCID: [PMC5537536](#)

DOI: [10.4162/nrp.2017.11.4.275](#)

[Free PMC Article](#)

Astaxanthin is effective in accelerating skin wound healing in mice.

[Clin Cosmet Investig Dermatol](#). 2017 Jul 13;10:259-265. doi: 10.2147/CCID.S142795. eCollection 2017.

Effect of astaxanthin on cutaneous wound healing.

[Meephansan J](#)¹, [Rungjang A](#)¹, [Yingmema W](#)², [Deenonpoe R](#)³, [Ponnikorn S](#)³.

Author information

Abstract

Wound healing consists of a complex series of convoluted processes which involve renewal of the skin after injury. ROS are involved in all phases of wound healing. A balance between oxidative and antioxidative forces is necessary for a favorable healing outcome. Astaxanthin, a member of the xanthophyll group, is considered a powerful antioxidant. In this study, we investigated the effect of topical astaxanthin on cutaneous wound healing. Full-thickness dermal wounds were created in 36 healthy female mice, which were divided into a control group and a group receiving 78.9 μ M topical astaxanthin treatment twice daily for 15 days. Astaxanthin-treated wounds showed noticeable contraction by day 3 of treatment and complete wound closure by day 9, whereas the wounds of control mice revealed only partial epithelialization and still carried scabs. Wound healing biological markers including Col1A1 and bFGF were significantly increased in the astaxanthin-treated group since day 1. Interestingly, the oxidative stress marker iNOS showed a significantly lower expression in the study. The results indicate that astaxanthin is an effective compound for accelerating wound healing.

KEYWORDS:

antioxidant; astaxanthin; reactive oxygen species; wound healing

PMID: 28761364

PMCID: [PMC5516620](#)

DOI: [10.2147/CCID.S142795](#)

[Free PMC Article](#)

Astaxanthin in eye drops prevents UV damage in mice.

[Mol Vis.](#) 2012;18:455-64. Epub 2012 Feb 14.

Amelioration of ultraviolet-induced photokeratitis in mice treated with astaxanthin eye drops.

[Lennikov A¹](#), [Kitaichi N](#), [Fukase R](#), [Murata M](#), [Noda K](#), [Ando R](#), [Ohguchi T](#), [Kawakita T](#), [Ohno S](#), [Ishida S](#).

Author information

Abstract

PURPOSE:

Ultraviolet (UV) acts as low-dose ionizing radiation. Acute UVB exposure causes photokeratitis and induces apoptosis in corneal cells. Astaxanthin (AST) is a carotenoid, present in seafood, that has potential clinical applications due to its high antioxidant activity. In the present study, we examined whether topical administration of AST has preventive and therapeutic effects on UV-photokeratitis in mice.

METHODS:

C57BL/6 mice were administered with AST diluted in polyethylene glycol (PEG) in instillation form (15 μ l) to the right eye. Left eyes were given vehicle alone as controls. Immediately after the instillation, the mice, under anesthesia, were irradiated with UVB at a dose of 400 mJ/cm². Eyeballs were collected 24 h after irradiation and stained with H&E and TUNEL. In an in vitro study, mouse corneal epithelial (TKE2) cells were cultured with AST before UV exposure to quantify the UV-derived cytotoxicity.

RESULTS:

UVB exposure induced cell death and thinning of the corneal epithelium. However, the epithelium was morphologically well preserved after irradiation in AST-treated corneas. Irradiated corneal epithelium was significantly thicker in eyes treated with AST eye drops, compared to those treated with vehicles ($p < 0.01$), in a dose-dependent manner. Significantly fewer apoptotic cells were observed in AST-treated eyes than controls after irradiation ($p < 0.01$). AST also reduced oxidative stress in irradiated corneas. The in vitro study showed less cytotoxicity of TKE2 cells in AST-treated cultures after UVB-irradiation ($p < 0.01$). The cytoprotective effect increased with the dose of AST.

CONCLUSIONS:

Topical AST administration may be a candidate treatment to limit the damages by UV irradiation with wide clinical applications.

PMID:

22393271

[PubMed - indexed for MEDLINE]

PMCID: PMC3291518

[Free PMC Article](#)

Astaxanthin reviewed for potential health benefits including prevention of skin diseases.

[Mol Nutr Food Res.](#) 2011 Jan;55(1):150-65. doi: 10.1002/mnfr.201000414. Epub 2010 Nov 18.

Potential health-promoting effects of astaxanthin: a high-value carotenoid mostly from microalgae.

[Yuan JP](#)¹, [Peng J](#), [Yin K](#), [Wang JH](#).

Author information

Abstract

The ketocarotenoid astaxanthin can be found in the microalgae *Haematococcus pluvialis*, *Chlorella zofingiensis*, and *Chlorococcum* sp., and the red yeast *Phaffia rhodozyma*. The microalga *H. pluvialis* has the highest capacity to accumulate astaxanthin up to 4-5% of cell dry weight. Astaxanthin has been attributed with extraordinary potential for protecting the organism against a wide range of diseases, and has considerable potential and promising applications in human health. Numerous studies have shown that astaxanthin has potential health-promoting effects in the prevention and treatment of various diseases, such as cancers, chronic inflammatory diseases, metabolic syndrome, diabetes, diabetic nephropathy, cardiovascular diseases, gastrointestinal diseases, liver diseases, neurodegenerative diseases, eye diseases, skin diseases, exercise-induced fatigue, male infertility, and HgCl₂-induced acute renal failure. In this article, the currently available scientific literature regarding the most significant activities of astaxanthin is reviewed.

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PMID:

21207519

[PubMed - indexed for MEDLINE]

Astaxanthin reviewed for potential health benefits including UV-light protection.

[Trends Biotechnol.](#) 2003 May;21(5):210-6.

Haematococcus astaxanthin: applications for human health and nutrition.

[Guerin M¹](#), [Huntley ME](#), [Olaizola M](#).

Author information

Abstract

The carotenoid pigment astaxanthin has important applications in the nutraceutical, cosmetics, food and feed industries. *Haematococcus pluvialis* is the richest source of natural astaxanthin and is now cultivated at industrial scale. Astaxanthin is a strong coloring agent and a potent antioxidant - its strong antioxidant activity points to its potential to target several health conditions. This article covers the antioxidant, UV-light protection, anti-inflammatory and other properties of astaxanthin and its possible role in many human health problems. The research reviewed supports the assumption that protecting body tissues from oxidative damage with daily ingestion of natural astaxanthin might be a practical and beneficial strategy in health management.

PMID:

12727382

[PubMed - indexed for MEDLINE]

Astaxanthin's reviewed as a beauty from within supplement.

Fragr J VOL.34;NO.3;PAGE.21-27(2006)

[Biological activities of astaxanthin and its cosmeceutical application.](#)
[YAMASHITA EIJI](#)

The present review covers cosmeceutical benefits of astaxanthin that is one of the most abundant carotenoids in nature, particularly in marine based life. The anti-oxidant properties of astaxanthin without any pro-oxidative nature working at cell membrane and cosmeceutical effects such as anti-hyperpigmentation, anti-photoaging, melanin inhibition and visual wrinkle reduction by topical or internal use and one of the action mechanisms of astaxanthin on NF-kB dependent inflammation are introduced. And current and future cosmeceutical applications of astaxanthin particularly from a green microalgae *Haematococcus pluvialis* that is the most ideal source in the earth are discussed describing actual examples of astaxanthin containing skin care products in Japanese market.

Astaxanthin's benefits reviewed including anti-aging.

[Altern Med Rev.](#) 2011 Dec;16(4):355-64.

Astaxanthin, cell membrane nutrient with diverse clinical benefits and anti-aging potential.

[Kidd P¹.](#)

Author information

Abstract

Astaxanthin, a xanthophyll carotenoid, is a nutrient with unique cell membrane actions and diverse clinical benefits. This molecule neutralizes free radicals or other oxidants by either accepting or donating electrons, and without being destroyed or becoming a pro-oxidant in the process. Its linear, polar-nonpolar-polar molecular layout equips it to precisely insert into the membrane and span its entire width. In this position, astaxanthin can intercept reactive molecular species within the membrane's hydrophobic interior and along its hydrophilic boundaries. Clinically, astaxanthin has shown diverse benefits, with excellent safety and tolerability. In double-blind, randomized controlled trials (RCTs), astaxanthin lowered oxidative stress in overweight and obese subjects and in smokers. It blocked oxidative DNA damage, lowered C-reactive protein (CRP) and other inflammation biomarkers, and boosted immunity in the tuberculin skin test. Astaxanthin lowered triglycerides and raised HDL-cholesterol in another trial and improved blood flow in an experimental microcirculation model. It improved cognition in a small clinical trial and boosted proliferation and differentiation of cultured nerve stem cells. In several Japanese RCTs, astaxanthin improved visual acuity and eye accommodation. It improved reproductive performance in men and reflux symptoms in *H. pylori* patients. In preliminary trials it showed promise for sports performance (soccer). In cultured cells, astaxanthin protected the mitochondria against endogenous oxygen radicals, conserved their redox (antioxidant) capacity, and enhanced their energy production efficiency. The concentrations used in these cells would be attainable in humans by modest dietary intakes. Astaxanthin's clinical success extends beyond protection against oxidative stress and inflammation, to demonstrable promise for slowing age-related functional decline.

PMID:

22214255

[PubMed - indexed for MEDLINE]

Free full text

Astaxanthin reviewed as a preventer of skin photoaging.

[Photochem Photobiol.](#) 2018 Oct 19. doi: 10.1111/php.13039. [Epub ahead of print]

The Xanthophyll Carotenoid Astaxanthin has Distinct Biological Effects to Prevent the Photoaging of the Skin Even by its Postirradiation Treatment.

[Imokawa G](#)^{1,2}.

Author information

Abstract

Exposure of human skin to ultraviolet (UV) radiation causes significant damage to that tissue. The effects of UV on the skin mainly include acute inflammation (erythema/edema) and abnormal keratinization wherein prostaglandin E₂ (produced by cyclooxygenase-2), interleukin-8 and transglutaminase 1 (a major regulatory factor of keratinization) play pivotal roles. Later phases of UV-induced skin reactions include hyperpigmentation, wrinkle formation and carcinogenesis, the former two being associated with the UVB-induced production and/or secretion of endothelin-1, stem cell factor and granulocyte-macrophage colony-stimulating factor by keratinocytes in the epidermis. Those paracrine factors then stimulate expression of the critical melanogenic enzyme tyrosinase by melanocytes in the epidermis and increase expression of neprilysin, an enzyme that degrades elastin, by fibroblasts in the dermis. This review summarizes the biological effects of the xanthophyll carotenoid astaxanthin, which prevents UV-induced cutaneous inflammation, abnormal keratinization and wrinkling as well as pigmentation of the skin even by its postirradiation treatment.

PMID: 30338860

DOI: [10.1111/php.13039](https://doi.org/10.1111/php.13039)

Astaxanthin reviewed as a preventer of skin photo-aging Part 2.

[Photochem Photobiol.](#) 2018 Oct 13. doi: 10.1111/php.13034. [Epub ahead of print]

Intracellular Signaling Mechanisms Involved in the Biological Effects of the Xanthophyll Carotenoid Astaxanthin to Prevent the Photo-aging of the Skin in a Reactive Oxygen Species Depletion-independent Manner: The Key Role of Mitogen and Stress-activated Protein Kinase 1.

[Imokawa G](#)^{1,2}.

[Author information](#)

Abstract

In the first review, we summarized the biological effects of the xanthophyll carotenoid astaxanthin (AX) to prevent UV-induced cutaneous inflammation, abnormal keratinization, pigmentation, and wrinkling in a manner independent of the depletion of reactive oxygen species. In this manuscript, we review what is known about the intracellular signaling mechanisms that are involved in those effects in keratinocytes and in melanocytes. Our research has characterized the intracellular stress signaling mechanism(s) that are involved in the up-regulated expression of genes encoding cyclooxygenase (COX2), interleukin (IL)-8, granulocyte macrophage colony stimulatory factor (GM-CSF), and transglutaminase (TGase)1 in UVB-exposed keratinocytes as well as in the stimulated transcription and/or translation of melanogenic factors, including microphthalmia-associated transcription factor (MITF), in stem cell factor (SCF)-treated melanocytes. The results reveal that while the expression of COX2, IL-8, GM-CSF, and TGase1 stimulated by UVB is due to effects primarily via the NFκB pathway, that stimulation can be abrogated by specifically interrupting the p38/MSK1/NFκBp65Ser276 axis. Further, the stimulation of melanogenesis by SCF can be inhibited by disrupting the phosphorylation of MSK1 via the p38, MSK1, CREB, and MITF axis. The sum of these findings provides new evidence for the interruption of ROS depletion independent-signaling by antioxidants.

PMID: 30317634

DOI: [10.1111/php.13034](https://doi.org/10.1111/php.13034)

ASTAXANTHIN: REVIEW OF SKIN HEALTH HUMAN CLINICAL RESEARCH.

J Diet Suppl. 2021;18(2):169-182.

doi: 10.1080/19390211.2020.1739187. Epub 2020 Mar 23.

Effects of Astaxanthin Supplementation on Skin Health: A Systematic Review of Clinical Studies

[Qin Xiang Ng^{1,2}](#), [Michelle Lee Zhi Qing De Deyn³](#), [Wayren Loke¹](#), [Nadine Xinhui Foo¹](#), [Hwei Wuen Chan^{4,5}](#), [Wee Song Yeo^{4,5}](#)

PMID: **32202443** DOI: [10.1080/19390211.2020.1739187](https://doi.org/10.1080/19390211.2020.1739187)

Abstract

Astaxanthin (AST), a naturally-occurring keto-carotenoid found in several species of bacteria and microalgae, has demonstrated diverse biological activities *in vitro* and *in vivo*. There is growing commercial interest in the application of astaxanthin in nutraceuticals and cosmeceuticals, due to its purported photoprotective, DNA repair, antioxidant, and anti-inflammatory benefits. This systematic review therefore aimed to summarize current clinical evidence on the effects of astaxanthin supplementation on skin health. Using the following combinations of broad Major Exploded Subject Headings (MeSH) terms or text words [astaxanthin OR AST OR ASX OR carotenoid OR xanthophyll] AND [skin OR dermat*], a comprehensive search of PubMed, EMBASE, Medline, Clinicaltrials.gov, and Google Scholar databases found a total of eleven clinical studies. There were six randomized, placebo-controlled, double-blind trials, while the rest were prospective, open-label studies. In many of the randomized, controlled trials reviewed, AST supplementation improved skin texture, appearance (wrinkles), and moisture content at the end of the study period. AST also appeared to protect against UV-induced skin damage. No serious adverse events were reported in any of the studies. However, most available studies had a relatively small sample size and were conducted on healthy Japanese females. Many of the studies were also funded by commercial entities, with potential conflicts of interests. This was difficult to account for in our analyses. Overall, there is some clinical data to support the benefits of astaxanthin supplementation (in the range of 3 to 6 mg/d) on skin health, especially for photoaged skin.

ASTAXANTHIN REVIEWED FOR ITS PHOTO-AGING SKIN HEALTH PROPERTIES.

Photochem Photobiol. 2019 Mar;95(2):480-489.

doi: 10.1111/php.13034. Epub 2018 Nov 29.

Intracellular Signaling Mechanisms Involved in the Biological Effects of the Xanthophyll Carotenoid Astaxanthin to Prevent the Photo-aging of the Skin in a Reactive Oxygen Species Depletion-independent Manner: The Key Role of Mitogen and Stress-activated Protein Kinase 1

[Genji Imokawa](#)^{1,2}

PMID: 30317634 DOI: [10.1111/php.13034](https://doi.org/10.1111/php.13034)

Abstract

In the first review, we summarized the biological effects of the xanthophyll carotenoid astaxanthin (AX) to prevent UV-induced cutaneous inflammation, abnormal keratinization, pigmentation, and wrinkling in a manner independent of the depletion of reactive oxygen species. In this manuscript, we review what is known about the intracellular signaling mechanisms that are involved in those effects in keratinocytes and in melanocytes. Our research has characterized the intracellular stress signaling mechanism(s) that are involved in the up-regulated expression of genes encoding cyclooxygenase (COX2), interleukin (IL)-8, granulocyte macrophage colony stimulatory factor (GM-CSF), and transglutaminase (TGase)1 in UVB-exposed keratinocytes as well as in the stimulated transcription and/or translation of melanogenic factors, including microphthalmia-associated transcription factor (MITF), in stem cell factor (SCF)-treated melanocytes. The results reveal that while the expression of COX2, IL-8, GM-CSF, and TGase1 stimulated by UVB is due to effects primarily via the NFκB pathway, that stimulation can be abrogated by specifically interrupting the p38/MSK1/NFκBp65Ser276 axis. Further, the stimulation of melanogenesis by SCF can be inhibited by disrupting the phosphorylation of MSK1 via the p38, MSK1, CREB, and MITF axis. The sum of these findings provides new evidence for the interruption of ROS depletion independent-signaling by antioxidants.

ASTAXANTHIN REVIEWED FOR ITS UV-PROTECTIVE PROPERTIES RELATED TO SKIN HEALTH.

Photochem Photobiol. 2019 Mar;95(2):490-500.

doi: 10.1111/php.13039. Epub 2018 Dec 1.

The Xanthophyll Carotenoid Astaxanthin has Distinct Biological Effects to Prevent the Photoaging of the Skin Even by its Postirradiation Treatment

[Genji Imokawa](#)^{1,2}

- PMID: **30338860**
- DOI: [10.1111/php.13039](https://doi.org/10.1111/php.13039)

Abstract

Exposure of human skin to ultraviolet (UV) radiation causes significant damage to that tissue. The effects of UV on the skin mainly include acute inflammation (erythema/edema) and abnormal keratinization wherein prostaglandin E₂ (produced by cyclooxygenase-2), interleukin-8 and transglutaminase 1 (a major regulatory factor of keratinization) play pivotal roles. Later phases of UV-induced skin reactions include hyperpigmentation, wrinkle formation and carcinogenesis, the former two being associated with the UVB-induced production and/or secretion of endothelin-1, stem cell factor and granulocyte-macrophage colony-stimulating factor by keratinocytes in the epidermis. Those paracrine factors then stimulate expression of the critical melanogenic enzyme tyrosinase by melanocytes in the epidermis and increase expression of neprilysin, an enzyme that degrades elastin, by fibroblasts in the dermis. This review summarizes the biological effects of the xanthophyll carotenoid astaxanthin, which prevents UV-induced cutaneous inflammation, abnormal keratinization and wrinkling as well as pigmentation of the skin even by its postirradiation treatment.

ASTAXANTHIN REVIEWED FOR ITS PHARMACOKINETIC PROPERTIES AND SKIN HEALTH BENEFITS.

J Cosmet Dermatol. 2020 Jan;19(1):22-27.

doi: 10.1111/jocd.13019. Epub 2019 May 29.

Protective effects of astaxanthin on skin: Recent scientific evidence, possible mechanisms, and potential indications

[Kritarth Naman Singh](#)¹, [Saiprasad Patil](#)¹, [Hanmant Barkate](#)¹

- PMID: [31141292](#)
- DOI: [10.1111/jocd.13019](#)

Abstract

Astaxanthin is a naturally occurring ketocarotenoid which has been found to have numerous biological functions, with its strong antioxidant property being the prominent feature. The compound has attracted a great amount of interest with respect to its potential utilization in the betterment of human health. In the recent past, astaxanthin has been extensively studied with respect to its possible effect on skin health, with positive results. Astaxanthin has also shown to have anti-inflammatory, immune-modulating, and DNA repair properties, which have further encouraged its usage to maintain skin health and tackle skin damage. In this review article, we highlight the pharmacokinetic profile of the antioxidant in brief and describe the findings of various recent published research articles which studied the effect of astaxanthin in improvement of skin health. We also mention the possible mechanisms which form the basis of the positive dermatological effects of astaxanthin and the potential indications of the antioxidant molecule in cosmetology and dermatology.

Astaxanthin reviewed for its effects on skin health.

[Nutrients](#). 2018 Apr 22;10(4). pii: E522. doi: 10.3390/nu10040522.

Astaxanthin in Skin Health, Repair, and Disease: A Comprehensive Review.

[Davinelli S](#)¹, [Nielsen ME](#)², [Scapagnini G](#)³.

Author information

Abstract

Astaxanthin, a xanthophyll carotenoid, is a secondary metabolite naturally synthesized by a number of bacteria, microalgae, and yeasts. The commercial production of this pigment has traditionally been performed by chemical synthesis, but the microalga *Haematococcus pluvialis* appears to be the most promising source for its industrial biological production. Due to its collective diverse functions in skin biology, there is mounting evidence that astaxanthin possesses various health benefits and important nutraceutical applications in the field of dermatology. Although still debated, a range of potential mechanisms through which astaxanthin might exert its benefits on skin homeostasis have been proposed, including photoprotective, antioxidant, and anti-inflammatory effects. This review summarizes the available data on the functional role of astaxanthin in skin physiology, outlines potential mechanisms involved in the response to astaxanthin, and highlights the potential clinical implications associated with its consumption.

KEYWORDS:

DNA repair; aging; anti-inflammatory; antioxidant; astaxanthin; clinical trials; immune-enhancing; skin; ultraviolet

PMID: 29690549

PMCID: [PMC5946307](#)

DOI: [10.3390/nu10040522](#)

[Indexed for MEDLINE]

[Free PMC Article](#)

Astaxanthin reviewed as an anti-pigmenting agent.

[Int J Mol Sci](#). 2014 May 12;15(5):8293-315. doi: 10.3390/ijms15058293.

Inhibitors of intracellular signaling pathways that lead to stimulated epidermal pigmentation: perspective of anti-pigmenting agents.

[Imokawa G](#)¹, [Ishida K](#)².

Author information

Abstract

Few anti-pigmenting agents have been designed and developed according to their known hyperpigmentation mechanisms and corresponding intracellular signaling cascades. Most anti-pigmenting agents developed so far are mechanistically involved in the interruption of constitutional melanogenic mechanisms by which skin color is maintained at a normal and unstimulated level. Thus, owing to the difficulty of confining topical application to a specific hyperpigmented skin area, potent anti-pigmenting agents capable of attenuating the natural unstimulated pigmentation process have the risk of leading to hypopigmentation. Since intracellular signaling pathways within melanocytes do not function substantially in maintaining normal skin color and are activated only by environmental stimuli such as UV radiation, specifically down-regulating the activation of melanogenesis to the constitutive level would be an appropriate strategy to develop new potent anti-pigmenting agents with a low risk of hypopigmentation. In this article, we review the hyperpigmentation mechanisms and intracellular signaling pathways that lead to the stimulation of melanogenesis. We also discuss a screening and evaluation system to select candidates for new anti-melanogenic substances by focusing on inhibitors of endothelin-1 or stem cell factor-triggered intracellular signaling cascades. From this viewpoint, we show that extracts of the herbs *Withania somnifera* and *Melia toosendan* and the natural chemicals Withaferin A and Astaxanthin are new candidates for potent anti-pigmenting substances that avoid the risk of hypopigmentation.

PMID: 24823877 PMCID: [PMC4057732](#)

DOI:

[10.3390/ijms15058293](#)

[PubMed - indexed for MEDLINE]

[Free PMC Article](#)

Athletic Performance, Strength, **Endurance and Energy**

Astaxanthin increases power output and improves racing time in competitive cyclists in placebo-controlled study sponsored by Gatorade®.

[Int J Sports Med.](#) 2011 Oct 7. [Epub ahead of print]

Effect of Astaxanthin on Cycling Time Trial Performance.

[Earnest CP](#), [Lupo M](#), [White KM](#), [Church TS](#).

Source

Pennington Biomedical Research Center.

Abstract

We examined the effect of Astaxanthin (AST) on substrate metabolism and cycling time trial (TT) performance by randomly assigning 21 competitive cyclists to 28d of encapsulated AST (4 mg/d) or placebo (PLA) supplementation. Testing included a VO₂max test and on a separate day a 2 h constant intensity pre-exhaustion ride, after a 10 h fast, at 5% below VO₂max stimulated onset of 4 mmol/L lactic acid followed 5 min later by a 20 km TT. Analysis included ANOVA and post-hoc testing. Data are Mean (SD) and (95% CI) when expressed as change (pre vs. post). Fourteen participants successfully completed the trial. Overall, we observed significant improvements in 20 km TT performance in the AST group (n=7; -121 s; 95% CI, -185, -53), but not the PLA (n=7; -19 s; 95% CI, -84, 45). The AST group was significantly different vs. PLA (P<0.05). The AST group significantly increased power output (20 W; 95% CI, 1, 38), while the PLA group did not (1.6 W; 95% CI, -17, 20). The mechanism of action for these improvements remains unclear, as we observed no treatment effects for carbohydrate and fat oxidation, or blood indices indicative of fuel mobilization. While AST significantly improved TT performance the mechanism of action explaining this effect remains obscure.

Georg Thieme Verlag KG Stuttgart · New York.

PMID: 21984399 [PubMed - as supplied by publisher]

Astaxanthin promotes recovery from exercise and prevents muscle fatigue and also reduces LDL cholesterol in double-blind, placebo-controlled human clinical study.

Hiro to Kyuyo no Kagaku VOL.18;NO.1;PAGE.35-46(2003)

Effects of Astaxanthin on Recovery from Whole Fatigue with Three Stepwise Exercises

NAGATA AKIRA; TAJIMA TAEKO; HAMAMATSU HOZUMI

This study was designed to evaluate the effects of astaxanthin (A) ingestion upon recovery from whole fatigue, that were generated by progressive loads of three stepwise exercise-30%HRmax, 50%HRmax, and 70%HRmax. Nineteen healthy volunteers were randomized into two groups: Group A (10 subjects) received oral astaxanthin capsule (5mg) daily for two weeks, while Group C (9 subjects) ingested oral placebo (C) capsule (5mg) with the double blind method. After a month from this ingestion, another capsules were taken again with cross-over system for the same subjects respectively. Comparative detections were practiced to estimate with effectiveness of A ingestion upon changing ratios between two groups. Significant difference between A and C groups were obtained to inhibit the increase of respiratory-circulatory function from expired gases analysis. Additionally sympathetic nervous activities (LF/HF ratio) during exercise and parasympathetic nervous activities (HF/TF 100) during recovery were observed to significant increase. Otherwise, blood serum concentration of LDL cholesterol showed significant decrease, while concentration of creatine phosphokinase had increased to higher level than that of C ingestion, significantly. Then, findings of the present study indicated that with astaxanthin ingestion for human, respiratory-circulation ability and activities of sympathetic nervous system were augmented to make efficient metabolism during exercise load. Those anti-fatigue and anti-oxidative function might be promoted for human to make recovery ability from the whole fatigue generated by exercise stress.

Astaxanthin improves strength and endurance in young men doing deep knee bends in double-blind, placebo-controlled human clinical trial.

Carotenoid Science, Vol.13, 2008 ISSN 1880-5671

Dietary Supplementation with Astaxanthin-Rich Algal Meal Improves Strength Endurance – A Double Blind Placebo Controlled Study on Male Students

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(b) BioReal (Sweden) AB, Idrottsvagen 4, 13440 Gustavsberg, Sweden

The present study was designed to investigate the effect of dietary supplementation with astaxanthin on physical performance. Forty healthy paramedic students were recruited for this test in a double blind placebo controlled study. In this study, we used algal meal (AstaREAL® biomass) as astaxanthin supplementation. Twenty of the subjects received capsules filled with algal meal to provide 4 mg astaxanthin per capsule, whereas the other twenty received placebo capsules for six months. The physical parameters monitored were fitness, strength/endurance and strength/explosivity by standardized exercises. Before starting the dietary supplementation, base values for each of the subjects were obtained. At the end of the six month period of dietary supplementation, the average number of knee bendings (squats) increased by 27.05 (from 49.32 to 76.37) for subjects having received astaxanthin and by 9.0 (from 46.06 to 55.06) for the placebo subjects. Hence, the increase in the astaxanthin supplemented group was three times higher than that of the placebo group ($P=0.047$). None of the other parameters monitored differed significantly between the groups at the end of the study period. Based on this findings, it suggested that supplementation of astaxanthin is effective for the improvement of strength endurance that may lead to sports performance.

ASTAXANTHIN IMPROVED EXERCISE TOLERANCE; REDUCED OXIDATIVE STRESS; AND IMPROVED CARDIAC CONTRACTILITY IN HEART FAILURE PATIENTS IN HUMAN CLINICAL STUDY.

Nutrients. 2020 Jun 26;12(6):1896.
doi: 10.3390/nu12061896.

Effects of 3-Month Astaxanthin Supplementation on Cardiac Function in Heart Failure Patients with Left Ventricular Systolic Dysfunction-A Pilot Study

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PMID: [32604721](#) PMCID: [PMC7353230](#) DOI: [10.3390/nu12061896](#)

Abstract

Astaxanthin has strong antioxidant properties. We conducted a prospective pilot study on heart failure (HF) patients with left ventricular (LV) systolic dysfunction to investigate improvements in cardiac function and exercise tolerance in relation to suppression of oxidative stress by 3-month astaxanthin supplementation. Oxidative stress markers-serum Diacron reactive oxygen metabolite (dROM), biological antioxidant potential (BAP), and urinary 8-hydroxy-2'-deoxyguanosine (8-OHdG) concentrations, LV ejection fraction (LVEF), and 6-min walk distance (6MWD) were assessed before and after 3-month astaxanthin supplementation. Finally, the data of 16 HF patients were analyzed. Following 3-month astaxanthin supplementation, dROM level decreased from 385.6 ± 82.6 U.CARR to 346.5 ± 56.9 U.CARR ($p = 0.041$) despite no changes in BAP and urinary 8-OHdG levels. LVEF increased from $34.1 \pm 8.6\%$ to $38.0 \pm 10.0\%$ ($p = 0.031$) and 6MWD increased from 393.4 ± 95.9 m to 432.8 ± 93.3 m ($p = 0.023$). Significant relationships were observed between percent changes in dROM level and those in LVEF. In this study, following 3-month astaxanthin supplementation, suppressed oxidative stress and improved cardiac contractility and exercise tolerance were observed in HF patients with LV systolic dysfunction. Correlation between suppression of oxidative stress and improvement of cardiac contractility suggests that suppression of oxidative stress by astaxanthin supplementation had therapeutic potential to improve cardiac functioning.

Astaxanthin increases grip strength by 93% in eight weeks in double-blind, placebo-controlled human clinical study.

Effect of daily use of natural astaxanthin on symptoms associated with Tennis Elbow (lateral humeral epicondylitis)

Gene A. Spiller, PhD, CNS, Antonella Dewell, MS, RD, Sally Chaves, RN, Zaga Rakidzich, Health Research & Studies Center, Los Altos, CA
Study Report, January, 2006

ABSTRACT

Previous studies have provided data suggesting that daily use of a microalgal extract containing natural astaxanthin and marketed under the trade name BioAstin® can help alleviate pain associated with joint damage, specifically that seen in rheumatoid arthritis and carpal tunnel syndrome. For this study, the benefits of daily use natural astaxanthin provided by BioAstin® for the purpose of alleviating pain associated with Tennis Elbow (lateral humeral epicondylitis) was evaluated. It was found that grip strength measurements (GSM) for those on the active product were significantly improved by the end of the study. This correlation of improved GSM and use of natural astaxanthin may suggest that daily use can help alleviate pain associated with Tennis Elbow, and increase mobility. This improvement may greatly improve the standard of living for those who suffer from such joint disorders.

Astaxanthin prevents muscle fatigue by decreasing lactic acid levels and also improves visual acuity in two separate placebo-controlled human clinical trials reported here.

Journal of Clinical Therapeutics & Medicines VOL.18;NO.9;PAGE.1085-1100(2002)

Sports Performance Benefits from Taking Natural Astaxanthin Characterized by Visual Acuity and Muscle Fatigue Improvement in Humans

[SAWAKI KEISUKE](#); [YOSHIGI HIROSHI](#); [AOKI KAZUHIRO](#); [KOIKAWA NATSUE](#);
[AZUMANE AKITO](#); [KANEKO KESATOKI](#); [YAMAGUCHI MASAHIRO](#)

The effects of astaxanthin on visual acuity and muscle fatigue were studied. Astaxanthin (3,3'-Dihydroxy-β,β-carotene-4,4'-dione) is a red pigment found in salmon and krill and has strong antioxidant properties. In the two supplementation studies, astaxanthin extracted from algae (*Haematococcus pluvialis*) was used. Four visual acuity parameters were examined in experiment A in 18 healthy adult male volunteers that were equally divided into two groups (treatment and control). The measured parameters were deep vision, critical flicker fusion, static and kinetic visual acuity before and after supplementation. A second investigation (experiment B) involved 16 adult male volunteers to establish the effect of astaxanthin supplementation on the build up of lactic acid before and after running 1200 metres. In both experiments, the treated groups ingested an astaxanthin capsule per day for 4 weeks (6mg astaxanthin per day) and the control groups received a placebo capsule. Results: In experiment A, the deep vision and the critical flicker fusion of the treated groups were significantly improved compared to the control group. No effects of treated group were observed on static and kinetic visual acuity. In experiment B, serum lactic acid concentration at 2 minutes after activity (1,200m running) of the treatment group was significantly lower than that of the control one. No other effects related to supplementation of astaxanthin on serum biological and hematological examinations were observed. Based on these preliminary findings, it suggested that supplementation of astaxanthin is effective for the improvement of visual acuity and muscle fatigue that may lead to sports performance benefits.

Astaxanthin decreases respiratory parameters during exercise and decreases LDL cholesterol after exercise in double-blind, placebo-controlled human clinical trial.

Effects of Astaxanthin Ingestion on Exercise-Induced Physiological Changes

Authors: Taeko Tajima, Akira Nagata. Health and Behavior Sciences.,3(1):5-10(2004).

Abstract

The purpose of this study was to evaluate the effects of astaxanthin (ACT) ingestion on exercise-induced physiological functions. In this experiment we planned to investigate the autonomic nervous system (ANS) and the respiratory metabolism during different exercise intensities in subjects taking astaxanthin and those taking placebo. The design of this experiment was a double-blind crossover study.

Eighteen male volunteers (35.8 ± 4.51 years of age) took ACT or placebo (CON) capsule daily for two weeks. Exercise stress tests were done before and after the ingestion period. The exercise load was in the form of running exercise on a treadmill at intensities of 30%, 50% and 70% of maximum heart rate (HR_{max}). Heart rate variability (HRV), expired gases analysis and blood biochemical parameters were measured. Sympathetic nervous activity (SNA) and parasympathetic nervous activity (PNA) were estimated from the pattern of power density in three frequency ranges on the power spectrum.

During the exercise at an intensity of 70% HR_{max}, CV_{RR} and HF/TF increased significantly ($p < 0.05$) after ACT ingestion. Additionally, V_E decreased significantly ($p < 0.05$) during exercise at 70% HR_{max} after ACT ingestion. These data indicated that after ACT ingestion, SNA was decreased and PNA was enhanced during exercises at 70% HR_{max}. Furthermore LDL cholesterol decreased markedly after exercise ($p < 0.05$) and respiratory quotient decreased during exercise. These results suggest that ACT may contribute to enhancement of lipid metabolism. Decrease of respiratory parameters may indicate augmentation of the efficacy of exercise in energy metabolism.

Astaxanthin helps prevent muscle damage and inflammation in young soccer players and may support immune system modulation in randomized, placebo-controlled study.

[Evid Based Complement Alternat Med.](#) 2015;2015:783761. doi: 10.1155/2015/783761. Epub 2015 Jun 18.

Effect of Astaxanthin Supplementation on Salivary IgA, Oxidative Stress, and Inflammation in Young Soccer Players.

[Baralic I¹](#), [Andjelkovic M¹](#), [Djordjevic B²](#), [Dikic N¹](#), [Radivojevic N¹](#), [Suzin-Zivkovic V³](#), [Radojevic-Skodric S⁴](#), [Pejic S⁵](#).

Author information

Abstract

The physiologic stress induced by physical activity is reflected in immune system perturbations, oxidative stress, muscle injury, and inflammation. We investigated the effect of astaxanthin (Asx) supplementation on salivary IgA (sIgA) and oxidative stress status in plasma, along with changes in biochemical parameters and total/differential white cell counts. Forty trained male soccer players were randomly assigned to Asx and placebo groups. Asx group was supplemented with 4 mg of Asx. Saliva and blood samples were collected at the baseline and after 90 days of supplementation in preexercise conditions. We observed a rise of sIgA levels at rest after 90 days of Asx supplementation, which was accompanied with a decrease in prooxidant-antioxidant balance. The plasma muscle enzymes levels were reduced significantly by Asx supplementation and by regular training. The increase in neutrophil count and hs-CRP level was found only in placebo group, indicating a significant blunting of the systemic inflammatory response in the subjects taking Asx. This study indicates that Asx supplementation improves sIgA response and attenuates muscle damage, thus preventing inflammation induced by rigorous physical training. Our findings also point that Asx could show significant physiologic modulation in individuals with mucosal immunity impairment or under conditions of increased oxidative stress and inflammation.

PMID:

26167194

[PubMed]

PMCID:

PMC4488551

[Free PMC Article](#)

Astaxanthin may be effective in preventing exercise-induced free radical production in young elite soccer players in double-blind, placebo controlled study.

[J Sports Med Phys Fitness](#). 2012 Aug;52(4):382-92.

Effect of astaxanthin supplementation on muscle damage and oxidative stress markers in elite young soccer players.

[Djordjevic B¹](#), [Baralic I](#), [Kotur-Stevuljevic J](#), [Stefanovic A](#), [Ivanisevic J](#), [Radivojevic N](#), [Andjelkovic M](#), [Dikic N](#).

Author information

Abstract

AIM:

The purpose of the current study was to examine the effect of Astaxanthin (Asx) supplementation on muscle enzymes as indirect markers of muscle damage, oxidative stress markers and antioxidant response in elite young soccer players.

METHODS:

Thirty-two male elite soccer players were randomly assigned in a double-blind fashion to Asx and placebo (P) group. After the 90 days of supplementation, the athletes performed a 2 hour acute exercise bout. Blood samples were obtained before and after 90 days of supplementation and after the exercise at the end of observational period for analysis of thiobarbituric acid-reacting substances (TBARS), advanced oxidation protein products (AOPP), superoxide anion ($O_2^{\bullet-}$), total antioxidative status (TAS), sulphhydryl groups (SH), superoxide-dismutase (SOD), serum creatine kinase (CK) and aspartate aminotransferase (AST).

RESULTS:

TBARS and AOPP levels did not change throughout the study. Regular training significantly increased $O_2^{\bullet-}$ levels (main training effect, $P<0.01$). $O_2^{\bullet-}$ concentrations increased after the soccer exercise (main exercise effect, $P<0.01$), but these changes reached statistical significance only in the P group (exercise x supplementation effect, $P<0.05$). TAS levels decreased significantly post-exercise only in P group ($P<0.01$). Both Asx and P groups experienced increase in total SH groups content (by 21% and 9%, respectively) and supplementation effect was marginally significant ($P=0.08$). Basal SOD activity significantly decreased both in P and in Asx group by the end of the study (main training effect, $P<0.01$). All participants showed a significant decrease in basal CK and AST activities after 90 days (main training effect, $P<0.01$ and $P<0.001$, respectively). CK and AST activities in serum significantly increased as result of soccer exercise (main exercise effect, $P<0.001$ and $P<0.01$, respectively). Postexercise CK and AST levels were significantly lower in Asx group compared to P group ($P<0.05$)

CONCLUSION:

The results of the present study suggest that soccer training and soccer exercise are associated with excessive production of free radicals and oxidative stress, which might diminish antioxidant system efficiency. Supplementation with Asx could prevent exercise induced free radical production and depletion of non-enzymatic antioxidant defense in young soccer players.

PMID: 22828460

[PubMed - indexed for MEDLINE]

ASTAXANTHIN INCREASES PHYSICAL ACTIVITY AND IMPROVES BOTH PHYSICAL AND MENTAL QUALITY-OF-LIFE SELF-ASSESSMENT IN PATIENTS WITH HEART FAILURE IN HUMAN CLINICAL TRIAL.

Ann Palliat Med. 2020 Nov 10;apm-20-1378.

doi: 10.21037/apm-20-1378. Online ahead of print.

Changes in self-reported physical activity and health-related quality of life following 3-month astaxanthin supplementation in patients with heart failure: results from a pilot study

[Sayaki Ishiwata](#)¹, [Takao Kato](#)², [Takatoshi Kasai](#)³, [Akihiro Sato](#)¹, [Shoichiro Yatsu](#)², [Hiroki Matsumoto](#)², [Jun Shitara](#)², [Azusa Murata](#)², [Megumi Shimizu](#)², [Shoko Suda](#)², [Yuya Matsue](#)¹, [Ryo Naito](#)¹, [Masaru Hiki](#)², [Hiroyuki Daida](#)²

- PMID: 33183036
- DOI: [10.21037/apm-20-1378](https://doi.org/10.21037/apm-20-1378)

Free article

Abstract

Background: Astaxanthin has a strong antioxidant effect. We recently demonstrated that following 3-month astaxanthin supplementation, cardiac contractility and exercise tolerance improved, possibly through the suppression of oxidative stress in a small pilot study involving patients with heart failure with left ventricular systolic dysfunction. This is a sub-study of our pilot study to investigate whether improvements of self-reported physical activity and health-related quality of life were observed following 3-month astaxanthin supplementation.

Methods: We investigated the changes in physical activity by the Specific Activity Scale score and health-related quality of life by physical and mental component summary scores in Short Form-8 at baseline and after 3-month astaxanthin supplementation.

Results: Data from 17 patients with heart failure were assessed. Following 3-month astaxanthin supplementation, the Specific Activity Scale score increased from the median of 4.5 (interquartile range, 2.0) to 6.5 (interquartile range, 1.1) metabolic equivalent ($P=0.001$), and the physical and mental component summary scores increased from 46.1 ± 9.2 to 50.8 ± 6.8 ($P=0.015$) and from 48.9 ± 9.1 to 53.8 ± 4.8 ($P=0.022$), respectively. There was a linear relationship of the baseline heart rate, or mental component summary score with the percent change in the Specific Activity Scale score ($r=0.523$, $P=0.031$ and $r=-0.505$, $P=0.039$, respectively). In addition, there was a direct relationship of ischemic etiology with the percent change in the physical component summary score ($r=0.483$, $P=0.049$, respectively). Finally, there was a linear relationship between the percent change in the Specific Activity Scale score and that in the mental component summary score ($r=0.595$, $P=0.012$).

Conclusions: Following 3-month astaxanthin supplementation, improvements of the self-reported physical activity level and health-related quality of life in both mental and physical components were observed. In patients with heart failure, those with higher baseline heart rate, ischemic etiology, and poorer baseline health-related quality of life have potentials to have greater improvement of physical activity and/or health-related quality of life.

ASTAXANTHIN IMPROVES PERFORMANCE; ENHANCES WHOLE-BODY FAT OXIDATION RATES; AND REDUCES RESPIRATORY EXCHANGE RATIO IN RECREATIONAL CYCLISTS IN ONLY SEVEN DAYS OF SUPPLEMENTATION IN HUMAN CLINICAL TRIAL.

J Sci Med Sport. 2021 Jan;24(1):92-97.

doi: 10.1016/j.jsams.2020.06.017. Epub 2020 Jul 3.

The effect of astaxanthin supplementation on performance and fat oxidation during a 40 km cycling time trial

[Daniel R Brown](#)¹, [Ashley R Warner](#)², [Sanjoy K Deb](#)³, [Lewis A Gough](#)⁴, [S Andy Sparks](#)⁵, [Lars R McNaughton](#)⁶

PMID: 32660833 DOI: [10.1016/j.jsams.2020.06.017](https://doi.org/10.1016/j.jsams.2020.06.017)

Abstract

Objectives: This study aimed to investigate whether supplementation with 12 mg·day⁻¹ astaxanthin for 7 days can improve exercise performance and metabolism during a 40 km cycling time trial.

Design: A randomised, double-blind, crossover design was employed.

Methods: Twelve recreationally trained male cyclists (VO_{2peak} : 56.5 ± 5.5 mL·kg⁻¹·min⁻¹, W_{max} : 346.8 ± 38.4 W) were recruited. Prior to each experimental trial, participants were supplemented with either 12 mg·day⁻¹ astaxanthin or an appearance-matched placebo for 7 days (separated by 14 days of washout). On day 7 of supplementation, participants completed a 40 km cycling time trial on a cycle ergometer, with indices of exercise metabolism measured throughout.

Results: Time to complete the 40 km cycling time trial was improved by $1.2 \pm 1.7\%$ following astaxanthin supplementation, from 70.76 ± 3.93 min in the placebo condition to 69.90 ± 3.78 min in the astaxanthin condition (mean improvement = 51 ± 71 s, $p = 0.029$, $g = 0.21$). Whole-body fat oxidation rates were also greater ($+0.09 \pm 0.13$ g·min⁻¹, $p = 0.044$, $g = 0.52$), and the respiratory exchange ratio lower (-0.03 ± 0.04 , $p = 0.024$, $g = 0.60$) between 39-40 km in the astaxanthin condition.

Conclusions: Supplementation with 12 mg·day⁻¹ astaxanthin for 7 days provided an ergogenic benefit to 40 km cycling time trial performance in recreationally trained male cyclists and enhanced whole-body fat oxidation rates in the final stages of this endurance-type performance event.

ASTAXANTHIN-CONTAINING FORMULA INCREASES RESTING OXYGEN CONSUMPTION; DECREASES OXIDATION MARKER AFTER EXERCISE; AND INCREASES MAXIMAL VOLUNTARY CONTRACTION, LEADING TO CONCLUSION THAT THE FORMULA SUPPORTS RESISTANCE TRAINING-INDUCED STRENGTH AND METABOLIC APPLICATIONS IN HUMAN CLINICAL TRIAL.

Antioxidants (Basel). 2021 Jan 14;10(1):113.
doi: 10.3390/antiox10010113.

Astaxanthin-, β -Carotene-, and Resveratrol-Rich Foods Support Resistance Training-Induced Adaptation

[Aki Kawamura](#)^{1,2}, [Wataru Aoi](#)¹, [Ryo Abe](#)^{1,3}, [Yukiko Kobayashi](#)¹, [Masashi Kuwahata](#)¹, [Akane Higashi](#)¹

PMID: 33466842 PMCID: [PMC7830030](#) DOI: [10.3390/antiox10010113](#) [Free PMC article](#)

Abstract

Resistance training adaptively increases the muscle strength associated with protein anabolism. Previously, we showed that the combined intake of astaxanthin, β -carotene, and resveratrol can accelerate protein anabolism in the skeletal muscle of mice. The purpose of this study was to investigate the effect of anabolic nutrient-rich foods on muscle adaptation induced by resistance training. Twenty-six healthy men were divided into control and intervention groups. All participants underwent a resistance training program twice a week for 10 weeks. Astaxanthin-, β -carotene-, and resveratrol-rich foods were provided to the intervention group. Body composition, nutrient intake, maximal voluntary contraction of leg extension, oxygen consumption, and serum carbonylated protein level were measured before and after training. The skeletal muscle mass was higher after training than before training in both groups ($p < 0.05$). Maximal voluntary contraction was increased after training in the intervention group ($p < 0.05$), but not significantly increased in the control group. Resting oxygen consumption was higher after training in the intervention group only ($p < 0.05$). As an oxidative stress marker, serum carbonylated protein level tended to be lower immediately after exercise than before exercise in the intervention group only ($p = 0.056$). Intake of astaxanthin-, β -carotene-, and resveratrol-rich foods supported resistance training-induced strength and metabolic adaptations.

Astaxanthin improves oxidative status in young soccer players in double-blind, placebo-controlled clinical study.

[Phytother Res.](#) 2013 Oct;27(10):1536-42. doi: 10.1002/ptr.4898. Epub 2012 Nov 28.

Effect of astaxanthin supplementation on paraoxonase 1 activities and oxidative stress status in young soccer players.

[Baralic I¹](#), [Djordjevic B](#), [Dikic N](#), [Kotur-Stevuljevic J](#), [Spasic S](#), [Jelic-Ivanovic Z](#), [Radivojevic N](#), [Andjelkovic M](#), [Pejic S](#).

Author information

Abstract

The purpose of the study was to examine the effects of astaxanthin (Asx) on paraoxonase (PON1) activities and oxidative stress status in soccer players. Forty soccer players were randomly assigned in a double-blind fashion to Asx and placebo (P) group. Blood samples were obtained before, 45 and 90 days after supplementation. PON1 activity was assessed by using two substrates: paraoxon and diazoxon. The oxidative stress biomarkers were also examined: total sulphhydryl group content (-SH groups), thiobarbituric acid-reactive substances (TBARS), advanced oxidation protein products and redox balance. The significant interaction effect of supplementation and training ($p < 0.05$) on PON1 activity toward paraoxon was observed. The PON1 activity toward diazoxon increased in Asx group after 90 days ($p < 0.01$), while there was no significant difference in P group. SH groups content rose from pre- to post-supplementation period only in Asx group (supplementation and training, $p < 0.05$; training, $p < 0.01$). TBARS levels decreased after 45 days and increased after 90 days of regular soccer training in both groups (training, $p < 0.001$). Redox balance decreased significantly in response to the regular training, regardless of treatment group (training, $p < 0.001$). Asx supplementation might increase total SH groups content and improve PON1 activity through protection of free thiol groups against oxidative modification.

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KEYWORDS:

astaxanthin; oxidative stress; paraoxonase 1 activity; soccer

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[PubMed - indexed for MEDLINE]

Astaxanthin decreases heart rate in endurance athletes in double-blind, placebo-controlled human clinical trial.

[EC Nutr](#) 11.6 (2016) 253-259.

Effect of Astaxanthin Supplementation on Cardiorespiratory Function in Runners

Talbott, S., Hantla, D., Capelli, B., Ding, L., Li, Y., Artaria, C.

Abstract

Purpose: Marine microalgae is the predominant source of natural astaxanthin (NAX), a red-orange carotenoid with powerful antioxidant and anti-inflammatory properties. Studies in both rodents and humans suggest that NAX supplementation improves antioxidant capacity and reduces oxidative stress, while also improving fat utilization and exercise endurance. The purpose of this study was to assess the effects of a moderate dose of NAX supplementation (12mg/day for 8 weeks) on cardiorespiratory function during both higher and lower intensity exercise in recreational runners.

Patients and Methods: Using a double-blind parallel design, 28 recreational runners (male = 14, female = 14, age = 42) were supplemented with NAX (*Haematococcus pluvialis* algal extract) or a placebo. Before and after the supplementation period, subjects performed a maximal running test (VO₂max on treadmill) and a maximal cycling test (watts on cycle ergometer).

Results: There was no improvement in maximal oxygen uptake (running VO₂ max) or maximal power output (cycling watts) with NAX supplementation. However, subjects in the NAX group showed a significant ~10% lower average heart rate at submaximal running intensities compared to placebo (aerobic threshold, AeT; NAX 130+17 v. PL 145+14; and anaerobic threshold, AT; NAX 139+20 v. PL 154+11, $p < 0.05$).

Conclusion: Supplementation with 12 mg/day of NAX for 8 weeks reduced average heart rate at submaximal endurance intensities (AeT and AT), but not at higher “peak” intensities. These results suggest that NAX may be a beneficial ergogenic aid for long/ultradistance endurance athletes, but not necessarily for athletes competing in shorter higher intensity efforts. In addition, these data are also suggestive of a general “cardiotonic” effect of NAX, that should be investigated in non-athletic populations including elderly subjects and those with cardiac complications including post-myocardial infarction, heart failure, statin usage, mitochondrial dysfunction, chronic fatigue, and related conditions.

Astaxanthin decreases mental and physical fatigue in double-blind, placebo-controlled human clinical trial.

J. Clin. Thera & Med 32.7 (2016):277-91 (Japanese)

Randomized Controlled Trial of the Anti-Fatigue Effects of Astaxanthin on Mental and Physical Loads Simulating Daily Life.

Hongo, N. et al.

In a study designed to induce fatigue and stress encountered in daily life, natural astaxanthin from *Haematococcus pluvialis* microalgae was administered over eight weeks to the treatment group in a double-blind, placebo-controlled study. A mental challenge comprised of a number of timed calculations (the Uchida-Kraepelin test) and a physical test on a bicycle ergometer were assessed in both the placebo and treatment groups before and after the eight-week supplementation period. Participants consisted of 39 healthy subjects who were divided into two groups. The treatment group received 12mg per day of natural astaxanthin combined with 20mg of tocotrienols while the control group received 20mg of tocotrienols without any astaxanthin. A Visual Analogue Scale analysis showed that astaxanthin significantly reduced perceived symptoms of mental and physical fatigue compared to placebo. Results included improvements in clarity of thinking, concentration, motivation and mood. Irritation and feelings of body heaviness were reduced. In the mental challenge test, an increase in errors observed in the placebo group was almost eliminated in the astaxanthin group. Salivary cortisol (a marker for stress) was significantly reduced in the astaxanthin group. These results suggest that astaxanthin supplementation has beneficial effects on fatigue encountered in daily life.

ASTAXANTHIN IMPROVES METABOLIC ADAPTATION AND IMPROVES MUSCLE ENDURANCE IN ELDERLY SUBJECTS DURING AEROBIC TRAINING IN RANDOMIZED, PLACEBO-CONTROLLED HUMAN CLINICAL STUDY.

Physiol Rep. 2021 Jun;9(11):e14887.

doi: 10.14814/phy2.14887.

Astaxanthin supplementation enhances metabolic adaptation with aerobic training in the elderly

[Sophia Z Liu](#)¹, [Ana P Valencia](#)¹, [Matt P VanDoren](#)², [Eric G Shankland](#)¹, [Baback Roshanravan](#)³, [Kevin E Conley](#)^{1,4,5}, [David J Marcinek](#)^{1,5,6}

- PMID: 34110707 PMCID: [PMC8191397](#) DOI: [10.14814/phy2.14887](#) [Free PMC article](#)

Abstract

Endurance training (ET) is recommended for the elderly to improve metabolic health and aerobic capacity. However, ET-induced adaptations may be suboptimal due to oxidative stress and exaggerated inflammatory response to ET. The natural antioxidant and anti-inflammatory dietary supplement astaxanthin (AX) has been found to increase endurance performance among young athletes, but limited investigations have focused on the elderly. We tested a formulation of AX in combination with ET in healthy older adults (65-82 years) to determine if AX improves metabolic adaptations with ET, and if AX effects are sex-dependent. Forty-two subjects were randomized to either placebo (PL) or AX during 3 months of ET. Specific muscle endurance was measured in ankle dorsiflexors. Whole body exercise endurance and fat oxidation (FATox) was assessed with a graded exercise test (GXT) in conjunction with indirect calorimetry. Results: ET led to improved specific muscle endurance only in the AX group (Pre 353 ± 26 vs. Post 472 ± 41 contractions), and submaximal GXT duration improved in both groups (PL 40.8 ± 9.1% and AX 41.1 ± 6.3%). The increase in FATox at lower intensity after ET was greater in AX (PL 0.23 ± 0.15 g vs. AX 0.76 ± 0.18 g) and was associated with reduced carbohydrate oxidation and increased exercise efficiency in males but not in females.

Astaxanthin reduces body fat percentage versus placebo in individuals doing moderate exercise over six weeks in placebo-controlled human clinical trial.

Fukamauchi M. Food Style 21. 2007;11:1-4.15

Astaxanthin increases fat utilisation during exercise

A randomised, double-blind study on humans has confirmed that natural astaxanthin increases fat utilisation during exercise.¹⁵ In the study, 32 individuals were supplemented with 2 x 6mg of astaxanthin per day, or placebo, for six weeks. The participants were instructed to undertake 40 minutes of continuous exercise three times per week during the 6-week period. After six weeks, the astaxanthin group had a significant reduction in body fat percentage, whereas there was no difference in the placebo group. These results indicate that astaxanthin increases muscle endurance and reduces lactic acid during intensive training by promoting the use of fat compared with glycogen stores.

Astaxanthin improves mood state in athletes doing endurance exercise in double-blind, placebo-controlled human clinical study.

Published as a poster at American College of Lifestyle Medicine and to be published as a full manuscript in 2019.

Natural Astaxanthin Supplementation Improves Mental Wellness

Talbott, S., Hantla, D., Capelli, B., Ding, L., Li, Y., Artaria, C.

Introduction: Nutrition plays a major role in the pathophysiology of many “physical” disease states, including cardiovascular disease, cancer, obesity, and diabetes. The role of nutrition is less well-known with respect to “mental” disease states, including depression, anxiety, attention deficit disorder, psychological burnout and chronic pain. Diet-related changes in psychological mood state and mental wellness may be due to cellular, biochemical, and behavioral factors – and may be mediated by lifestyle factors including diet and exercise.

Purpose: Our objective was to assess changes in mental wellness by assessing psychological mood state in response to dietary supplementation with natural astaxanthin (12mg/day for 8 weeks). Marine microalgae is the predominant source of natural astaxanthin (NAX), a red-orange carotenoid with powerful antioxidant and anti-inflammatory properties. Studies in both rodents and humans suggest that NAX supplementation improves antioxidant capacity and reduces oxidative stress – effects which may be related to mental wellness.

Methods: Using a double-blind parallel design, 28 recreational runners (male = 14, female = 14, age = 42) were supplemented with NAX (*Haematococcus pluvialis* algal extract) or a placebo. Before and after the supplementation period, subjects completed the validated Profile of Mood States (POMS) survey to assess mental wellness parameters including global mood state (GM) and related subscales: Vigor (V), Tension (T), Depression (D), Anger (A), Fatigue (F), and Confusion (C).

Results & Conclusions: Significant changes (all, $p < 0.05$) were found for improvements in positive mood state parameters: GM (+11%) & V (+5%); as well as reductions in negative mood state parameters: T (-20%), D (-57%), A (-12%), F (-36%), and C (-28%). Previous studies have shown astaxanthin supplementation to be associated with improvements in fatigue, attention, and memory – with suggestions that it may also play a role in prevention of dementia and age-related memory loss. These data are the first to suggest that astaxanthin supplementation improves mental wellness parameters associated with improvements in mood state and depression.

Astaxanthin prevents muscle soreness after heavy exercise in men with high fiber content in their muscles in placebo-controlled human clinical trial.

Human Performance Laboratories, The University of Memphis,
Memphis, TN, USA 38152

ASTAXANTHIN SUPPLEMENTATION

A.C. Fry, B.K. Schilling, L.Z.F. Chiu, N. Hori, and L.W. Weiss, FACSM.

Abstract

PURPOSE: To determine the effects of astaxanthin anti-oxidant supplementation as a counter-measure for delayed onset muscular soreness (DOMS) in currently trained individuals, nine weight trained males ($X \pm SE$: age=25.1+1.6 yrs., hgt=1.79+0.02 m, wgt=86.8+4.4 kg) participated in this study. **METHODS:** All subjects provided muscle biopsy samples from the vastus lateralis m. prior to inducing DOMS in the knee extensor mm. (10 sets x 7-10 reps, 85% eccentric 1 RM). The subjects ingested either 4 mg.d-1 of astaxanthin (Suppl; n=4) or a placebo (Con; n=5) for a 3 week loading phase prior to the DOMS-inducing protocol, and during a 12 d recovery phase. Perceptions of DOMS at 48 hrs post-eccentric exercise were quantified by muscle soreness ratings (0-10 Likert scale). Muscle fiber characteristics were determined via mATPase histochemistry and digital imaging to determine % cross-sectional areas of the major fiber types (I, IIA, IIAB/B). Due to small numbers of IIB fibers in some subjects, IIAB hybrid fibers were included in this fiber type population. Simple regression was used to determine relationships between fiber characteristics and perceptions of soreness. **RESULTS:** No differences in perceptions of soreness between the Suppl or Con groups were observed ($p > 0.05$), with all subjects exhibiting a mean score of > 5 . Percent fiber type areas were similar ($p > 0.05$) for both groups (type I, Suppl=47.6+8.9%, Con=41.3+2.7%; type IIA, Suppl=44.3+5.6%, Con=53.0+2.8%; type IIAB/B, Suppl=8.2+3.6%, Con=5.7+1.6%). However, 48 hrs after the DOMS-inducing session, perceptions of soreness for the Suppl group were positively related to % area type I ($r=0.90$), and negatively related to % area types IIA ($r=-0.80$) and IIAB/B ($r=-0.99$). A distinctly different correlational pattern was observed for the Con group (% type I area, $r=-0.58$; % type IIA area, $r=0.32$; % type IIAB/B area, $r=0.40$). **CONCLUSIONS:** Collectively, these preliminary data suggest that astaxanthin supplementation may preferentially attenuate perceptions of DOMS in weight trained men with a high % area for fiber types IIA & AB/B.

ASTAXANTHIN IMPROVES AEROBIC EXERCISE RECOVERY IN HUMAN CLINICAL TRIAL.

Front Sports Act Living. 2019 Sep 4;1:17.
doi: 10.3389/fspor.2019.00017. eCollection 2019.

Astaxanthin Improves Aerobic Exercise Recovery Without Affecting Heat Tolerance in Humans

[Chen Fleischmann](#)^{1,2,3}, [Michal Horowitz](#)², [Ran Yanovich](#)^{1,2,4}, [Hany Raz](#)⁵, [Yuval Heled](#)²

PMID: 33344941 PMCID: [PMC7739736](#) DOI: [10.3389/fspor.2019.00017](#) [Free PMC article](#)

Abstract

Objectives: To examine the supplementation effects of the xanthophyll carotenoid Astaxanthin on physical performance and exertional heat strain in humans. **Design:** A randomized double blind placebo controlled trial. **Methods:** Twenty two male participants (Age: 23.14 ± 3.5 y, height: 175 ± 6 cm, body mass: 69.6 ± 8.7 kg, % body fat: 16.8 ± 3.8) received placebo (PLA, $n = 10$) or Astaxanthin (ATX, $n = 12$) 12 mg/day Per os (P.O), for 30 days, and were tested pre and post-supplementation with a maximal oxygen uptake (VO_2 Max) test and the heat tolerance test (HTT) (2 h walk at 40°C , 40% relative humidity (RH), 5 kph, 2% incline). NIH database registration no. [NCT02088242](#). Gas exchange, Heart rate (HR), Relative perceived exertion (RPE), and blood lactate were measured during the VO_2 Max test. Heart rate (HR), rectal (T_{rec}), and skin (T_{skin}) temperatures, RPE, and sweat rate (SR) were monitored in the HTT. Serum heat shock protein 72 (HSP72), Creatine phospho-kinase (CPK), C-reactive protein (CRP), and lipid profile were measured before and after the test. **Results:** The rise in blood lactate caused by the VO_2 Max test was significantly diminished in the ATX group (9.4 ± 3.1 and 13.0 ± 3.1 $\text{mmole}\cdot\text{l}^{-1}$ in the ATX and PLA groups, respectively $P < 0.02$), as was the change in oxygen uptake during recovery (-2.02 ± 0.64 and $0.83 \pm 0.79\%$ of VO_2 Max in the ATX and PLA group, respectively, $p = 0.001$). No significant differences were observed in the anaerobic threshold or VO_2 Max. In the HTT, no significant physiological or biochemical differences were observed (HR < 120 bpm, T_{rec} rose by $\sim 1^\circ\text{C}$ to $< 38^\circ\text{C}$, no difference in SR). **Conclusions:** Astaxanthin supplementation improved exercise recovery. No benefit was observed for ATX over PLA in response to heat stress. Further examination of Astaxanthin in higher exertional heat strain is required.

Astaxanthin combined with tocotrienols and zinc increases strength and endurance in elderly subjects in a double-blind, placebo-controlled randomized human clinical trial.

[J Cachexia Sarcopenia Muscle](#). 2018 Oct;9(5):826-833. doi: 10.1002/jcsm.12318. Epub 2018 Sep 26.

Building strength, endurance, and mobility using an astaxanthin formulation with functional training in elderly.

[Liu SZ](#)¹, [Ali AS](#)¹, [Campbell MD](#)¹, [Kilroy K](#)¹, [Shankland EG](#)¹, [Roshanravan B](#)², [Marcinek DJ](#)^{1,3,4}, [Conley KE](#)^{1,5,3}.

Author information

Abstract

BACKGROUND:

Building both strength and endurance has been a challenge in exercise training in the elderly, but dietary supplements hold promise as agents for improving muscle adaptation. Here, we test a formulation of natural products (AX: astaxanthin, 12 mg and tocotrienol, 10 mg and zinc, 6 mg) with both anti-inflammatory and antioxidant properties in combination with exercise. We conducted a randomized, double-blind, placebo-controlled study of elderly subjects (65-82 years) on a daily oral dose with interval walking exercise on an incline treadmill.

METHODS:

Forty-two subjects were fed AX or placebo for 4 months and trained 3 months (3x/week for 40-60 min) with increasing intervals of incline walking. Strength was measured as maximal voluntary force (MVC) in ankle dorsiflexion exercise, and tibialis anterior muscle size (cross-sectional area, CSA) was determined from magnetic resonance imaging.

RESULTS:

Greater endurance (exercise time in incline walking, >50%) and distance in 6 min walk (>8%) accompanied training in both treatments. Increases in MVC by 14.4% ($\pm 6.2\%$, mean \pm SEM, $P < 0.02$, paired t-test), CSA by 2.7% ($\pm 1.0\%$, $P < 0.01$), and specific force by 11.6% (MVC/CSA, $\pm 6.0\%$, $P = 0.05$) were found with AX treatment, but no change was evident in these properties with placebo treatment (MVC, $2.9\% \pm 5.6\%$; CSA, $0.6\% \pm 1.2\%$; MVC/CSA, $2.4 \pm 5.7\%$; $P > 0.6$ for all).

CONCLUSIONS:

The AX formulation improved muscle strength and CSA in healthy elderly in addition to the elevation in endurance and walking distance found with exercise training alone. Thus, the AX formulation in combination with a functional training programme uniquely improved muscle strength, endurance, and mobility in the elderly.

PMID: 30259703 PMCID: [PMC6204600](#) DOI: [10.1002/jcsm.12318](#)

Astaxanthin combined with Sesamin improves recovery from mental fatigue in double-blind, placebo-controlled crossover human clinical trial.

[Nutrients](#). 2018 Feb 28;10(3). pii: E281. doi: 10.3390/nu10030281.

Effects of Dietary Supplementation of Astaxanthin and Sesamin on Daily Fatigue: A Randomized, Double-Blind, Placebo-Controlled, Two-Way Crossover Study.

[Imai A](#)¹, [Oda Y](#)², [Ito N](#)³, [Seki S](#)⁴, [Nakagawa K](#)⁵, [Miyazawa T](#)^{6,7}, [Ueda F](#)⁸.

Author information

Abstract

Severe fatigue can negatively affect quality of life, and oxidative stress may play a role in its mechanism. The aim of this study was to evaluate the effect of dietary supplementation of astaxanthin and sesamin (AS), strong food-derived antioxidants, on fatigue. Twenty-four healthy volunteers were supplemented with AS and placebo, each for four weeks. After each supplementation period, participants underwent tasks inducing mental and physical fatigue (visual display terminal task and ergometer task, respectively). Subjective fatigue was evaluated using a visual analogue scale during and after the mental and physical tasks, and daily subjective fatigue was evaluated by the Chalder fatigue questionnaire. Secondary outcomes included other subjective feelings, work efficiency, autonomic nerve activity, levels of an oxidative stress marker (plasma phosphatidylcholine hydroperoxide (PCOOH)) and safety. AS supplementation was associated with significantly improved recovery from mental fatigue compared with placebo. Increased PCOOH levels during mental and physical tasks were attenuated by AS supplementation. No differences between AS and placebo were detected in secondary outcomes, and no adverse effects of AS supplementation were observed. In conclusion, AS supplementation may be a candidate to promote recovery from mental fatigue which is experienced by many healthy people.

KEYWORDS:

astaxanthin; fatigue; phosphatidylcholine hydroperoxide; sesame seed extract; sesamin; visual analogue scale

PMID: 29495607

PMCID: [PMC5872699](#)

DOI: [10.3390/nu10030281](#)

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ASTAXANTHIN FORMULA MODULATES TRAINING-INDUCED AEROBIC METABOLISM OF CARBS AND FAT DURING REST AND EXERCISE IN HEALTHY YOUNG MEN IN HUMAN CLINICAL TRIAL.

J Clin Biochem Nutr. 2019 Jan;64(1):79-85.

doi: 10.3164/jcbn.18-40. Epub 2018 Aug 8.

Effect of dietary antioxidant-rich foods combined with aerobic training on energy metabolism in healthy young men

[Maki Takami](#)¹, [Wataru Aoi](#)¹, [Hitomi Terajima](#)¹, [Yuko Tanimura](#)², [Sayori Wada](#)¹, [Akane Higashi](#)¹

PMID: 30705516 PMCID: [PMC6348409](#) DOI: [10.3164/jcbn.18-40](#) [Free PMC article](#)

Abstract

Although supplementation with several antioxidants has been suggested to improve aerobic metabolism during exercise, whether dietary foods containing such antioxidants can exert the metabolic modulation is unclear. This study aimed to investigate the effect of intake of the specific antioxidant-rich foods coupled with exercise training on energy metabolism. Twenty young healthy, untrained men were assigned to antioxidant and control groups: participants in the antioxidant group were encouraged to consume foods containing catechin, astaxanthin, quercetin, glutathione, and anthocyanin. All participants performed cycle training at 60% maximum oxygen consumption for 30 min, 3 days per week for 4 weeks. Maximum work load was significantly increased by training in both groups, while oxygen consumption during exercise was significantly increased in the antioxidant group only. There were positive correlations between maximum work load and fat/carbohydrate oxidations in the antioxidant group. Carbohydrate oxidation during rest was significantly higher in the post-training than that in the pre-training only in the antioxidant group. More decreased levels of serum insulin and HOMA-IR after training were observed in the antioxidant group than in the control group. This study suggests that specific antioxidant-rich foods could modulate training-induced aerobic metabolism of carbohydrate and fat during rest and exercise.

Astaxanthin user survey shows that 84% of respondents experiencing painful conditions found reduced joint, tendon & muscle pain and 60% experienced increased mobility.

Potential Clinical Applications of Natural Astaxanthin from Haematococcus Microalgae

Bob Capelli, Robert Corish, MD, Gerald R. Cysewski, PhD

Published at www.cyanotech.com

Natural Astaxanthin from Haematococcus Pluvialis microalgae has been used as a human nutritional supplement since the early 1990's. Researchers have studied potential benefits of Astaxanthin during and before its introduction as a commercially sold nutritional supplement. Among many different areas of research, our discussion will be limited specifically to research on antioxidant protection; anti-inflammatory applications including joint and tendon conditions; protection of the skin from UV radiation; and immune system enhancement. We first review research on Natural Astaxanthin as a potential preventative and/or curative agent in relation to the aforementioned areas of health. Additionally, we report the results of a survey of Natural Astaxanthin users. A use/benefit survey (Appendix A) was created and posted on an independent survey implementation and analysis website. A request was sent by e-mail to 1584 consumers who had purchased a commercially sold Natural Astaxanthin supplement (BioAstin® Natural Astaxanthin, Cyanotech Corporation) at least once during the last seven years. These consumers were asked to log onto the independent survey website and fill out the use/benefit survey. 423 consumers (26.7% of the total) completed the survey (full results in Appendix A). Of the 423 respondents, 121 respondents were classified as non-qualified due to three specific disqualifying factors, yielding a final total of 302 qualified respondents (qualified results in Appendix B). Respondents were surveyed about their use of the Natural Astaxanthin supplement including a) milligrams per day; b) frequency of use; c) duration of use; d) consumption with food. Respondents were further surveyed about the benefits they derived from their use of Natural Astaxanthin. Of the 302 qualified respondents, 85% experienced positive benefits from Natural Astaxanthin supplementation. Of those respondents who had experienced joint, tendon or muscle pain, 84% found that their condition ameliorated through Natural Astaxanthin supplementation; 83% experienced less pain while 60% experienced increased mobility. 75% found that Natural Astaxanthin worked the same or better than over-the-counter pain medications, while 64% found that Natural Astaxanthin worked the same or better than prescription anti-inflammatories. Additional results include: a) 68% experienced reduced UV damage from sun exposure; b) 65% experienced improvement in skin condition; c) 80% experienced improved immunity and/or resistance to colds and flu. Based on previous research and further validated by the results of this survey, we conclude that Natural Astaxanthin is a viable therapy 1) for joint and tendon conditions; 2) as a preventative for UV damage; 3) to improve immune function and increase resistance to colds and flu.

ASTAXANTHIN PREVENTS MUSCLE DAMAGE INDUCED BY ISCHEMIA-REPERFUSION IN ANIMAL MODEL.

Mar Drugs. 2019 Jun 14;17(6):354.
doi: 10.3390/md17060354.

Astaxanthin Complexes to Attenuate Muscle Damage after In Vivo Femoral Ischemia-Reperfusion

[Marisol Zuluaga Tamayo](#)¹, [Laurence Choudat](#)², [Rachida Aid-Launais](#)³, [Olivier Thibaudeau](#)⁴, [Liliane Louedec](#)⁵, [Didier Letourneur](#)⁶, [Virginie Gueguen](#)⁷, [Anne Meddahi-Pellé](#)⁸, [Anne Couvelard](#)^{9,10}, [Graciela Pavon-Djavid](#)¹¹

PMID: 31207871 PMCID: [PMC6627496](#) DOI: [10.3390/md17060354](#) [Free PMC article](#)

Abstract

(1) **Background:** Reperfusion injury refers to the cell and tissue damage induced, when blood flow is restored after an ischemic period. While reperfusion reestablishes oxygen supply, it generates a high concentration of radicals, resulting in tissue dysfunction and damage. Here, we aimed to challenge and achieve the potential of a delivery system based on astaxanthin, a natural antioxidant, in attenuating the muscle damage in an animal model of femoral hind-limb ischemia and reperfusion. (2) **Methods:** The antioxidant capacity and non-toxicity of astaxanthin was validated before and after loading into a polysaccharide scaffold. The capacity of astaxanthin to compensate stress damages was also studied after ischemia induced by femoral artery clamping and followed by varied periods of reperfusion. (3) **Results:** Histological evaluation showed a positive labeling for CD68 and CD163 macrophage markers, indicating a remodeling process. In addition, higher levels of Nrf2 and NQO1 expression in the sham group compared to the antioxidant group could reflect a reduction of the oxidative damage after 15 days of reperfusion. Furthermore, non-significant differences were observed in non-heme iron deposition in both groups, reflecting a cell population susceptible to free radical damage. (4) **Conclusions:** Our results suggest that the in situ release of an antioxidant molecule could be effective in improving the antioxidant defenses of ischemia/reperfusion (I/R)-damaged muscles.

ASTAXANTHIN REDUCES ANTIOXIDANT ENZYME ACTIVITY DURING MODERATE EXERCISE IN MICE.

Nutrients. 2019 May 31;11(6):1244.

doi: 10.3390/nu11061244.

High-Dose Astaxanthin Supplementation Suppresses Antioxidant Enzyme Activity during Moderate-Intensity Swimming Training in Mice

[Yingsong Zhou](#)¹, [Julien S Baker](#)², [Xiaoping Chen](#)³, [Yajun Wang](#)⁴, [Haimin Chen](#)⁵, [Gareth W Davison](#)⁶, [Xiaojun Yan](#)⁷

PMID: 31159211 PMCID: [PMC6627865](#) DOI: [10.3390/nu11061244](#) [Free PMC article](#)

Abstract

Exercise-induced reactive oxygen and nitrogen species are increasingly considered as beneficial health promotion. Astaxanthin (ASX) has been recognized as a potent antioxidant suitable for human ingestion. We investigated whether ASX administration suppressed antioxidant enzyme activity in moderate-intensity exercise. Seven-week-old male C57BL/6 mice ($n = 8/\text{group}$) were treated with ASX (5, 15, and 30 mg/kg BW) combined with 45 min/day moderate-intensity swimming training for four weeks. Results showed that the mice administered with 15 and 30 mg/kg of ASX decreased glutathione peroxidase, catalase, malondialdehyde, and creatine kinase levels in plasma or muscle, compared with the swimming control group. Beyond that, these two (15 and 30 mg/kg BW) dosages of ASX downregulated gastrocnemius muscle erythroid 2p45 (NF-E2)-related factor 2 (Nrf2). Meanwhile, mRNA of Nrf2 and Nrf2-dependent enzymes in mice heart were also downregulated in the ASX-treated groups. However, the mice treated with 15 or 30 mg/kg ASX had increased constitutive nitric oxidase synthase and superoxide dismutase activity, compared with the swimming and sedentary control groups. Our findings indicate that high-dose administration of astaxanthin can blunt antioxidant enzyme activity and downregulate transcription of Nrf2 and Nrf2-dependent enzymes along with attenuating plasma and muscle MDA.

Astaxanthin leads to improvement in muscle and joint soreness in vast majority of consumers surveyed.

Mera Pharmaceuticals, Inc. Review presented at the 1st Congress of the International Society for Applied Phycology/9th International Conference on Applied Phycology, May 2002, Almeria, Spain.

Haematococcus astaxanthin: health and nutrition applications: Exercise survey with 88% reporting improvement

Guerin, M, Huntley, M, Olaizola, M.

“In March 2001, a health survey looked at the various positive effects of Astaxanthin on exercise. The survey involved 247 between the ages of 20 and 87 years. 146 of those taking part reported problems with muscle and joint soreness. When taking Astaxanthin, 88% of participants reported improvement. In all cases, the more exercise an individual did, the more benefit was experienced.”

Astaxanthin from algae superior to Astaxanthin from mutated Phaffia yeast or Synthetic Astaxanthin from petrochemicals in increasing endurance and protecting tissues from oxidative damage in mice.

[J Clin Biochem Nutr.](#) 2018 Mar;62(2):161-166. doi: 10.3164/jcbn.17-89. Epub 2017 Dec 27.

Comparison of the effect of non-esterified and esterified astaxanthins on endurance performance in mice.

[Aoi W](#)¹, [Maoka T](#)², [Abe R](#)¹, [Fujishita M](#)³, [Tominaga K](#)³.

Author information

Abstract

Astaxanthin, a natural antioxidant, exists in non-esterified and esterified forms. Although it is known that astaxanthin can improve exercise endurance and cause metabolic improvement in skeletal muscle, the effects of the two different forms are unclear. We investigated the effects of the different forms of astaxanthin on endurance in mice. Eight-week-old ICR mice were divided into four groups: control; astaxanthin extracted from *Haematococcus pluvialis* in an esterified form; astaxanthin extracted from *Phaffia rhodozyma* in a non-esterified form; and astaxanthin synthesized chemically in a non-esterified form. After 5 weeks of treatment, each group was divided into sedentary and exercise groups. In the group fed astaxanthin from *Haematococcus*, the running time to exhaustion was longest, and the plasma and tissue concentrations of astaxanthin were significantly higher than those in the other groups. Astaxanthin from *Haematococcus* increased 5'-adenosine monophosphate-activated protein kinase levels in the skeletal muscle. Although the mice in the *Haematococcus* group ran for longer, hexanoyl lysine adduct levels in the skeletal muscle mitochondria were similar in the control and *Haematococcus* groups. Our results suggested that esterified astaxanthin promoted energy production and protected tissues from oxidative damage during exercise owing to its favorable absorption properties, leading to a longer running time.

KEYWORDS:

astaxanthin; energy metabolism; esterified form and non-esterified form; oxidative damage; running exercise

PMID: 29610556

PMCID: [PMC5874239](#)

DOI: [10.3164/jcbn.17-89](#)

[Free PMC Article](#)

Astaxanthin prevents fatigue in rats during treadmill exercise.

[Vopr Pitan.](#) 2015;84(5):46-55.

[Enrichment of the rats diet with docosahexaenoic acid and astaxanthin: physiological and biochemical efficiency].

[Sidorova YS](#), [Zorin SN](#), [Petrov NA](#), [Makarenko MA](#), [Sarkisyan VA](#), [Mazo VK](#), [Kodentsova VM](#), [Bessonov VV](#), [Kochetkova AA](#).

Abstract

To investigate the effect of enrichment of the rats diet with polyunsaturated fatty acids (PUFA) ω -3 (220 mg docosahexaenoic acid per 1 kg of animal body weight per day) and astaxanthin (5 mg/kg body weight) on serum corticosterone concentration, physical fatigue, anxiety of rats after exhausting the load. During 30 days the rats of the test group received the diet in which the usual fat component comprising sunflower oil and lard (1:1) was completely replaced by the mixture of oils (high oleic sunflower (89%), coconut (6%), and marine oil from microalgae *Schizochytrium* sp. (5%) with a high content of docosahexaenoic acid with the addition of astaxanthin). Ratio of ω -6 and ω -3 PUFA in the lipid component of the experimental diet was 5.2:1 (n=12) and 135:1 in the diet of rats in the control group (n=12). DHA enrichment of the diet resulted in a significant 10-fold increase of the DHA liver content and ω -6 PUFA reducing (in particular of linoleic acid in 2.7-fold). No significant differences have been identified between the groups in terms of anxiety, estimated on the elevated plus maze at the beginning and on 24th day of the experiment. Results of the exhausting load on a treadmill (25th day) showed a significant reduction in physical fatigue in rats of the experimental group compared with the control group of rats: the number of contacts with the electrical grid was 4.2 ± 0.9 versus 19.7 ± 4.4 , fulltime shock was 0.9 ± 0.2 versus 3.3 ± 0.8 sec. Significantly lower serum corticosterone concentration took place in the subjected to exhausting exertion animals receiving lipid module (15.0 ± 3.9 ng/ml) compared to control animals (31.0 ± 5.4 ng/ml). Thus, modification of the lipid component of the diet by its enrichment with DHA and astaxanthin led to decrease of the rat fatigue during exercise training (test treadmill) and prevent from the serum corticosterone raise, that indicates animal stress adaptation ability.

PMID: 29363930

[Indexed for MEDLINE]

Astaxanthin delays exhaustion and improves oxidative balance in the mitochondria of muscles in rats.

[Nutrients](#). 2014 Dec 12;6(12):5819-38. doi: 10.3390/nu6125819.

Astaxanthin supplementation delays physical exhaustion and prevents redox imbalances in plasma and soleus muscles of Wistar rats.

[Polotow TG](#)¹, [Vardaris CV](#)², [Mihaliuc AR](#)³, [Gonçalves MS](#)⁴, [Pereira B](#)⁵, [Ganini D](#)⁶, [Barros MP](#)⁷.

Author information

Abstract

Astaxanthin (ASTA) is a pinkish-orange carotenoid commonly found in marine organisms, especially salmon. ASTA is a powerful antioxidant and suggested to provide benefits for human health, including the inhibition of LDL oxidation, UV-photoprotection, and prophylaxis of bacterial stomach ulcers. Exercise is associated to overproduction of free radicals in muscles and plasma, with pivotal participation of iron ions and glutathione (GSH). Thus, ASTA was studied here as an auxiliary supplement to improve antioxidant defenses in soleus muscles and plasma against oxidative damage induced by exhaustive exercise. Long-term 1 mg ASTA/kg body weight (BW) supplementation in Wistar rats (for 45 days) significantly delayed time to exhaustion by 29% in a swimming test. ASTA supplementation increased scavenging/iron-chelating capacities (TEAC/FRAP) and limited exercise-induced iron overload and its related pro-oxidant effects in plasma of exercising animals. On the other hand, ASTA induced significant mitochondrial Mn-dependent superoxide dismutase and cytosolic glutathione peroxidase antioxidant responses in soleus muscles that, in turn, increased GSH content during exercise, limited oxidative stress, and delayed exhaustion. We also provided significant discussion about a putative "mitochondrial-targeted" action of ASTA based on previous publications and on the positive results found in the highly mitochondrial populated (oxidative-type) soleus muscles here.

PMID:

25514562

[PubMed - in process]

PMCID:

PMC4277001

[Free PMC Article](#)

Astaxanthin increases time to exhaustion and improves utilization of fatty acids as an energy source in mice.

[Biol Pharm Bull.](#) 2006 Oct;29(10):2106-10.

Effects of astaxanthin supplementation on exercise-induced fatigue in mice.

[Ikeuchi M](#), [Koyama T](#), [Takahashi J](#), [Yazawa K](#).

Laboratory of Nutraceuticals and Functional Foods Science, Graduate School of Marine Science and Technology, Tokyo University of Marine Science and Technology, Tokyo, Japan.

The present study was designed to determine the effect of astaxanthin on endurance capacity in male mice aged 4 weeks. Mice were given orally either vehicle or astaxanthin (1.2, 6, or 30 mg/kg body weight) by stomach intubation for 5 weeks. The astaxanthin group showed a significant increase in swimming time to exhaustion as compared to the control group. Blood lactate concentration in the astaxanthin groups was significantly lower than in the control group. In the control group, plasma non-esterified fatty acid (NEFA) and plasma glucose were decreased by swimming exercise, but in the astaxanthin group, NEFA and plasma glucose were significantly higher than in the control group. Astaxanthin treatment also significantly decreased fat accumulation. These results suggest that improvement in swimming endurance by the administration of astaxanthin is caused by an increase in utilization of fatty acids as an energy source.

PMID: 17015959 [PubMed - indexed for MEDLINE]

Astaxanthin increases endurance and fat metabolism during exercise in mice.

[Biochem Biophys Res Commun.](#) 2008 Feb 22;366(4):892-7. Epub 2007 Dec 17.

Astaxanthin improves muscle lipid metabolism in exercise via inhibitory effect of oxidative CPT I modification.

[Aoi W](#), [Naito Y](#), [Takanami Y](#), [Ishii T](#), [Kawai Y](#), [Akagiri S](#), [Kato Y](#), [Osawa T](#), [Yoshikawa T](#).

Department of Inflammation and Immunology, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, Kyoto 602-8566, Japan.

Intracellular redox balance may affect nutrient metabolism in skeletal muscle. Astaxanthin, a carotenoid contained in various natural foods, exerts high antioxidative capacity in the skeletal muscles. The present study investigated the effect of astaxanthin on muscle lipid metabolism in exercise. ICR mice (8 weeks old) were divided into four different groups: sedentary, sedentary treated with astaxanthin, running exercise, and exercise treated with astaxanthin. After 4 weeks of treatment, exercise groups performed treadmill running. Astaxanthin increased fat utilization during exercise compared with mice on a normal diet with prolongation of the running time to exhaustion. Colocalization of fatty acid translocase with carnitine palmitoyltransferase I (CPT I) in skeletal muscle was increased by astaxanthin. We also found that hexanoyl-lysine modification of CPT I was increased by exercise, while astaxanthin prevented this increase. In additional experiment, we found that astaxanthin treatment accelerated the decrease of body fat accumulation with exercise training. Our results suggested that astaxanthin promoted lipid metabolism rather than glucose utilization during exercise via CPT I activation, which led to improvement of endurance and efficient reduction of adipose tissue with training.

Publication Types:

- [Research Support, Non-U.S. Gov't](#)

PMID: 18082622 [PubMed - indexed for MEDLINE]

Astaxanthin improves lipid metabolism during exercise and prevents inter-muscular pH decrease due to exercise in mice.

[J Clin Biochem Nutr.](#) 2014 Mar;54(2):86-9. doi: 10.3164/jcbn.13-110. Epub 2014 Feb 19.

The astaxanthin-induced improvement in lipid metabolism during exercise is mediated by a PGC-1 α increase in skeletal muscle.

[Liu PH¹](#), [Aoi W²](#), [Takami M²](#), [Terajima H²](#), [Tanimura Y¹](#), [Naito Y¹](#), [Itoh Y¹](#), [Yoshikawa T¹](#).

Author information

Abstract

Astaxanthin, a xanthophyll carotenoid, accelerates lipid utilization during aerobic exercise, although the underlying mechanism is unclear. The present study investigated the effect of astaxanthin intake on lipid metabolism associated with peroxisome proliferator-activated receptor- γ coactivator-1 α (PGC-1 α) in mice. Mice were divided into 4 groups: sedentary, sedentary and astaxanthin-treated, exercised, and exercised and astaxanthin-treated. After 2 weeks of treatment, the exercise groups performed treadmill running at 25 m/min for 30 min. Immediately after running, intermuscular pH was measured in hind limb muscles, and blood was collected for measurements. Proteins were extracted from the muscle samples and PGC-1 α and its downstream proteins were measured by western blotting. Levels of plasma fatty acids were significantly decreased after exercise in the astaxanthin-fed mice compared with those fed a normal diet. Intermuscular pH was significantly decreased by exercise, and this decrease was inhibited by intake of astaxanthin. Levels of PGC-1 α and its downstream proteins were significantly elevated in astaxanthin-fed mice compared with mice fed a normal diet. Astaxanthin intake resulted in a PGC-1 α elevation in skeletal muscle, which can lead to acceleration of lipid utilization through activation of mitochondrial aerobic metabolism.

KEYWORDS:

PGC-1 α ; astaxanthin; lipid metabolism; running exercise; skeletal muscle

PMID:

24688216

[PubMed]

PMCID:

PMC3947967

Free PMC Article

Astaxanthin prevents exercise-induced skeletal and cardiac muscle damage in mice.

[Antioxid Redox Signal](#). 2003 Feb;5(1):139-44.

Astaxanthin limits exercise-induced skeletal and cardiac muscle damage in mice.

[Aoi W](#), [Naito Y](#), [Sakuma K](#), [Kuchide M](#), [Tokuda H](#), [Maoka T](#), [Toyokuni S](#), [Oka S](#),
[Yasuhara M](#), [Yoshikawa T](#).

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Dietary antioxidants may attenuate oxidative damage from strenuous exercise in various tissues. Beneficial effects of the antioxidant astaxanthin have been demonstrated in vitro, but not yet in vivo. We investigated the effect of dietary supplementation with astaxanthin on oxidative damage induced by strenuous exercise in mouse gastrocnemius and heart. C57BL/6 mice (7 weeks old) were divided into groups: rested control, intense exercise, and exercise with astaxanthin supplementation. After 3 weeks of exercise acclimation, both exercise groups ran on a treadmill at 28 m/min until exhaustion. Exercise-increased 4-hydroxy-2-nonenal-modified protein and 8-hydroxy-2'-deoxyguanosine in gastrocnemius and heart were blunted in the astaxanthin group. Increases in plasma creatine kinase activity, and in myeloperoxidase activity in gastrocnemius and heart, also were lessened by astaxanthin. Astaxanthin showed accumulation in gastrocnemius and heart from the 3 week supplementation. Astaxanthin can attenuate exercise-induced damage in mouse skeletal muscle and heart, including an associated neutrophil infiltration that induces further damage.

PMID: 12626126 [PubMed - indexed for MEDLINE]

Astaxanthin reduces exercise-induced oxidative stress in muscles.

[Subcell Biochem.](#) 2014;77:175-87. Doi: 10.1007/978-94-007-7920-4_15.

Potential role of oxidative protein modification in energy metabolism in exercise.

[Aoi W¹](#), [Naito Y](#), [Yoshikawa T](#).

Author information

Abstract

Exercise leads to the production of reactive oxygen species (ROS) via several sources in the skeletal muscle. In particular, the mitochondrial electron transport chain in the muscle cells produces ROS along with an elevation in the oxygen consumption during exercise. Such ROS generated during exercise can cause oxidative modification of proteins and affect their functionality. Many evidences have been suggested that some muscle proteins, i.e., myofiber proteins, metabolic signaling proteins, and sarcoplasmic reticulum proteins can be a targets modified by ROS generated due to exercise. We detected the modification of carnitine palmitoyltransferase I (CPT I) by N ϵ -(hexanoyl)lysine (HEL), one of the lipid peroxides, in exercised muscles, while the antioxidant astaxanthin reduced this oxidative stress-induced modification. Exercise-induced ROS may diminish CPT I activity caused by HEL modification, leading to a partly limited lipid utilization in the mitochondria. This oxidative protein modification may be useful as a potential biomarker to examine the oxidative stress levels, antioxidant compounds, and their possible benefits in exercise.

PMID:

24374928

[PubMed – indexed for MEDLINE]

Astaxanthin prevents muscular atrophy in rat study.

Japanese Journal of Physical Fitness and Sports Medicine. Vol. 54, No. 6, pg 466. December 2005.

Effect of Astaxanthin on Muscular Atrophy

Tateo Sugiura, Yoshiharu Iida, Hisashi Naito, Daijiro Ohmori, Katsumasa Goto, Toshitada Yoshioka

Objective: Patients wearing casts or other devices that hinder mobility are reported to have muscular atrophy. It is commonly thought that the cause is from reactive oxygen species (ROS). The use of Vitamin E, along with other antioxidants, prevents ROS from causing muscular atrophy that arises from lack of movement; however there has been conflicting reports on its effectiveness, varying from some claiming that it works and others that it does not.

Results and Analysis: Groups that were administered Ax had significantly less muscle atrophy than those in the Control group ($p < 0.05$). The level of Cu/Zn-SOD expressed was higher in the rats with casts than those without casts in the control group; however, in the Ax group, the level expressed was insignificantly different from those with casts and those without. In addition, the level expressed in the control group with casts was significantly higher than the Ax group with casts on. The level of calpain and ubiquitin expressed was higher in the control group with casts than those in the Ax group with casts, but the difference was insignificant. Also, significantly less (of calpain and ubiquitin) was expressed in the Ax 0.2% with casts compared to the control group with casts. The same pattern was seen with Capthesin L expression.

Presently, it is reported that muscular atrophy in patients who are immobile due to casts was caused by oxidative stress. The increase in oxidative stress accelerates the reaction of lipoperoxide, which causes distress in the cell membrane and sarcoendoplasmic reticulum, leading to an increase in Ca^{2+} in the cytoplasm and concurrently causing a decrease in its discharge. An increase in Ca^{2+} concentration activates calpain along with cathepsin. In addition, the presence of lipoperoxide causes disruption in the cell membrane of the mitochondria, causing iron ions and ROS to leak in the cytoplasm, which leads to ubiquitination (of proteins.) Ax is the same as beta-carotene in that they are both carotenoids. They both prevent lipoperoxides from disturbing the cell membrane in many biological organisms, but Ax is more active than other antioxidants. Based on this information, we believe Ax intake prevents muscular atrophy by protecting membranes; preventing oxidative stress which results in atrophy; preventing the facilitation protease and ubiquitination. The effects due to the quantity of Ax uptake were not clear in this study.

ASTAXANTHIN PREVENTS MUSCLE ATROPHY AND PROTECTS AGAINST MUSCLE OXIDATION IN RATS.

J Physiol Sci. 2019 Sep;69(5):757-767.

doi: 10.1007/s12576-019-00692-7. Epub 2019 Jul 4.

Effects of astaxanthin supplementation and electrical stimulation on muscle atrophy and decreased oxidative capacity in soleus muscle during hindlimb unloading in rats

[Miho Kanazashi](#)¹, [Masayuki Tanaka](#)², [Ryosuke Nakanishi](#)³, [Noriaki Maeshige](#)⁴, [Hidemi Fujino](#)⁵

- PMID: [31273678](#)
- DOI: [10.1007/s12576-019-00692-7](#)

Abstract

The effects of a combination of the antioxidant astaxanthin (AX) and electrical stimulation (ES) on muscle mass and mitochondrial oxidative capacity were investigated in the soleus muscle of hindlimb unloaded rats. Five groups of male Sprague-Dawley rats were used; control, 1-week hindlimb unloading (HU), HU + AX, HU + ES, and HU + AX + ES. Respective rats in the AX groups received 50-mg/kg AX twice daily during HU. Calf muscles of rats in the ES groups were electrically stimulated for 240 s/day during HU. One-week HU decreased muscle mass along with decreased FoxO3a phosphorylation and increased ubiquitinated proteins expressions, decreased oxidative enzymatic activity accompanied with decline in PGC-1 α protein expression, and increased reactive oxygen species production. However, the combination treatment could synergistically attenuate/suppress all HU-related changes, suggesting protective effects on muscle atrophy and decreased muscle oxidative capacity due to chronic neuromuscular inactivity.

Astaxanthin prevents sarcopenia [muscular atrophy due to aging] in rats.

Long term dietary antioxidant intakes attenuate sarcopenia

Tsubasa SHIBAGUCHI¹, Talmo SUGIURA¹, Tsukasa FURUMOTO¹, Koshiro I-OUEI,
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Japanese Journal of Physical Fitness and Sports Medicine. 2008, 57:541-52

Oxidative stress is thought to be one of significant contributing factors to age-related sarcopenia. We tested the hypothesis that the long term dietary antioxidant (astaxanthin intakes attenuate sarcopenia. Wistar strain male rats, aged 45 weeks old, were given either control (Cont) or astaxanthin feed (0.004%, Ax) for 1 year. The soleus muscle weights and muscle weight-to-body weight ratios in Ax group were significantly heavier than in Cont group, but tibialis anterior muscle mass remained similar between the two dietary groups. The level of ubiquitinated proteins was significantly lower in soleus muscles of Ax group, but not in tibialis anterior muscles when compared with Cont group. Tibialis anterior levels of cathepsin L and calpain were tended to be lower in Ax group than in Cont group, especially significant differences observed in cathepsin L, whereas no differences between Cont and Ax were observed in soleus calpain levels. There were no effects of Ax supplementation on calpain 1 and 2, UBC3B, Cu/Zn SOD and nitrotyrosine levels in both soleus and tibialis anterior muscles. Our data suggest that the long term dietary astaxanthin intakes attenuate the age related muscle atrophy, due in part, to reductions in oxidative stress and ubiquitination of myofibrillar protein in slow soleus muscles, but not in fast tibialis anterior muscles.

Astaxanthin prevents age-related mitochondrial dysfunction in dogs.

[J Anim Sci](#). 2013 Jan;91(1):268-75. Doi: 10.2527/jas.2012-5341. Epub 2012 Oct 16.

Astaxanthin modulates age-associated mitochondrial dysfunction in healthy dogs.

[Park JS¹](#), [Mathison BD](#), [Hayek MG](#), [Zhang J](#), [Reinhart GA](#), [Chew BP](#).

Author information

Abstract

Young (2.97±0.01 yr; 8.16±0.15 kg BW) and geriatric (10.71±0.01 yr; 9.46±0.18 kg BW) healthy female Beagle dogs (n=14/age group) were fed 0 or 20 mg astaxanthin daily for 16 wk to examine modulation of mitochondrial function. Fasted blood was sampled on wk 0, 8, and 16. Mitochondria membrane permeability, ATP production, cytochrome c oxidase/reductase, and number were assessed in leukocytes whereas astaxanthin uptake, glutathione, superoxide dismutase, nitric oxide, 8-hydroxy-2'-deoxyguanosine, 8-isoprostane, and protein carbonyl were measured in plasma. Aging increased (P<0.05) complex III cytochrome c oxidoreductase but decreased (P<0.05) 8-hydroxy-2'-deoxyguanosine and protein carbonyl. Mitochondrial function improved in both young and geriatric dogs by increasing (P<0.05) ATP production, mitochondria mass, and cytochrome c oxidoreductase activity, especially in geriatric dogs compared with young dogs. Astaxanthin feeding also increased (P<0.05) the reduced glutathione to oxidized glutathione ratio in young dogs and decreased (P<0.05) nitric oxide in both young and geriatric dogs. Dietary astaxanthin improved mitochondrial function in blood leukocytes, most likely by alleviating oxidative damage to cellular DNA and protein.

PMID:

23100599

[PubMed – indexed for MEDLINE]

Free full text

Astaxanthin protects heart mitochondria in mice.

[Anticancer Res.](#) 2010 Jul;30(7):2721-5.

Effect of astaxanthin supplementation on inflammation and cardiac function in BALB/c mice.

[Nakao R](#), [Nelson OL](#), [Park JS](#), [Mathison BD](#), [Thompson PA](#), [Chew BP](#).

School of Food Science, Washington State University, Pullman, WA 99164, USA.

Abstract

Astaxanthin is an antioxidant with immunomodulatory, anti-inflammatory and anticancer properties. This study evaluated the use of dietary astaxanthin to decrease oxidative stress and improve cardiac function, thereby providing a potential cardioprotective supplement. Female BALB/c mice (8 weeks of age) were fed a semi-synthetic diet containing 0, 0.02 or 0.08% astaxanthin for 8 weeks. Cardiac function was assessed by echocardiography bi-weekly, and blood and tissue samples were collected at 8 weeks. Plasma astaxanthin concentrations increased ($p < 0.05$) dose-dependently to 0.5 and 4 $\mu\text{mol/l}$ in the astaxanthin-supplemented mice. Blood glutathione concentrations and lymphocyte mitochondrial membrane potential were not significantly affected by astaxanthin treatment. However, mice fed 0.08% astaxanthin had higher ($p < 0.05$) heart mitochondrial membrane potential and contractility index compared to the control group. These results support the possible use of dietary astaxanthin for cardiac protection.

PMID: 20683004 [PubMed - indexed for MEDLINE]

Astaxanthin extends the lifespan of a model organism *C. elegans* by protecting the mitochondria and nucleus of its cells.

[Oxid Med Cell Longev](#). 2011;2011:596240. doi: 10.1155/2011/596240. Epub 2011 Oct 12.

Supplemental cellular protection by a carotenoid extends lifespan via Ins/IGF-1 signaling in *Caenorhabditis elegans*.

[Yazaki K¹](#), [Yoshikoshi C](#), [Oshiro S](#), [Yanase S](#).

Author information

Abstract

Astaxanthin (AX), which is produced by some marine animals, is a type of carotenoid that has antioxidative properties. In this study, we initially examined the effects of AX on the aging of a model organism *C. elegans* that has the conserved intracellular pathways related to mammalian longevity. The continuous treatments with AX (0.1 to 1 mM) from both the prereproductive and young adult stages extended the mean lifespans by about 16-30% in the wild-type and long-lived mutant age-1 of *C. elegans*. In contrast, the AX-dependent lifespan extension was not observed even in a daf-16 null mutant. Especially, the expression of genes encoding superoxide dismutases and catalases increased in two weeks after hatching, and the DAF-16 protein was translocated to the nucleus in the AX-exposed wild type. These results suggest that AX protects the cell organelle mitochondria and nucleus of the nematode, resulting in a lifespan extension via an Ins/IGF-1 signaling pathway during normal aging, at least in part.

PMID:

22013497

[PubMed - indexed for MEDLINE]

PMCID:

PMC3195502

[Free PMC Article](#)

Astaxanthin protects against mitochondrial dysfunction and reactive oxygen species in-vivo and in-vitro.

[Food Chem Toxicol.](#) 2011 Jan;49(1):271-80. Epub 2010 Nov 5.

Astaxanthin protects against MPTP/MPP⁺-induced mitochondrial dysfunction and ROS production in vivo and in vitro.

[Lee DH](#), [Kim CS](#), [Lee YJ](#).

Source

Department of Surgery, School of Medicine, University of Pittsburgh, Pittsburgh, PA 15213, USA.

Abstract

Astaxanthin (AST) is a powerful antioxidant that occurs naturally in a wide variety of living organisms. We have investigated the role of AST in preventing 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)-induced apoptosis of the substantia nigra (SN) neurons in the mouse model of Parkinson's disease (PD) and 1-methyl-4-phenylpyridinium (MPP⁺)-induced cytotoxicity of SH-SY5Y human neuroblastoma cells. In in vitro study, AST inhibits MPP⁺-induced production of intracellular reactive oxygen species (ROS) and cytotoxicity in SH-SY5Y human neuroblastoma cells. Preincubation of AST (50 μ M) significantly attenuates MPP⁺-induced oxidative damage. Furthermore, AST is able to enhance the expression of Bcl-2 protein but reduce the expression of α -synuclein and Bax, and suppress the cleavage of caspase-3. Our results suggest that the protective effects of AST on MPP⁺-induced apoptosis may be due to its anti-oxidative properties and anti-apoptotic activity via induction of expression of superoxide dismutase (SOD) and catalase and regulating the expression of Bcl-2 and Bax. Pretreatment with AST (30 mg/kg) markedly increases tyrosine hydroxylase (TH)-positive neurons and decreases the argyrophilic neurons compared with the MPTP model group. In summary, AST shows protection from MPP⁺/MPTP-induced apoptosis in the SH-SY5Y cells and PD model mouse SN neurons, and this effect may be attributable to upregulation of the expression of Bcl-2 protein, downregulation of the expression of Bax and α -synuclein, and inhibition of the activation of caspase-3. These data indicate that AST may provide a valuable therapeutic strategy for the treatment of progressive neurodegenerative disease such as Parkinson's disease.

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PMID: 21056612 [PubMed - indexed for MEDLINE]

PMCID: PMC3010303 [Available on 2012/1/1]

Astaxanthin protects mitochondria from damage in rats better than a-tocopherol.

[Physiol Chem Phys Med NMR](#). 1990;22(1):27-38.

Inhibition of oxidative injury of biological membranes by astaxanthin.

[Kurashige M](#), [Okimasu E](#), [Inoue M](#), [Utsumi K](#).

Department of Medical Biology, Kochi Medical School, Japan.

The value of astaxanthin, a carotenoid pigment, in the treatment of oxidative injury is assessed. Astaxanthin protects the mitochondria of vitamin E-deficient rats from damage by Fe²⁺-catalyzed lipid peroxidation both in vivo and in vitro. The inhibitory effect of astaxanthin on mitochondrial lipid peroxidation is stronger than that of alpha-tocopherol. Thin layer chromatographic analysis shows that the change in phospholipid components of erythrocytes from vitamin E-deficient rats induced by Fe²⁺ and Fe³⁺-xanthine/xanthine oxidase system was significantly suppressed by astaxanthin. Carrageenan-induced inflammation of the paw is also significantly inhibited by administration of astaxanthin. These data indicate that astaxanthin functions as a potent antioxidant both in vivo and in vitro.

PMID: 2084711 [PubMed - indexed for MEDLINE]

Astaxanthin protects mitochondria subject to oxidative stress.

[J Nutr Biochem](#). 2009 May 6. [Epub ahead of print]

Astaxanthin protects mitochondrial redox state and functional integrity against oxidative stress.

[Wolf AM](#), [Asoh S](#), [Hiranuma H](#), [Ohsawa I](#), [Iio K](#), [Satou A](#), [Ishikura M](#), [Ohta S](#).

Department of Biochemistry and Cell Biology, Institute of Development and Aging Sciences, Nippon Medical School, Nakahara-ku, Kawasaki, Kanagawa 211-8533, Japan.

Mitochondria combine the production of energy with an efficient chain of reduction-oxidation (redox) reactions but also with the unavoidable production of reactive oxygen species. Oxidative stress leading to mitochondrial dysfunction is a critical factor in many diseases, such as cancer and neurodegenerative and lifestyle-related diseases. Effective antioxidants thus offer great therapeutic and preventive promise. Investigating the efficacy of antioxidants, we found that a carotenoid, astaxanthin (AX), decreased physiologically occurring oxidative stress and protected cultured cells against strong oxidative stress induced with a respiratory inhibitor. Moreover, AX improved maintenance of a high mitochondrial membrane potential and stimulated respiration. Investigating how AX stimulates and interacts with mitochondria, a redox-sensitive fluorescent protein (roGFP1) was stably expressed in the cytosol and mitochondrial matrix to measure the redox state in the respective compartments. AX at nanomolar concentrations was effective in maintaining mitochondria in a reduced state. Additionally, AX improved the ability of mitochondria to remain in a reduced state under oxidative challenge. Taken together, these results suggest that AX is effective in improving mitochondrial function through retaining mitochondria in the reduced state.

PMID: 19423317 [PubMed - as supplied by publisher]

Astaxanthin improves muscle atrophy from heat stress in rats.

[J Zhejiang Univ Sci B](#). 2018 Nov.;19(11):844-852. doi: 10.1631/jzus.B1800076.

Effect of a combination of astaxanthin supplementation, heat stress, and intermittent reloading on satellite cells during disuse muscle atrophy.

[Yoshihara T](#)¹, [Sugiura T](#)², [Miyaji N](#)³, [Yamamoto Y](#)⁴, [Shibaguchi T](#)⁵, [Kakigi R](#)⁶, [Naito H](#)¹, [Goto K](#)⁷, [Ohmori D](#)⁸, [Yoshioka T](#)⁹.

Author information

Abstract

We examined the effect of a combination of astaxanthin (AX) supplementation, repeated heat stress, and intermittent reloading (IR) on satellite cells in unloaded rat soleus muscles. Forty-nine male Wistar rats (8-week-old) were divided into control, hind-limb unweighting (HU), IR during HU, IR with AX supplementation, IR with repeated heat stress (41.0-41.5 °C for 30 min), and IR with AX supplementation and repeated heat stress groups. After the experimental period, the antigravitational soleus muscle was analyzed using an immunohistochemical technique. Our results revealed that the combination of dietary AX supplementation and heat stress resulted in protection against disuse muscle atrophy in the soleus muscle. This protective effect may be partially due to a higher satellite cell number in the atrophied soleus muscle in the IR/AX/heat stress group compared with the numbers found in the other groups. We concluded that the combination treatment with dietary AX supplementation and repeated heat stress attenuates soleus muscle atrophy, in part by increasing the number of satellite cells.

KEYWORDS:

Antioxidant astaxanthin; Disuse muscle atrophy; Heat stress; Satellite cell

PMID: 30387334

PMCID: [PMC6238114](#)

DOI: [10.1631/jzus.B1800076](#)

[Free PMC Article](#)

Astaxanthin protects liver cells and improves mitochondrial function.

[Yao Xue Xue Bao](#). 2011 May;46(5):521-6.

[Astaxanthin inhibits sodium azide-induced cytotoxicity in hepatocyte L-02 cells probably by H⁺ transferring function].

[Article in Chinese]

[Ma J](#), [Chen HM](#), [Yan XJ](#), [Wang F](#), [Xu WF](#).

Source

Key Laboratory of Applied Marine Biotechnology, Ningbo University, Ningbo 315211, China.

Abstract

This study is to investigate the protective effect of astaxanthin against injured hepatocyte L-02 cells induced by sodium azide (NaN₃) and reveal the possible mechanisms. Hepatocyte L-02 cells were exposed to 100 mmol.L⁻¹ NaN₃ with various concentrations of astaxanthin pre-incubated, then the cell viability was measured by MTT method; The level of reactive oxygen species (ROS) was determined by DCFH-DA method; The changes of mitochondrial membrane potential (MMP) and apoptosis ratio were detected by JC-1 method and Annexin V-FITC/PI double stain method, respectively. Results showed that after cells were exposed to 100 mmol.L⁻¹ NaN₃ for 3 hours, the cell viability significantly decreased; ROS level and the percentage of late phase apoptosis increased obviously; MMP was also declined. When cells were pretreated with astaxanthin, the cell damage and late phase apoptosis ratio reduced and MMP was maintained. However, the level of ROS showed insignificant decrease (P>0.05). The beneficial concentration of astaxanthin in improving cell viability and MMP was not in a dose dependent manner and the most effective of which was 0.10 nmol.L⁻¹ (P<0.01). In order to reveal its possible non-antioxidant mechanism, mitochondrial membrane was imitated and H⁺ transferring function of astaxanthin was also detected by bilayer lipid membrane (BLM) method. Results showed that 2.0% astaxanthin could transfer H⁺ efficiently. These suggested the mechanisms of astaxanthin in protection of hepatocyte L-02 cells not via its ROS quenching capability but via its H⁺ transferring function, which improved the mitochondrial function and had the sequence biology effects.

PMID: 21800538 [PubMed - in process]

Astaxanthin protects neuronal cells against oxidative damage through its mitochondrial protection and antioxidant activity.

[Forum Nutr.](#) 2009;61:129-35. Epub 2009 Apr 7.

Astaxanthin protects neuronal cells against oxidative damage and is a potent candidate for brain food.

[Liu X](#), [Osawa T](#).

Graduate School of Bioagricultural Science, Nagoya University, Nagoya, Japan.

Astaxanthin (AST) is a powerful antioxidant that occurs naturally in a wide variety of living organisms. Based on the report claiming that AST could cross the brain-blood barrier, the aim of this study was to investigate the neuroprotective effect of AST by using an oxidative stress-induced neuronal cell damage system. The treatment with DHA hydroperoxide (DHA-OOH) or 6-hydroxydopamine (6-OHDA), either of which is a reactive oxygen species (ROS)-inducing neurotoxin, led to a significant decrease in viable dopaminergic SH-SY5Y cells by the MTT assay, whereas a significant protection was shown when the cells were pretreated with AST. Moreover, 100 nM AST pretreatment significantly inhibited intracellular ROS generation that occurred in either DHA-OOH- or 6-OHDA-treated cells. The neuroprotective effect of AST is suggested to be dependent upon its antioxidant potential and mitochondria protection; therefore, it is strongly suggested that treatment with AST may be effective for oxidative stress-associated neurodegeneration and a potential candidate for natural brain food.

PMID: 19367117 [PubMed - in process]

Astaxanthin's neuroprotective effect is attributed to its antioxidant potential and mitochondria protection.

[Brain Res.](#) 2009 Feb 13;1254:18-27. Epub 2008 Dec 3.

Astaxanthin inhibits reactive oxygen species-mediated cellular toxicity in dopaminergic SH-SY5Y cells via mitochondria-targeted protective mechanism.

[Liu X](#), [Shibata T](#), [Hisaka S](#), [Osawa T](#).

Laboratory of Food and Biodynamics, Graduate School of Bioagricultural Science, Nagoya University, Furo-cho, Nagoya 464-8601, Japan.

Astaxanthin is a powerful antioxidant that occurs naturally in a wide variety of living organisms. The aim of this study is to investigate the effect and the mechanism of astaxanthin on reactive oxygen species (ROS)-mediated apoptosis in dopaminergic SH-SY5Y cells. The treatment with DHA hydroperoxide (DHA-OOH) or 6-hydroxydopamine (6-OHDA), either of which is ROS-inducing neurotoxin, led to a significant decrease in viable dopaminergic SH-SY5Y cells by MTT assay, whereas a significant protection was shown while the cells were pretreated with astaxanthin. Moreover, 100 nM astaxanthin pretreatment significantly inhibited apoptosis, mitochondrial abnormalities and intracellular ROS generation occurred in either DHA-OOH- or 6-OHDA-treated cells. The neuroprotective effect of astaxanthin is suggested to be dependent upon its antioxidant potential and mitochondria protection; therefore, it is suggested that astaxanthin may be an effective treatment for oxidative stress-associated neurodegeneration.

PMID: 19101523 [PubMed - indexed for MEDLINE]

ASTAXANTHIN PRESERVES MITOCHONDRIAL INTEGRITY; REDUCES HEAT-INDUCED SKELETAL MUSCLE INJURY; AND IMPROVES OXIDATIVE STRESS IN-VITRO WHILE QUERCETIN HAD NO EFFECT.

J Cell Physiol. 2019 Aug;234(8):13292-13302.
doi: 10.1002/jcp.28006. Epub 2019 Jan 4.

Astaxanthin but not quercetin preserves mitochondrial integrity and function, ameliorates oxidative stress, and reduces heat-induced skeletal muscle injury

[Tianzheng Yu](#)¹, [Jacob Dohl](#)¹, [Yifan Chen](#)¹, [Heath G Gasier](#)¹, [Patricia A Deuster](#)¹

PMID: 30609021 DOI: [10.1002/jcp.28006](https://doi.org/10.1002/jcp.28006)

Abstract

Heat stress causes mitochondrial dysfunction and increases mitochondrial production of reactive oxygen species (ROS), both of which contribute to heat-induced skeletal muscle injury. In this study, we tested whether either astaxanthin or quercetin, two dietary antioxidants, could ameliorate heat-induced skeletal muscle oxidative injury. In mouse C2C12 myoblasts exposed to 43°C heat stress, astaxanthin inhibited heat-induced ROS production in a concentration-dependent manner (1-20 μM), whereas the ROS levels remained high in cells treated with quercetin over a range of concentrations (2-100 μM). Because mitochondria are both the main source and a primary target of heat-induced ROS, we then tested the effects of astaxanthin and quercetin on mitochondrial integrity and function, under both normal temperature (37°C) and heat stress conditions. Quercetin treatment at 37°C induced mitochondrial fragmentation and decreased membrane potential ($\Delta\Psi_m$), accompanied by reduced protein expression of the master regulator of mitochondrial biogenesis peroxisome proliferator-activated receptor- γ coactivator-1 α (PGC-1 α). It also induced cleavage of mitochondrial inner-membrane fusion protein OPA1. In contrast, astaxanthin at 37°C increased protein expression of PGC-1 α and mitochondrial transcription factor A (TFAM), and maintained tubular structure and normal $\Delta\Psi_m$. Under 43°C heat stress conditions, whereas quercetin failed to rescue C2C12 cells from injury, astaxanthin treatment prevented heat-induced mitochondrial fragmentation and depolarization, and apoptotic cell death. We also isolated rat flexor digitorum brevis myofibers and confirmed the data from C2C12 myoblasts that astaxanthin but not quercetin preserves mitochondrial integrity and function and ameliorates heat-induced skeletal muscle injury. These results confirm that mitochondria may be a potential therapeutic target for heat-related illness and suggest that astaxanthin may potentially be an effective preventive strategy.

Astaxanthin protects mitochondrial membrane potential and prevents DNA damage and cell death in-vitro.

[J Food Sci.](#) 2009 Sep;74(7):H225-31.

Antioxidative and anti-inflammatory neuroprotective effects of astaxanthin and canthaxanthin in nerve growth factor differentiated PC12 cells.

[Chan KC](#), [Mong MC](#), [Yin MC](#).

Dept of Food and Nutrition, Providence Univ, Taichung County, Taiwan.

Abstract

Nerve growth factor differentiated PC12 cells were used to examine the antioxidative and anti-inflammatory effects of astaxanthin (AX) and canthaxanthin (CX). PC12 cells were pretreated with AX or CX at 10 or 20 μM , and followed by exposure of hydrogen peroxide (H_2O_2) or 1-methyl-4-phenylpyridinium ion (MPP⁺) to induce cell injury. H_2O_2 or MPP⁺ treatment significantly decreased cell viability, increased lactate dehydrogenase (LDH) release, enhanced DNA fragmentation, and lowered mitochondrial membrane potential (MMP) ($P < 0.05$). The pretreatments from AX or CX concentration-dependently alleviated H_2O_2 or MPP⁺-induced cell death, LDH release, DNA fragmentation, and MMP reduction ($P < 0.05$). Either H_2O_2 or MPP⁺ treatment significantly increased malonyldialdehyde (MDA) and reactive oxygen species (ROS) formations, decreased glutathione content, and lowered glutathione peroxidase (GPX) and catalase activities ($P < 0.05$). The pretreatments from AX or CX significantly retained GPX and catalase activities, and decreased MDA and ROS formations ($P < 0.05$). H_2O_2 or MPP⁺ treatment significantly decreased Na^+ - K^+ -ATPase activity, elevated caspase-3 activity and levels of interleukin (IL)-1, IL-6, and tumor necrosis factor (TNF)- α ($P < 0.05$); and the pretreatments from these agents significantly restored Na^+ - K^+ -ATPase activity, suppressed caspase-3 activity and release of IL-1, IL-6, and TNF- α ($P < 0.05$). Based on the observed antioxidative and anti-inflammatory protection from AX and CX, these 2 compounds were potent agents against neurodegenerative disorder.

PMID: 19895474 [PubMed - indexed for MEDLINE]

Astaxanthin protects neural cell mitochondria and prevents cell death in-vitro.

[Brain Res.](#) 2010 Sep 21. [Epub ahead of print]

Neuroprotective effect of astaxanthin on H₂O₂-induced neurotoxicity in vitro and on focal cerebral ischemia in vivo.

[Lu YP](#), [Liu SY](#), [Sun H](#), [Wu XM](#), [Li JJ](#), [Zhu L](#).

Institute of Nautical Medicine, Nantong University, Nantong 226001, China.

Abstract

Astaxanthin (AST) is a powerful antioxidant that occurs naturally in a wide variety of living organisms. Much experimental evidence has proved that AST has the function of eliminating oxygen free radicals and can protect organisms from oxidative damage. The present study was carried out to further investigate the neuroprotective effect of AST on oxidative stress induced toxicity in primary culture of cortical neurons and on focal cerebral ischemia-reperfusion induced brain damage in rats. AST, over a concentration range of 250-1000nM, attenuated 50μM H₂O₂-induced cell viability loss. 500nM AST pretreatment significantly inhibited H₂O₂-induced apoptosis measured by Hoechst 33342 staining and restored the mitochondrial membrane potential (MMP) measured by a fluorescent dye, Rhodamine 123. In vivo, AST prevented cerebral ischemic injury induced by 2h middle cerebral artery occlusion (MCAO) and 24h reperfusion in rats. Pretreatment of AST intragastrically twice at 5h and 1h prior to ischemia dramatically diminished infarct volume and improved neurological deficit in a dose-dependent manner. Nissl staining showed that the neuronal injury was significantly improved by pretreatment of AST at 80mg/kg. Taken together, these results suggest that pretreatment with AST exhibits noticeable neuroprotection against brain damage induced by ischemia-reperfusion and the antioxidant activity of AST maybe partly responsible for it.

PMID: 20846510 [PubMed - as supplied by publisher]

Astaxanthin induces mitochondria-mediated liver cancer cell death.

[Biol Pharm Bull.](#) 2011;34(6):839-44.

Astaxanthin induces mitochondria-mediated apoptosis in rat hepatocellular carcinoma CBRH-7919 cells.

[Song XD](#), [Zhang JJ](#), [Wang MR](#), [Liu WB](#), [Gu XB](#), [Lv CJ](#).

Source

Medicine Research Center, Binzhou Medical University, Yantai, China.

Abstract

We designed to study the role of mitochondria in astaxanthin-induced apoptosis in hepatocellular carcinoma cells. Effect of astaxanthin on cell proliferation was studied by using methyl thiazolyl tetrazolium (MTT) in three tumor cell lines (CBRH-7919, SHZ-88 and Lewis) and normal human hepatocyte HL-7702 cell. Cell apoptosis rate, changes of mitochondrial morphology, mitochondrial transmembrane potential and electron transport chain were evaluated respectively. Expressions of B cell lymphoma/leukemia-2 (Bcl-2) and Bcl-2 associated X protein (Bax) were detected by Western blot. Results as following, astaxanthin had little effect on HL-7702 cell, however its inhibition was most pronounced in CBRH-7919 cell line with an IC_{50} of 39 μ M. This dose of astaxanthin and CBRH-7919 cell line were chosen for further studies. Astaxanthin could induce cell apoptosis and mitochondrial membrane damage. The mitochondrial transmembrane potential and function of electron transport chain were decreased. The expression of Bcl-2 protein was down-regulated but that of Bax protein was up-regulated. In conclusion, astaxanthin showed anticancer effect by inducing cell apoptosis through the regulation of mitochondrial-dependent manner.

PMID: 21628881 [PubMed - indexed for MEDLINE]

Astaxanthin protects kidney mitochondria cells from reactive oxygen species.

[J Cell Biochem.](#) 2008 Apr 15;103(6):1925-37.

Astaxanthin protects mesangial cells from hyperglycemia-induced oxidative signaling.

[Manabe E](#), [Handa O](#), [Naito Y](#), [Mizushima K](#), [Akagiri S](#), [Adachi S](#), [Takagi T](#), [Kokura S](#), [Maoka T](#), [Yoshikawa T](#).

School of Nursing, Kyoto Prefectural University of Medicine, Kyoto 602-8566, Japan.

Astaxanthin (ASX) is a carotenoid that has potent protective effects on diabetic nephropathy in mice model of type 2 diabetes. In this study, we investigated the protective mechanism of ASX on the progression of diabetic nephropathy using an in vitro model of hyperglycemia, focusing on mesangial cells. Normal human mesangial cells (NHMCs) were cultured in the medium containing normal (5 mM) or high (25 mM) concentrations of D-glucose. Reactive oxygen species (ROS) production, the activation of nuclear transcription factors such as nuclear factor kappa B (NFkappaB) and activator protein-1 (AP-1), and the expression/production of transforming growth factor-beta 1 (TGFbeta(1)) and monocyte chemoattractant protein-1 (MCP-1) were evaluated in the presence or absence of ASX. High glucose (HG) exposure induced significant ROS production in mitochondria of NHMCs, which resulted in the activation of transcription factors, and subsequent expression/production of cytokines that plays an important role in the mesangial expansion, an important event in the pathogenesis of diabetic nephropathy. ASX significantly suppressed HG-induced ROS production, the activation of transcription factors, and cytokine expression/production by NHMCs. In addition, ASX accumulated in the mitochondria of NHMCs and reduced the production of ROS-modified proteins in mitochondria. ASX may prevent the progression of diabetic nephropathy mainly through ROS scavenging effect in mitochondria of mesangial cells and thus is expected to be very useful for the prevention of diabetic nephropathy.

PMID: 17955498 [PubMed - indexed for MEDLINE]

Astaxanthin prevents cell death of epithelial cells through ROS-dependent mitochondrial pathway.

[J Cell Mol Med.](#) 2014 Nov;18(11):2198-212. doi: 10.1111/jcmm.12347. Epub 2014 Sep 12.

Astaxanthin inhibits apoptosis in alveolar epithelial cells type II in vivo and in vitro through the ROS-dependent mitochondrial signalling pathway.

[Song X¹](#), [Wang B](#), [Lin S](#), [Jing L](#), [Mao C](#), [Xu P](#), [Lv C](#), [Liu W](#), [Zuo J](#).

Author information

Abstract

Oxidative stress is an important molecular mechanism underlying lung fibrosis. The mitochondrion is a major organelle for oxidative stress in cells. Therefore, blocking the mitochondrial signalling pathway may be the best therapeutic manoeuvre to ameliorate lung fibrosis. Astaxanthin (AST) is an excellent antioxidant, but no study has addressed the pathway of AST against pulmonary oxidative stress and free radicals by the mitochondrion-mediated signalling pathway. In this study, we investigated the antioxidative effects of AST against H₂O₂ - or bleomycin (BLM)-induced mitochondrial dysfunction and reactive oxygen species (ROS) production in alveolar epithelial cells type II (AECs-II) in vivo and in vitro. Our data show that AST blocks H₂O₂ - or BLM-induced ROS generation and dose-dependent apoptosis in AECs-II, as characterized by changes in cell and mitochondria morphology, translocation of apoptotic proteins, inhibition of cytochrome c (Cyt c) release, and the activation of caspase-9, caspase-3, Nrf-2 and other cytoprotective genes. These data suggest that AST inhibits apoptosis in AECs-II cells through the ROS-dependent mitochondrial signalling pathway and may be of potential therapeutic value in lung fibrosis treatment.

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KEYWORDS:

ROS; astaxanthin; lung fibrosis; mitochondrial signalling pathway; oxidative stress

PMID:

25215580

[PubMed - indexed for MEDLINE]

PMCID:

PMC4224554

[Free PMC Article](#)

Astaxanthin improves muscle fibrosis caused by immobilization by reducing oxidative stress.

[J Physiol Sci](#). 2017 Sep;67(5):603-611. doi: 10.1007/s12576-016-0492-x. Epub 2016 Oct 6.

Astaxanthin supplementation attenuates immobilization-induced skeletal muscle fibrosis via suppression of oxidative stress.

[Maezawa T](#)¹, [Tanaka M](#)^{1,2}, [Kanazashi M](#)³, [Maeshige N](#)¹, [Kondo H](#)⁴, [Ishihara A](#)⁵, [Fujino H](#)⁶.

Author information

Abstract

Immobilization induces skeletal muscle fibrosis characterized by increasing collagen synthesis in the perimysium and endomysium. Transforming growth factor- β 1 (TGF- β 1) is associated with this lesion via promoting differentiation of fibroblasts into myofibroblasts. In addition, reactive oxygen species (ROS) are shown to mediate TGF- β 1-induced fibrosis in tissues. These reports suggest the importance of ROS reduction for attenuating skeletal muscle fibrosis. Astaxanthin, a powerful antioxidant, has been shown to reduce ROS production in disused muscle. Therefore, we investigated the effects of astaxanthin supplementation on muscle fibrosis under immobilization. In the present study, immobilization increased the collagen fiber area, the expression levels of TGF- β 1, α -smooth muscle actin, and superoxide dismutase-1 protein and ROS production. However, these changes induced by immobilization were attenuated by astaxanthin supplementation. These results indicate the effectiveness of astaxanthin supplementation on skeletal muscle fibrosis induced by ankle joint immobilization.

KEYWORDS:

Astaxanthin; Immobilization; Reactive oxygen species; Skeletal muscle fibrosis; Transforming growth factor- β 1

PMID: 27714500

DOI: [10.1007/s12576-016-0492-x](#)

[Indexed for MEDLINE]

ASTAXANTHIN PREVENTS ATROPHY IN MUSCLE BY REDUCING OXIDATION IN MITOCHONDRIA.

Nutrients. 2021 Jan 26;13(2):379.
doi: 10.3390/nu13020379.

Astaxanthin Prevents Atrophy in Slow Muscle Fibers by Inhibiting Mitochondrial Reactive Oxygen Species via a Mitochondria-Mediated Apoptosis Pathway

[Luchuan yang Sun](#)¹, [Nobuyuki Miyaji](#)², [Min Yang](#)¹, [Edward M Mills](#)³, [Shigeto Taniyama](#)¹, [Takayuki Uchida](#)⁴, [Takeshi Nikawa](#)⁴, [Jifeng Li](#)⁵, [Jie Shi](#)⁵, [Katsuyasu Tachibana](#)¹, [Katsuya Hirasaka](#)^{1,6}

PMID: 33530505 PMCID: [PMC7912339](#) DOI: [10.3390/nu13020379](#) [Free PMC article](#)

Abstract

Astaxanthin (AX) is a carotenoid that exerts potent antioxidant activity and acts in the lipid bilayer. This study aimed to investigate the effects of AX on muscle-atrophy-mediated disturbance of mitochondria, which have a lipid bilayer. Tail suspension was used to establish a muscle-atrophied mouse model. AX diet fed to tail-suspension mice prevented loss of muscle weight, inhibited the decrease of myofiber size, and restrained the increase of hydrogen peroxide (H₂O₂) production in the soleus muscle. Additionally, AX improved downregulation of mitochondrial respiratory chain complexes I and III in the soleus muscle after tail suspension. Meanwhile, AX promoted mitochondrial biogenesis by upregulating the expressions of *adenosine 5'-monophosphate-activated protein kinase (AMPK) α-1*, *peroxisome proliferator-activated receptor (PPAR)-γ*, and *creatine kinase in mitochondrial (Ckmt) 2* in the soleus muscle of tail-suspension mice. To confirm the AX phenotype in the soleus muscle, we examined its effects on mitochondria using Sol8 myotubes derived from the soleus muscle. We found that AX was preferentially detected in the mitochondrial fraction; it significantly suppressed mitochondrial reactive oxygen species (ROS) production in Sol8 myotubes. Moreover, AX inhibited the activation of caspase 3 via inhibiting the release of cytochrome c into the cytosol in antimycin A-treated Sol8 myotubes. These results suggested that AX protected the functional stability of mitochondria, alleviated mitochondrial oxidative stress and mitochondria-mediated apoptosis, and thus, prevented muscle atrophy.

Astaxanthin reduces muscle atrophy in rats.

[Exp Physiol.](#) 2014 Aug;99(8):1065-77. doi: 10.1113/expphysiol.2014.079988. Epub 2014 Jun 6.

Amelioration of capillary regression and atrophy of the soleus muscle in hindlimb-unloaded rats by astaxanthin supplementation and intermittent loading.

[Kanazashi M¹](#), [Tanaka M¹](#), [Murakami S²](#), [Kondo H³](#), [Nagatomo F⁴](#), [Ishihara A⁴](#), [Roy RR⁵](#), [Fujino H⁶](#).

Author information

Abstract

A chronic decrease in neuromuscular activity (activation and/or loading) results in muscle atrophy and capillary regression that are due, in part, to the overproduction of reactive oxygen species. We have reported that antioxidant treatment with astaxanthin attenuates the overexpression of reactive oxygen species in atrophied muscles that, in turn, ameliorates capillary regression in hindlimb-unloaded rats. Astaxanthin supplementation, however, had little effect on muscle mass and fibre cross-sectional area. In contrast, intermittent loading of the hindlimbs of hindlimb-unloaded rats ameliorates muscle atrophy. Therefore, we hypothesized that the combination of astaxanthin supplementation and intermittent loading would attenuate both muscle atrophy and capillary regression during hindlimb unloading. As expected, 2 weeks of hindlimb unloading resulted in atrophy, a decrease in capillary volume and a shift towards smaller-diameter capillaries in the soleus muscle. Intermittent loading alone (1 h of cage ambulation per day) attenuated atrophy of the soleus, while astaxanthin treatment alone maintained the capillary network to near control levels. The combination of intermittent loading and astaxanthin treatment, however, ameliorated atrophy of the soleus and maintained the capillary volume and luminal diameters and the superoxide dismutase-1 protein levels near control values. These results indicate that intermittent loading combined with astaxanthin supplementation could be an effective therapy for both the muscle atrophy and the capillary regression associated with a chronic decrease in neuromuscular activity.

PMID: 24907028

DOI: [10.1113/expphysiol.2014.079988](https://doi.org/10.1113/expphysiol.2014.079988)

[Indexed for MEDLINE]

Free full text

Astaxanthin reduces muscle atrophy caused by immobilization in rats.

[Physiol Rep.](#) 2016 Aug;4(15). pii: e12885. doi: 10.14814/phy2.12885.

Astaxanthin intake attenuates muscle atrophy caused by immobilization in rats.

[Shibaguchi T](#)¹, [Yamaguchi Y](#)², [Miyaji N](#)³, [Yoshihara T](#)⁴, [Naito H](#)⁴, [Goto K](#)⁵, [Ohmori D](#)⁶, [Yoshioka T](#)⁷, [Sugiura T](#)⁸.

Author information

Abstract

Astaxanthin is a carotenoid pigment and has been shown to be an effective inhibitor of oxidative damage. We tested the hypothesis that astaxanthin intake would attenuate immobilization-induced muscle atrophy in rats. Male Wistar rats (14-week old) were fed for 24 days with either astaxanthin or placebo diet. After 14 days of each experimental diet intake, the hindlimb muscles of one leg were immobilized in plantar flexion position using a plaster cast. Following 10 days of immobilization, both the atrophic and the contralateral plantaris muscles were removed and analyzed to determine the level of muscle atrophy along with measurement of the protein levels of CuZn-superoxide dismutase (CuZn-SOD) and selected proteases. Compared with placebo diet animals, the degree of muscle atrophy in response to immobilization was significantly reduced in astaxanthin diet animals. Further, astaxanthin supplementation significantly prevented the immobilization-induced increase in the expression of CuZn-SOD, cathepsin L, calpain, and ubiquitin in the atrophied muscle. These results support the postulate that dietary astaxanthin intake attenuates the rate of disuse muscle atrophy by inhibiting oxidative stress and proteolysis via three major proteolytic pathways.

KEYWORDS:

Astaxanthin; muscle atrophy; oxidative stress; protease

PMID: 27482075

PMCID: [PMC4985550](#)

DOI: [10.14814/phy2.12885](#)

[Indexed for MEDLINE]

[Free PMC Article](#)

Astaxanthin reduces muscle atrophy in rats.

[J Physiol Sci](#). 2017 Jan;67(1):181-190. doi: 10.1007/s12576-016-0453-4. Epub 2016 Apr 27.

Dietary astaxanthin supplementation attenuates disuse-induced muscle atrophy and myonuclear apoptosis in the rat soleus muscle.

[Yoshihara T](#)¹, [Yamamoto Y](#)², [Shibaguchi T](#)³, [Miyaji N](#)⁴, [Kakigi R](#)⁵, [Naito H](#)⁶, [Goto K](#)⁷, [Ohmori D](#)⁸, [Yoshioka T](#)⁹, [Sugiura T](#)¹⁰.

Author information

Abstract

Extended periods of skeletal muscle disuse results in muscle atrophy and weakness. Currently, no therapeutic treatment is available for the prevention of this problem. Nonetheless, growing evidence suggests that prevention of disuse-induced oxidative stress in inactive muscle fibers can delay inactivity-induced muscle wasting. Therefore, this study tested the hypothesis that dietary supplementation with the antioxidant astaxanthin would protect against disuse muscle atrophy, in part, by prevention of myonuclear apoptosis. Wistar rats (8 weeks old) were divided into control (CT, n = 9), hindlimb unloading (HU, n = 9), and hindlimb unloading with astaxanthin (HU + AX, n = 9) groups. Following 2 weeks of dietary supplementation, rats in the HU and HU + AX groups were exposed to unloading for 7 days. Seven-day unloading resulted in reduced soleus muscle weight and myofiber cross-sectional area (CSA) by ~30 and ~47 %, respectively. Nonetheless, relative muscle weights and CSA of the soleus muscle in the HU + AX group were significantly greater than those of the HU group. Moreover, astaxanthin prevented disuse-induced increase in the number of terminal deoxynucleotidyl transferase dUTP nick end labeling (TUNEL)-positive nuclei. We conclude that astaxanthin supplementation prior to and during hindlimb unloading attenuates soleus muscle atrophy, in part, by suppressing myonuclear apoptosis.

KEYWORDS:

Antioxidant; Apoptosis; Disuse muscle atrophy; Protein degradation

PMID: 27117878

DOI: [10.1007/s12576-016-0453-4](https://doi.org/10.1007/s12576-016-0453-4)

[Indexed for MEDLINE]

Astaxanthin's positive effect on the mitochondria responsible for its protection from heat stress in-vitro.

[J Assist Reprod Genet.](#) 2013 Jun;30(5):623-31. doi: 10.1007/s10815-013-9987-z. Epub 2013 Mar 29.

Astaxanthin ameliorates heat stress-induced impairment of blastocyst development in vitro:--astaxanthin colocalization with and action on mitochondria--.

[Kuroki T¹](#), [Ikeda S](#), [Okada T](#), [Maoka T](#), [Kitamura A](#), [Sugimoto M](#), [Kume S](#).

Author information

Abstract

PURPOSE:

The effects of astaxanthin (Ax) on the in vitro development of bovine embryos cultured under heat stress were investigated in combination with the assessment of its cellular accumulation and action on mitochondrial membrane potential ($\Delta\Psi_m$).

METHODS:

Bovine ≥ 8 -cell embryos were collected on day 3 after in vitro fertilization and exposed to single (day 4) or repeated (day 4 and 5) heat stress (10 h/day at 40.5 °C). Ax was added into culture medium under the repeated heat stress and blastocyst development was evaluated. The cellular uptake of Ax in embryos was examined using bright-field and confocal laser-scanning microscopy, and high-performance liquid chromatography. The relationship between Ax and mitochondria localization was assessed using MitoTracker dye. The effects of Ax on $\Delta\Psi_m$ were investigated using JC-1 dye.

RESULTS:

Blastocyst development in the repeated heat stress treatment decreased significantly ($P < 0.05$) compared with those in single heat stress or normal thermal treatment. The addition of Ax into culture medium did lead to a significant recovery in blastocyst development in the repeated heat-treated group. Ax was detected in cytoplasm of embryos and observed to colocalize with mitochondria. Ax recovered $\Delta\Psi_m$ in embryos that was decreased by the heat treatment.

CONCLUSIONS:

Ax ameliorated the heat stress-induced impairment of blastocyst development. Our results suggest that the direct action of Ax on mitochondrial activity via cellular uptake is a mechanism of the ameliorating effects.

PMID:

23536152

[PubMed - indexed for MEDLINE]

PMCID:

PMC3663973

[Free PMC Article](#)

Astaxanthin's prevention of damage to the mitochondria is offered as the mechanism by which it can benefit people suffering from non-alcoholic fatty liver disease.

[Med Hypotheses](#). 2011 Oct;77(4):550-6. doi: 10.1016/j.mehy.2011.06.029. Epub 2011 Jul 20.

Full-spectrum antioxidant therapy featuring astaxanthin coupled with lipoprivic strategies and salsalate for management of non-alcoholic fatty liver disease.

[McCarty MF](#)¹.

Author information

Abstract

Owing to the worldwide epidemic of obesity, and the popularity of diets rich in sugar and saturated fat, nonalcoholic fatty liver disease (NAFLD) is increasingly common; it is usually associated with insulin resistance, and may be considered a component of the metabolic syndrome. The pathologies which can complicate hepatic steatosis--steatohepatitis, cirrhosis, and hepatic cancer--appear to result from an interaction of hepatic lipid overload and hepatic oxidative stress. It is therefore proposed that comprehensive regimens which effectively target each of these precipitating factors should achieve the best therapeutic benefit in NAFLD. Appropriate weight loss, and a diet low in saturated fat, glycemic index, and added sugars, should decrease hepatic lipid load. Measures which enhance adipocyte insulin sensitivity--such as pioglitazone, astaxanthin, and spirulina--may also be helpful in this regard, as may agents that boost hepatocyte capacity for fatty acid oxidation, such as metformin, carnitine, hydroxycitrate, long-chain omega-3 fats, and glycine. Astaxanthin and spirulina appear to have considerable potential for controlling the oxidative stress associated with NAFLD - the former because it may help to prevent the mitochondrial damage that renders mitochondria a key source of superoxide in this syndrome, the latter because it is exceptionally rich in phycocyanobilin, a phytochemical inhibitor of NADPH oxidase. Other antioxidants which show some promise in this syndrome include high-dose folate, lipoic acid, melatonin, N-acetylcysteine, vitamin E, and taurine. Finally, treatment with salsalate, an inhibitor of IkappaB kinase-beta, has potential for blunting the adverse impact of hepatic steatosis on oxidative stress and inflammation.

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Astaxanthin reviewed for exercise metabolism, performance and recovery.

[Front Nutr.](#) 2018 Jan 18;4:76. doi: 10.3389/fnut.2017.00076. eCollection 2017.

Astaxanthin in Exercise Metabolism, Performance and Recovery: A Review.

[Brown DR¹](#), [Gough LA¹](#), [Deb SK¹](#), [Sparks SA¹](#), [McNaughton LR^{1,2}](#).

Author information

Abstract

During periods of heavy exercise training and competition, lipid, protein, and nucleic molecules can become damaged due to an overproduction of reactive oxygen and nitrogen species (RONS) within the exercising organism. As antioxidants can prevent and delay cellular oxidative damage through removing, deactivating, and preventing the formation of RONS, supplementation with exogenous antioxidant compounds has become a commercialized nutritional strategy commonly adopted by recreationally active individuals and athletes. The following review is written as a critical appraisal of the current literature surrounding astaxanthin and its potential application as a dietary supplement in exercising humans. Astaxanthin is a lipid-soluble antioxidant carotenoid available to supplement through the intake of *Haematococcus pluvialis*-derived antioxidant products. Based upon *in vitro* and *in vivo* research conducted in mice exercise models, evidence would suggest that astaxanthin supplementation could potentially improve indices of exercise metabolism, performance, and recovery because of its potent antioxidant capacity. In exercising humans, however, these observations have yet to be consistently realized, with equivocal data reported. Implicated, in part, by the scarcity of well-controlled, scientifically rigorous research, future investigation is necessary to enable a more robust conclusion in regard to the efficacy of astaxanthin supplementation and its potential role in substrate utilization, endurance performance, and acute recovery in exercising humans.

KEYWORDS:

Haematococcus pluvialis; antioxidants; carotenoids; delayed onset muscle soreness; endurance exercise; fat oxidation; inflammation; oxidative stress

PMID: 29404334

PMCID: [PMC5778137](#)

DOI: [10.3389/fnut.2017.00076](#)

[Free PMC Article](#)

Astaxanthin and other antioxidants reviewed for their potential in sports nutrition.

Well-Known Antioxidants and Newcomers in Sport Nutrition: Coenzyme Q10, Quercetin, Resveratrol, Pterostilbene, Pycnogenol and Astaxanthin.

Authors

[Belviranli M](#), [Okudan N](#).

Editors

In: [Lamprecht M](#), editor.

Source

Antioxidants in Sport Nutrition. Boca Raton (FL): CRC Press; 2015. Chapter 5.

Excerpt

Physical exercise induces an increase in production of free radicals and other reactive oxygen species (ROS) (Davies et al. 1982, Borzone et al. 1994, Halliwell and Gutteridge 1999). Current evidence indicates that ROS are the primary reason of exercise-induced disturbances in muscle redox balance. Severe disturbances in redox balance have been shown to promote oxidative injury and muscle fatigue (Reid et al. 1992, O'Neill et al. 1996) and thus impair the exercise performance. There are several potential sources of ROS that can be activated by exercise such as mitochondrial electron transfer chain, in the purine degradation pathway the reaction catalysed by xanthine oxidase, macrophage infiltration and metabolic degradation of catecholamines (Urso and Clarkson 2003, Finaud et al. 2006). The high production of ROS during exercise is also responsible for muscular damage (Aguiló et al. 2007). On the basis of the above-mentioned information, sportsmen have to improve their antioxidant defence systems to overcome the exercise-induced oxidative damage. Over the past few decades, many attempts have been made to improve antioxidant potential and therefore increase physical performance by improving nutrition, training programmes and other related factors. An antioxidant is generally defined as any substance that significantly delays or prevents oxidative damage of a target molecule (Halliwell 2007). The antioxidant defence system of the body consists of antioxidant enzymes (superoxide dismutases, catalase and glutathione peroxidase, etc.) and non-enzymatic antioxidants (vitamins A, C and E, coenzyme Q10 (CoQ10) and glutathione, etc.) (Deaton and Marlin 2003). There is a cooperative interaction between endogenous antioxidants and dietary antioxidants; therefore, antioxidant supplementation may improve the muscle fibre's ability to scavenge ROS and protect the exercising muscle against exercise-induced oxidative damage and fatigue. However, antioxidant nutrient deficiency could induce an increased susceptibility to exercise-induced damage and thus leads to impaired exercise performance (Stear et al. 2009). Recently, the problem of whether or not athletes should use antioxidant supplements is an important and highly debated topic. To prevent these hypothetically negative or side effects of physical exercise, supplementation with different types of antioxidants has been used in a great number of studies (Snider et al. 1992, Rokitzki et al. 1994, Reid et al. 1994, Margaritis et al. 1997, Aguiló et al. 2007, Bloomer et al. 2012). In the context of this chapter, information in brief about the well-known and recently used antioxidants such as CoQ10, quercetin, resveratrol, pterostilbene, pycnogenol and astaxanthine is given. The effects of these antioxidants on exercise performance and exercise-induced oxidative stress are also explained.

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PMID: 26065085 [PubMed]

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Astaxanthin reviewed for its many potential health benefits including prevention of exercise-induced fatigue.

[Mol Nutr Food Res.](#) 2011 Jan;55(1):150-65. doi: 10.1002/mnfr.201000414. Epub 2010 Nov 18.

Potential health-promoting effects of astaxanthin: a high-value carotenoid mostly from microalgae.

[Yuan JP](#)¹, [Peng J](#), [Yin K](#), [Wang JH](#).

Author information

Abstract

The ketocarotenoid astaxanthin can be found in the microalgae *Haematococcus pluvialis*, *Chlorella zofingiensis*, and *Chlorococcum* sp., and the red yeast *Phaffia rhodozyma*. The microalga *H. pluvialis* has the highest capacity to accumulate astaxanthin up to 4-5% of cell dry weight. Astaxanthin has been attributed with extraordinary potential for protecting the organism against a wide range of diseases, and has considerable potential and promising applications in human health. Numerous studies have shown that astaxanthin has potential health-promoting effects in the prevention and treatment of various diseases, such as cancers, chronic inflammatory diseases, metabolic syndrome, diabetes, diabetic nephropathy, cardiovascular diseases, gastrointestinal diseases, liver diseases, neurodegenerative diseases, eye diseases, skin diseases, exercise-induced fatigue, male infertility, and HgCl₂-induced acute renal failure. In this article, the currently available scientific literature regarding the most significant activities of astaxanthin is reviewed.

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PMID:

21207519

[PubMed - indexed for MEDLINE]

Astaxanthin reviewed for its many potential benefits including protection of the mitochondria.

[Altern Med Rev.](#) 2011 Dec;16(4):355-64.

Astaxanthin, cell membrane nutrient with diverse clinical benefits and anti-aging potential.

[Kidd P¹.](#)

Author information

Abstract

Astaxanthin, a xanthophyll carotenoid, is a nutrient with unique cell membrane actions and diverse clinical benefits. This molecule neutralizes free radicals or other oxidants by either accepting or donating electrons, and without being destroyed or becoming a pro-oxidant in the process. Its linear, polar-nonpolar-polar molecular layout equips it to precisely insert into the membrane and span its entire width. In this position, astaxanthin can intercept reactive molecular species within the membrane's hydrophobic interior and along its hydrophilic boundaries. Clinically, astaxanthin has shown diverse benefits, with excellent safety and tolerability. In double-blind, randomized controlled trials (RCTs), astaxanthin lowered oxidative stress in overweight and obese subjects and in smokers. It blocked oxidative DNA damage, lowered C-reactive protein (CRP) and other inflammation biomarkers, and boosted immunity in the tuberculin skin test. Astaxanthin lowered triglycerides and raised HDL-cholesterol in another trial and improved blood flow in an experimental microcirculation model. It improved cognition in a small clinical trial and boosted proliferation and differentiation of cultured nerve stem cells. In several Japanese RCTs, astaxanthin improved visual acuity and eye accommodation. It improved reproductive performance in men and reflux symptoms in H. pylori patients. In preliminary trials it showed promise for sports performance (soccer). In cultured cells, astaxanthin protected the mitochondria against endogenous oxygen radicals, conserved their redox (antioxidant) capacity, and enhanced their energy production efficiency. The concentrations used in these cells would be attainable in humans by modest dietary intakes. Astaxanthin's clinical success extends beyond protection against oxidative stress and inflammation, to demonstrable promise for slowing age-related functional decline.

PMID:

22214255

[PubMed - indexed for MEDLINE]

Free full text

ASTAXANTHIN REVIEWED FOR ITS POTENTIAL TO TREAT SARCOPENIA.

Exp Ther Med. 2020 Oct;20(4):2941-2952.

doi: 10.3892/etm.2020.9075. Epub 2020 Jul 29.

Effects of astaxanthin on the protection of muscle health (Review)

[Sok Kuan Wong](#)¹, [Soelaiman Ima-Nirwana](#)¹, [Kok-Yong Chin](#)¹

- PMID: 32855659
- PMCID: [PMC7444411](#)
- DOI: [10.3892/etm.2020.9075](#)

Free PMC article

Abstract

Sarcopenia refers to the involuntary and generalized deterioration of skeletal muscle mass and strength, which may lead to falls, frailty, physical disability, loss of independence, morbidity and mortality. The majority of molecular and cellular changes involved in the degeneration of muscle tissues are mediated by oxidative stress. Therefore, astaxanthin may act as a potential adjunct therapy for sarcopenia owing to its antioxidant activity. The present review examines the effects of astaxanthin on the promotion of skeletal muscle performance and prevention of muscle atrophy and the potential mechanisms underlying these effects. The available evidence till date was retrieved from PubMed and Medline electronic databases. The present review reported the beneficial effects of astaxanthin in preventing muscle degeneration in various animal models of sarcopenia. In humans, the effects of astaxanthin in combination with other antioxidants on muscle health are mixed, wherein positive and negligible effects were reported. Mechanistic studies revealed that astaxanthin promotes muscle health by reducing oxidative stress, myoblast apoptosis and proteolytic pathways while promoting mitochondria regeneration and formation of blood vessels. Thus, astaxanthin is a potential therapeutic agent for sarcopenia but its effects in humans require further validation.

Immunity

Astaxanthin at 2mg per day enhances immune response in healthy adults and decreases DNA damage in double-blind, placebo-controlled human clinical trial.

[Nutr Metab \(Lond\)](#). 2010 Mar 5;7:18.

Astaxanthin decreased oxidative stress and inflammation and enhanced immune response in humans.

[Park JS](#), [Chyun JH](#), [Kim YK](#), [Line LL](#), [Chew BP](#).

School of Food Science, Washington State University, Pullman, WA 99164-6376 USA.

boonchew@wsu.edu.

ABSTRACT:

BACKGROUND: Astaxanthin modulates immune response, inhibits cancer cell growth, reduces bacterial load and gastric inflammation, and protects against UVA-induced oxidative stress in in vitro and rodent models. Similar clinical studies in humans are unavailable. Our objective is to study the action of dietary astaxanthin in modulating immune response, oxidative status and inflammation in young healthy adult female human subjects.

METHODS: Participants (averaged 21.5 yr) received 0, 2, or 8 mg astaxanthin (n = 14/diet) daily for 8 wk in a randomized double-blind, placebo-controlled study. Immune response was assessed on wk 0, 4 and 8, and tuberculin test performed on wk 8.

RESULTS: Plasma astaxanthin increased ($P < 0.01$) dose-dependently after 4 or 8 wk of supplementation. Astaxanthin decreased a DNA damage biomarker after 4 wk but did not affect lipid peroxidation. Plasma C-reactive protein concentration was lower ($P < 0.05$) on wk 8 in subjects given 2 mg astaxanthin. Dietary astaxanthin stimulated mitogen-induced lymphoproliferation, increased natural killer cell cytotoxic activity, and increased total T and B cell subpopulations, but did not influence populations of Thelper, Tcytotoxic or natural killer cells. A higher percentage of leukocytes expressed the LFA-1 marker in subjects given 2 mg astaxanthin on wk 8. Subjects fed 2 mg astaxanthin had a higher tuberculin response than unsupplemented subjects. There was no difference in TNF and IL-2 concentrations, but plasma IFN-gamma and IL-6 increased on wk 8 in subjects given 8 mg astaxanthin.

CONCLUSION: Therefore, dietary astaxanthin decreases a DNA damage biomarker and acute phase protein, and enhances immune response in young healthy females.

PMID: 20205737 [PubMed - in process]PMCID: PMC2845588

Astaxanthin raises immunoglobulin levels in healthy young athletes in double-blind, placebo-controlled human clinical study.

[Evid Based Complement Alternat Med.](#) 2015;2015:783761. doi: 10.1155/2015/783761. Epub 2015 Jun 18.

Effect of Astaxanthin Supplementation on Salivary IgA, Oxidative Stress, and Inflammation in Young Soccer Players.

[Baralic I¹](#), [Andjelkovic M¹](#), [Djordjevic B²](#), [Dikic N¹](#), [Radivojevic N¹](#), [Suzin-Zivkovic V³](#), [Radojevic-Skodric S⁴](#), [Pejic S⁵](#).

Author information

Abstract

The physiologic stress induced by physical activity is reflected in immune system perturbations, oxidative stress, muscle injury, and inflammation. We investigated the effect of astaxanthin (Asx) supplementation on salivary IgA (sIgA) and oxidative stress status in plasma, along with changes in biochemical parameters and total/differential white cell counts. Forty trained male soccer players were randomly assigned to Asx and placebo groups. Asx group was supplemented with 4 mg of Asx. Saliva and blood samples were collected at the baseline and after 90 days of supplementation in preexercise conditions. We observed a rise of sIgA levels at rest after 90 days of Asx supplementation, which was accompanied with a decrease in prooxidant-antioxidant balance. The plasma muscle enzymes levels were reduced significantly by Asx supplementation and by regular training. The increase in neutrophil count and hs-CRP level was found only in placebo group, indicating a significant blunting of the systemic inflammatory response in the subjects taking Asx. This study indicates that Asx supplementation improves sIgA response and attenuates muscle damage, thus preventing inflammation induced by rigorous physical training. Our findings also point that Asx could show significant physiologic modulation in individuals with mucosal immunity impairment or under conditions of increased oxidative stress and inflammation.

PMID:

26167194

[PubMed]

PMCID:

PMC4488551

[Free PMC Article](#)

Astaxanthin increases salivary output and decreases an oxidative stress marker in human clinical trial on patients with an auto-immune disease.

[J Clin Biochem Nutr.](#) 2010 Sep;47(2):130-7. Epub 2010 Jun 22.

Evaluation of therapeutic effects of astaxanthin on impairments in salivary secretion.

[Yamada T](#), [Ryo K](#), [Tai Y](#), [Tamaki Y](#), [Inoue H](#), [Mishima K](#), [Tsubota K](#), [Saito I](#).

Department of Pathology, Tsurumi University School of Dental Medicine, 2-1-3, Tsurumi, Tsurumi-ku, Yokohama 230-8501, Japan.

Abstract

The involvement of reactive oxygen species (ROS) in the pathophysiology of Sjögren's syndrome (SS), an autoimmune disorder, and irradiation-induced impairments in salivary secretion has been reported. Meanwhile, the strong antioxidant astaxanthin (Ast) has been suggested to have therapeutic effects on various diseases. In the present study, we examined the ROS scavenging capacity of Ast using a human salivary gland epithelial cell line (HSY) and investigated the effects of Ast on salivary secretion in a mouse model of irradiation-induced salivary gland dysfunction. Furthermore, we performed a clinical study of Ast in six SS patients and six normal individuals, quantifying the volume of saliva secretion and the level of oxidative stress markers in the saliva. Ast partially suppressed hydrogen peroxide-induced ROS in HSY cells. The mouse model demonstrated that the pre-administration of Ast resulted in the suppression of irradiation-induced hyposalivation. Furthermore, the administration of Ast appeared to increase salivary output in both the SS and normal groups. The level of oxidative stress marker, hexanoyl-lysine, in the saliva was reduced after Ast intake. These results suggest that Ast might act as an ROS scavenger, providing benefits to SS patients with impaired salivary secretion.

PMID: 20838568 [PubMed - in process]PMCID: PMC2935153

Astaxanthin suppresses lymphocyte activation more effectively than ginkgolide B in-vitro in patients with allergic rhinitis and pollen-related asthma.

[Acta Physiol Hung.](#) 2012 Jun;99(2):173-84. doi: 10.1556/APhysiol.99.2012.2.11.

In vitro suppression of lymphocyte activation in patients with seasonal allergic rhinitis and pollen-related asthma by cetirizine or azelastine in combination with ginkgolide B or astaxanthin.

[Mahmoud FF¹](#), [Haines D](#), [Al-Awadhi R](#), [Arifhodzic N](#), [Abal A](#), [Azeamouzi C](#), [Al-Sharah S](#), [Tosaki A](#).

Author information

Abstract

Novel strategies are evaluated for management of allergic rhinitis and asthma in patients co-afflicted with both disorders. It is hypothesized that the platelet activating factor receptor antagonist ginkgolide B (GB) and the carotenoid antioxidant astaxanthin (ASX) interact with antihistamines cetirizine dihydrochloride (CTZ) and azelastine (AZE) to potentiate their ability to downregulate potentially pathological immune activation. Peripheral blood mononuclear cells from asthmatics and healthy subjects, cultured 24 hours with 50 µg/ml phytohemagglutinin (PHA) or PHA plus each drug are analyzed by flow cytometry for expression of CD25+ or HLA-DR+ by CD3+ (T cells). Results are reported as stimulation indices for CD3+CD25+ (SICD3+CD25+) and CD3+HLA-DR+ (SICD3+HLADR+) cells in cultures treated with PHA alone, versus cultures treated with both PHA and drugs. Optimal suppression of activated cells was observed in cultures stimulated with ASX 10⁻⁶ M + CTZ 10⁻⁶ M (SICD3+CD25+, p = 0.016; SICD3+HLADR, p = 0.012); ASX 10⁻⁶ M + AZE 10⁻⁶ M (SICD3+CD25+, p = 0.012; SICD3+HLADR, p = 0.015); GB 10⁻⁶ M + CTZ 10⁻⁶ M (SICD3+CD25+, p = 0.024, SICD3+HLADR+, p = 0.019). Results demonstrate improved activity of antihistamines by 2 phytochemicals, suggesting dosing strategies for animal trials of ASX- or GB-augmented formulations for seasonal allergic rhinitis and asthma.

PMID:

22849842

[PubMed - indexed for MEDLINE]

Astaxanthin affects various markers in patients with sickle cell disease in clinical human trial.

Free Radicals and Antioxidants (2013). <http://dx.doi.org/10.1016/j.fra.2013.10.1003>

Supplementation of patients with sickle cell disease with astaxanthin increases plasma- and erythrocyte-astaxanthin and may improve the hemolytic component of the disease

Begoña Ruiz-Núñez^aStéphanie A.De Rooij^aPieter J.Offringa^bGert E.Schuitemaker^cTomTeerlink^dHose S.M.Booi^eJanneke D.A.Dijck-Brouwer^aFrits A.J.Muskiet^a

<https://doi.org/10.1016/j.fra.2013.10.1003>Get rights and content

Aim & background: [Sickle cell disease](#) (SCD) is characterized by hemolytic and vaso-occlusive components. [Astaxanthin](#) is a [carotenoid](#) of marine origin, without [pro-oxidant](#) properties.

Methods: In this open label pilot study, we investigated whether orally administered astaxanthin incorporates into erythrocytes (RBC) of SCD patients and studied the effect on hematological and clinical chemical parameters. Ten SCD patients (6–52 years) in Sint Maarten received 8–12 mg astaxanthin during 3 months.

Results: Baseline plasma- (33 nmol/L) and RBC- (11 nmol/L packed RBC) astaxanthin increased to 225, 174, 167 nmol/L (plasma) and 149, 100, 71 nmol/L packed RBC at 1–3 months, respectively. [Reticulocytes](#) decreased from baseline and 2 months (9.5 and 8.8%) to 3 months (5.6%), [MCV](#) from 2 to 3 months (88–86 fL), [MCH](#) from baseline to 3 months (30–28 pg) and [RDW](#) from baseline and 2 months (19.2 and 19.0%) to 3 months (16.7%). Plasma [arginine](#) decreased from 2 to 3 months (46.6–39.4 μmol/L). [Asymmetric dimethylarginine](#) (ADMA) did not change. Reticulocytes at baseline correlated with relative changes in reticulocytes from baseline to 3 months. Relative changes in reticulocytes correlated with relative changes in RBC, [RDW](#), [LDH](#), [ALAT](#), but not [hematocrit](#), within the same period.

Conclusion: Astaxanthin incorporates into SCD RBC and may favorably affect the hemolytic component. A larger randomized controlled trial is indicated, using similar or [higher dose](#), preferably during more than 3 months, concomitant with (other) [low dose antioxidants](#) (vitamin E, [beta-carotene](#), [vitamin C](#), folic acid), minerals (zinc, if necessary, selenium), arginine, [fish oil](#) and [vitamin D](#).

ASTAXANTHIN EFFECTIVE IN ENHANCING IMMUNITY IN MICE WITHOUT ANY SIGN OF TOXICITY.

Foods 2021 Aug 10;10(8):1847. doi: 10.3390/foods10081847.

Study on the Enhancement of Immune Function of Astaxanthin from *Haematococcus pluvialis*

[Qingsheng Fan](#)¹, [Zhan Chen](#)¹, [Yating Wu](#)¹, [Jiangxin Zhu](#)¹, [Zhou Yu](#)¹

- PMID: 34441624 PMCID: [PMC8394466](#) DOI: [10.3390/foods10081847](#)

Free PMC article

Abstract

This study was aimed at investigating the effect of astaxanthin on the immune function and its safety in mice. It was administered once daily at low, medium and high doses (4.2, 8.35, 16.70 mg/kg BW) to mice for 30 days. Subsequently, the spleen and thymus index, spleen lymphocyte transformation activity, delayed allergy reaction, amounts of antibody-producing cells, half-hemolytic value HC_{50} , carbon particle clearance rate, macrophage phagocytosis, and natural killer cell (NK) activity were determined. Acute oral toxicity and genotoxicity tests were conducted to evaluate the safety of astaxanthin. Compared with the control group, medium and high doses of astaxanthin significantly increased the proliferation and transformation activities of spleen lymphocytes, activities of antibody-producing cells, serum hemolysin levels, and carbon particle clearance rate in mice (phagocytic index). High doses significantly improved delayed allergy reaction and NK cell activity. Results of acute oral toxicity and genotoxicity tests were negative. Gross anatomical observations and histopathological examination showed no abnormal changes associated with the treatments. In the article, it is confirmed that astaxanthin treatments significantly improve immune functions and show no toxic effects in the experimental doses.

Astaxanthin enhances immunity, improves resistance to environmental stress, increases growth rates and supports the antioxidant defense system in pufferfish.

[Fish Physiol Biochem.](#) 2018 Feb;44(1):209-218. doi: 10.1007/s10695-017-0425-5. Epub 2017 Sep 21.

Effect of dietary astaxanthin on the growth performance, non-specific immunity, and antioxidant capacity of pufferfish (*Takifugu obscurus*) under high temperature stress.

[Cheng CH](#)^{1,2}, [Guo ZX](#)^{3,4}, [Ye CX](#)^{2,5}, [Wang AL](#)^{6,7}.

Author information

Abstract

The present study was conducted to investigate the effects of astaxanthin on growth performance, biochemical parameters, ROS production, and immune-related gene expressions of the pufferfish (*Takifugu obscurus*) under high temperature stress. The experimental basal diets supplemented with astaxanthin at the rates of 0 (control), 20, 40, 80, 160, and 320 mg kg⁻¹ were fed to fish for 8 weeks. The results showed that the fish fed diet with 80, 160, and 320 mg kg⁻¹ astaxanthin significantly improved weight gain and specific growth rate. Furthermore, fish fed the moderate dietary astaxanthin increased plasma alkaline phosphatase activities, and decrease plasma aspartate aminotransferase and alanine aminotransferase activities. After the feeding trial, the fish were exposed to high temperature stress for 48 h. The results shown that astaxanthin could suppress ROS production induced by high temperature stress. Meanwhile, compared with the control group, the astaxanthin groups increased SOD, CAT, and HSP70 mRNA levels under high temperature stress. These results showed that the basal diet supplemented with 80-320 mg kg⁻¹ astaxanthin could enhance growth, nonspecific immune responses, and antioxidant defense system and improve resistance against high temperature stress in pufferfish.

KEYWORDS:

Astaxanthin; Growth performance; High temperature stress; Immune response; *Takifugu obscurus*

PMID: 28936571

DOI: [10.1007/s10695-017-0425-5](https://doi.org/10.1007/s10695-017-0425-5)

[Indexed for MEDLINE]

Astaxanthin improves immune capacity, increases survival and reduces susceptibility to environmental stress in shrimp.

[Fish Shellfish Immunol.](#) 2018 Sep;80:452-457. doi: 10.1016/j.fsi.2018.06.039. Epub 2018 Jun 20.

Dietary supplementation of *Haematococcus pluvialis* improved the immune capacity and low salinity tolerance ability of post-larval white shrimp, *Litopenaeus vannamei*.

[Xie S](#)¹, [Fang W](#)¹, [Wei D](#)¹, [Liu Y](#)¹, [Yin P](#)¹, [Niu J](#)¹, [Tian L](#)².

Author information

Abstract

A 25-days experiment was conducted to evaluate the effect of dietary *Haematococcus pluvialis* on growth, survival, immune response and stress tolerance ability of post-larval *Litopenaeus vannamei*. Post-larval white shrimp (mean initial weight 2.1 mg) were fed five isoenergetic and isonitrogenous diets containing grade levels of *Haematococcus pluvialis* (0, 1.7, 3.3, 6.7 and 13.3 g kg⁻¹ diet, respectively). Results indicated that 3.3 g *Haematococcus pluvialis* kg⁻¹ diet increased the survival rate of post-larval white shrimp. Specific growth rate (SGR) and weight gain (WG) showed no difference among each groups. After the acute salinity stress (salinity decreased rapidly from 28‰ to 5‰), survival of shrimp fed 6.7 g *Haematococcus pluvialis* kg⁻¹ diet significant higher than the control ($P < 0.05$), and the total antioxidant capacity (T-AOC) was increased with the increasing dietary *Haematococcus pluvialis* levels. The malonaldehyde (MDA) contents in whole body decreased with the increasing dietary *Haematococcus pluvialis* levels before and after the salinity stress. Before the salinity stress, relative mRNA levels of Caspase 3, Rho and Janus kinase (JAK) decreased in shrimp fed diets contain *Haematococcus pluvialis*. After the salinity stress, relative mRNA levels of anti-oxidative related genes and immune related genes decreased with the dietary *Haematococcus pluvialis* level increased to 3.3 g kg⁻¹. Based on the effect of *Haematococcus pluvialis* on survival, salinity stress tolerance ability and the immune response of post-larval *L. vannamei*, the optimal level of *Haematococcus pluvialis* was 3.3-6.7 g kg⁻¹ diet (100-200 mg astaxanthin kg⁻¹ diet).

KEYWORDS:

Haematococcus pluvialis; Immune capacity; NF-κB pathway; Post-larval; Salinity stress

PMID: 29933110

DOI: [10.1016/j.fsi.2018.06.039](https://doi.org/10.1016/j.fsi.2018.06.039)

Astaxanthin stimulates cell-mediated and humoral immune response in cats.

[Vet Immunol Immunopathol.](#) 2011 Sep 3. [Epub ahead of print]

Astaxanthin stimulates cell-mediated and humoral immune responses in cats.

[Park JS](#), [Mathison BD](#), [Hayek MG](#), [Massimino S](#), [Reinhart GA](#), [Chew BP](#).

Source

School of Food Science, Washington State University, Pullman, WA 99164-6376, USA.

Abstract

Astaxanthin is a potent antioxidant carotenoid and may play a role in modulating immune response in cats. Blood was taken from female domestic shorthair cats (8-9mo old; 3.2±0.04kg body weight) fed 0, 1, 5 or 10mg astaxanthin daily for 12wk to assess peripheral blood mononuclear cell (PBMC) proliferation response, leukocyte subpopulations, natural killer (NK) cell cytotoxic activity, and plasma IgG and IgM concentration. Cutaneous delayed-type hypersensitivity (DTH) response against concanavalin A and an attenuated polyvalent vaccine was assessed on wk 8 (prior to vaccination) and 12 (post-vaccination). There was a dose-related increase in plasma astaxanthin concentrations, with maximum concentrations observed on wk 12. Dietary astaxanthin enhanced DTH response to both the specific (vaccine) and nonspecific (concanavalin A) antigens. In addition, cats fed astaxanthin had heightened PBMC proliferation and NK cell cytotoxic activity. The population of CD3(+) total T and CD4(+) T helper cells were also higher in astaxanthin-fed cats; however, no treatment difference was found with the CD8(+) T cytotoxic and MHC II(+) activated lymphocyte cell populations. Dietary astaxanthin increased concentrations of plasma IgG and IgM. Therefore, dietary astaxanthin heightened cell-mediated and humoral immune responses in cats.

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PMID: 21930306 [PubMed - as supplied by publisher]

Astaxanthin enhances immune response in dogs.

[Vet Immunol Immunopathol.](#) 2011 Apr 15;140(3-4):199-206. Epub 2010 Dec 14.

Dietary astaxanthin enhances immune response in dogs.

[Chew BP](#), [Mathison BD](#), [Hayek MG](#), [Massimino S](#), [Reinhart GA](#), [Park JS](#).

Source

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Abstract

No information is available on the possible role of astaxanthin on immune response in domestic canine. Female Beagle dogs (9-10 mo old; 8.2 ± 0.2 kg body weight) were fed 0, 10, 20 or 40 mg astaxanthin daily and blood sampled on wk 0, 6, 12, and 16 for assessing the following: lymphoproliferation, leukocyte subpopulations, natural killer (NK) cell cytotoxicity, and concentrations of blood astaxanthin, IgG, IgM and acute phase proteins. Delayed-type hypersensitivity (DTH) response was assessed on wk 0, 12 and 16. Plasma astaxanthin increased dose-dependently and reached maximum concentrations on wk 6. Dietary astaxanthin enhanced DTH response to vaccine, concanavalin A-induced lymphocyte proliferation (with the 20mg dose at wk 12) and NK cell cytotoxic activity. In addition, dietary astaxanthin increased concentrations of IgG and IgM, and B cell population. Plasma concentrations of C reactive protein were lower in astaxanthin-fed dogs. Therefore, dietary astaxanthin heightened cell-mediated and humoral immune response and reduced DNA damage and inflammation in dogs.

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PMID: 21208664 [PubMed - indexed for MEDLINE]

Astaxanthin stimulates immune response in-vitro and in mice.

[Int J Mol Sci](#). 2015 Dec 29;17(1). pii: E44. doi: 10.3390/ijms17010044.

Astaxanthin, a Carotenoid, Stimulates Immune Responses by Enhancing IFN- γ and IL-2 Secretion in Primary Cultured Lymphocytes in Vitro and ex Vivo.

[Lin KH](#)^{1,2}, [Lin KC](#)^{3,4}, [Lu WJ](#)⁵, [Thomas PA](#)⁶, [Jayakumar T](#)⁷, [Sheu JR](#)⁸.

Author information

Abstract

Astaxanthin, a potent antioxidant carotenoid, plays a major role in modulating the immune response. In this study, we examined the immunomodulatory effects of astaxanthin on cytokine production in primary cultured lymphocytes both in vitro and ex vivo. Direct administration of astaxanthin (70-300 nM) did not produce cytotoxicity in lipopolysaccharide (LPS, 100 μ g/ mL)- or concanavalin A (Con A, 10 μ g/ mL)-activated lymphocytes, whereas astaxanthin alone at 300 nM induced proliferation of splenic lymphocytes ($p < 0.05$) in vitro. Although astaxanthin, alone or with Con A, had no apparent effect on interferon (INF- γ) and interleukin (IL-2) production in primary cultured lymphocytes, it enhanced LPS-induced INF- γ production. In an ex vivo experiment, oral administration of astaxanthin (0.28, 1.4 and 7 mg/kg/day) for 14 days did not cause alterations in the body or spleen weights of mice and also was not toxic to lymphocyte cells derived from the mice. Moreover, treatment with astaxanthin significantly increased LPS-induced lymphocyte proliferation ex vivo but not Con A-stimulated lymphocyte proliferation ex vivo. Enzyme linked immunosorbent assay (ELISA) analysis revealed that administration of astaxanthin significantly enhanced INF- γ production in response to both LPS and Con A stimulation, whereas IL-2 production increased only in response to Con A stimulation. Also, astaxanthin treatment alone significantly increased IL-2 production in lymphocytes derived from mice, but did not significantly change production of INF- γ . These findings suggest that astaxanthin modulates lymphocytic immune responses in vitro, and that it partly exerts its ex vivo immunomodulatory effects by increasing INF- γ and IL-2 production without inducing cytotoxicity.

KEYWORDS:

Con A; IL-2; INF- γ ; LPS; astaxanthin; immunomodulation; lymphocytes; mice

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[PubMed - in process]

PMCID: PMC4730289

[Free PMC Article](#)

ASTAXANTHIN HAS POTENTIAL TO ALLEVIATE CYTOKINE STORM (A SEVERE IMMUNE REACTION) DUE TO COVID-19.

Biomed Pharmacother. 2020 Dec;132:110886.

doi: 10.1016/j.biopha.2020.110886. Epub 2020 Oct 16.

Potential of natural astaxanthin in alleviating the risk of cytokine storm in COVID-19

[Jayanta Talukdar](#)¹, [Bhaskar Bhadra](#)², [Tomal Dattaroy](#)², [Vinod Nagle](#)², [Santanu Dasgupta](#)²

PMID: **33113418** PMCID: [PMC7566765](#) DOI: [10.1016/j.biopha.2020.110886](#) **Free PMC article**

Abstract

Host excessive inflammatory immune response to SARS-CoV-2 infection is thought to underpin the pathogenesis of COVID-19 associated severe pneumonitis and acute lung injury (ALI) or acute respiratory distress syndrome (ARDS). Once an immunological complication like cytokine storm occurs, anti-viral based monotherapy alone is not enough. Additional anti-inflammatory treatment is recommended. It must be noted that anti-inflammatory drugs such as JAK inhibitors, IL-6 inhibitors, TNF- α inhibitors, colchicine, etc., have been either suggested or are under trials for managing cytokine storm in COVID-19 infections. Natural astaxanthin (ASX) has a clinically proven safety profile and has antioxidant, anti-inflammatory, and immunomodulatory properties. There is evidence from preclinical studies that supports its preventive actions against ALI/ARDS. Moreover, ASX has a potent PPARs activity. Therefore, it is plausible to speculate that ASX could be considered as a potential adjunctive supplement. Here, we summarize the mounting evidence where ASX is shown to exert protective effect by regulating the expression of pro-inflammatory factors IL-1 β , IL-6, IL-8 and TNF- α . We present reports where ASX is shown to prevent against oxidative damage and attenuate exacerbation of the inflammatory responses by regulating signaling pathways like NF- κ B, NLRP3 and JAK/STAT. These evidences provide a rationale for considering natural astaxanthin as a therapeutic agent against inflammatory cytokine storm and associated risks in COVID-19 infection and this suggestion requires further validation with clinical studies.

Astaxanthin may exert anti-tumor activity through the enhancement of the immune response in mice.

NUTRITION AND CANCER, 36(1), 59-65

Antitumor Activity of Astaxanthin and Its Mode of Action

Harumi Jyonouchi, Sinine Sun, KoJi [I]Iima, and Myron D. Gross

Astaxanthin, a carotenoid without Vitamin A activity, may exert antitumor activity through the enhancement of immune response. Here, we determined the effects of dietary astaxanthin on tumor growth and tumor immunity against transplantable methylcholanthrene-induced fibrosarcoma (Meth-A tumor) cells. These tumor cells express a tumor antigen that induces T cell-mediated immune responses in syngenic mice. BALB/c mice were fed astaxanthin (0.02%, 40 µg/kg body wt/day in a beadlet form) mixed in a chemically defined diet starting zero, one, and three weeks before subcutaneous inoculation with tumor cells (3×10^5 cells, 2 times the minimal tumorigenic dose). Three weeks after inoculation, tumor size and weight were determined. We also determined cytotoxic T lymphocyte (CTL) activity and interferon- γ (IFN- γ) production by tumor-draining lymph node (TDLN) and spleen cells by restimulating cells with Meth-A tumor cells in culture. The astaxanthin-fed mice had significantly lower tumor size and weight than controls when supplementation was started one and three weeks before tumor inoculation. This antitumor activity was paralleled with higher CTL activity and IFN- γ production by TDLN and spleen cells in the astaxanthin-fed mice. CTL activity by TDLN cells was highest in mice fed astaxanthin for three weeks before inoculation. When the astaxanthin-supplemented diet was started at the same time as tumor inoculation, none of these parameters were altered by dietary astaxanthin-supplemented diet was started at the same time as tumor inoculation, none of these parameters were altered by dietary astaxanthin, except IFN- γ production by spleen cells. Total serum astaxanthin concentrations were approximately 1.2 µmol/l when mice were fed astaxanthin (0.02%) for four weeks and appeared to increase in correlation with the length of astaxanthin supplementation. Our results indicate that dietary astaxanthin suppressed Meth-A tumor cell growth and stimulated immunity against Meth-A tumor antigen.

Astaxanthin improves tumor immune response in mice.

[Life Sci.](#) 2002 Apr 21;70(21):2509-20.

Contribution of the antioxidative property of astaxanthin to its protective effect on the promotion of cancer metastasis in mice treated with restraint stress.

[Kurihara H](#)¹, [Koda H](#), [Asami S](#), [Kiso Y](#), [Tanaka T](#).

Author information

Abstract

We investigated the effects of astaxanthin on the antitumor effector activity of natural killer (NK) cells suppressed by stress in mice in order to define the immunological significance of astaxanthin (ASX) when combined with restraint stress treatment. When the mice were treated with restraint stress alone, the total number of spleen cells, and the level NK cell activity per spleen were reduced to a nadir on day 3. The stress also caused a significant increase in the lipid peroxidation of liver tissue. ASX (100 mg/kg/day, p.o., 4 days) improved the immunological dysfunction induced by restraint stress. On the other hand, metastatic nodules were observed in the livers of syngenic DBA/2 mice on day 12 after inoculation of P815 mastocytoma cells. Hepatic metastasis was promoted further by restraint stress when applied on day 3 before the inoculation of P815. Daily oral administration of ASX (1 mg/kg/day, p.o., 14 days) markedly attenuated the promotion of hepatic metastasis induced by restraint stress. These results suggested that astaxanthin improves antitumor immune responses by inhibiting of lipid peroxidation induced by stress.

PMID:

12173414

[PubMed - indexed for MEDLINE]

Astaxanthin reduces immune liver injury in rat model of autoimmune hepatitis.

[PLoS One](#). 2015 Mar 11;10(3):e0120440. doi: 10.1371/journal.pone.0120440. eCollection 2015.

Protective effects of astaxanthin on ConA-induced autoimmune hepatitis by the JNK/p-JNK pathway-mediated inhibition of autophagy and apoptosis.

[Li J¹](#), [Xia Y¹](#), [Liu T¹](#), [Wang J¹](#), [Dai W¹](#), [Wang F¹](#), [Zheng Y¹](#), [Chen K¹](#), [Li S¹](#), [Abudumijiti H¹](#), [Zhou Z²](#), [Wang J²](#), [Lu W²](#), [Zhu R²](#), [Yang J¹](#), [Zhang H³](#), [Yin Q³](#), [Wang C¹](#), [Zhou Y³](#), [Lu J¹](#), [Zhou Y¹](#), [Guo C¹](#).

Author information

Abstract

OBJECTIVE:

Astaxanthin, a potent antioxidant, exhibits a wide range of biological activities, including antioxidant, atherosclerosis and antitumor activities. However, its effect on concanavalin A (ConA)-induced autoimmune hepatitis remains unclear. The aim of this study was to investigate the protective effects of astaxanthin on ConA-induced hepatitis in mice, and to elucidate the mechanisms of regulation.

MATERIALS AND METHODS:

Autoimmune hepatitis was induced in Balb/C mice using ConA (25 mg/kg), and astaxanthin was orally administered daily at two doses (20 mg/kg and 40 mg/kg) for 14 days before ConA injection. Levels of serum liver enzymes and the histopathology of inflammatory cytokines and other marker proteins were determined at three time points (2, 8 and 24 h). Primary hepatocytes were pretreated with astaxanthin (80 μ M) in vitro 24 h before stimulation with TNF- α (10 ng/ml). The apoptosis rate and related protein expression were determined 24 h after the administration of TNF- α .

RESULTS:

Astaxanthin attenuated serum liver enzymes and pathological damage by reducing the release of inflammatory factors. It performed anti-apoptotic effects via the descending phosphorylation of Bcl-2 through the down-regulation of the JNK/p-JNK pathway.

CONCLUSION:

This research firstly expounded that astaxanthin reduced immune liver injury in ConA-induced autoimmune hepatitis. The mode of action appears to be downregulation of JNK/p-JNK-mediated apoptosis and autophagy.

PMID:

25761053

[PubMed - in process]

PMCID:

PMC4356569

Free PMC Article

Astaxanthin modulates immune response and delays tumor growth in mice.

[Anticancer Res.](#) 2010 Jun;30(6):2171-5.

Effect of dietary astaxanthin at different stages of mammary tumor initiation in BALB/c mice.

[Nakao R¹](#), [Nelson OL](#), [Park JS](#), [Mathison BD](#), [Thompson PA](#), [Chew BP](#).

Author information

Abstract

The effects of astaxanthin on tumor growth, cardiac function and immune response in mice were studied. Female BALB/c mice were fed a control diet (diet C) for 8 weeks, 0.005% astaxanthin for 8 weeks (diet A), or diet C for weeks 1-5 followed by diet A thereafter (diet CA). Mice were injected with a mammary tumor cell line on day 7 and tumor growth was measured daily. Mice fed diet A had extended tumor latency and lower tumor volume ($p < 0.05$). Interestingly, those fed diet CA showed the fastest tumor growth. Astaxanthin feeding elevated plasma astaxanthin concentrations; there was no difference in plasma astaxanthin between mice fed CA and those fed A. Mice fed diet A, but not CA, had a higher ($p < 0.05$) natural killer cell subpopulation and plasma interferon-gamma concentration compared to those fed diet C. Astaxanthin delayed tumor growth and modulated immune response, but only when astaxanthin was given before tumor initiation. This suggests that an adequate blood astaxanthin status is needed to protect against tumor initiation; conversely, astaxanthin supplementation after tumor initiation may be contraindicated.

PMID:

20651366

[PubMed - indexed for MEDLINE]

ASTAXANTHIN STIMULATES THE IMMUNE RESPONSE OF *H. PYLORI*-INFECTED MICE.

Mar Drugs. 2019 Jun 26;17(7):382.
doi: 10.3390/md17070382.

Astaxanthin from Shrimp Cephalothorax Stimulates the Immune Response by Enhancing IFN- γ , IL-10, and IL-2 Secretion in Splenocytes of *Helicobacter Pylori*-Infected Mice

[Sergio Davinelli](#)¹, [Heidi Mikkelsen Melvang](#)², [Leif Percival Andersen](#)³, [Giovanni Scapagnini](#)⁴, [Michael Engelbrecht Nielsen](#)⁵

- PMID: **31248010**
- PMCID: [PMC6669458](#)
- DOI: [10.3390/md17070382](#)

Abstract

Infection with *Helicobacter pylori* is a critical cause of gastrointestinal diseases. A crucial host response associated with *H. pylori* infection includes gastric inflammation, which is characterized by a sustained recruitment of T-helper (Th) cells to the site of infection and distinct patterns of cytokine production. Adequate nutritional status, especially frequent consumption of dietary antioxidants, appears to protect against infection with *H. pylori*. The aim of the present study was to investigate whether astaxanthin (AXT) from shrimp cephalothorax may modulate cytokine release of splenocytes in *H. pylori*-infected mice ($n = 60$). Six- to eight-week-old female mice were divided into three groups ($n = 20$ per group) to receive a daily oral dose of 10 or 40 mg of AXT for six weeks. After six weeks, a trend toward interferon gamma (IFN- γ) upregulation was found (40 mg; $p < 0.05$) and a significant dose-dependent increase of interleukin 2 (IL-2) and IL-10 (both $p < 0.05$) was observed. These results suggest that AXT induces higher levels of IL-2 and a shift to a balanced Th1/Th2 response by increasing IFN- γ and augmenting IL-10. We concluded that AXT may influence the pattern of cytokines during *H. pylori* infection.

ASTAXANTHIN ENHANCES INTESTINAL MUCOSAL FUNCTIONS IN IMMUNODEFICIENT MICE WHICH MAY AUGMENT IMMUNITY.

Food Funct. 2020 Apr 1;11(4):3371-3381.

doi: 10.1039/c9fo02555c. Epub 2020 Mar 31.

Astaxanthin (ATX) enhances the intestinal mucosal functions in immunodeficient mice

[Lirong Zhang](#)[†], [Wanxiu Cao](#), [Yuan Gao](#), [Ruili Yang](#), [Xu Zhang](#), [Jie Xu](#), [Qingjuan Tang](#)

- PMID: [32232254](#)
- DOI: [10.1039/c9fo02555c](#)

Abstract

Increasing pressure of life may bring some disease risks and stress injuries, which may destroy the immune system and result in intestinal mucosal immune disorders. In this study, the effects of different doses of ATX (30 mg per kg b.w., 60 mg per kg b.w. and 120 mg per kg b.w.) on intestinal mucosal functions were explored in cyclophosphamide (Cy)-induced immunodeficient mice. The results showed that continuous intraperitoneal injection of 100 mg per kg b.w. Cy for three days led to a persistent decrease of body weight and a range of abnormalities in the intestine of C57BL/6 mice. However, administration of ATX at 60 and 120 mg per kg b.w. could effectively prevent intestinal mucosa from this damage, including reduced levels of oxidative stress (MDA, GSH and GSH-PX), increased intestinal morphological structural integrity, stimulative growth of goblet cells and mucous secretion, decreased development of Paneth cells and expression levels of antimicrobial peptides (AMPs) (Reg-3 γ and lysozyme), increased IgA secretion, ameliorative main gut flora (especially total bacteria, Lactobacillus and Enterobacteriaceae spp.) and its metabolites (acetic acid, propionic acid and butyric acid). These protective effects of ATX were better than those of control- β -carotene in general. Our results may provide a new protective measure to keep intestinal mucosal barriers, which is of great significance for maintaining immune function in the body.

ASTAXANTHIN SHOWS ANTI-AGING PROPERTIES; IMPROVES IMMUNITY; AND REDUCES OXIDATIVE STRESS IN AGING RATS.

Food Funct. 2020 Sep 23;11(9):8099-8111.

doi: 10.1039/d0fo01663b.

Astaxanthin attenuates oxidative stress and immune impairment in D-galactose-induced aging in rats by activating the Nrf2/Keap1 pathway and suppressing the NF- κ B pathway

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- PMID: **32857080**
- DOI: [10.1039/d0fo01663b](https://doi.org/10.1039/d0fo01663b)

Abstract

As a potential antioxidant, astaxanthin (AST) exhibits anti-aging effects. However, its relationships to oxidative stress and immunity have yet to be sufficiently investigated. In this research, integrated analysis of oxidative stress and immunosenescence was performed to elucidate the efficacy and potential mechanisms of AST in d-galactose-induced aging in rats. The results showed that AST significantly decreased malonaldehyde (MDA) levels and increased antioxidant activity, in addition to demonstrating the ability to repair histopathological injuries to the liver, thereby attenuating oxidative stress. Nuclear factor erythroid 2-related factor 2 (Nrf2) expression was up-regulated by 117.95%, whereas Kelch-like ECH-associated protein-1 (Keap1) expression was simultaneously down-regulated by 51.22%. Moreover, AST significantly reduced interleukin-1 β (IL-1 β) and interleukin-6 (IL-6) levels, as well as expression of nuclear factor-kappa B (NF- κ B) (p65) and i-kappa-B-alpha (I κ B α) proteins. Findings of repair of immune organs, as well as elevated levels of interleukin-2 (IL-2), immunoglobulin M (IgM) and immunoglobulin G (IgG), suggest a novel mechanism by which AST could regulate cellular immunity and humoral immunity to attenuate immunosenescence. The anti-aging effects of AST were shown to be due in part to the Nrf2/Keap1 and NF- κ B pathways, and AST treatment ameliorated oxidative stress and immune impairment overall.

Astaxanthin stimulates splenocyte function in mice while canthaxanthin does not.

[Anticancer Res.](#) 1999 Nov-Dec;19(6B):5223-7.

Dietary beta-carotene and astaxanthin but not canthaxanthin stimulate splenocyte function in mice.

[Chew BP](#), [Wong MW](#), [Park JS](#), [Wong TS](#).

Department of Animal Sciences, Washington State University, Pullman 99164, USA. The in vivo modulatory effect of beta-carotene, astaxanthin and canthaxanthin on lymphocyte function was investigated. Female BALB/c mice (8 wk old) were fed a basal diet containing 0, 0.1% or 0.4% beta-carotene, astaxanthin or canthaxanthin for 0, 2 or 4 wk (n = 8/diet/period). Splenic lymphocytes were isolated and mitogen-stimulated proliferation, IL-2 production and lymphocyte cytotoxicity were assessed. Body weight and feed intake were not different among dietary treatments. Plasma carotenoids were undetectable in unsupplemented mice but concentrations of the respective carotenoids were elevated in mice fed 0.1 or 0.4% beta-carotene (0.22 and 0.39 $\mu\text{mol/L}$), astaxanthin (16.4 and 50.2 $\mu\text{mol/L}$) and canthaxanthin (5.00 and 7.02 $\mu\text{mol/L}$) respectively. Mice fed both dietary levels of beta-carotene and astaxanthin had enhanced phytohemagglutinin-induced lymphoblastogenesis compared to unsupplemented mice ($P < 0.03$). No treatment difference was detected with concanavalin A- or lipopolysaccharide-induced lympho-proliferation nor with IL-2 production ($P < 0.05$). Astaxanthin (0.1%) also enhanced lymphocyte cytotoxic activity ($P < 0.08$). In contrast, canthaxanthin did not significantly influence any of the lymphocyte functions measured. Results indicate that beta-carotene and astaxanthin but not canthaxanthin exert enhanced splenic lymphocyte function in mice.

Astaxanthin enhances humoral immune response in old mice better than lutein and beta-carotene.

[Nutr Cancer](#). 1994;21(1):47-58.

Immunomodulating actions of carotenoids: enhancement of in vivo and in vitro antibody production to T-dependent antigens.

[Jyonouchi H](#), [Zhang L](#), [Gross M](#), [Tomita Y](#).

Department of Pediatrics, University of Minnesota, Minneapolis 55455.

Previously, we demonstrated an enhancement of in vitro antibody (Ab) production in response to T-dependent antigens (TD-Ag) by astaxanthin, a carotenoid without vitamin A activity. The effects of beta-carotene, a carotenoid with vitamin A activity, and lutein, another carotenoid without vitamin A activity, on in vitro Ab production were examined with spleen cells from young and old B6 mice. In addition, the in vivo effects of lutein, astaxanthin, and beta-carotene on Ab production were studied in young and old B6 mice. Lutein, but not beta-carotene, enhanced in vitro Ab production in response to TD-Ags. The depletion of T-helper cells prevented the enhancement of Ab production by lutein and astaxanthin. In vivo Ab production in response to TD-Ag was significantly enhanced by lutein, astaxanthin, and beta-carotene. The numbers of immunoglobulin M- and G-secreting cells also increased in vivo with the administration of these carotenoids when mice were primed with TD-Ags. Antibody production in response to TD-Ags in vivo and in vitro was significantly lower in old than in young B6 mice. Astaxanthin supplements partially restored decreased in vivo Ab production in response to TD-Ags in old B6 mice. Lutein and beta-carotene also enhanced in vivo Ab production in response to TD-Ags in old B6 mice, although to a lesser extent than did astaxanthin. However, none of the carotenoids had an effect on in vivo or in vitro Ab production in response to T-independent antigen. These results indicate significant immunomodulating actions of carotenoids for humoral immune responses to TD-Ags and suggest that carotenoid supplementation may be beneficial in restoring humoral immune responses in older animals.

Publication Types:

PMID: 8183722 [PubMed - indexed for MEDLINE]

Astaxanthin modulates the immune system in fish.

[Fish Shellfish Immunol.](#) 2014 Dec;41(2):674-80.

Effect of dietary astaxanthin against *Aeromonas hydrophila* infection in common carp, *Cyprinus carpio*.

[Jagruthi C¹](#), [Yogeshwari G](#), [Anbazahan SM](#), [Mari LS](#), [Arockiaraj J](#), [Mariappan P](#), [Sudhakar GR](#), [Balasundaram C](#), [Harikrishnan R](#).

Author information

Abstract

The effect of astaxanthin at 0, 25, 50, and 100 mg kg⁻¹ incorporated in basal feed on immune response and disease resistance in *Cyprinus carpio* against *Aeromonas hydrophila* was investigated. When fed with 25 mg kg⁻¹ diet, the cumulative mortality was 35% whereas it was 10% and 20% with 50 and 100 mg kg⁻¹ diets. With all enriched diets the growth rate increased significantly from week 1 to 4 when compared with control. However, the specific growth rate (SGR), feed conversion ratio (FCR), and protein efficiency ratio (PER) did not vary significantly from that of the control except with 50 mg kg⁻¹ diet. When fed with 50 and 100 mg kg⁻¹ diets the red blood cells, white blood cells, hemoglobin, and hematocrit values significantly increased. However, the serum total protein, albumin, and globulin contents significantly increased only when fed with 50 and 100 mg kg⁻¹ diets. The phagocytic ratio also significantly raised with 50 and 100 mg kg⁻¹ diets on week 2 and 4 whereas the phagocytic index significantly increased with all groups only on fourth week. The respiratory burst activity significantly increased in 25 mg kg⁻¹ diet group on first week whereas in 50 and 100 mg kg⁻¹ diet groups the activity increased on weeks 2 and 4; a similar trend was observed in the anti-protease activity only on weeks 2 and 4. The serum lysozyme activity and bactericidal activity registered a significant increase with all enriched diets. This study suggests that supplementation of astaxanthin at 50 and 100 mg kg⁻¹ with the basal diet significantly promotes the growth restores hematology and modulates the immune system in *C. carpio* against *A. hydrophila*.

PMID:

25462460

[PubMed - indexed for MEDLINE]

Astaxanthin superior to other carotenoids in enhancing immunity in-vitro.

[Int J Immunopharmacol.](#) 1996 Dec;18(12):753-8.

Possible immunomodulating activities of carotenoids in in vitro cell culture experiments.

Okai Y, Higashi-Okai K.

Division of Food and Nutrition, Osaka Kun-Ei Women's College, Japan.

Immunomodulating activities of beta-carotene and carotene-associated carotenoids such as canthaxanthin (beta, beta-carotene-4,4 dione) and astaxanthin (3,3'-dihydroxyl beta, beta-carotene 4,4-dione) were analyzed by in vitro cell culture experiments. (i) beta-Carotene, canthaxanthin and astaxanthin caused significant stimulatory effects on the cell proliferative response of spleen cells and thymocytes from BALB/c mice at the concentrations of 2×10^{-8} to 10^{-7} M, although they showed the activities different from each other. (ii) Astaxanthin exhibited the highest activity on the polyclonal antibody (immunoglobulin M and G) production of murine spleen cells at the concentrations of 2×10^{-8} to 10^{-7} M but beta-carotene did not cause a significant effect at a low concentration (2×10^{-8} M) although stimulated at a high concentration (2×10^{-7} M). Canthaxanthin expressed moderate activities at the same concentrations. (iii) All tested carotenoids significantly enhanced the release of interleukin-1 alpha and tumor necrosis factor-alpha from murine peritoneal adherent cells at the concentrations of 2×10^{-8} to 10^{-7} M and the ranks of cytokine-inducing activities were astaxanthin > canthaxanthin > beta-carotene. These results indicate that carotenoids such as beta-carotene, canthaxanthin and astaxanthin have possible immunomodulating activities to enhance the proliferation and functions of murine immunocompetent cells.

PMID: 9172019 [PubMed - indexed for MEDLINE]

ASTAXANTHIN INCREASES IMMUNITY, ANTIOXIDANT CAPABILITY AND STRESS RESISTANCE IN YOUNG CRABS.

Fish Shellfish Immunol. 2020 Jul;102:499-510.
doi: 10.1016/j.fsi.2020.05.021. Epub 2020 May 11.

Micro-algal astaxanthin could improve the antioxidant capability, immunity and ammonia resistance of juvenile Chinese mitten crab, *Eriocheir sinensis*

[Xiaodong Jiang](#)¹, [Lu Zu](#)², [Zhiyan Wang](#)², [Yongxu Cheng](#)³, [Yuhong Yang](#)⁴, [Xugan Wu](#)⁵

- PMID: **32408019**
- DOI: [10.1016/j.fsi.2020.05.021](https://doi.org/10.1016/j.fsi.2020.05.021)

Abstract

Green alga *Haematococcus pluvialis* is an important source of natural astaxanthin (Ast), which have been shown to be beneficial for the color formulation, survival, antioxidation, immunity and stress resistance of many crustacean. This study was conducted to investigate the effects of dietary supplementation of *H. pluvialis* meal on growth, antioxidant status, ammonia resistance, color parameters, and carotenoids composition of juvenile Chinese mitten crab *Eriocheir sinensis*. Five diets were formulated to contain 0, 30, 60, 90 and 120 mg/kg dry diets of natural Ast (defined as Diet 1-5) using *H. pluvialis* meal as astaxanthin source. The results showed that: (1) Although all treatments with Ast supplementation had the relatively higher growth performance and survival than the control (Diet 1 treatment), no significant differences were found on growth performance, feed conversion ratio and hepatosomatic index among all treatments. (2) The highest total antioxidant capacity (T-AOC) in hepatopancreas and hemolymph were observed in Diet 4 and 3 treatments respectively, while the lowest malondialdehyde (MDA) contents in hepatopancreas and hemolymph were also found in these two treatments. Furthermore, the significantly positive relationships were detected on acid phosphatase (ACP) activities and dietary Ast contents for hepatopancreas and hemolymph. (3) Diet 3 treatment had the highest

mRNA levels of EsLecA, EsTrx, and EsPrx6 in hepatopancreas, while both Diet 3 and 4 treatments reached the peaks for mRNA expression levels of EsMyd88 and EsHc, respectively. (4) The stress test with ammonia-N indicated Diet 1 treatment had the highest mortality among all treatments, and the lowest mortality was found on Diet 3 treatment during the stress test. (5) Dietary Ast significantly improved the redness (a^*) of carapace and hepatopancreas, which were consistent with the Ast contents in these tissues from the different treatments. Ast concentrations in carapace reached the plateau for Diet 3 treatment while hepatopancreatic Ast concentration kept increasing with elevating dietary Ast contents. In conclusion, natural astaxanthin could enhance the antioxidative capability, non-specific immunity, tissue Ast contents and stress resistance to ammonia-N, and these results suggested the optimal diet micro-algal astaxanthin was around 60 mg/kg for juvenile *E. sinensis*.

ASTAXANTHIN SHOWS POTENTIAL IMMUNE SYSTEM BENEFIT IN CELL AND MICE STUDIES.

Mar Drugs. 2021 Jun 17;19(6):346.

doi: [10.3390/md19060346](https://doi.org/10.3390/md19060346).

Astaxanthin Protects Dendritic Cells from Lipopolysaccharide-Induced Immune Dysfunction

[Yinyan Yin](#)^{1,2}, [Nuo Xu](#)¹, [Yi Shi](#)¹, [Bangyue Zhou](#)¹, [Dongrui Sun](#)^{1,3}, [Bixia Ma](#)⁴, [Zhengzhong Xu](#)⁵, [Jin Yang](#)³, [Chunmei Li](#)⁴

- PMID: **34204220**
- DOI: [10.3390/md19060346](https://doi.org/10.3390/md19060346)

Abstract

Astaxanthin, originating from seafood, is a naturally occurring red carotenoid pigment. Previous studies have focused on its antioxidant properties; however, whether astaxanthin possesses a desired anti-inflammatory characteristic to regulate the dendritic cells (DCs) for sepsis therapy remains unknown. Here, we explored the effects of astaxanthin on the immune functions of murine DCs. Our results showed that astaxanthin reduced the expressions of LPS-induced inflammatory cytokines (TNF- α , IL-6, and IL-10) and phenotypic markers (MHCII, CD40, CD80, and CD86) by DCs. Moreover, astaxanthin promoted the endocytosis levels in LPS-treated DCs, and hindered the LPS-induced migration of DCs via downregulating CCR7 expression, and then abrogated allogeneic T cell proliferation. Furthermore, we found that astaxanthin inhibited the immune dysfunction of DCs induced by LPS via the activation of the HO-1/Nrf2 axis. Finally, astaxanthin with oral administration remarkably enhanced the survival rate of LPS-challenged mice. These data showed a new approach of astaxanthin for potential sepsis treatment through avoiding the immune dysfunction of DCs.

Astaxanthin improves the function of human neutrophils (a type of white blood cells).

[Eur J Nutr.](#) 2010 Dec;49(8):447-57. doi: 10.1007/s00394-010-0103-1. Epub 2010 Apr 2.

Astaxanthin addition improves human neutrophils function: in vitro study.

[Macedo RC¹](#), [Bolin AP](#), [Marin DP](#), [Otton R](#).

Author information

Abstract

PURPOSE:

The aim of the present study was to evaluate the in vitro effect of carotenoid astaxanthin (ASTA) on the phagocytic and microbicidal capacities, cytokine release, and reactive oxygen species production in human neutrophils.

METHODS:

The following parameters were evaluated: cytotoxic effect of ASTA on human neutrophils viability, phagocytic and microbicidal capacities of neutrophils by using *Candida albicans* assay, intracellular calcium mobilization (Fura 2-AM fluorescent probe), superoxide anion (Lucigenin and DHE probes), hydrogen peroxide (H₂O₂, phenol red), and nitric oxide (NO·) (Griess reagent) production, activities of antioxidant enzymes (total/Mn-SOD, CAT, GPx, and GR), oxidative damages in biomolecules (TBARS assay and carbonyl groups), and cytokine (IL-6 and TNF-alpha) release.

RESULTS:

Astaxanthin significantly improves neutrophil phagocytic and microbicidal capacity, and increases the intracellular calcium concentration and NO· production. Both functional parameters were accompanied by a decrease in superoxide anion and hydrogen peroxide and IL-6 and TNF-α production. Oxidative damages in lipids and proteins were significantly decreased after ASTA-treatment.

CONCLUSIONS:

Taken together our results are supportive to a beneficial effect of astaxanthin-treatment on human neutrophils function as demonstrated by increased phagocytic and fungicide capacity as well as by the reduced superoxide anion and hydrogen peroxide production, however, without affecting neutrophils capacity to kill *C. albicans*. This process appears to be mediated by calcium released from intracellular storages as well as nitric oxide production.

PMID:

20361333

[PubMed - indexed for MEDLINE]

Astaxanthin inhibits human gastric cancer cell line proliferation.

[Gut Liver](#). 2016 May 23;10(3):369-74. doi: 10.5009/gnl15208.

Astaxanthin Inhibits Proliferation of Human Gastric Cancer Cell Lines by Interrupting Cell Cycle Progression.

[Kim JH¹](#), [Park JJ¹](#), [Lee BJ¹](#), [Joo MK¹](#), [Chun HJ²](#), [Lee SW³](#), [Bak YT¹](#).

Author information

Abstract

BACKGROUND/AIMS:

Astaxanthin is a carotenoid pigment that has antioxidant, antitumoral, and anti-inflammatory properties. In this in vitro study, we investigated the mechanism of anticancer effects of astaxanthin in gastric carcinoma cell lines.

METHODS:

The human gastric adenocarcinoma cell lines AGS, KATO-III, MKN-45, and SNU-1 were treated with various concentrations of astaxanthin. A cell viability test, cell cycle analysis, and immunoblotting were performed.

RESULTS:

The viability of each cancer cell line was suppressed by astaxanthin in a dose-dependent manner with significantly decreased proliferation in KATO-III and SNU-1 cells. Astaxanthin increased the number of cells in the G0/G1 phase but reduced the proportion of S phase KATO-III and SNU-1 cells. Phosphorylated extracellular signal-regulated kinase (ERK) was decreased in an inverse dose-dependent correlation with astaxanthin concentration, and the expression of p27(kip-1) increased in the KATO-III and SNU-1 cell lines in an astaxanthin dose-dependent manner.

CONCLUSIONS:

Astaxanthin inhibits proliferation by interrupting cell cycle progression in KATO-III and SNU-1 gastric cancer cells. This may be caused by the inhibition of the phosphorylation of ERK and the enhanced expression of p27(kip-1).

KEYWORDS:

Astaxanthin; Extracellular signal-regulated kinase; Human gastric adenocarcinoma; Proliferation; p27kip-1

PMID: 26470770

[PubMed - in process]

PMCID: PMC4849689

[Free PMC Article](#)

Astaxanthin inhibits proliferation and induces cell death of human liver cancer cells.

[Mar Drugs](#). 2015 Sep 24;13(10):6064-81. doi: 10.3390/md13106064.

Astaxanthin Inhibits Proliferation and Induces Apoptosis of Human Hepatocellular Carcinoma Cells via Inhibition of Nf-Kb P65 and Wnt/B-Catenin in Vitro.

[Li J](#)¹, [Dai W](#)², [Xia Y](#)³, [Chen K](#)⁴, [Li S](#)⁵, [Liu T](#)⁶, [Zhang R](#)^{7,8}, [Wang J](#)^{9,10}, [Lu W](#)^{11,12}, [Zhou Y](#)^{13,14}, [Yin Q](#)^{15,16}, [Abudumijiti H](#)¹⁷, [Chen R](#)¹⁸, [Zheng Y](#)¹⁹, [Wang F](#)²⁰, [Lu J](#)¹, [Zhou Y](#)²¹, [Guo C](#)²².

Author information

Abstract

Hepatocellular carcinoma (HCC) is a malignant tumor that can cause systemic invasion; however, the exact etiology and molecular mechanism are unknown. Astaxanthin (ASX), a powerful antioxidant, has efficient anti-oxidant, anti-inflammatory, and other activities, and has great research prospects in cancer therapy. We selected the human hepatoma cell lines, LM3 and SMMC-7721, to study the anti-tumor effect and related mechanisms of ASX. The cell lines were treated with different concentrations of ASX, and its solvent DMSO as a control, for different time periods and the results were determined using CCK8, qRT-PCR, WB, apoptotic staining, and flow cytometry. ASX induced significant apoptosis of HCC cells, and its effect may have been caused by NF- κ B p65 and Wnt/ β -catenin down-regulation via negative activation of PI3K/Akt and ERK. Antitumor research on ASX has provided us with a potential therapy for patients with hepatomas.

KEYWORDS:

apoptosis; astaxanthin; hepatocellular carcinoma

PMID:

26404320

[PubMed - in process]

PMCID:

PMC4626679

[Free PMC Article](#)

Astaxanthin effective in enhancing immunity in-vitro and was the sole carotenoid of several tested that performs as a T1-helper cell clone.

[Nutr Cancer](#). 1996;26(3):313-24.

Effects of various carotenoids on cloned, effector-stage T-helper cell activity.

[Jyonouchi H](#), [Sun S](#), [Mizokami M](#), [Gross MD](#).

Department of Pediatrics, School of Medicine, University of Minnesota, Minneapolis 55455, USA. jyono001@maroon.tc.umn.edu

Astaxanthin, a carotenoid without provitamin A activity, enhances murine T-helper (Th) cell clone-mediated antibody (Ab) production with suboptimal antigen (Ag) challenges. It also suppresses interferon-gamma (IFN-gamma) production by cloned murine Th1 cells. beta-Carotene is less effective than astaxanthin. This study evaluates the effects of various carotenoids with various relative polarity, provitamin A activity, and antioxidant activity. Carotenoids tested include astaxanthin, cantaxanthin, zeaxanthin, lutein, and lycopene, and their effects were tested at a concentration at which astaxanthin's effect was most potent. A.E7 and CDC35 cells are used as representative type 1 and type 2 Th cell (Th1 and Th2) clones, respectively. In the Th1 clone, astaxanthin, but not other carotenoids, suppressed IFN-gamma production and increased the number of Ab-secreting cells with the use of primed spleen cells. With cultures of Th1 cells and unprimed spleen cells, astaxanthin and zeaxanthin augmented the number of immunoglobulin M Ab-secreting cells. In the cultures of Th2 clone and primed spleen cells, astaxanthin, but not other carotenoids, enhanced the number of Ab-secreting cells. With unprimed spleen cells, lycopene suppressed Th2 clone-mediated Ab production. Interleukin-5 production by the Th2 clone was not significantly altered with the carotenoids tested, irrespective of the use of unprimed or primed spleen cells. Carotenoid actions on Th cells may vary in each carotenoid and do not seem to be closely associated with carotenoid antioxidant activity or relative polarity.

Publication Types:

PMID: 8910913 [PubMed - indexed for MEDLINE]

Astaxanthin increases antibody response in-vitro.

[J Nutr.](#) 1995 Oct;125(10):2483-92.

Astaxanthin, a carotenoid without vitamin A activity, augments antibody responses in cultures including T-helper cell clones and suboptimal doses of antigen.

[Jyonouchi H](#), [Sun S](#), [Tomita Y](#), [Gross MD](#).

Department of Pediatrics, School of Medicine, University of Minnesota, Minneapolis 55455, USA.

Astaxanthin, a carotenoid without vitamin A activity, enhances T-dependent antigen (Ag)-specific humoral immune responses. We examined carotenoid actions on T-helper (Th) cell activity in a direct manner with reconstitution experiments; spleen Th cells were replaced with Ag-specific Type 1 and Type 2 (Th1 and Th2) Th cell clones. The Ag for the Th1 and Th2 clones were pigeon cytochrome C and rabbit gamma-globulin, respectively. Astaxanthin and beta-carotene augmented the number of IgM antibody (Ab)-secreting cells when unprimed B cells were incubated with Th clones and stimulated with suboptimal doses of Ag specific for each Th clone. The number of IgG Ab-secreting cells were greater with use of in vivo primed B cells than with unprimed B cells in both Th clones. Astaxanthin but not beta-carotene augmented the number of IgG Ab-secreting cells when primed B cells and Th cell clones were stimulated with suboptimal doses of Ag specific for each Th clone. In the presence of optimal doses of Ag for each Th clone, neither carotenoid augmented the number of Ab-secreting cells. Astaxanthin and beta-carotene may enhance the actions of both Th1 and Th2 cells for humoral immune responses with suboptimal Ag challenges; certain carotenoids may help maintain Ag-mediated immune responses at optimal levels.

Publication Types:

PMID: 7562082 [PubMed - indexed for MEDLINE]

Astaxanthin but not beta-carotene enhances human immunoglobulin in culture.

[Nutr Cancer](#). 1995;23(2):171-83.

Effect of carotenoids on in vitro immunoglobulin production by human peripheral blood mononuclear cells: astaxanthin, a carotenoid without vitamin A activity, enhances in vitro immunoglobulin production in response to a T-dependent stimulant and antigen.

[Jyonouchi H](#), [Sun S](#), [Gross M](#).

Department of Pediatrics, School of Medicine, University of Minnesota, Minneapolis 55455, USA.

The effect of carotenoids on in vitro immunoglobulin (Ig) production by peripheral blood mononuclear cells (PBMNC) was examined by employing blood samples from adult volunteers and full-term newborn babies (umbilical cord blood). Under carotenoid-supplemented culture conditions, cells were stimulated by polyclonal stimulants, neoantigens, and a recall antigen (Ag), and IgM, IgA, and IgG levels in the culture supernatant were measured. Beta-carotene and astaxanthin were used as representatives of carotenoids with and without vitamin A activity, respectively. Astaxanthin enhanced IgM production in response to T-dependent Ag (TD-Ag) and a T-dependent polyclonal stimulant. Astaxanthin also augmented IgG production in response to a recall Ag. IgA production without supplemental carotenoids was negligible for all stimuli. However, in carotenoid-supplemented cultures, IgA production was significantly higher in response to a T-dependent polyclonal stimulant than in unsupplemented cultures. IgM and IgA production was augmented at 10^{-8} mol/l astaxanthin, whereas astaxanthin enhanced IgG production in response to a recall Ag at 10^{-10} - 10^{-9} mol/l. Similar enhancing actions of astaxanthin on IgM production were observed in cord blood mononuclear cells (CBMNC), although CBMNC produced less IgM than adult PBMNC. Beta-carotene did not have a significant effect on human Ig production. The carotenoid actions were not demonstrated under serum-free culture conditions; serum is essential for solubilization of carotenoids. In summary, this study has shown for the first time that astaxanthin, a carotenoid without vitamin A activity, enhances human Ig production in response to T-dependent stimuli.

Publication Types:

Astaxanthin enhances in-vitro antibody production to T-dependent antigens.

[Nutr Cancer](#). 1993;19(3):269-80.

Studies of immunomodulating actions of carotenoids. II. Astaxanthin enhances in vitro antibody production to T-dependent antigens without facilitating polyclonal B-cell activation.

[Jyonouchi H](#), [Zhang L](#), [Tomita Y](#).

Department of Pediatrics, University of Minnesota, Minneapolis 55455.

Previously we have shown that astaxanthin, a carotenoid without provitamin A activity, enhances in vitro antibody (Ab) production to sheep red blood cells in normal B6 mice. In this study, we further attempted to examine the mechanisms of this enhancing action of carotenoids on specific Ab production in vitro in relation to different antigen (Ag) stimuli, cytokine production, and T- and B-cell interactions in both normal and autoimmune strains of mice. When the actions of carotenoids were tested in normal strains of mice, we found that astaxanthin enhanced in vitro Ab production to T cell-dependent Ag, but not to T-independent Ag, and did not augment total immunoglobulin production. Astaxanthin exerted maximum enhancing actions when it was present at the initial period of Ag priming. This action of astaxanthin was abolished when T cells were depleted from spleen cell suspensions and appeared to require direct interactions between T and B cells. The results also indicated that carotenoids may modulate the production of interferon-tau in this assay system. When the actions of carotenoids were tested in autoimmune-prone MRL and NZB mice, the enhancing action of astaxanthin on in vitro Ab production was less significant. Furthermore, carotenoids did not potentiate or augment spontaneous Ab and immunoglobulin production by spleen cells in these strains. Taken together, carotenoids without provitamin A activity may be able to augment in vitro specific Ab production to T cell-dependent Ag partly through affecting the initial stage of Ag presentation without facilitating polyclonal B-cell activation or autoantibody production.

Publication Types:

PMID: 8346076 [PubMed - indexed for MEDLINE]

Astaxanthin superior to beta-carotene in preventing formation of cancer in mice.

[Autoimmunity](#). 1993;16(2):95-102.

Preventive action of carotenoids on the development of lymphadenopathy and proteinuria in MRL-lpr/lpr mice.

[Tomita Y](#)¹, [Jyonouchi H](#), [Engelman RW](#), [Day NK](#), [Good RA](#).

Author information

Abstract

The chemopreventive action of carotenoids on proteinuria and lymphadenopathy were examined in autoimmune-prone MRL-lpr/lpr (MRL/l) mice. They were fed a synthetic full-fed diet (16-18 kcal/mouse/day) with supplementation of beta-carotene or astaxanthin (0.19 mumoles/mouse, 3 times a week), and the development of lymphadenopathy and proteinuria were examined. MRL/l mice fed a full-fed diet without the supplementation of carotenoids or those fed a calorie-restricted (CR) diet (10-11 kcal/mouse/day, 60% calorie intake of full-fed mice) were employed as controls. CR dramatically delayed the development of proteinuria and lymphadenopathy, as reported previously. Carotenoids also significantly delayed the onset of these symptoms in MRL/l mice fed a full-fed diet. Carotenoids were half as effective as CR and astaxanthin, a carotenoid without provitamin A activity, which appeared to exert more significant preventive actions than beta-carotene in delaying the development of these symptoms. Similar chemopreventive actions of carotenoids were also demonstrated in MRL/l mice fed a regular diet (Lab Chow). CR has been shown to augment IL-2 production and to decrease serum prolactin levels in this strain, which may be related to its dramatic preventive action of autoimmunity. However, carotenoids did not affect IL-2 production nor prolactin levels in full-fed MRL/l mice. The chemopreventive actions of carotenoids observed in autoimmune-prone MRL/l mice may be attributed to yet unknown mechanisms, apart from their provitamin A activity or oxygen-quenching activity.

PMID:

8180322

[PubMed - indexed for MEDLINE]

Astaxanthin superior to beta-carotene in immune modulation in-vitro.

[Nutr Cancer](#). 1991;16(2):93-105.

Studies of immunomodulating actions of carotenoids. I. Effects of beta-carotene and astaxanthin on murine lymphocyte functions and cell surface marker expression in in vitro culture system.

[Jyonouchi H](#), [Hill RJ](#), [Tomita Y](#), [Good RA](#).

Department of Pediatrics, University of South Florida/All Children's Hospital, St. Petersburg 33701.

The immunomodulating effects of carotenoids (beta-carotene and astaxanthin) on mouse lymphocytes were studied in in vitro culture system by use of assay for mitogen responses of spleen cells, thymocyte proliferation, interleukin 2 production, and antibody (Ab) production in vitro in response to sheep red blood cells. Changes of cell surface markers on spleen lymphocytes including Ia antigen (Ag), surface immunoglobulin, B220, and Thy-1 Ag were also examined. At a concentration of 10^{-8} M, carotenoids did not show any significant effect on mitogen responses (phytohemagglutinin P and concanavalin A) on murine spleen cells, irrespective of the concentrations of mitogens used. Interleukin 2 production by murine spleen cells was not significantly altered by carotenoids in the culture media (10^{-7} to 10^{-9} M). [^3H]thymidine incorporation by B6 thymocytes was somewhat enhanced in the presence of astaxanthin or beta-carotene when cultured in the concentration of 10^6 /ml. At higher concentrations of cells (5×10^6 /ml), such an effect was not observed. In assays of in vitro Ab production in response to sheep red blood cells, B6 spleen cells produced significantly more Ab-forming cells (plaque-forming cells, immunoglobulins M and G) in the presence of astaxanthin (greater than 10^{-8} M) but not beta-carotene. Expression of Ia Ag seemed to be moderately enhanced on both Thy-1+ and Thy-1- spleen cells in the presence of astaxanthin (greater than 10^{-9} M) but not beta-carotene. The expression of Thy-1 and surface immunoglobulin seemed unchanged with the treatment of these carotenoids. These results indicate that immunomodulating actions of carotenoids are not necessarily related to provitamin A activity, because astaxanthin, which does not have provitamin A activity, showed more significant effects in these bioassays and also indicate that such actions of carotenoid demonstrated in this study may be difficult to explain only by its oxygen-quenching capacity.

Publication Types:

PMID: 1796012 [PubMed - indexed for MEDLINE]

Astaxanthin superior to beta-carotene and canthaxanthin in inhibiting the growth of mammary tumors in mice.

[Anticancer Res.](#) 1999 May-Jun;19(3A):1849-53.

A comparison of the anticancer activities of dietary beta-carotene, canthaxanthin and astaxanthin in mice in vivo.

[Chew BP](#)¹, [Park JS](#), [Wong MW](#), [Wong TS](#).

[Author information](#)

Abstract

The anticancer activities of beta-carotene, astaxanthin and canthaxanthin against the growth of mammary tumors were studied in female eight-wk-old BALB/c mice. The mice were fed a synthetic diet containing 0, 0.1 or 0.4% beta-carotene, astaxanthin or canthaxanthin. After 3 weeks, all mice were inoculated with 1 x 10⁶ WAZ-2T tumor cells into the mammary fat pad. All animals were killed on 45 d after inoculation with the tumor cells. No carotenoids were detectable in the plasma or tumor tissues of unsupplemented mice. Concentrations of plasma astaxanthin (20 to 28 μmol/L) were greater (P < 0.05) than that of beta-carotene (0.1 to 0.2 μmol/L) and canthaxanthin (3 to 6 nmol/L). However, in tumor tissues, the concentration of canthaxanthin (4.9 to 6.0 nmol/g) was higher than that of beta-carotene (0.2 to 0.5 nmol/g) and astaxanthin (1.2 to 2.7 nmol/g). In general, all three carotenoids decreased mammary tumor volume. Mammary tumor growth inhibition by astaxanthin was dose-dependent and was higher than that of canthaxanthin and beta-carotene. Mice fed 0.4% beta-carotene or canthaxanthin did not show further increases in tumor growth inhibition compared to those fed 0.1% of each carotenoid. Lipid peroxidation activity in tumors was lower (P < 0.05) in mice fed 0.4% astaxanthin, but not in those fed beta-carotene and canthaxanthin. Therefore, beta-carotene, canthaxanthin and especially astaxanthin inhibit the growth of mammary tumors in mice; their anti-tumor activity is also influenced by the supplemental dose.

PMID:

10470126

[PubMed - indexed for MEDLINE]

Astaxanthin changes the immune response to *H. pylori* bacteria.

[Clin Microbiol Infect.](#) 2002 Jul;8(7):438-41.

Effect of antioxidants on the immune response of *Helicobacter pylori*.

[Akyön Y.](#)

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Antioxidants are substances capable of inhibiting oxidation. In chronic diseases, inflammatory response cells produce oxygen free radicals. Oxygen free radicals cause DNA damage, and this may lead to gene modifications that might be carcinogenic. Chronic *Helicobacter pylori* infection causes the production of DNA-damaging free radicals. In recent years, various groups have studied the effects of antioxidants, especially on *H. pylori*-associated gastric cancer. In most of the studies, it has been shown that *H. pylori* infection does affect the level of antioxidants measured in the gastric juice, but there are also controversial results. Recent experimental studies, both in vivo and in vitro, have shown that vitamin C and astaxanthin, a carotenoid, are not only free radical scavengers but also show antimicrobial activity against *H. pylori*. It has been shown that astaxanthin changes the immune response to *H. pylori* by shifting the Th1 response towards a Th2 T-cell response. Very few experimental studies support the epidemiologic studies, and further studies are needed to describe the effect and the mechanism of antioxidants in the *H. pylori* immune response.

Astaxanthin shows preventive properties in mouse model of multiple sclerosis.

[Bratisl Lek Listy](#). 2018;119(3):160-166. doi: 10.4149/BLL_2018_031.

Astaxanthin effectiveness in preventing multiple sclerosis in animal model.

[Bidaran S](#), [Ahmadi AR](#), [Yaghmaei P](#), [Sanati MH](#), [Ebrahim-Habibi A](#).

Abstract

OBJECTIVE: The aim of the present study was to reveal the effect of therapeutic and prophylactic potential of astaxanthin in experimental autoimmune encephalomyelitis (EAE) as an acceptable model for the study of multiple sclerosis (MS).

BACKGROUND: Astaxanthin has powerful antioxidant activities as well as several essential biological functions while multiple sclerosis prevention is highly regarded by researchers.

METHODS: The astaxanthin potential in prevention of multiple sclerosis was examined in the chronic model of experimental autoimmune encephalomyelitis (EAE) by using female C57BL/6 mice induced with oligodendrocyte glycoprotein (MOG). Splenocytes were assessed to measure the levels of proinflammatory and anti-inflammatory cytokines, proliferation rate and FoxP3+Treg cell frequency. Immunohistochemical examinations were performed on spinal cord and brain tissue.

RESULTS: Astaxanthin reduced splenocytes proliferation index and proinflammatory cytokine levels, and vice versa increased the anti-inflammatory cytokine levels. Immunohistochemical studies of the spinal cord and brain showed that the infiltration with inflammatory cells was highly confined in the central nervous system. Protective effects of astaxanthin were visible by assigning low score recording in clinical behavior and disease severity.

CONCLUSION: Astaxanthin is a powerful tool for intervention in EAE on a model of multiple sclerosis, so it can be studied further to prevent and treat MS (Tab. 2, Fig. 3, Ref. 41).

KEYWORDS: Haematococcus pluvialis multiple sclerosis.; astaxanthin; experimental autoimmune encephalomyelitis; female C57BL/6 mice

PMID: 29536745

DOI: [10.4149/BLL_2018_031](#)

[Indexed for MEDLINE]

Astaxanthin reviewed along with other carotenoids for its action on immune response.

[J Nutr.](#) 2004 Jan;134(1):257S-261S.

Carotenoid action on the immune response.

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Early studies demonstrating the ability of dietary carotenes to prevent infections have left open the possibility that the action of these carotenoids may be through their prior conversion to vitamin A. Subsequent studies to demonstrate the specific action of dietary carotenoids have used carotenoids without provitamin A activity such as lutein, canthaxanthin, lycopene and astaxanthin. In fact, these nonprovitamin A carotenoids were as active, and at times more active, than beta-carotene in enhancing cell-mediated and humoral immune response in animals and humans. Another approach to study the possible specific role of dietary carotenoids has used animals that are inefficient converters of carotenoids to vitamin A, for example the domestic cat. Results have similarly shown immuno-enhancement by nonprovitamin A carotenoids, based either on the relative activity or on the type of immune response affected compared to beta-carotene. Certain carotenoids, acting as antioxidants, can potentially reduce the toxic effects of reactive oxygen species (ROS). These ROS, and therefore carotenoids, have been implicated in the etiology of diseases such as cancer, cardiovascular and neurodegenerative diseases and aging. Recent studies on the role of carotenoids in gene regulation, apoptosis and angiogenesis have advanced our knowledge on the possible mechanism by which carotenoids regulate immune function and cancer.

Publication Types:

PMID: 14704330 [PubMed - indexed for MEDLINE]

Astaxanthin reviewed for its health benefits including enhancing immunity.

[Crit Rev Food Sci Nutr](#). 2006;46(2):185-96.

Astaxanthin: a review of its chemistry and applications.

Higuera-Ciapara I, Félix-Valenzuela L, Goycoolea FM.

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Astaxanthin is a carotenoid widely used in salmonid and crustacean aquaculture to provide the pink color characteristic of that species. This application has been well documented for over two decades and is currently the major market driver for the pigment. Additionally, astaxanthin also plays a key role as an intermediary in reproductive processes. Synthetic astaxanthin dominates the world market but recent interest in natural sources of the pigment has increased substantially. Common sources of natural astaxanthin are the green algae *Haematococcus pluvialis*, the red yeast, *Phaffia rhodozyma*, as well as crustacean byproducts. Astaxanthin possesses an unusual antioxidant activity which has caused a surge in the nutraceutical market for the encapsulated product. Also, health benefits such as cardiovascular disease prevention, immune system boosting, bioactivity against *Helicobacter pylori*, and cataract prevention, have been associated with astaxanthin consumption. Research on the health benefits of astaxanthin is very recent and has mostly been performed in vitro or at the pre-clinical level with humans. This paper reviews the current available evidence regarding astaxanthin chemistry and its potential beneficial effects in humans.

Publication Types:

PMID: 16431409 [PubMed - indexed for MEDLINE]

Astaxanthin reviewed for its potential health benefits including ameliorating the immune system.

[J Nat Prod.](#) 2006 Mar;69(3):443-9.

Astaxanthin, a carotenoid with potential in human health and nutrition.

[Hussein G¹](#), [Sankawa U](#), [Goto H](#), [Matsumoto K](#), [Watanabe H](#).

Author information

Abstract

Astaxanthin (1), a red-orange carotenoid pigment, is a powerful biological antioxidant that occurs naturally in a wide variety of living organisms. The potent antioxidant property of 1 has been implicated in its various biological activities demonstrated in both experimental animals and clinical studies. Compound 1 has considerable potential and promising applications in human health and nutrition. In this review, the recent scientific literature (from 2002 to 2005) is covered on the most significant activities of 1, including its antioxidative and anti-inflammatory properties, its effects on cancer, diabetes, the immune system, and ocular health, and other related aspects. We also discuss the green microalga *Haematococcus pluvialis*, the richest source of natural 1, and its utilization in the promotion of human health, including the antihypertensive and neuroprotective potentials of 1, emphasizing our experimental data on the effects of dietary astaxanthin on blood pressure, stroke, and vascular dementia in animal models, is described.

PMID:

16562856

[PubMed - indexed for MEDLINE]

Astaxanthin reviewed for its health benefits including boosting immunity in the tuberculin skin test.

[Altern Med Rev.](#) 2011 Dec;16(4):355-64.

Astaxanthin, cell membrane nutrient with diverse clinical benefits and anti-aging potential.

[Kidd P¹.](#)

Author information

Abstract

Astaxanthin, a xanthophyll carotenoid, is a nutrient with unique cell membrane actions and diverse clinical benefits. This molecule neutralizes free radicals or other oxidants by either accepting or donating electrons, and without being destroyed or becoming a pro-oxidant in the process. Its linear, polar-nonpolar-polar molecular layout equips it to precisely insert into the membrane and span its entire width. In this position, astaxanthin can intercept reactive molecular species within the membrane's hydrophobic interior and along its hydrophilic boundaries. Clinically, astaxanthin has shown diverse benefits, with excellent safety and tolerability. In double-blind, randomized controlled trials (RCTs), astaxanthin lowered oxidative stress in overweight and obese subjects and in smokers. It blocked oxidative DNA damage, lowered C-reactive protein (CRP) and other inflammation biomarkers, and boosted immunity in the tuberculin skin test. Astaxanthin lowered triglycerides and raised HDL-cholesterol in another trial and improved blood flow in an experimental microcirculation model. It improved cognition in a small clinical trial and boosted proliferation and differentiation of cultured nerve stem cells. In several Japanese RCTs, astaxanthin improved visual acuity and eye accommodation. It improved reproductive performance in men and reflux symptoms in H. pylori patients. In preliminary trials it showed promise for sports performance (soccer). In cultured cells, astaxanthin protected the mitochondria against endogenous oxygen radicals, conserved their redox (antioxidant) capacity, and enhanced their energy production efficiency. The concentrations used in these cells would be attainable in humans by modest dietary intakes. Astaxanthin's clinical success extends beyond protection against oxidative stress and inflammation, to demonstrable promise for slowing age-related functional decline.

PMID:

22214255

[PubMed - indexed for MEDLINE]

Free full text

Reproductive and Hormonal Health

Astaxanthin improves sperm functioning in placebo-controlled human clinical trial leading to the conclusion that Astaxanthin may be used to decrease male infertility.

[Mar Drugs](#). 2015 Aug 25;13(9):5533-51. doi: 10.3390/md13095533.

Astaxanthin Improves Human Sperm Capacitation by Inducing Lyn Displacement and Activation.

[Andrisani A](#)¹, [Donà G](#)², [Tibaldi E](#)³, [Brunati AM](#)⁴, [Sabbadin C](#)⁵, [Armanini D](#)⁶, [Alvisi G](#)⁷, [Gizzo S](#)⁸, [Ambrosini G](#)⁹, [Ragazzi E](#)¹⁰, [Bordin L](#)¹¹.

Author information

Abstract

Astaxanthin (Asta), a photo-protective red pigment of the carotenoid family, is known for its multiple beneficial properties. In this study, the effects of Asta on isolated human sperm were evaluated. Capacitation involves a series of transformations to let sperm acquire the correct features for potential oocyte fertilization, including the generation of a controlled amount of reactive oxygen species (ROS), cholesterol depletion of the sperm outer membrane, and protein tyrosine phosphorylation (Tyr-P) process in the head region. Volunteers, with normal spermiogram values, were divided in two separate groups on the basis of their ability to generate the correct content of endogenous ROS. Both patient group (PG) and control group (CG) were analysed for Tyr-phosphorylation (Tyr-P) pattern and percentages of acrosome-reacted cells (ARC) and non-viable cells (NVC), in the presence or absence of Asta. In addition, the involvement of ROS on membrane reorganization and the presence of Lyn, a Src family kinase associated with lipid rafts, were investigated. Results show that Lyn is present in the membranes of human sperm, mainly confined in midpiece in resting conditions. Following capacitation, Lyn translocated to the head concomitantly with raft relocation, thus allowing the Tyr-P of head proteins. Asta succeeded to trigger Lyn translocation in PG sperm thus bypassing the impaired ROS-related mechanism for rafts and Lyn translocation. In this study, we showed an interdependence between ROS generation and lipid rafts and Lyn relocation leading the cells to undergo the successive acrosome reaction (AR). Asta, by ameliorating PG sperm functioning, may be utilised to decrease male idiopathic infertility.

KEYWORDS:

: astaxanthin; acrosome reaction; cholera toxin subunit B (CTB); human sperm capacitation; tyrosine kinase Lyn

PMID: 26308013 [PubMed - in process] PMID: PMC4584338

[Free PMC Article](#)

Male fertility increased and sperm quality and motility increased in double-blind, placebo-controlled randomized human clinical trial.

[Asian J Androl.](#) 2005 Sep;7(3):257-62.

Combined conventional/antioxidant "Astaxanthin" treatment for male infertility: a double blind, randomized trial.

[Comhaire FH](#), [El Garem Y](#), [Mahmoud A](#), [Eertmans F](#), [Schoonjans F](#).

Ghent University Hospital, Department of Medical and Urological Andrology, 9k12 IE, De Pintelaan, 185, B 9000, Gent, Belgium. frank.comhaire@ugent.be

AIM: To evaluate the treatment of male infertility with a strong natural antioxidant, in addition to conventional treatment. **METHODS:** Using a double blind, randomized trial design, 30 men with infertility of > or =12 months and female partners with no demonstrable cause of infertility received conventional treatment according to the guidelines of the World Health Organization (WHO), and either a strong antioxidant Astaxanthin 16 mg/day (AstaCarox, AstaReal AB, Gustavsberg, Sweden) or placebo for 3 months. The effects of treatment on semen parameters, reactive oxygen species (ROS), zona-free hamster oocyte test, serum hormones including testosterone, luteinizing hormone (LH), follicle stimulating hormone (FSH) and Inhibin B, and spontaneous or intrauterine insemination (IUI)-induced pregnancies were evaluated. **RESULTS:** ROS and Inhibin B decreased significantly and sperm linear velocity increased in the Astaxanthin group (n = 11), but not in the placebo group (n = 19). The results of the zona-free hamster oocyte test tended to improve in the Astaxanthin group in contrast with the placebo group, though not reaching statistical significance. The total and per cycle pregnancy rates among the placebo cases (10.5 % and 3.6 %) were lower compared with 54.5 % and 23.1 % respectively in the Astaxanthin group (P = 0.028; P = 0.036). **CONCLUSION:** Although the present study suggests a positive effect of Astaxanthin on sperm parameters and fertility, the results need to be confirmed in a larger trial before recommending Astaxanthin for the complementary treatment of infertile men.

Publication Types:

[Clinical Trial](#)

[Randomized Controlled Trial](#)

[Research Support, Non-U.S. Gov't](#)

PMID: 16110353 [PubMed - indexed for MEDLINE]

Astaxanthin improves conception rate and sperm quality in Infertile Men in placebo-controlled human clinical trial.

XIII International Carotenoid Symposium Hawaii January 2002. Patent Cooperation Treaty Application
WO99 / 29313. AstaCarotene AB, Sweden.

Natural Astaxanthin Improves Semen Quality in Infertile Men

GAREM, Y.E., A. LIGNELL u. F. COMHAIRE

Summary: Natural Astaxanthin from Haematococcus Algae has been shown in a double blind, placebo controlled clinical to improve fertility in infertile men. Natural Astaxanthin had previously been shown to improve fertility in male animals such as boars and stallions. This study was conducted on men who were diagnosed as infertile due to abnormal sperm quality. The experimental group received 16 mg of Natural Astaxanthin per day for three months. The results were an improvement in conception rate in the experimental group by 478% over the placebo group. The scientist concluded that supplementation with Natural Astaxanthin improved the quality of the spermatozoa, which is suggested to be the plausible explanation for the increased frequency of conception.

Astaxanthin improves human sperm capacitation.

[Mar Drugs](#). 2013 Jun 3;11(6):1909-19. doi: 10.3390/md11061909.

Effect of astaxanthin on human sperm capacitation.

[Donà G¹](#), [Kožuh I](#), [Brunati AM](#), [Andrisani A](#), [Ambrosini G](#), [Bonanni G](#), [Ragazzi E](#), [Armanini D](#), [Clari G](#), [Bordin L](#).

Author information

Abstract

In order to be able to fertilize oocytes, human sperm must undergo a series of morphological and structural alterations, known as capacitation. It has been shown that the production of endogenous sperm reactive oxygen species (ROS) plays a key role in causing cells to undergo a massive acrosome reaction (AR). Astaxanthin (Asta), a photo-protective red pigment belonging to the carotenoid family, is recognized as having anti-oxidant, anti-cancer, anti-diabetic and anti-inflammatory properties and is present in many dietary supplements. This study evaluates the effect of Asta in a capacitating buffer which induces low ROS production and low percentages of acrosome-reacted cells (ARC). Sperm cells were incubated in the presence or absence of increasing concentrations of Asta or diamide (Diam) and analyzed for their ROS production, Tyr-phosphorylation (Tyr-P) pattern and percentages of ARC and non-viable cells (NVC). Results show that Asta ameliorated both sperm head Tyr-P and ARC values without affecting the ROS generation curve, whereas Diam succeeded in enhancing the Tyr-P level but only of the flagellum without increasing ARC values. It is suggested that Asta can be inserted in the membrane and therefore create capacitation-like membrane alteration which allow Tyr-P of the head. Once this has occurred, AR can take place and involves a higher numbers of cells.

PMID:

23736766

[PubMed - indexed for MEDLINE]

PMCID:

PMC3721213

Free PMC Article

Astaxanthin improves sperm quality and function.

e - Vol 7. No 4. 385-391 Reproductive BioMedicine Online; www.rbmonline.com/Article/918 on web 27 June 2003

Commentary

The role of food supplements in the treatment of the infertile man

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Astaxanthin is a lipophilic carotenoid produced by the alga *Haematococcus pluvialis*, and it has a strong antioxidant capacity (Iwamoto *et al.*, 2000; Goto *et al.*, 2001). In a pilot double-blind randomized trial, 16 mg per day of the natural astaxanthin (AstaCarox, Astacarotene AB, Gustavsberg, Sweden) was given to the male partners of 20 infertile couples, whose semen characteristics were below the WHO recommended reference values. This food supplementation resulted in a significant reduction of seminal reactive oxygen species and serum inhibin B concentration among treated cases, but not in the placebo controls. Rapid linear progressive motility significantly increased, and sperm morphology presented an insignificant increase in the astaxanthin group, but sperm concentration remained unchanged. In the treated group, the total and monthly pregnancy rates were 54.5% and 23.1%, respectively, compared with 11.1% and 3.6% in the placebo group (OR: 9.6, $P = 0.08$) (Comhaire *et al.*, submitted).

Astaxanthin with Saw Palmetto increases testosterone levels in men in human clinical trial.

[J Int Soc Sports Nutr.](#) 2014 Aug 23;11:43. doi: 10.1186/s12970-014-0043-x. eCollection 2014.

Evaluation of Resettin® on serum hormone levels in sedentary males.

[Anderson ML](#)¹.

Author information

Abstract

BACKGROUND: Comparisons of hormones such as dihydrotestosterone (DHT), estradiol (E2), and testosterone indicate their impact on metabolism and body composition. While less is known regarding DHT and E2, testosterone is an androgenic metabolic hormone capable of positively regulating a variety of anabolic and androgenic processes in the body. Accordingly, it has been postulated that the age-related reduction in serum testosterone levels leads to reductions in lean muscle mass, bone mineral density, and other physical conditions that impair physical performance and decrease quality of life. Preliminary studies suggest that key ingredients found in Resettin®/MyTosterone™, a natural supplement containing the carotenoid astaxanthin from *Haematococcus pluvialis* and Saw Palmetto berry lipid extract from *Serenoa repens*, could positively impact testosterone levels. To investigate the clinical efficacy of Resettin®, the serum profiles of testosterone, E2 and DHT in healthy sedentary males before and after Resettin® treatment were evaluated in a randomized, placebo controlled clinical trial.

METHOD: Twenty healthy, sedentary men between the ages of 21 and 70 were randomized into either an 800 mg/day or 1200 mg/day Resettin®/MyTosterone™ treatment group or lecithin, which was used as the placebo. After a 14-day treatment period, there was a 14-day washout period. After the wash-out period, participants were crossed over within their respective group to either Resettin®/MyTosterone™ or the lecithin placebo for 14 days.

RESULTS: After 14 days, participants receiving 800 mg per day of Resettin® had significantly reduced baseline-subtracted serum DHT levels in comparison to the placebo control group. While after 14 days, participants receiving 1200 mg per day of Resettin® had significantly reduced baseline-subtracted serum DHT and E2 levels in comparison to the placebo control group. Moreover, participants receiving 1200 mg per day of Resettin® experienced a 38% increase in serum testosterone levels in comparison to the placebo control group, but the effect did not reach statistical significance.

CONCLUSION: Although additional studies will be required to evaluate how Resettin® may promote proper testosterone regulation, these findings indicate that Resettin® can favorably influence serum hormone profiles in men.

PMID: 25183955 PMCID: [PMC4151021](#) DOI: [10.1186/s12970-014-0043-x](#) [Free PMC Article](#)

Astaxanthin combined with Saw Palmetto increases Testosterone in healthy men in human clinical trial.

[J Int Soc Sports Nutr](#). 2008 Aug 12;5:12. doi: 10.1186/1550-2783-5-12.

An open label, dose response study to determine the effect of a dietary supplement on dihydrotestosterone, testosterone and estradiol levels in healthy males.

[Angwafor F 3rd^{#1}](#), [Anderson ML^{#2}](#).

Author information

Abstract

BACKGROUND:

Maintaining endogenous testosterone (T) levels as men age may slow the symptoms of sarcopenia, andropause and decline in physical performance. Drugs inhibiting the enzyme 5alpha-reductase (5AR) produce increased blood levels of T and decreased levels of dihydrotestosterone (DHT). However, symptoms of gynecomastia have been reported due to the aromatase (AER) enzyme converting excess T to estradiol (ES). The carotenoid astaxanthin (AX) from *Haematococcus pluvialis*, Saw Palmetto berry lipid extract (SPLE) from *Serenoa repens* and the precise combination of these dietary supplements, Alphastat(R) (Mytosterone(trade mark)), have been reported to have inhibitory effects on both 5AR and AER in-vitro. Concomitant regulation of both enzymes in-vivo would cause DHT and ES blood levels to decrease and T levels to increase. The purpose of this clinical study was to determine if patented Alphastat(R) (Mytosterone(trade mark)) could produce these effects in a dose dependent manner.

METHODS:

To investigate this clinically, 42 healthy males ages 37 to 70 years were divided into two groups of twenty-one and dosed with either 800 mg/day or 2000 mg/day of Alphastat(R) (Mytosterone(trade mark)) for fourteen days. Blood samples were collected on days 0, 3, 7 and 14 and assayed for T, DHT and ES. Body weight and blood pressure data were collected prior to blood collection. One-way, repeated measures analysis of variance (ANOVA-RM) was performed at a significance level of alpha = 0.05 to determine differences from baseline within each group. Two-way analysis of variance (ANOVA-2) was performed after baseline subtraction, at a significance level of alpha = 0.05 to determine differences between dose groups. Results are expressed as means +/- SEM.

RESULTS:

ANOVA-RM showed significant within group increases in serum total T and significant decreases in serum DHT from baseline in both dose groups at a significance level of alpha = 0.05. Significant decreases in serum ES are reported for the 2000 mg/day dose group and not the 800 mg/day dose

group. Significant within group effects were confirmed using ANOVA-2 analyses after baseline subtraction. ANOVA-2 analyses also showed no significant difference between dose groups with regard to the increase of T or the decrease of DHT. It did show a significant dose dependant decrease in serum ES levels.

CONCLUSION:

Both dose groups showed significant ($p = 0.05$) increases in T and decreases in DHT within three days of treatment with Alphastat(R) (Mytosterone(trade mark)). Between group statistical analysis showed no significant ($p = 0.05$) difference, indicating the effect was not dose dependent and that 800 mg/per day is equally effective as 2000 mg/day for increasing T and lowering DHT. Blood levels of ES however, decreased significantly ($p = 0.05$) in the 2000 mg/day dose group but not in the 800 mg/day dose group indicating a dose dependant decrease in E levels.

PMID: 18700016

PMCID: [PMC2525623](#)

DOI: [10.1186/1550-2783-5-12](#)

[Free PMC Article](#)

Astaxanthin improves sperm quality in rats.

[Zhonghua Nan Ke Xue](#). 2017 Mar;23(3):206-211.

[Protective effect of astaxanthin against epididymal oxidative damage in rats with ornidazole-induced oligoasthenozoospermia].

[Article in Chinese; Abstract available in Chinese from the publisher]

[Liu W](#)¹, [Kang XF](#)², [Zhang GW](#)¹, [Cai HC](#)¹, [Li KQ](#)¹, [Wang LL](#)³, [Shang XJ](#)¹.

Author information

Abstract

in [English](#), [Chinese](#)

OBJECTIVE: To investigate the improving effect of astaxanthin (AST) on the sperm quality of rats with ornidazole (ORN)-induced oligoasthenozoospermia and its action mechanism.

METHODS: Forty adult male SD rats were equally randomized into groups A (solvent control), B (low-dose ORN [400 mg/ (kg·d)]), C (high-dose ORN [800 mg/ (kg·d)]), D (low-dose ORN [400 mg/ (kg·d)] + AST [20 mg/ (kg·d)]), and E (high-dose ORN [800 mg/ (kg·d)] + AST [20 mg/ (kg·d)]), all treated intragastrically for 3 weeks. After treatment, the epididymal tails on one side were taken for determination of sperm concentration and activity, and the epididymides on the other side were harvested for measurement of the activities of GSH-Px, GR, CAT and SOD and the MDA content in the homogenate.

RESULTS: Compared with group A, sperm motility in the epididymal tail and GSH-Px and SOD activities in the epididymis were markedly decreased while the MDA content significantly increased in group B ($P < 0.05$), sperm motility and concentration in the epididymal tail, testis index, and the activities of GSH-Px, GR, CAT and SOD in the epididymis were remarkably reduced while the MDA content significantly increased in group C ($P < 0.05$). In comparison with group B, group D showed markedly increased sperm motility ([45.3±8.7] % vs [66.3±8.9] %, $P < 0.05$) in the epididymal tail and SOD activity in the epididymis ([116.7±25.3] U/mg prot vs [146.1±23.8] U/mg prot, $P < 0.05$), decreased MDA content ([1.68±0.45] nmol/mg prot vs [1.19±0.42] nmol/mg prot, $P < 0.05$). Compared with group C, group E exhibited significant increases in the weight gained ([89.0±9.5] vs [99.9±4.1] %, $P < 0.05$) and sperm motility ([17.9±3.5] % vs [27.3±5.3] %, $P < 0.05$) but a decrease in the content of MDA ([2.03±0.30] nmol/mg prot vs [1.52±0.41] nmol/mg prot, $P < 0.05$).

CONCLUSIONS: AST can improve sperm quality in rats with ORN-induced oligoasthenozoospermia, which may be associated with its enhancing effect on the antioxidant capacity of the epididymis.

KEYWORDS: ; SD rat; antioxidant; astaxanthin; oligoasthenozoospermia; ornidazole; oxidative damage

PMID: 29706039 [Indexed for MEDLINE]

Astaxanthin improves the quality of boar sperm.

[Reprod Domest Anim.](#) 2018 Apr;53(2):463-471. doi: 10.1111/rda.13133. Epub 2018 Jan 14.

Effect of astaxanthin on the quality of boar sperm stored at 17°C, incubated at 37°C or under in vitro conditions.

[Basioura A](#)¹, [Boscos CM](#)¹, [Parrilla I](#)², [Tsousis G](#)¹, [Tsakmakidis IA](#)¹.

Author information

Abstract

The aim of the study was to investigate the effect of the antioxidant astaxanthin on boar semen. Twenty ejaculates from 10 boars (two ejaculates/boar) were extended and split in three groups: semen control (SC), solvent control (C; semen with dimethyl sulfoxide, the diluent of astaxanthin) and semen with astaxanthin (A) in concentration 0.5 µmol/L. Sperm quality parameters (motility and kinetics, morphology, viability, functional integrity of sperm plasma membrane by Hypo-Osmotic Swelling Test [HOST] and DNA integrity) were assessed at 0, 24 and 48 hr of storage at 17°C (experiment I), before (0 hr) and after (1 hr) of sperm thermal resistance assay at 37°C (experiment II) and finally before (0 hr) and after (1 hr) sperm in vitro incubation (38.5°C, 5% CO₂, maximum humidity [experiment III]). In experiment I, group A performed overall better than group SC and as a tendency better than group C regarding viability. Total motility, rapid spermatozoa and HOST remained constant across time in group A, whereas they decreased in the remaining groups. In experiment II, regarding motility and viability, group A displayed better results across time than the other two groups. In experiment III, viability and total motility decreased in groups SC and C, while in group A, these parameters were not significantly different between the examination time points. In conclusion, astaxanthin has a beneficial and protective effect on boar semen quality under the investigated conditions.

KEYWORDS:

antioxidants; astaxanthin; boar semen; in vitro incubation; storage; thermal resistance assay

PMID: 29333626

DOI: [10.1111/rda.13133](https://doi.org/10.1111/rda.13133)

[Indexed for MEDLINE]

Astaxanthin increases progesterone production in bovine cells with the isomer found in algae-based Astaxanthin outperforming the isomer found in Phaffia yeast Astaxanthin and Synthetic Astaxanthin.

[J Vet Med Sci](#). 2017 Jun 29;79(6):1103-1109. doi: 10.1292/jvms.17-0044. Epub 2017 Apr 23.

Astaxanthin increases progesterone production in cultured bovine luteal cells.

[Kamada H¹](#), [Akagi S¹](#), [Watanabe S¹](#).

Author information

Abstract

Although astaxanthin (AST) is known to be a strong antioxidant, its effects on reproductive function in domestic animals have not yet been elucidated in detail. Therefore, we investigated the effects of AST on luteal cells, which produce progesterone (P4), an important hormone for maintaining pregnancy. Luteal cells were prepared by collagenase dispersion of the corpus luteum (CL). The addition of racemic AST at a low concentration (<10 nM) to cultured bovine luteal cells increased P4 in the culture medium (P<0.05). This effect was attributed to an increase in the ability of luteal cells to produce P4 (P4/cell·DNA); however, the level of lipid peroxide (TBARS: thiobarbituric acid reactive substances) per cell did not decrease with the addition of AST, whose values were similar to that with the addition of luteinizing hormone. When optical isomers of AST (SS and RR types) were added to the culture medium, respectively, SS-AST was more effective in increasing P4 production than RR-AST. When 1 mg/kg·body weight of SS-AST derived from green algae was fed to cows for 2 weeks, its concentration in blood plasma was 10.9 nM on average, which was sufficient to expect an in vitro effect on the production of P4 in cows. These results suggested the potential of SS-AST supplements for cows to elevate luteal function.

KEYWORDS:

TBARS; astaxanthin; cow; luteal cells; progesterone

PMID: 28442639

PMCID: [PMC5487791](#)

DOI: [10.1292/jvms.17-0044](#)

[Indexed for MEDLINE]

[Free PMC Article](#)

ASTAXANTHIN REDUCES NEGATIVE SIDE EFFECTS OF CEMOTHERAPY DRUG IN SPERM CELLS.

Reprod Sci 2021 Jun 15. doi: 10.1007/s43032-021-00651-x. Online ahead of print.

Astaxanthin Relieves Busulfan-Induced Oxidative Apoptosis in Cultured Human Spermatogonial Stem Cells by Activating the Nrf-2/HO-1 pathway

[Azita Afzali](#)¹, [Fardin Amidi](#)¹, [Morteza Koruji](#)², [Hassan Nazari](#)³, [Mohammad Ali Sadighi Gilani](#)⁴, [Aligholi Sobhani Sanjbad](#)⁵

- PMID: 34129218 DOI: [10.1007/s43032-021-00651-x](https://doi.org/10.1007/s43032-021-00651-x)

Abstract

Many child cancer patients endure anticancer therapy containing alkylating agents before sexual maturity. Busulfan (BU), as an alkylating agent, is a chemotherapy drug, causing DNA damage and cytotoxicity in germ cells. In the present study, we aimed to investigate the protective effect of astaxanthin (AST), as a potent antioxidant and powerful reactive oxygen species (ROS) scavenger, on BU-induced toxicity in human spermatogonial stem cells. For this purpose, testes were obtained from four brain-dead donors. After tissue enzymatic digestions, testicular cells were cultured for 3 weeks for spermatogonial stem cell (SSC) isolation and purification. K562 cell line was cultured to survey the effect of AST on cancer treatment. The cultured SSCs and K562 cell line were finally treated with AST (10 μ M), BU (0.1nM), and AST+BU. The expression of NRF-2, HO-1, SOD2, SOD3, TP53, and apoptotic genes, including CASP9, CASP3, BCL2, and BAX, were assayed using real-time PCR. Moreover, ROS level in different groups and malondialdehyde level and total antioxidant capacity in cell contraction of SSCs were measured using ELISA. Data showed that AST significantly upregulated the expression of NRF-2 gene (P<0.001) and protein (P<0.005) and also significantly decreased the production of BU-induced ROS (P<0.001). AST activated the NRF-2/HO-1 pathway that could remarkably restrain BU-induced apoptosis in SSCs. Interestingly, AST upregulated the expression level of apoptosis genes in the K562 cell line. The results of this study indicated that AST reduces the side effects of BU on SSCs without interference with its chemotherapy effect on cancerous cells through modulation of the NRF-2/HO-1 and mitochondria-mediated apoptosis pathways.

Astaxanthin Induces the Expression of *CatSper1* Gene and Protects Sperms in Toxicity Induced by Cadmium in Mice

[Ensieh Saberi](#)¹, [Fereshteh Mir Mohammadrezaei](#)¹, [Omid Jazayeri](#)², [Nazanin Fathi](#)¹, [Akbar Hajizadeh Moghadam](#)¹

Affiliations expand

- PMID: 34407557 DOI: [10.1055/a-1553-3265](https://doi.org/10.1055/a-1553-3265)

Abstract

Cadmium (Cd) as a heavy metal damages testis and decreases fertility, however, antioxidants can improve sperm parameters and decrease male infertility. In this study we investigated the effect of astaxanthin (AST) on sperm parameters, expression levels of *CatSper1* and *CatSper2* genes in presence of Cd in mice. Thirty adults' mice were divided into 4 groups, sham group received olive oil and saline (olive oil is the solvent of AST and saline is the solvent of Cd), Cd group received 1 mg/kg CdCl₂, a group received 10 mg/kg AST and 1 mg/kg CdCl₂ and a group received 10 mg/kg AST. The treatments were done intraperitoneally for 14 days. After 14 days sperm parameters were analyzed. Malondialdehyde level, catalase enzyme activity, the alteration of *CatSper1* and *CatSper2* genes expression were measured in testis. Results showed that Sperm count, viability, *CatSper1* gene expression and catalase activity significantly decreased by Cd compared to sham group. Cd significantly increased sperm DNA fragmentation (SDF), abnormal sperm morphology and malondialdehyd level compared to sham group. AST significantly increased sperm count, viability and *CatSper1* gene expression and decreased SDF and abnormal sperm in comparison with Cd group. AST protected testis and decreased oxidative stress induced by Cd. Our findings indicated that AST could protect sperm DNA, enhanced *CatSper1* gene expression and sperm quality in presence of Cd. No significant differences were found in *CatSper2* expression among treatments. Therefore, AST as a strong antioxidant can help to protect the potential of fertility against Cd toxicity.

Astaxanthin improves sperm parameters in diabetic rats.

[Clin Exp Reprod Med.](#) 2016 Jun;43(2):90-6. doi: 10.5653/cerm.2016.43.2.90. Epub 2016 Jun 23.

Dietary supplementation with astaxanthin may ameliorate sperm parameters and DNA integrity in streptozotocin-induced diabetic rats.

[Bahmanzadeh M](#)¹, [Vahidinia A](#)², [Mehdinejadi S](#)³, [Shokri S](#)⁴, [Alizadeh Z](#)¹.

Author information

Abstract

OBJECTIVE:

Diabetes mellitus (DM) is known to cause many systemic complications as well as male infertility. Astaxanthin (ASTX) is a powerful antioxidant that is involved in a variety of biologically active processes, including those with anti-diabetes effects. The present study investigates the effect of ASTX on the spermatozoa function in streptozotocin (STZ)-induced diabetic rats.

METHODS:

We divided 30 adult rats into three groups (10 rats per group), with a control group that received corn oil mixed with chow. DM was induced by intra-peritoneal injection of STZ. Eight weeks after the STZ injection, half of the diabetic animals were used as diabetic controls, and the rest were treated with ASTX for 56 days. Then the parameters and chromatin integrity of the epididymal sperm were analyzed using chromomycin A3, toluidine blue (TB), and acridine orange (AO) staining.

RESULTS:

The count, viability, and motility of the epididymal sperm were decreased significantly in the STZ group in comparison with the control group (count and viability, $p < 0.001$; motility, $p < 0.001; 0.01$). ASTX increased normal morphology and viable spermatozoa compared to the STZ group (morphology, $p = 0.001$; viability, $p < 0.001; 0.05$). The percentage of abnormal chromatins in TB and AO staining was higher in the STZ group compared to the control group ($p < 0.001; 0.001$). The mean percentage of TB and AO positive spermatozoa in STZ rats was significantly lower in the STZ+ASTX group (TB, $p = 0.001$; AO, $p < 0.001; 0.05$).

CONCLUSION:

This study observed that in vivo ASTX treatment partially attenuates some detrimental effect of diabetes. Conversely, ASTX improved sperm viability, normal morphology, and DNA integrity.

KEYWORDS:

Astaxanthin; Chromatin; Diabetes mellitus; Sperm; Streptozotocin

PMID: 27358826 PMCID: [PMC4925872](#) DOI: [10.5653/cerm.2016.43.2.90](#) [PubMed] [Free PMC Article](#)

ASTAXANTHIN IMPROVES SPERM MOTILITY, MORPHOLOGY, VIABILITY AND ACTIVITY IN SPERM SUBJECTED TO LIPOPOLYSACCHARIDES TO INDUCE REDUCED FERTILITY IN MICE.

Dose Response. 2019 Sep 25;17(3):1559325819878537.
doi: 10.1177/1559325819878537. eCollection Jul-Sep 2019.

Astaxanthin Ameliorates the Lipopolysaccharides-Induced Subfertility in Mouse via Nrf2/HO-1 Antioxidant Pathway

[Lei Wang¹](#), [Lili Zhuang²](#)

Affiliations expand

- PMID: **31598118**
- PMCID: [PMC6764055](#)
- DOI: [10.1177/1559325819878537](#)

Free PMC article

Abstract

The endotoxin lipopolysaccharide (LPS) exists in human semen, which is associated with reduced sperm quality. Studying the LPS-impaired spermatozoa motility and viability, and discovering effective therapeutic treatments have crucial importance. The time-course and dose-response experiments were performed to optimize the treatment dose and time of astaxanthin and LPS on mouse spermatozoa motility and viability. Sperm kinetics and morphology, reactive oxygen species production, in vitro fertilization, and developmental competence were examined to evaluate the protective effects of astaxanthin on spermatozoa after LPS exposure. The activity of nuclear factor erythroid 2-related factor-2/heme oxygenase 1 (Nrf2/HO-1) pathway was detected by quantitative reverse transcription polymerase chain reaction and Western blot. Astaxanthin improves LPS-impaired spermatozoa motility, viability, morphology, and activity; reduces LPS-induced spermatozoa oxidative stress; and alleviates LPS-impaired fertilization and embryo development through activating Nrf2/HO-1 antioxidant signaling pathway. Astaxanthin might be a potential treatment for LPS-induced subfertility.

ASTAXANTHIN IMPROVES SEMEN QUALITY IN DIABETIC MICE.

Chem Biol Interact. 2020 Dec 1;332:109303.

doi: 10.1016/j.cbi.2020.109303. Epub 2020 Oct 24.

Astaxanthin improves serum cytokine expression and semen quality of diabetes mellitus KKAY mice

[Zhiqiang Hao](#)¹

- PMID: **33132140**
- DOI: [10.1016/j.cbi.2020.109303](https://doi.org/10.1016/j.cbi.2020.109303)

Abstract

The present study aims to explore the effects of astaxanthin on the semen quality of diabetes mellitus (DM) KKAY mice. A total of 60 DM KKAY mice with similar body weights and initial blood glucose and serum lipid levels were assigned to four groups, namely, one control and three astaxanthin treatments (10, 50, or 100 mg/kg astaxanthin). Results show that oral astaxanthin administration reduced fasting blood glucose and serum total cholesterol, low-density lipoprotein cholesterol, insulin and nitrate oxide levels in the testis of DM KKAY mice. Astaxanthin also improved the high-density lipoprotein cholesterol, protein and superoxide dismutase levels in the testis; serum interleukin-11, tumour necrosis factor- α and interferon- γ levels; and sperm density, sperm movement and normal morphology rate of DM KKAY mice. Based on the results, astaxanthin can effectively affect serum cytokines and ameliorate semen quality of DM KKAY mice; thus, it may be developed as an adjuvant drug to treat diabetes mellitus-induced infertility.

Astaxanthin increases testosterone levels and testis weight and improves oxidative status in rats fed a high fructose diet.

[Andrologia](#). 2018 May 9:e13042. doi: 10.1111/and.13042. [Epub ahead of print]

Effects of astaxanthin on biochemical and histopathological parameters related to oxidative stress on testes of rats on high fructose regime.

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Author information

Abstract

Astaxanthin (ASX) is a xanthophyll family of hydroxycarotenoids which contains several double bonds. It is produced by *Haemococcus pluvialis*, a microalgae and possesses antioxidant and anti-inflammatory properties. The aim of this study was to test whether ASX could protect against oxidative damage in the testicular tissues of rats receiving high fructose. The rats (n = 24) were randomly divided into two main groups: control and fructose (30%, via drinking water) and then each main group either not supplemented or supplemented with ASX (1 mg kg⁻¹ day⁻¹, within 0.2 ml olive oil) via oral gavage. Data were subjected to two-way ANOVA. High fructose consumption tended to increase testis weight and serum testosterone concentration and decreased testicular tissue glutathione-S-transferase (GST) and superoxide dismutase (SOD) levels, but did not affect testicular tissue malondialdehyde (MDA) concentration. Astaxanthin administration increased testosterone, GST and SOD levels and testis weight and decreased MDA concentration. However, ASX administration did not reverse alterations in antioxidant parameters caused by high fructose consumption. Inducible nitric oxide synthase (iNOS) tended to increase in sertoli cell, spermatid and spermatogonia, but not in spermatocytes and leydig cell in response to high fructose consumption. Astaxanthin administration tended to reverse elevation in iNOS in testis cells. In conclusion, ASX could help alleviate oxidative damage caused by high fructose consumption.

KEYWORDS:

astaxanthin; fructose; oxidative stress; testes

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Astaxanthin improves testes weight, sperm count, sperm head morphology, sperm comet assay, restores sperm DNA damage and protects against testicular toxicity in mouse cells subjected to Cyclophosphamide (an alkylating agent used in the treatment of cancer).

[Toxicology](#). 2008 Jun 27;248(2-3):96-103. doi: 10.1016/j.tox.2008.03.015. Epub 2008 Mar 27.

Astaxanthin inhibits cytotoxic and genotoxic effects of cyclophosphamide in mice germ cells.

[Tripathi DN¹](#), [Jena GB](#).

Author information

Abstract

Cyclophosphamide (CP), an alkylating agent used in the treatment of several cancers as well as an immunosuppressant in rheumatoid arthritis. It is used against several cancers due to its broad spectrum efficacy, but at the same time possesses unwanted risks for occupational exposure as well as therapy related toxicities to patients. The present study was aimed to investigate the protective effect of astaxanthin (AST) a red carotenoid pigment on CP induced germ cell toxicity in male mice. CP was administered intraperitoneally (i.p.) at the dose of 50, 100 and 200mg/kg body weight to mice (20-25 g) once in a week for a period of five weeks. AST was given at the dose of 25mg/kg per oral (p.o.) for five consecutive days in a week for five weeks. The animals were sacrificed one week after the last injection of CP. The protective effect of AST against CP induced male germ cell toxicity was evaluated using body weight, testes and epididymis weight, sperm count, sperm head morphology, sperm comet assay, histology of testes and TUNEL assay. AST treatment significantly improved the testes weight, sperm count and sperm head morphology as compared to only CP treated animals. The result of comet assay showed that AST treatment significantly restored the sperm DNA damage induced by CP. Further, AST treatment showed protection against CP induced testicular toxicity as evident from testes histology and TUNEL assay. The present results indicate the chemoprotective potential of AST against CP induced germ cell toxicity in mice.

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18485558

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[PubMed - indexed for MEDLINE]

Astaxanthin increases the number and size of ovarian eggs in crayfish more effectively than Vitamin C, Vitamin A and Beta-Carotene.

[Cell Mol Biol \(Noisy-le-grand\)](#). 2016 Dec 30;62(14):1-10. doi: 10.14715/cmb/ 2016.62.14.1.

The influence of dietary antioxidant on ovarian eggs and levels of vitamin E, C, A, astaxanthin, β -carotene and oxidative stress in tissues of *Astacus leptodactylus* (Eschscholtz) during reproduction.

[Barim-Oz O¹](#), [Sahin H²](#).

[Author information](#)

Abstract

The experiment was conducted to determine the most effective antioxidant (among the vitamin E (VE), vitamin C (VC), vitamin A (VA), astaxanthine (AX), β -carotene (β C)) on the ovarian egg number and size, level of VE, VC, VA, AX, β C and oxidative stress (as malondialdehyde (MDA)) in the hepatopancreas, ovarian, gills and muscle tissue during ovarian development of *Astacus leptodactylus*. One control (C) and five experimental diets (EE, EC, EA, EAX and E β C) were prepared. The EE, EC, EA, EAX and E β C groups were formed by added 150 mg kg⁻¹ VE, 200 mg kg⁻¹ VC, 240 mg kg⁻¹ VA, 200 mg kg⁻¹ AX and 200 mg kg⁻¹ β C to diet C, respectively. At the end of the experiment found that the dietary antioxidants increased ovarian egg number and size and reduced the level of MDA in the tissues. Ovarian egg number and size were highest in the EE and EAX diet groups in the comparison to control ($p < 0.001$). The level of MDA in the tissues was lowest in the EAX diet group in the comparison to control ($p < 0.001$). The highest levels of VE, VC, VA, AX and β C were found in the hepatopancreas and ovarian compared with muscle and gills. The highest level of MDA also was determined in the ovarian according to other tissues. In conclusion, the VE and AX in broodstock diets were the most effective antioxidants on the ovarian egg number and size of *A. leptodactylus*.

PMID: 28145851

DOI: [10.14715/cmb/ 2016.62.14.1](https://doi.org/10.14715/cmb/2016.62.14.1)

[Indexed for MEDLINE]

Astaxanthin decreases oxidative stress in testicular mouse cells and improves hormone production.

[Mar Drugs](#). 2015 Mar 16;13(3):1375-88. doi: 10.3390/md13031375.

Astaxanthin protects steroidogenesis from hydrogen peroxide-induced oxidative stress in mouse Leydig cells.

[Wang JY](#)¹, [Lee YJ](#)², [Chou MC](#)³, [Chang R](#)⁴, [Chiu CH](#)⁵, [Liang YJ](#)⁶, [Wu LS](#)⁷.

Author information

Abstract

Androgens, especially testosterone produced in Leydig cells, play an essential role in development of the male reproductive phenotype and fertility. However, testicular oxidative stress may cause a decline in testosterone production. Many antioxidants have been used as reactive oxygen species (ROS) scavengers to eliminate oxidative stress to protect steroidogenesis. Astaxanthin (AST), a natural extract from algae and plants ubiquitous in the marine environment, has been shown to have antioxidant activity in many previous studies. In this study, we treated primary mouse Leydig cells or MA-10 cells with hydrogen peroxide (H₂O₂) to cause oxidative stress. Testosterone and progesterone production was suppressed and the expression of the mature (30 kDa) form of StAR protein was down-regulated in MA-10 cells by H₂O₂ and cAMP co-treatment. However, progesterone production and expression of mature StAR protein were restored in MA-10 cells by a one-hour pretreatment with AST. AST also reduced ROS levels in cells so that they were lower than the levels in untreated controls. These results provide additional evidence of the potential health benefits of AST as a potential food additive to ease oxidative stress.

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25786065

[PubMed - in process]

PMCID:

PMC4377989

Free PMC Article

ASTAXANTHIN PREVENTS DAMAGE OF THE URINARY AND GENITAL ORGANS CAUSED BY OXIDATION, INFLAMMATION AND CELL DEATH IN FEMALE RATS.

Arch Gynecol Obstet. 2021 Feb 20.

doi: 10.1007/s00404-021-06000-2. Online ahead of print.

Methotrexate-induced toxic effects and the ameliorating effects of astaxanthin on genitourinary tissues in a female rat model

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- PMID: 33608803
- DOI: [10.1007/s00404-021-06000-2](https://doi.org/10.1007/s00404-021-06000-2)

Abstract

Purpose: The purpose of the study was to explore the possible deleterious effects of Methotrexate (MTX) treatment on the urogenital tissues and the potential protective effects of Astaxanthin (AXA).

Methods: Twenty-four female Wistar Albino rats (12 months old) were divided into 3 groups as follows: Group I (Control group): rats received a single dose of 0.1 ml saline by gavage and intraperitoneal injection. Group II (MTX group): rats received a single dose of 20 mg/kg MTX, i.p, on the 2nd day. Group III (MTX + AXA group): rats received 100 mg/kg AXA orally for 7 days in addition to a single dose of MTX. The levels of total oxidant status (TOS), total antioxidant status (TAS), oxidative stress index (OSI), and histopathological and immunohistochemical markers (Caspase-3, iNOS, CRP, G-CSF) were evaluated in urogenital tissues.

Results: In ovarian tissues, a statistically significant increase in TOS levels ($p = 0.001$) and OSI index ($p = 0.028$) were observed in Group II compared to Group I. TAS level was significantly higher in Group III compared to Group II and I ($p = 0.009$ and 0.002 , respectively). However, a significant decrease in OSI level was observed in Group III compared to Group II ($p = 0.035$). In fallopian tube tissues, TAS level was significantly

decreased in Group II compared to Group I ($p = 0.047$). Histopathologically, marked hyperemia was observed in MTX group. AXA treatment ameliorated all the pathological findings. Immunohistochemically, all the studied markers were considerably increased in Group II, however, they were decreased by AXA.

Conclusion: These findings revealed that MTX treatment caused oxidative stress, apoptosis, and inflammation in the urogenital tissue. We found that AXA significantly ameliorated the damage caused by MTX in the urogenital tissue. The results of the study have indicated that AXA may be a promising nutritional support substance against the damage caused by chemotherapeutic and cytotoxic agents, such as MTX, to the urogenital tissue.

Astaxanthin protects bovine reproductive cells from heat shock.

[Reprod Fertil Dev.](#) 2018 Mar 28. doi: 10.1071/RD17271. [Epub ahead of print]

Astaxanthin counteracts the effects of heat shock on the maturation of bovine oocytes.

[Ispada J](#), [Rodrigues TA](#), [Risolia PHB](#), [Lima RS](#), [Gonçalves DR](#), [Rettori D](#), [Nichi M](#), [Feitosa WB](#), [Paula-Lopes FF](#).

Abstract

The cellular mechanisms induced by elevated temperature on oocytes are not fully understood. However, there is evidence that some of the deleterious effects of heat shock are mediated by a heat-induced increase in reactive oxygen species (ROS). In this context, carotenoid antioxidants might have a thermoprotective effect. Therefore, the objective of this study was to determine the role of astaxanthin (AST) on oocyte ROS production and on the redox profile and developmental competency of cumulus-oocyte complexes (COCs) after 14h heat shock (41°C) during in vitro maturation (IVM). Exposure of oocytes to heat shock during IVM increased ROS and reduced the ability of the oocyte to cleave and develop to the blastocyst stage. However, 12.5 and 25nM astaxanthin rescued these negative effects of heat shock; astaxanthin counteracted the heat shock-induced increase in ROS and restored oocyte developmental competency. There was no effect of astaxanthin on maturation medium lipid peroxidation or on glutathione peroxidase and catalase activity in oocytes and cumulus cells. However, astaxanthin stimulated superoxide dismutase (SOD) activity in heat-shocked cumulus cells. In conclusion, direct heat shock reduced oocyte competence, which was restored by astaxanthin, possibly through regulation of ROS and SOD activity in oocytes and COCs.

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DOI: [10.1071/RD17271](https://doi.org/10.1071/RD17271)

Dietary *Haematococcus pluvialis* improves egg quality in fish.

[Anim Reprod Sci.](#) 2012 Jan;130(1-2):119-23. doi: 10.1016/j.anireprosci.2011.12.010. Epub 2012 Jan 10.

Effects of *Haematococcus pluvialis* in maternal diet on reproductive performance and egg quality in rainbow trout (*Oncorhynchus mykiss*).

[Sheikhzadeh N¹](#), [Panchah IK](#), [Asadpour R](#), [Tayefi-Nasrabadi H](#), [Mahmoudi H](#).

Author information

Abstract

The aim of this study was to clarify the effects of dietary *Haematococcus pluvialis* (H.p) on reproductive performance in female rainbow trout and egg quality in terms of antioxidant system and biochemical parameters. 60 rainbow trout (2475.5 ± 64.4 g) were randomly assigned to 2 groups in triplicates and fed diet containing 3 g H.p kg(-1) feed equivalent to 30 mg astaxanthin kg(-1) die or control diet for 30 days. On days 20 and 30 during feeding trial, mature fish were weighed and sampled for stripping. Results indicated that supplementation of H.p did not improve total egg weight, egg number per gram and fecundity. There were few changes in triglyceride and total protein content in fish eggs. Level of glucose decreased markedly on day 30 while on day 20 of feeding trial, a non-significant decrease was shown in treatment group. On day 20, the level of malondialdehyde (MDA) indicating lipid peroxidation product significantly decreased in eggs of the treatment group. The activities of enzymes of the antioxidant system did not change during this study, even though slight increase in glutathione peroxidase in treatment group was revealed during this study. In conclusion, this study showed that female rainbow trout appear to benefit from inclusion of H.p in diet during their reproductive stages in terms of improved egg quality.

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22277839

[PubMed - indexed for MEDLINE]

Astaxanthin improves fertilization, maturation and development of ovarian cells exposed to heat stress in pigs.

[Reprod Biol.](#) 2015 Jun;15(2):86-93. doi: 10.1016/j.repbio.2015.01.002. Epub 2015 Jan 29.

Astaxanthin present in the maturation medium reduces negative effects of heat shock on the developmental competence of porcine oocytes.

[Do LT](#)¹, [Luu VV](#)¹, [Morita Y](#)¹, [Taniguchi M](#)¹, [Nii M](#)², [Peter AT](#)³, [Otoi T](#)⁴.

Author information

Abstract

Astaxanthin, one of the most common carotenoids, elicits antioxidant effects on cellular viability and embryonic development. This study was conducted to investigate the effects of astaxanthin on maturation, fertilization and development of porcine oocytes matured in vitro under heat stress conditions, and then fertilized and cultured under standard conditions. Porcine oocytes were cultured in maturation medium supplemented with different concentrations of astaxanthin (0, 0.25, 0.5 or 1 ppm) for 46 h at either 38.5 or 41 °C. In comparison to oocytes cultured at 38.5 °C, the exposure of porcine oocytes to 41.0 °C during in vitro maturation (IVM) significantly inhibited maturation and development of fertilized oocytes to the blastocyst stage. Supplementation of maturation medium with astaxanthin (0.5 ppm) significantly improved oocyte maturation, fertilization and development to the blastocysts stage in both oocyte groups. However, the total cell number and apoptosis index of blastocysts did not differ among groups. Moreover, astaxanthin (0.5 ppm) significantly increased the rate of oocytes that reached metaphase II and decreased proportion of apoptotic oocytes exposed to H₂O₂ (1.0mM) during IVM. In summary, we demonstrated that supplementation of maturation medium with astaxanthin (0.5 ppm) exerted antioxidative effects and improved the ability of maturation, fertilization, and development of porcine oocytes exposed to heat stress.

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KEYWORDS:

Antioxidants; Carotenoid; Heat stress; Oxidative stress; Porcine oocyte

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[PubMed - indexed for MEDLINE]

ASTAXANTHIN FOUND TO BE A POTENTIAL THERAPEUTIC AGENT FOR INFLAMMATION OF THE UTERUS AND MAY BE AN IMPORTANT INTERVENTION DUE TO THE OVERUSE OF ANTIBIOTICS.

Biol Reprod. 2020 Feb 14;102(2):339-347.

doi: 10.1093/biolre/ioz187.

Protective effects of astaxanthin on lipopolysaccharide-induced inflammation in bovine endometrial epithelial cells†

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PMID: 31566218 DOI: [10.1093/biolre/ioz187](https://doi.org/10.1093/biolre/ioz187)

Abstract

Astaxanthin (AST), a natural antioxidant carotenoid, has been shown to exert anti-inflammatory effects. However, to our knowledge, no study has specifically addressed the potential protective effects of AST against bovine endometritis. The purpose of this study was to examine whether treatment with AST could protect endometrial epithelial cells against lipopolysaccharide (LPS)-induced inflammatory injury. Treatment of bovine endometrial (BEND) epithelial cell line with AST reduced LPS-induced production of interleukin-6 and tumor necrosis factor-alpha, increased the cellular activity of superoxide dismutase and catalase, decreased the proportion of apoptotic cells, and promoted the production of insulin-like growth factor and epithelial growth factor. The effects of AST were mediated through the downregulation of B-cell lymphoma 2 (Bcl-2) associated X, apoptosis regulator (Bax), and cleaved caspase-3 and through the upregulation of Bcl-2. Moreover, AST significantly increased the expression of the tight junction proteins (TJP) claudin, cadherin-1, and TJP1, which play an essential role in the maintenance of host endometrial defense barrier against pathogen infection. Collectively, these results demonstrated that treatment with AST protected against oxidative stress, prevented cell apoptosis, promoted BEND cells viability, and increased the production of growth factors, in addition to activating the endometrial defense barrier. Therefore, AST is a promising therapeutic agent for the prevention and treatment of endometritis. This finding is of utmost importance in the present times when the excessive use of antibiotics has resulted in the development of antibiotic-resistant bacteria.

ASTAXANTHIN IMPROVES BOVINE OVARY CELLS DESTINED TO FORM AN OVUM BY EXERTING AN ANTIOXIDANT EFFECT AND MAY LEAD TO INCREASED FEMALE FERTILITY.

Reprod Fertil Dev. 2019 Jan;31(2):272-281.

doi: [10.1071/RD17527](https://doi.org/10.1071/RD17527).

Astaxanthin improves the developmental competence of in vitro-grown oocytes and modifies the steroidogenesis of granulosa cells derived from bovine early antral follicles

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- PMID: **30071922**
- DOI: [10.1071/RD17527](https://doi.org/10.1071/RD17527)

Abstract

In this study we investigated the effect of astaxanthin (Ax), which exhibits strong antioxidant activity, during invitro growth (IVG) on the developmental competence of oocytes and steroidogenesis of granulosa cells derived from early antral follicles. Bovine oocyte-cumulus-granulosa complexes collected from early antral follicles were cultured for 12 days in the presence or absence (control) of 500µM Ax. The viability of oocytes and antrum formation in the granulosa cell layer during IVG culture were greater in the presence than absence of Ax (P<0.05). Regardless of Ax treatment, 17β-oestradiol production increased during IVG culture; however, progesterone production was significantly lower in the presence than absence of Ax (P<0.05). Reactive oxygen species levels were lower in Ax-treated oocytes than in controls after IVG (P<0.05). Although nuclear maturation and cleavage rates did not differ between the Ax-treated and control groups, Ax treatment led to weaker cathepsin B activity in oocytes and better blastocyst rates than in controls (P<0.05). Accordingly, Ax treatment during IVG increased the total number of cells in blastocysts (P<0.05). These results indicate that Ax supplementation of IVG medium improves the quality of bovine oocytes due to its antioxidative effects on growing oocytes and its suppression of the luteinisation of granulosa cells.

ASTAXANTHIN PROTECTS SPERM BY COMBATTING HUMAN PAPILOMAVIRUS IN HUMAN SPERM MEMBRANES.

Mar Drugs. 2018 Nov 2;16(11):427.
doi: 10.3390/md16110427.

Astaxanthin Prevents Human Papillomavirus L1 Protein Binding in Human Sperm Membranes

[Gabiella Donà¹](#), [Alessandra Andrisani²](#), [Elena Tibaldi³](#), [Anna Maria Brunati⁴](#), [Chiara Sabbadin⁵](#), [Decio Armanini⁶](#), [Guido Ambrosini⁷](#), [Eugenio Ragazzi⁸](#), [Luciana Bordin⁹](#)

- PMID: [30400141](#)
- PMCID: [PMC6266165](#)
- DOI: [10.3390/md16110427](#)

Free PMC article

Abstract

Astaxanthin (Asta), red pigment of the carotenoid family, is known for its anti-oxidant, anti-cancer, anti-diabetic, and anti-inflammatory properties. In this study, we evaluated the effects of Asta on isolated human sperm in the presence of human papillomavirus (HPV) 16 capsid protein, L1. Sperm, purified by gradient separation, were treated with HPV16-L1 in both a dose and time-dependent manner in the absence or presence of 30 min-Asta pre-incubation. Effects of HPV16-L1 alone after Asta pre-incubation were evaluated by rafts (CTB) and Lyn dislocation, Tyr-phosphorylation (Tyr-P) of the head, percentages of acrosome-reacted cells (ARC) and endogenous reactive oxygen species (ROS) generation. Sperm membranes were also analyzed for the HPV16-L1 content. Results show that HPV16-L1 drastically reduced membrane rearrangement with percentage of sperm showing head CTB and Lyn displacement decreasing from 72% to 15.8%, and from 63.1% to 13.9%, respectively. Accordingly, both Tyr-P of the head and ARC decreased from 68.4% to 10.2%, and from 65.7% to 14.6%, respectively. Asta pre-incubation prevented this drop and restored values of the percentage of ARC up to 40.8%. No alteration was found in either the ROS generation curve or sperm motility. In conclusion, Asta is able to preserve sperm by reducing the amount of HPV16-L1 bound onto membranes.

ASTAXANTHIN PROVIDES ANTI-AGING BENEFITS TO PIG OVARY CELLS BY EXERTING ITS ANTIOXIDANT PROPERTIES.

Sci Rep. 2020 Nov 19;10(1):20217.
doi: 10.1038/s41598-020-77359-6.

Inhibitory effects of astaxanthin on postovulatory porcine oocyte aging in vitro

[Bao-Yu Jia](#)¹, [De-Cai Xiang](#)², [Qing-Yong Shao](#)², [Bin Zhang](#)², [Shao-Na Liu](#)², [Qiong-Hua Hong](#)², [Guo-Bo Quan](#)³, [Guo-Quan Wu](#)⁴

- PMID: [33214659](#)
- PMCID: [PMC7677382](#)
- DOI: [10.1038/s41598-020-77359-6](#)

Free PMC article

Abstract

Mammalian oocytes represent impaired quality after undergoing a process of postovulatory aging, which can be alleviated through various effective ways such as reagent treatment. Accumulating evidences have revealed the beneficial effects of astaxanthin (Ax) as a potential antioxidant on reproductive biology. Here, porcine matured oocytes were used as a model to explore whether Ax supplement can protect against oocyte aging in vitro and the underlying mechanism, and therefore they were cultured with or without 2.5 μ M Ax for an additional 24 h. Aged oocytes treated with Ax showed improved yield and quality of blastocysts as well as recovered expression of maternal genes. Importantly, oxidative stress in aged oocytes was relieved through Ax treatment, based on reduced reactive oxygen species and enhanced glutathione and antioxidant gene expression. Moreover, inhibition in apoptosis and autophagy of aged oocyte by Ax was confirmed through decreased caspase-3, cathepsin B and autophagic activities. Ax could also maintain spindle organization and actin expression, and rescue functional status of organelles including mitochondria, endoplasmic reticulum, Golgi apparatus and lysosomes according to restored fluorescence intensity. In conclusion, Ax might provide an alternative for ameliorating the oocyte quality following aging in vitro, through the mechanisms mediated by its antioxidant properties.

ASTAXANTHIN SHOWS BENEFITS IN RAT STUDY OF TESTICULAR TORSION-DETORSION INJURY.

J Pediatr Urol. 2021 Mar 27;S1477-5131(21)00142-X.

doi: 10.1016/j.jpurol.2021.03.020. Online ahead of print.

The effect of astaxanthin on testicular torsion-detorsion injury in rats - Detailed morphometric evaluation of histological sections

[Marko Bašković¹](#), [Ana Katušić Bojanac²](#), [Nino Sinčić²](#), [Marta Himmelreich Perić²](#), [Dajana Krsnik²](#), [Davor Ježek³](#)

- PMID: 33839034
- DOI: [10.1016/j.jpurol.2021.03.020](https://doi.org/10.1016/j.jpurol.2021.03.020)

Abstract

Introduction: Testicular torsion is one of the conditions of the acute scrotum that requires immediate surgical intervention. If not recognized at time, it can result of ischemic injuries and testicular loss. Restoration of blood flow is essential to save ischemic tissue, but reperfusion itself paradoxically causes further damage. Seaweed and sponges are considered to be the richest source of bioactive compounds that have antioxidant activity. The antioxidant activity of astaxanthin is 10 times higher than zeaxanthin, lutein, canthaxanthin, β -carotene and 100 times higher than α -tocopherol. Since to date there is no drug given to patients with torsion-detorsion testicular injury, we have investigated the effect of this powerful antioxidant.

Objective: The aim of this study was to determine the effect of astaxanthin (ASX) on testicular torsion-detorsion injury in rats.

Materials and methods: Thirty-two male Fischer prepubertal rats were divided into 4 groups of 8 individuals. Group 1 underwent sham surgery to determine basal values for histological evaluation. In group 2 (torsion-detorsion group), right testis was twisted at 720° for 90 min. After 90min of reperfusion, the testis was removed. Astaxanthin was administered intraperitoneally at the time of detorsion (group 3) and 45 min after

detorsion (group 4) in the treatment groups. Using software ImageJ®, histological morphometric values were measured.

Results: MSTD (mean seminiferous tubule diameter) values increase statistically significantly in ASX groups compared to T/D group. MSLD (mean seminiferous lumen diameter) value was statistically significantly lower in the ASX group 3 compared to the T/D group. Epithelial height was statistically significantly higher in ASX groups compared to the T/D group. Tubular area is statistically significantly higher in ASX group 4, while the luminal area is statistically significantly lower in the ASX group 3 compared to the T/D group. Johnsen score was statistically significantly higher in the ASX groups compared to the T/D group.

Discussion: This is the first scientific paper to study the effects of a single powerful antioxidant on all morphometric parameters. In previous scientific papers, scientists have mainly measured MSTD and the Johnsen score.

Conclusion: By measuring all histological morphometric parameters (mean seminiferous tubule diameter, mean seminiferous lumen diameter, epithelial height, tubular area, luminal area, Johnsen score) it can be concluded that astaxanthin has a favorable effect comparing the treated groups to untreated group.

ASTAXANTHIN IMPROVES SEVERAL MARKERS INCLUDING LOWERING REACTIVE OXYGEN SPECIES, INCREASING GLUTATHIONE, AND ENHANCING MITOCHONDRIAL ACTIVITY IN PIG OVARIAN CELLS.

Theriogenology. 2021 Jun;167:13-23.

doi: 10.1016/j.theriogenology.2021.03.006. Epub 2021 Mar 9.

Role of astaxanthin as an efficient antioxidant on the in vitro maturation and vitrification of porcine oocytes

[De-Cai Xiang](#)¹, [Bao-Yu Jia](#)², [Xiang-Wei Fu](#)³, [Jian-Xiong Guo](#)², [Qiong-Hua Hong](#)¹, [Guo-Bo Quan](#)⁴, [Guo-Quan Wu](#)⁵

- PMID: 33743504 DOI: [10.1016/j.theriogenology.2021.03.006](https://doi.org/10.1016/j.theriogenology.2021.03.006)

Abstract

As one of the most powerful natural antioxidants, astaxanthin (Ax) has begun to be applied to the field of reproductive biology. Here we used porcine oocyte as a model to explore how Ax improves the oocyte potential during in vitro maturation (IVM), and we also investigated the cytoprotective effects of Ax on the vitrified oocytes. Ax supplementation (final concentration of 2.5 μ M) was subjected for immature oocytes during vitrification and subsequent IVM; fresh oocytes were also matured in vitro in the presence or absence of 2.5 μ M Ax. Our results showed that Ax significantly increased the survival rate of vitrified oocytes, and promoted the blastocyst yield of both fresh and vitrified oocytes after parthenogenetic activation and somatic cell nuclear transfer. The oocytes treated with Ax displayed significantly lower reactive oxygen species generation and higher glutathione level. Vitrification of oocytes had no impact on caspase-3, cathepsin B and autophagic activities; Ax significantly decreased the cathepsin B activity in both fresh and vitrified oocytes. Moreover, the relative fluorescence intensity of lysosomes was significantly increased in vitrified oocytes, which was recovered by Ax treatment. The mitochondrial activity did not differ between fresh and vitrified oocytes, and was significantly enhanced in Ax-treated oocytes. Furthermore, Ax significantly restored the decreased expression of BMP15, ZAR1, POU5F1, GPX4 and LAMP2 genes in vitrified oocytes. Both fresh and vitrified oocytes treated with Ax showed significantly higher mRNA levels of GDF9, POU5F1, SOD2, NRF2 and ATG5. Taken together, this study provides new perspectives in understanding the mechanisms by which Ax improves the developmental competence of both fresh and vitrified porcine oocytes.

Astaxanthin restores progesterone production in mouse Leydig cells subjected to oxidative stress.

[Mar Drugs](#). 2015 Mar 16;13(3):1375-88. doi: 10.3390/md13031375.

Astaxanthin protects steroidogenesis from hydrogen peroxide-induced oxidative stress in mouse Leydig cells.

[Wang JY](#)¹, [Lee YJ](#)², [Chou MC](#)³, [Chang R](#)⁴, [Chiu CH](#)⁵, [Liang YJ](#)⁶, [Wu LS](#)⁷.

Author information

Abstract

Androgens, especially testosterone produced in Leydig cells, play an essential role in development of the male reproductive phenotype and fertility. However, testicular oxidative stress may cause a decline in testosterone production. Many antioxidants have been used as reactive oxygen species (ROS) scavengers to eliminate oxidative stress to protect steroidogenesis. Astaxanthin (AST), a natural extract from algae and plants ubiquitous in the marine environment, has been shown to have antioxidant activity in many previous studies. In this study, we treated primary mouse Leydig cells or MA-10 cells with hydrogen peroxide (H₂O₂) to cause oxidative stress. Testosterone and progesterone production was suppressed and the expression of the mature (30 kDa) form of StAR protein was down-regulated in MA-10 cells by H₂O₂ and cAMP co-treatment. However, progesterone production and expression of mature StAR protein were restored in MA-10 cells by a one-hour pretreatment with AST. AST also reduced ROS levels in cells so that they were lower than the levels in untreated controls. These results provide additional evidence of the potential health benefits of AST as a potential food additive to ease oxidative stress.

PMID:

[25786065](#)

PMCID:

[PMC4377989](#)

DOI:

[10.3390/md13031375](#)

[PubMed - indexed for MEDLINE]

Free PMC Article

Astaxanthin protects sperm plasma membrane from free radicals and lipid peroxidation in pigs.

[Biomed Res Int](#). 2018 Apr 19;2018:6784591. doi: 10.1155/2018/6784591. eCollection 2018.

Effects of Astaxanthin on Miniature Pig Sperm Cryopreservation.

[Lee E¹](#), [Kim D¹](#).

[Author information](#)

Abstract

The purpose of this study is to evaluate the effects of astaxanthin added to freezing buffer on semen parameters, total sperm oxidation stress after postthawing of boar sperm, and lipid peroxidation (LPO) which is caused by reactive oxygen species (ROS) in sperm membrane. Varying concentrations of astaxanthin (0, 10, 50, 100, and 500 μM) were used in the freezing buffer during cryopreservation to protect the DNA of thawed miniature pig sperm. Semen parameter was measured using computer-assisted sperm analysis (CASA) for sperm motility, and then ROS rate and oxidative stress of boar sperm were determined using fluorescence-activated cell sorting (FACS). Sperm motility was higher ($p < 0.05$) in the astaxanthin group than in the control group. Sperm motility and the number of progressive motile sperm were higher ($p < 0.05$) in the astaxanthin 500 μM group than in the control group. In ROS evaluation, the astaxanthin group had lower intracellular O_2 and H_2O_2 in viable sperm. Yo-Pro-I/HE and PI/H2DCFDA staining as revealed using flow cytometry was lower in astaxanthin groups than in the other groups. As a result, we found that astaxanthin could protect the sperm plasma membrane from free radicals and LPO during boar sperm postthawing.

PMID: 29850549

PMCID: [PMC5933026](#)

DOI: [10.1155/2018/6784591](#)

[Indexed for MEDLINE]

[Free PMC Article](#)

Astaxanthin improves fertilization rate, osmolality, motility and sperm concentration in goldfish.

[Theriogenology](#). 2015 Oct 15;84(7):1111-7. doi: 10.1016/j.theriogenology.2015.06.011. Epub 2015 Jun 21.

Effects of dietary supplementation with astaxanthin and β -carotene on the semen quality of goldfish (*Carassius auratus*).

[Tizkar B](#)¹, [Kazemi R](#)², [Alipour A](#)², [Seidavi A](#)³, [Naseralavi G](#)⁴, [Ponce-Palafox JT](#)⁵.

Author information

Abstract

This study was conducted to investigate the effects of two carotenoids (astaxanthin and β -carotene) on the sperm quality of goldfish *Carassius auratus* (Linnaeus, 1758). For this purpose, six diets containing concentrations of 50, 100, and 150 mg/kg of synthetic astaxanthin and β -carotene were added to a basic carp diet. One group of fish was also fed with a control diet (no added carotenoids). Osmolality, spermatocrit value, and sperm concentration significantly increased in the treatment supplemented with 150 mg/kg of astaxanthin (296.6 ± 1.1 mOsm/kg; $29.2 \pm 0.6\%$; $17.2 \pm 0.4 \times 10^9$) cells/mL, respectively) and β -carotene (295.2 ± 2.1 mOsm/kg; $32.5 \pm 1.6\%$; $17.9 \pm 0.5 \times 10^9$) cells/mL, respectively). The highest concentration of astaxanthin (10.4 ± 1.4 mg/kg) was recorded in the treatment of A150 ($P < 0.05$) and did not differ between β -carotene treatments. The highest motility was observed in the A150 and B150 treatments, and the lowest was observed in the control group ($P < 0.05$). The artificial fertilization of the treated males with the similar females (fed with the control diet) showed that the fertilization rate in the A150 treatments was higher than in the other treatments ($P < 0.05$). In conclusion, dietary supplementation with 150 mg/kg of astaxanthin improves osmolality, motility, fertilization rate, and sperm concentration.

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KEYWORDS:

Carotenoid; Diet; Goldfish; Reproductive; Sperm quality

PMID:

26166170

DOI:

[10.1016/j.theriogenology.2015.06.011](https://doi.org/10.1016/j.theriogenology.2015.06.011)

[PubMed - indexed for MEDLINE]

Astaxanthin positively affects human prostate cells in-vitro.

[AAPS J.](#) 2017 Mar;19(2):421-430. doi: 10.1208/s12248-016-0016-x. Epub 2016 Dec 2.

Epigenetic CpG Methylation of the Promoter and Reactivation of the Expression of GSTP1 by Astaxanthin in Human Prostate LNCaP Cells.

[Yang Y](#)^{1,2,3}, [Fuentes F](#)^{1,2}, [Shu L](#)^{1,2}, [Wang C](#)^{1,2}, [Pung D](#)^{1,2,3}, [Li W](#)^{1,2}, [Zhang C](#)^{1,2,3}, [Guo Y](#)^{1,2,3}, [Kong AN](#)^{4,5,6}.

Author information

Abstract

Astaxanthin (AST), a red dietary carotenoid, has synergistic antioxidant effects with polyunsaturated fatty acids at low concentrations via Nuclear factor (erythroid-derived 2)-like 2 (NFE2L2 or Nrf2)/antioxidant response element (ARE) signaling. In addition, chromatin remodeling and DNA methylation-based gene silencing represent a common mechanism in prostate carcinogenesis and tumor progression from normal cells to pre-initiated cells and ultimately to invasive carcinoma. Therefore, the control of epigenetic modification and the transcriptional/translational control of the activation of Nrf2 and Nrf2-target genes, including glutathione S-transferases (GSTs), appear to be an important mechanism that protects cells against injuries from oxidative stress and cancer development. In this study, we aim to investigate the role of AST in reactivating the expression of Nrf2 and GSTP1 through epigenetic modification in human prostate LNCaP cells. Treatment with AST in human LNCaP cells reduced the methylation of 21 CpG sites of the GSTP1 CpG island but did not affect the three CpG sites of the Nrf2 promoter region. AST induced the mRNA expression and protein expression of both Nrf2 and GSTP1. It also increased the mRNA expression of NQO1 in sh-mock LNCaP cells but not in sh-SETD7 LNCaP cells. Furthermore, AST reduced the protein expression of DNMT3b and significantly inhibited DNMT and HDAC activities in vitro. Taken together, these results suggest that AST decreased the methylation status of the GSTP1, and these epigenetic modifying effects may originate from the decreasing activities of epigenetic modification enzymes, contributing to the overall beneficial health effects of AST.

KEYWORDS:

DNA methylation; GSTP1; astaxanthin; epigenetics; prostate cancer

PMID: 27913949

DOI: [10.1208/s12248-016-0016-x](https://doi.org/10.1208/s12248-016-0016-x)

[Indexed for MEDLINE]

ASTAXANTHIN REDUCES THE MIGRATION DELAY CAUSED BY PRENATAL STRESS.

Cereb Cortex. 2019 Dec 17;29(12):5116-5130. doi: 10.1093/cercor/bhz052.

The Role of Redox Dysregulation in the Effects of Prenatal Stress on Embryonic Interneuron Migration

[Jada Bittle](#)^{1,2}, [Edenia C Menezes](#)¹, [Michael L McCormick](#)³, [Douglas R Spitz](#)³, [Michael Dailey](#)^{2,4}, [Hanna E Stevens](#)^{1,2,4}

PMID: 30877797 PMCID: [PMC7199998](#) DOI: [10.1093/cercor/bhz052](#) **Free PMC article**

Abstract

Maternal stress during pregnancy is associated with increased risk of psychiatric disorders in offspring, but embryonic brain mechanisms disrupted by prenatal stress are not fully understood. Our lab has shown that prenatal stress delays inhibitory neural progenitor migration. Here, we investigated redox dysregulation as a mechanism for embryonic cortical interneuron migration delay, utilizing direct manipulation of pro- and antioxidants and a mouse model of maternal repetitive restraint stress starting on embryonic day 12. Time-lapse, live-imaging of migrating GAD67GFP⁺ interneurons showed that normal tangential migration of inhibitory progenitor cells was disrupted by the pro-oxidant, hydrogen peroxide. Interneuron migration was also delayed by in utero intracerebroventricular rotenone. Prenatal stress altered glutathione levels and induced changes in activity of antioxidant enzymes and expression of redox-related genes in the embryonic forebrain. Assessment of dihydroethidium (DHE) fluorescence after prenatal stress in ganglionic eminence (GE), the source of migrating interneurons, showed increased levels of DHE oxidation. Maternal antioxidants (N-acetylcysteine and astaxanthin) normalized DHE oxidation levels in GE and ameliorated the migration delay caused by prenatal stress. Through convergent redox manipulations, delayed interneuron migration after prenatal stress was found to critically involve redox dysregulation. Redox biology during prenatal periods may be a target for protecting brain development.

Astaxanthin inhibits human papillomavirus in sperm membranes.

[Mar Drugs](#). 2018 Nov 2;16(11). pii: E427. doi: 10.3390/md16110427.

Astaxanthin Prevents Human Papillomavirus L1 Protein Binding in Human Sperm Membranes.

[Donà G](#)¹, [Andrisani A](#)², [Tibaldi E](#)³, [Brunati AM](#)⁴, [Sabbadin C](#)⁵, [Armanini D](#)⁶, [Ambrosini G](#)⁷, [Ragazzi E](#)⁸, [Bordin L](#)⁹.

Author information

Abstract

Astaxanthin (Asta), red pigment of the carotenoid family, is known for its anti-oxidant, anti-cancer, anti-diabetic, and anti-inflammatory properties. In this study, we evaluated the effects of Asta on isolated human sperm in the presence of human papillomavirus (HPV) 16 capsid protein, L1. Sperm, purified by gradient separation, were treated with HPV16-L1 in both a dose and time-dependent manner in the absence or presence of 30 min-Asta pre-incubation. Effects of HPV16-L1 alone after Asta pre-incubation were evaluated by rafts (CTB) and Lyn dislocation, Tyr-phosphorylation (Tyr-P) of the head, percentages of acrosome-reacted cells (ARC) and endogenous reactive oxygen species (ROS) generation. Sperm membranes were also analyzed for the HPV16-L1 content. Results show that HPV16-L1 drastically reduced membrane rearrangement with percentage of sperm showing head CTB and Lyn displacement decreasing from 72% to 15.8%, and from 63.1% to 13.9%, respectively. Accordingly, both Tyr-P of the head and ARC decreased from 68.4% to 10.2%, and from 65.7% to 14.6%, respectively. Asta pre-incubation prevented this drop and restored values of the percentage of ARC up to 40.8%. No alteration was found in either the ROS generation curve or sperm motility. In conclusion, Asta is able to preserve sperm by reducing the amount of HPV16-L1 bound onto membranes.

KEYWORDS:

L1 protein; acrosome reaction; astaxanthin (Asta); cholera toxin subunit B (CTB); human papillomavirus 16 (HPV16)

PMID: 30400141

PMCID: [PMC6266165](#)

DOI: [10.3390/md16110427](#)

[Free PMC Article](#)

Astaxanthin in combination with Vitamins A & E improves sperm parameters in rats fed a high fat diet.

[J Reprod Infertil.](#) 2014 Jan;15(1):22-8.

Protective Effects of Antioxidants on Sperm Parameters and Seminiferous Tubules Epithelium in High Fat-fed Rats.

[Mortazavi M](#)¹, [Salehi I](#)², [Alizadeh Z](#)¹, [Vahabian M](#)³, [Roushandeh AM](#)⁴.

Author information

BACKGROUND:

Prescription of antioxidants might increase the quality of sperm parameters and improve the rate of pregnancy in obese people who suffer from infertility. Therefore, the present study investigated protective effects of vitamin A, E and astaxanthin on sperm parameters and seminiferous tubules epithelium in high-fat diet model.

METHODS:

Thirty-six numbers of 3 months old albino Wistar rats were divided to control, high-fat diet and high-fat diet with antioxidants groups. After 12 weeks, levels of LDL-C and HDL-C were detected in the groups. Sperm was obtained from the tail of epididymis and its parameters (count, vitality, motility and morphology) were analyzed. Testes were fixed in 10% formalin and after tissue processing, stained with Hematoxylin and Eosine (H&E) for histological evaluation. Data were analyzed by a one-way ANOVA and $p < 0.05$ was considered significant.

RESULTS:

Our results indicated that viability, motility and normal morphology of sperm in high-fat diet (HFD) decreased significantly compared to high-fat diet with antioxidant (HFD + A) and the control groups ($p < 0.05$). Also spermatogonium and the number of Sertoli cells increased significantly in HFD + A compared to the control ($p < 0.05$).

CONCLUSION:

As it is shown in our study, application of antioxidants decreased serum triglyceride, cholesterol and HDL-C/LDL-C in high-fat diet model and improved the semen parameters. Therefore, it is suggested that the low quality of sperm can be improved in obese men through antioxidant prescription. Finally, it seems that the antioxidants in obese patients with subfertility or infertility is a new and efficient strategy with few side effects.

KEYWORDS:

Antioxidant; Astaxanthin; High-fat diet; Spermatogenesis; Testis; Vitamin A; Vitamin C

PMID: 24696792 PMCID: [PMC3955420](#) [PubMed] [Free PMC Article](#)

Astaxanthin improves the development of bovine reproductive cells grown in-vitro.

[Reprod Fertil Dev](#). 2018 Aug 3. doi: 10.1071/RD17527. [Epub ahead of print]

Astaxanthin improves the developmental competence of invitro-grown oocytes and modifies the steroidogenesis of granulosa cells derived from bovine early antral follicles.

[Abdel-Ghani MA](#), [Yanagawa Y](#), [Balboula AZ](#), [Sakaguchi K](#), [Kanno C](#), [Katagiri S](#), [Takahashi M](#), [Nagano M](#).

Abstract

In this study we investigated the effect of astaxanthin (Ax), which exhibits strong antioxidant activity, during invitro growth (IVG) on the developmental competence of oocytes and steroidogenesis of granulosa cells derived from early antral follicles. Bovine oocyte-cumulus-granulosa complexes collected from early antral follicles were cultured for 12 days in the presence or absence (control) of 500µM Ax. The viability of oocytes and antrum formation in the granulosa cell layer during IVG culture were greater in the presence than absence of Ax ($P<0.05$). Regardless of Ax treatment, 17β -oestradiol production increased during IVG culture; however, progesterone production was significantly lower in the presence than absence of Ax ($P<0.05$). Reactive oxygen species levels were lower in Ax-treated oocytes than in controls after IVG ($P<0.05$). Although nuclear maturation and cleavage rates did not differ between the Ax-treated and control groups, Ax treatment led to weaker cathepsin B activity in oocytes and better blastocyst rates than in controls ($P<0.05$). Accordingly, Ax treatment during IVG increased the total number of cells in blastocysts ($P<0.05$). These results indicate that Ax supplementation of IVG medium improves the quality of bovine oocytes due to its antioxidative effects on growing oocytes and its suppression of the luteinisation of granulosa cells.

PMID: 30071922

DOI: [10.1071/RD17527](https://doi.org/10.1071/RD17527)

Astaxanthin in combination with Vitamins C & E improves male infertility in rats.

[J Diet Suppl.](#) 2017 May 4;14(3):252-263. Epub 2016 Aug 2.

Effect of Astaxanthin, Vitamin E, and Vitamin C in Combination with Calorie Restriction on Sperm Quality and Quantity in Male Rats.

[Vahidinia A¹](#), [Rahbar AR²](#), [Shakoori Mahmoodabadi MM¹](#).

Author information

Abstract

The aim of this study was to investigate the effect of calorie restriction and dietary antioxidant supplementation, separately or in combination, on the quality and quantity of sperm in male rats. Forty male rats were randomly allocated to four groups of 10 animals each, and fed for at least 86 days with an ad libitum diet (group 1), a restricted diet (group 2), an ad libitum diet and astaxanthin, vitamin E, and vitamin C supplements (group 3), or a restricted diet with astaxanthin, vitamin E, and vitamin C supplements (group 4). At the end of the study period, sperm count and motility were determined with a hemocytometer, and differences between the groups were analyzed by analysis of variance. In addition, total antioxidant capacity and 8-epi prostaglandin F2 alpha were measured at the beginning and end of the study period with an enzyme-linked immunosorbent assay method. After 86 days, a significantly higher sperm count was seen in group 4 compared to other groups. The percentage of immotile sperm was significantly decreased in groups 2, 3, and 4 compared to group 1. A significant increase in total antioxidant capacity was observed in group 3 ($p = 0.02$) and group 4 ($p = 0.02$) compared to groups 1 and 2. Antioxidant supplementation with or without calorie restriction had no significant effect on the serum isoprostane level in any group. Astaxanthin, combined with vitamin E, vitamin C, and calorie restriction, was able to ameliorate, in part, infertility in male rats.

KEYWORDS:

(8-epi-PGF2 α); 8-epi prostaglandin F2 alpha; astaxanthin; infertility; male; total antioxidant capacity; vitamin C; vitamin E

PMID:

27485919

DOI:

[10.1080/19390211.2016.1211783](https://doi.org/10.1080/19390211.2016.1211783)

Astaxanthin reviewed as a male reproductive enhancer.

[Zhonghua Nan Ke Xue](#). 2016 Oct;22(10):938-943.

[Astaxanthin in male reproduction: Advances in studies].

[Article in Chinese; Abstract available in Chinese from the publisher]

[Liu W](#)¹, [Kang XF](#)², [Shang XJ](#)¹.

Author information

Abstract

in [English](#), [Chinese](#)

Astaxanthin (AST) is a carotenoid with a strong antioxidant activity and has many biological functions, such as anti-inflammation, immune regulation, anti-tumor, anti-oxidation, anti-aging, and anti-apoptosis. Recent studies show that AST can effectively regulate the dynamic balance between oxidation and antioxidants in the male reproductive system, protect sperm mitochondrial function, ameliorate testicular heat stress and reproductive poison damage, promote the occurrence of sperm capacitation and acrosome reaction, regulate reproductive endocrine hormone balance, and act favorably on primary infertility or metabolic syndrome-related infertility. It also helps the treatment of late-onset hypogonadism and prostate health care. This review updates the studies of AST in male reproductive health and provides some new ideas for the prevention and treatment of male reproductive problems.

KEYWORDS:

antioxidant; astaxanthin; male infertility; oxidative stress; spermatozoa

PMID: 29278478

[Indexed for MEDLINE]

Anti-Aging, DNA and Cellular Health

Abstracts

Astaxanthin decreases DNA damage, inflammation and oxidative stress and enhances immune response in randomized, double-blind, placebo-controlled human clinical trial.

[Nutr Metab \(Lond\)](#). 2010 Mar 5;7:18. doi: 10.1186/1743-7075-7-18.

Astaxanthin decreased oxidative stress and inflammation and enhanced immune response in humans.

[Park JS¹](#), [Chyun JH](#), [Kim YK](#), [Line LL](#), [Chew BP](#).

[Author information](#)

Abstract

BACKGROUND:

Astaxanthin modulates immune response, inhibits cancer cell growth, reduces bacterial load and gastric inflammation, and protects against UVA-induced oxidative stress in in vitro and rodent models. Similar clinical studies in humans are unavailable. Our objective is to study the action of dietary astaxanthin in modulating immune response, oxidative status and inflammation in young healthy adult female human subjects.

METHODS:

Participants (averaged 21.5 yr) received 0, 2, or 8 mg astaxanthin (n = 14/diet) daily for 8 wk in a randomized double-blind, placebo-controlled study. Immune response was assessed on wk 0, 4 and 8, and tuberculin test performed on wk 8.

RESULTS:

Plasma astaxanthin increased (P < 0.01) dose-dependently after 4 or 8 wk of supplementation. Astaxanthin decreased a DNA damage biomarker after 4 wk but did not affect lipid peroxidation. Plasma C-reactive protein concentration was lower (P < 0.05) on wk 8 in subjects given 2 mg astaxanthin. Dietary astaxanthin stimulated mitogen-induced lymphoproliferation, increased natural killer cell cytotoxic activity, and increased total T and B cell subpopulations, but did not influence populations of Thelper, Tcytotoxic or natural killer cells. A higher percentage of leukocytes expressed the LFA-1 marker in subjects given 2 mg astaxanthin on wk 8. Subjects fed 2 mg astaxanthin had a higher tuberculin response than unsupplemented subjects. There was no difference in TNF and IL-2 concentrations, but plasma IFN-gamma and IL-6 increased on wk 8 in subjects given 8 mg astaxanthin.

CONCLUSION:

Therefore, dietary astaxanthin decreases a DNA damage biomarker and acute phase protein, and enhances immune response in young healthy females.

PMID: 20205737 [PubMed] PMCID: PMC2845588 [Free PMC Article](#)

Astaxanthin decreases DNA damage by 40% in four weeks at a dose of 2mg per day in human subjects.

Comparison of Astaxanthin's Singlet Oxygen Quenching Activity with Common Fat and Water Soluble Antioxidants

United States Patent Application

20060217445

Kind Code

A1

Chew; Boon P. ; et al.

September 28, 2006

Natural astaxanthin extract reduces DNA oxidation

Abstract

Provided herein are methods for reducing oxidative DNA damage in a subject, by administering to the subject astaxanthin, for instance a natural, astaxanthin-enriched extract from *Haematococcus pluvialis*. It is shown that doses as low as 2 mg/day, given orally to a human subject for a period of four weeks, is sufficient to reduced measurable endogenous oxidative DNA damage by about 40%.

Astaxanthin shows efficacy for age-related decline in cognitive and psycho-motor function in human clinical study.

[J Clin Biochem Nutr.](#) 2009 May;44(3):280-4. Epub 2009 Apr 25.

Preliminary Clinical Evaluation of Toxicity and Efficacy of A New Astaxanthin-rich Haematococcus pluvialis Extract.

[Sato A](#), [Tsuji S](#), [Okada Y](#), [Murakami N](#), [Urami M](#), [Nakagawa K](#), [Ishikura M](#), [Katagiri M](#), [Koga Y](#), [Shirasawa T](#).

Life Science Institute, Yamaha Motor Co., Ltd., 3001-10 Kuno, Fukuroi, Shizuoka 437-0061, Japan.

Astaxanthin (Ax), a carotenoid ubiquitously distributed in microorganisms, fish, and crustaceans, has been known to be a potent antioxidant and hence exhibit various physiological effects. We attempted in these studies to evaluate clinical toxicity and efficacy of long-term administration of a new Ax product, by measuring biochemical and hematological blood parameters and by analyzing brain function (using CogHealth and P300 measures). Ax-rich Haematococcus pluvialis extracts equivalent to 4, 8, 20 mg of Ax dialcohol were administered to 73, 38, and 16 healthy adult volunteers, respectively, once daily for 4 weeks to evaluate safety. Ten subjects with age-related forgetfulness received an extract equivalent to 12 mg in a daily dosing regimen for 12 weeks to evaluate efficacy. As a result, no abnormality was observed and efficacy for age-related decline in cognitive and psychomotor functions was suggested.

PMID: 19430618 [PubMed - in process]

PMCID: PMC2675019

Astaxanthin shows potential to prevent dementia in aging subjects in double-blind, placebo-controlled human clinical study.

[Br J Nutr.](#) 2011 Jun;105(11):1563-71. Doi: 10.1017/S0007114510005398. Epub 2011 Jan 31.

Antioxidant effect of astaxanthin on phospholipid peroxidation in human erythrocytes.

[Nakagawa K¹](#), [Kiko T](#), [Miyazawa T](#), [Carpentero Burdeos G](#), [Kimura F](#), [Satoh A](#), [Miyazawa T](#).

Author information

Abstract

Phospholipid hydroperoxides (PLOOH) accumulate abnormally in the erythrocytes of dementia patients, and dietary xanthophylls (polar carotenoids such as astaxanthin) are randomized to prevent the accumulation. In the present study, we conducted a randomized, double-blind, placebo-controlled human trial to assess the efficacy of 12-week astaxanthin supplementation (6 or 12 mg/d) on both astaxanthin and PLOOH levels in the erythrocytes of thirty middle-aged and senior subjects. After 12 weeks of treatment, erythrocyte astaxanthin concentrations were higher in both the 6 and 12 mg astaxanthin groups than in the placebo group. In contrast, erythrocyte PLOOH concentrations were lower in the astaxanthin groups than in the placebo group. In the plasma, somewhat lower PLOOH levels were found after astaxanthin treatment. These results suggest that astaxanthin supplementation results in improved erythrocyte antioxidant status and decreased PLOOH levels, which may contribute to the prevention of dementia.

PMID:

21276280

[PubMed – indexed for MEDLINE]

ASTAXANTHIN IMPROVED EXERCISE TOLERANCE; REDUCED OXIDATIVE STRESS; AND IMPROVED CARDIAC CONTRACTILITY IN HEART FAILURE PATIENTS IN HUMAN CLINICAL STUDY.

Nutrients. 2020 Jun 26;12(6):1896.

doi: 10.3390/nu12061896.

Effects of 3-Month Astaxanthin Supplementation on Cardiac Function in Heart Failure Patients with Left Ventricular Systolic Dysfunction-A Pilot Study

[Takao Kato](#)¹, [Takatoshi Kasai](#)^{1,2,3}, [Akihiro Sato](#)^{1,2}, [Sayaki Ishiwata](#)^{1,2}, [Shoichiro Yatsu](#)¹, [Hiroki Matsumoto](#)¹, [Jun Shitara](#)¹, [Azusa Murata](#)¹, [Megumi Shimizu](#)¹, [Shoko Suda](#)^{1,3}, [Masaru Hiki](#)¹, [Ryo Naito](#)^{1,2,3}, [Hiroyuki Daida](#)¹

PMID: [32604721](#) PMCID: [PMC7353230](#) DOI: [10.3390/nu12061896](#)

Abstract

Astaxanthin has strong antioxidant properties. We conducted a prospective pilot study on heart failure (HF) patients with left ventricular (LV) systolic dysfunction to investigate improvements in cardiac function and exercise tolerance in relation to suppression of oxidative stress by 3-month astaxanthin supplementation. Oxidative stress markers-serum Diacron reactive oxygen metabolite (dROM), biological antioxidant potential (BAP), and urinary 8-hydroxy-2'-deoxyguanosine (8-OHdG) concentrations, LV ejection fraction (LVEF), and 6-min walk distance (6MWD) were assessed before and after 3-month astaxanthin supplementation. Finally, the data of 16 HF patients were analyzed. Following 3-month astaxanthin supplementation, dROM level decreased from 385.6 ± 82.6 U.CARR to 346.5 ± 56.9 U.CARR ($p = 0.041$) despite no changes in BAP and urinary 8-OHdG levels. LVEF increased from $34.1 \pm 8.6\%$ to $38.0 \pm 10.0\%$ ($p = 0.031$) and 6MWD increased from 393.4 ± 95.9 m to 432.8 ± 93.3 m ($p = 0.023$). Significant relationships were observed between percent changes in dROM level and those in LVEF. In this study, following 3-month astaxanthin supplementation, suppressed oxidative stress and improved cardiac contractility and exercise tolerance were observed in HF patients with LV systolic dysfunction. Correlation between suppression of oxidative stress and improvement of cardiac contractility suggests that suppression of oxidative stress by astaxanthin supplementation had therapeutic potential to improve cardiac functioning.

Astaxanthin improves cognitive function in healthy subjects in randomized double-blind, placebo-controlled human clinical trial.

[J Clin Biochem Nutr.](#) 2012 Sep;51(2):102-7. doi: 10.3164/jcbn.11-00017. Epub 2012 Mar 30.

Effects of astaxanthin-rich Haematococcus pluvialis extract on cognitive function: a randomised, double-blind, placebo-controlled study.

[Katagiri M¹](#), [Satoh A](#), [Tsuji S](#), [Shirasawa T](#).

Author information

Abstract

In this study we tried to confirm the effect of an astaxanthin-rich Haematococcus pluvialis extract on cognitive function in 96 subjects by a randomised double-blind placebo-controlled study. Healthy middle-aged and elderly subjects who complained of age-related forgetfulness were recruited. Ninety-six subjects were selected from the initial screen, and ingested a capsule containing astaxanthin-rich Haematococcus pluvialis extract, or a placebo capsule for 12 weeks. Somatometry, haematology, urine screens, and CogHealth and Groton Maze Learning Test were performed before and after every 4 weeks of administration. Changes in cognitive performance and the safety of astaxanthin-rich Haematococcus pluvialis extract administration were evaluated. CogHealth battery scores improved in the high-dosage group (12 mg astaxanthin/day) after 12 weeks. Groton Maze Learning Test scores improved earlier in the low-dosage (6 mg astaxanthin/day) and high-dosage groups than in the placebo group. The sample size, however, was small to show a significant difference in cognitive function between the astaxanthin-rich Haematococcus pluvialis extract and placebo groups. No adverse effect on the subjects was observed throughout this study. In conclusion, the results suggested that astaxanthin-rich Haematococcus pluvialis extract improves cognitive function in the healthy aged individuals.

KEYWORDS:

Astaxanthin; Haematococcus pluvialis; aging; clinical efficacy; cognitive function

PMID:

22962526

[PubMed]

PMCID:

PMC3432818

[Free PMC Article](#)

Astaxanthin combined with tocotrienols and zinc increases strength and endurance in elderly subjects in a double-blind, placebo-controlled randomized human clinical trial.

[J Cachexia Sarcopenia Muscle](#). 2018 Oct;9(5):826-833. doi: 10.1002/jcsm.12318. Epub 2018 Sep 26.

Building strength, endurance, and mobility using an astaxanthin formulation with functional training in elderly.

[Liu SZ](#)¹, [Ali AS](#)¹, [Campbell MD](#)¹, [Kilroy K](#)¹, [Shankland EG](#)¹, [Roshanravan B](#)², [Marcinek DJ](#)^{1,3,4}, [Conley KE](#)^{1,5,3}.

Author information

Abstract

BACKGROUND:

Building both strength and endurance has been a challenge in exercise training in the elderly, but dietary supplements hold promise as agents for improving muscle adaptation. Here, we test a formulation of natural products (AX: astaxanthin, 12 mg and tocotrienol, 10 mg and zinc, 6 mg) with both anti-inflammatory and antioxidant properties in combination with exercise. We conducted a randomized, double-blind, placebo-controlled study of elderly subjects (65-82 years) on a daily oral dose with interval walking exercise on an incline treadmill.

METHODS:

Forty-two subjects were fed AX or placebo for 4 months and trained 3 months (3x/week for 40-60 min) with increasing intervals of incline walking. Strength was measured as maximal voluntary force (MVC) in ankle dorsiflexion exercise, and tibialis anterior muscle size (cross-sectional area, CSA) was determined from magnetic resonance imaging.

RESULTS:

Greater endurance (exercise time in incline walking, >50%) and distance in 6 min walk (>8%) accompanied training in both treatments. Increases in MVC by 14.4% ($\pm 6.2\%$, mean \pm SEM, $P < 0.02$, paired t-test), CSA by 2.7% ($\pm 1.0\%$, $P < 0.01$), and specific force by 11.6% (MVC/CSA, $\pm 6.0\%$, $P = 0.05$) were found with AX treatment, but no change was evident in these properties with placebo treatment (MVC, $2.9\% \pm 5.6\%$; CSA, $0.6\% \pm 1.2\%$; MVC/CSA, $2.4 \pm 5.7\%$; $P > 0.6$ for all).

CONCLUSIONS:

The AX formulation improved muscle strength and CSA in healthy elderly in addition to the elevation in endurance and walking distance found with exercise training alone. Thus, the AX formulation in combination with a functional training programme uniquely improved muscle strength, endurance, and mobility in the elderly.

PMID: 30259703 PMCID: [PMC6204600](#) DOI: [10.1002/jcsm.12318](#)

Astaxanthin added to dark chocolate decreases oxidative stress in aging volunteers in randomized, placebo-controlled human clinical study.

[J Nutr Health Aging](#). 2018;22(9):1092-1098. doi: 10.1007/s12603-018-1063-z.

Markers of Hypoxia and Oxidative Stress in Aging Volunteers Ingesting Licosomal Formulation of Dark Chocolate Containing Astaxanthin.

[Petyaev IM¹](#), [Klochkov VA](#), [Chalyk NE](#), [Pristensky DV](#), [Chernyshova MP](#), [Kyle NH](#), [Bashmakov YK](#).

Author information

Abstract

OBJECTIVE: To determine if ingestion of licosome-formulated dark chocolate (DC) containing astaxanthin (ASTX) improves bioavailability of ASTX and affects markers of hypoxia and oxidative stress in aging individuals.

DESIGN: Randomized, blinded, four-arm, prospective study.

SETTINGS: Lycotec Ltd, Cambridge, United Kingdom and Institute of Cardiology, Saratov, Russian Federation.

PARTICIPANTS: 32 healthy individuals aged 60-70 years with confirmed signs of oxidative stress (increased serum levels of oxidized LDL and malonic dialdehyde) randomized into four study groups (8 volunteers each).

INTERVENTION: Volunteers of first group were given orally 10 gr of dark chocolate (DC). Individuals from the second group received 7 mg of astaxanthin (ASTX). Third group of volunteers was supplemented with 10 gr of DC and 7 mg of ASTX ingested simultaneously as two separate formulations. Last group of the individuals was given 10 gr of a licosomal formulation of DC containing 7 mg of co-crystalized ASTX (L-DC-ASTX), a newly developed highly bioavailable nutraceutical composition of DC containing 2 groups of antioxidants (cocoa flavanols and ASTX). All formulations were given orally, once daily for a month.

MEASUREMENTS: Serum ASTX was measured by high-performance liquid chromatography. Nitric oxide, malonic dialdehyde and oxidized LDL were quantified spectrophotometrically. Oxygenation parameters were evaluated by near-infrared spectroscopy.

RESULTS: One month ingestion of singular formulation of ASTX lead to a 20 fold buildup in serum ASTX level whereas the 4 week ingestion of L-DC-ASTX formulation was accompanied by more prominent accumulation of ASTX in serum (a 40 fold increase over the basal values) at the same daily dose of ASTX. Both antioxidants taken separately decreased serum levels of oxidized LDL and malonic dialdehyde. However effect of L-DC-ASTX formulation was more prominent. ASTX ingested alone caused a borderline increase ($p=0.054$) in serum nitric oxide (NO) levels, whereas

DC ingestion lead to small but statistically significant increase in serum NO concentration. Higher values of NO level were seen after co-ingestion of DC and ASTX, especially in case of L-DC-ASTX formulation suggesting additive/synergistic effects of DC and ASTX on nitric oxide production.

These changes were in agreement with the increase in plasma oxygen transport and tissue oxygen saturation seen in the volunteers supplemented with L-DC-ASTX formulation.

CONCLUSION: The nutraceutical formulation of DC and ASTX with an enhanced bioavailability of ASTX can be efficiently used for the correction of oxidative status in aging individuals.

KEYWORDS:

Dark chocolate; astaxanthin; nitric oxide; oxidized LDL

PMID: 30379308

DOI: [10.1007/s12603-018-1063-z](https://doi.org/10.1007/s12603-018-1063-z)

Astaxanthin supplementation improves oxidative stress markers in soccer players in randomized, double-blind, placebo-controlled human clinical study.

[Phytother Res.](#) 2013 Oct;27(10):1536-42. doi: 10.1002/ptr.4898. Epub 2012 Nov 28.

Effect of astaxanthin supplementation on paraoxonase 1 activities and oxidative stress status in young soccer players.

[Baralic I¹](#), [Djordjevic B](#), [Dikic N](#), [Kotur-Stevuljevic J](#), [Spasic S](#), [Jelic-Ivanovic Z](#), [Radivojevic N](#), [Andjelkovic M](#), [Pejic S](#).

Author information

Abstract

The purpose of the study was to examine the effects of astaxanthin (Asx) on paraoxonase (PON1) activities and oxidative stress status in soccer players. Forty soccer players were randomly assigned in a double-blind fashion to Asx and placebo (P) group. Blood samples were obtained before, 45 and 90 days after supplementation. PON1 activity was assessed by using two substrates: paraoxon and diazoxon. The oxidative stress biomarkers were also examined: total sulphhydryl group content (-SH groups), thiobarbituric acid-reactive substances (TBARS), advanced oxidation protein products and redox balance. The significant interaction effect of supplementation and training ($p < 0.05$) on PON1 activity toward paraoxon was observed. The PON1 activity toward diazoxon increased in Asx group after 90 days ($p < 0.01$), while there was no significant difference in P group. SH groups content rose from pre- to post-supplementation period only in Asx group (supplementation and training, $p < 0.05$; training, $p < 0.01$). TBARS levels decreased after 45 days and increased after 90 days of regular soccer training in both groups (training, $p < 0.001$). Redox balance decreased significantly in response to the regular training, regardless of treatment group (training, $p < 0.001$). Asx supplementation might increase total SH groups content and improve PON1 activity through protection of free thiol groups against oxidative modification.

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KEYWORDS:

astaxanthin; oxidative stress; paraoxonase 1 activity; soccer

PMID:

23192897

[PubMed - indexed for MEDLINE]

Astaxanthin improves oxidative stress markers in healthy smokers in randomized placebo-controlled human clinical study and may be suitable as a supplement to prevent oxidative damage in smokers by suppressing lipid peroxidation and stimulating the activity of the antioxidant system.

[J Med Food](#). 2011 Nov;14(11):1469-75. doi: 10.1089/jmf.2011.1626. Epub 2011 Sep 1.

Protective effects of Haematococcus astaxanthin on oxidative stress in healthy smokers.

[Kim JH](#)¹, [Chang MJ](#), [Choi HD](#), [Youn YK](#), [Kim JT](#), [Oh JM](#), [Shin WG](#).

Author information

Abstract

Free radicals induced by cigarette smoking have been strongly linked to increased oxidative stress in vivo, contributing to the pathobiology of various diseases. This study was performed to investigate the effects of Haematococcus astaxanthin (ASX), which has been known to be a potent antioxidant, on oxidative stress in smokers. Thirty-nine heavy smokers (≥ 20 cigarettes/day) and 39 non-smokers were enrolled in this study. Smokers were randomly divided into three dosage groups to receive ASX at doses of 5, 20, or 40 mg (n=13, each) once daily for 3 weeks. Oxidative stress biomarkers such as malondialdehyde, isoprostane, superoxide dismutase, and total antioxidant capacity, and ASX levels in plasma were measured at baseline and after 1, 2, and 3 weeks of treatment. Compared with baseline, the plasma malondialdehyde and isoprostane levels decreased, whereas superoxide dismutase level and total antioxidant capacity increased in all ASX intervention groups over the 3-week period. In particular, isoprostane levels showed a significant dose-dependent decrease after ASX intake. The results suggest that ASX supplementation might prevent oxidative damage in smokers by suppressing lipid peroxidation and stimulating the activity of the antioxidant system in smokers.

PMID:

21883001

[PubMed - indexed for MEDLINE]

Astaxanthin shows potential benefits for lipid peroxidation in healthy men in double-blind, placebo-controlled randomized human clinical trial.

[Int J Vitam Nutr Res.](#) 2007 Jan;77(1):3-11.

Effects of astaxanthin supplementation on lipid peroxidation.

[Karppi J¹](#), [Rissanen TH](#), [Nyyssönen K](#), [Kaikkonen J](#), [Olsson AG](#), [Voutilainen S](#), [Salonen JT](#).

Author information

Abstract

Astaxanthin, the main carotenoid pigment in aquatic animals, has greater antioxidant activity in vitro (protecting against lipid peroxidation) and a more polar configuration than other carotenoids. We investigated the effect of three-month astaxanthin supplementation on lipid peroxidation in healthy non-smoking Finnish men, aged 19-33 years by using a randomized double-blind study design. Also absorption of astaxanthin from capsules into bloodstream and its safety were evaluated. The intervention group received two 4-mg astaxanthin (Astaxin) capsules daily, and the control group two identical-looking placebo capsules. Astaxanthin supplementation elevated plasma astaxanthin levels to 0.032 pmol/L ($p < 0.001$ for the change compared with the placebo group). We observed that levels of plasma 12- and 15-hydroxy fatty acids were reduced statistically significantly in the astaxanthin group ($p = 0.048$ and $p = 0.047$ respectively) during supplementation, but not in the placebo group and the change of 15-hydroxy fatty acid was almost significantly greater ($p = 0.056$) in the astaxanthin group, as compared with the placebo group. The present study suggests that intestinal absorption of astaxanthin delivered as capsules is adequate, and well tolerated. Supplementation with astaxanthin may decrease in vivo oxidation of fatty acids in healthy men.

PMID:

17685090

[PubMed - indexed for MEDLINE]

Astaxanthin shows positive effects on sperm parameters and fertility and reduces reactive oxygen species in double-blind, placebo-controlled randomized human clinical trial.

[Asian J Androl.](#) 2005 Sep;7(3):257-62.

Combined conventional/antioxidant "Astaxanthin" treatment for male infertility: a double blind, randomized trial.

[Comhaire FH¹](#), [El Garem Y](#), [Mahmoud A](#), [Eertmans F](#), [Schoonjans F](#).

Author information

Abstract

AIM:

To evaluate the treatment of male infertility with a strong natural antioxidant, in addition to conventional treatment.

METHODS:

Using a double blind, randomized trial design, 30 men with infertility of > or =2 months and female partners with no demonstrable cause of infertility received conventional treatment according to the guidelines of the World Health Organization (WHO), and either a strong antioxidant Astaxanthin 16 mg/day (AstaCarox, AstaReal AB, Gustavsberg, Sweden) or placebo for 3 months. The effects of treatment on semen parameters, reactive oxygen species (ROS), zona-free hamster oocyte test, serum hormones including testosterone, luteinizing hormone (LH), follicle stimulating hormone (FSH) and Inhibin B, and spontaneous or intrauterine insemination (IUI)-induced pregnancies were evaluated.

RESULTS:

ROS and Inhibin B decreased significantly and sperm linear velocity increased in the Astaxanthin group (n = 11), but not in the placebo group (n = 19). The results of the zona-free hamster oocyte test tended to improve in the Astaxanthin group in contrast with the placebo group, though not reaching statistical significance. The total and per cycle pregnancy rates among the placebo cases (10.5 % and 3.6 %) were lower compared with 54.5 % and 23.1 % respectively in the Astaxanthin group (P = 0.028; P = 0.036).

CONCLUSION:

Although the present study suggests a positive effect of Astaxanthin on sperm parameters and fertility, the results need to be confirmed in a larger trial before recommending Astaxanthin for the complementary treatment of infertile men.

PMID:

16110353

[PubMed - indexed for MEDLINE]

Free full text

Astaxanthin dose-dependently prolongs the oxidation lag time in-vitro and inhibits low-density lipoprotein oxidation in a human clinical trial leading to the conclusion that it may contribute to the prevention of atherosclerosis.

[J Atheroscler Thromb.](#) 2000;7(4):216-22.

Inhibition of low-density lipoprotein oxidation by astaxanthin.

[Iwamoto T](#)¹, [Hosoda K](#), [Hirano R](#), [Kurata H](#), [Matsumoto A](#), [Miki W](#), [Kamiyama M](#), [Itakura H](#), [Yamamoto S](#), [Kondo K](#).

[Author information](#)

Abstract

Marine animals produce astaxanthin which is a carotenoid and antioxidant. In this study we determined the in vitro and ex vivo effects of astaxanthin on LDL oxidation. The oxidation of LDL was measured in a 1 ml reaction system consisting of increasing concentrations of astaxanthin (12.5, 25.0, 50.0 microg/ml), 400 microM V-70 (2, 2'-azobis(4-methoxy-2, 4-dimethylvaleronitrile)), and LDL (70 microg/ml protein). Astaxanthin dose, dependently significantly prolonged the oxidation lag time (31.5, 45.4, 65.0 min) compared with the control (19.9 min). For the ex vivo study 24 volunteers (mean age 28.2 [SD 7.8] years) consumed astaxanthin at doses of 1.8, 3.6, 14.4 and 21.6 mg per day for 14 days. No other changes were made in the diet. Fasting venous blood samples were taken at days 0, +14. LDL lag time was longer (5.0, 26.2, 42.3 and 30.7% respectively) compared with day 0 after consuming astaxanthin at doses of 1.8, 3.6, 14.4 and 21.6 mg for 14 days compared with day 0, but there was no difference in oxidation of LDL between day 0 (lag time 59.9+/-7.2 min) and day 14 (57.2+/-6.0 min) in the control group. Our results provide evidence that consumption of marine animals producing astaxanthin inhibits LDL oxidation and possibly therefore contributes to the prevention of atherosclerosis.

PMID:

11521685

[PubMed - indexed for MEDLINE]

Astaxanthin improves LDL cholesterol levels, ApoB and oxidative stress biomarkers in overweight subjects in double-blind, placebo-controlled randomized human clinical study.

[Plant Foods Hum Nutr.](#) 2011 Nov;66(4):363-9. doi: 10.1007/s11130-011-0258-9.

Positive effects of astaxanthin on lipid profiles and oxidative stress in overweight subjects.

[Choi HD¹](#), [Youn YK](#), [Shin WG](#).

Author information

Abstract

Astaxanthin, a carotenoid, has antioxidant activity as well as many positive effects, such as anticancer and anti-inflammatory effects. We performed a randomized, double-blind, placebo-controlled study to investigate the effects of astaxanthin on lipid profiles and oxidative stress in overweight and obese adults in Korea. In total, 27 subjects with body mass index >25.0 kg/m² were enrolled and randomly assigned into two groups administered astaxanthin or placebo capsules for 12 weeks. Total cholesterol, triglycerides, high density lipoprotein (HDL) cholesterol, low density lipoprotein (LDL) cholesterol, apolipoprotein A1 (ApoA1), and apolipoprotein B (ApoB) were measured before and after intervention. Malondialdehyde (MDA), isoprostane (ISP), superoxide dismutase (SOD), and total antioxidant capacity (TAC), as oxidative stress biomarkers, were measured at baseline and at 4, 8, and 12 weeks after intervention. LDL cholesterol and ApoB were significantly lower after treatment with astaxanthin, compared with the start of administration, whereas none of the lipid profiles was changed in the placebo group. At the baseline, all four biomarkers were not significantly different between the two groups. Compared with the placebo group, MDA and ISP were significantly lower, but TAC was significantly higher in the astaxanthin group at 12 weeks. These results suggest that supplementary astaxanthin has positive effects by improving the LDL cholesterol, ApoB, and oxidative stress biomarkers.

PMID:

21964877

[PubMed - indexed for MEDLINE]

Astaxanthin dose-dependently inhibits LDL oxidation and may prevent atherosclerosis in human clinical trial.

Prog Med F0664B 0287-3648 VOL.24;NO.6;PAGE.1437-1442(2004)

Multivitamin and Carotenoid Supplements

[ITAKURA HIROSHIGE](#) (Dep. Life Sci., Ibaraki Christian Univ., JPN)

Abstract; Vitamins are regarded as essential nutrients for health and maintain stable tissue environments. Vitamins and carotenoids have multiple roles both as participants in many important metabolic processes throughout the body and to counter the oxidative stress resulting from normal metabolism and daily exposure to environmental agents. Epidemiological studies have consistently indicated that the consumption of vegetables and fruits is inversely related to the incidence of cardiovascular and cerebrovascular diseases and cancer. Although the majority of vitamins and carotenoids are derived from these foods, foods of animal origin also contribute supplementation of these nutrients. Marine animals supply astaxanthin which is a carotenoid and antioxidant. We studied the effects of astaxanthin on in vitro and ex vivo LDL oxidation. Astaxanthin prolonged dose-dependently the oxidation lag time compared with the control. For the ex vivo study 24 volunteers consumed astaxanthin at doses of 1.8, 3.6, 14.4, 21.6 mg per day for 14 days. LDL lag time was longer in the groups who intaked astaxanthin compared with day 0, but there was no difference in oxidation of LDL in the control group. Our results provide evidence that consumption of marine animals producing astaxanthin inhibits LDL oxidation and possibly therefore contributes to the prevention of atherosclerosis.

Astaxanthin could prevent exercise-induced free radical production and depletion of non-enzymatic antioxidant defense in elite soccer players as evidenced in double-blind, placebo-controlled randomized human clinical study.

[J Sports Med Phys Fitness](#). 2012 Aug;52(4):382-92.

Effect of astaxanthin supplementation on muscle damage and oxidative stress markers in elite young soccer players.

[Djordjevic B¹](#), [Baralic I](#), [Kotur-Stevuljevic J](#), [Stefanovic A](#), [Ivanisevic J](#), [Radivojevic N](#), [Andielkovic M](#), [Dikic N](#).

Author information

Abstract

AIM:

The purpose of the current study was to examine the effect of Astaxanthin (Asx) supplementation on muscle enzymes as indirect markers of muscle damage, oxidative stress markers and antioxidant response in elite young soccer players.

METHODS:

Thirty-two male elite soccer players were randomly assigned in a double-blind fashion to Asx and placebo (P) group. After the 90 days of supplementation, the athletes performed a 2 hour acute exercise bout. Blood samples were obtained before and after 90 days of supplementation and after the exercise at the end of observational period for analysis of thiobarbituric acid-reacting substances (TBARS), advanced oxidation protein products (AOPP), superoxide anion ($O_2^{\bullet-}$), total antioxidative status (TAS), sulphhydryl groups (SH), superoxide-dismutase (SOD), serum creatine kinase (CK) and aspartate aminotransferase (AST).

RESULTS:

TBARS and AOPP levels did not change throughout the study. Regular training significantly increased $O_2^{\bullet-}$ levels (main training effect, $P<0.01$). $O_2^{\bullet-}$ concentrations increased after the soccer exercise (main exercise effect, $P<0.01$), but these changes reached statistical significance only in the P group (exercise x supplementation effect, $P<0.05$). TAS levels decreased significantly post-exercise only in P group ($P<0.01$). Both Asx and P groups experienced increase in total SH groups content (by 21% and 9%, respectively) and supplementation effect was marginally significant ($P=0.08$). Basal SOD activity significantly decreased both in P and in Asx group by the end of the study (main training effect, $P<0.01$). All participants showed a significant decrease in basal CK and AST activities after 90 days (main training effect, $P<0.01$ and $P<0.001$, respectively). CK and AST activities in serum significantly increased as result of soccer exercise (main exercise effect, $P<0.001$ and $P<0.01$, respectively). Postexercise CK and AST levels were significantly lower in Asx group compared to P group ($P<0.05$)

CONCLUSION:

The results of the present study suggest that soccer training and soccer exercise are associated with excessive production of free radicals and oxidative stress, which might diminish antioxidant system efficiency. Supplementation with Asx could prevent exercise induced free radical production and depletion of non-enzymatic antioxidant defense in young soccer players.

PMID: 22828460 [PubMed - indexed for MEDLINE]

Astaxanthin improves oxidative stress biomarkers in overweight adults in randomized human clinical study.

[Phytother Res.](#) 2011 Dec;25(12):1813-8. doi: 10.1002/ptr.3494. Epub 2011 Apr 8.

Effects of astaxanthin on oxidative stress in overweight and obese adults.

[Choi HD¹](#), [Kim JH](#), [Chang MJ](#), [Kyu-Youn Y](#), [Shin WG](#).

Author information

Abstract

Oxidative stress is caused by an imbalance between the antioxidant and the reactive oxygen species, which results in damage to cells or tissues. Recent studies have reported that oxidative stress is involved in obesity, in addition to many other human diseases and aging. A prospective, randomized, double-blind study was performed to investigate the effect of astaxanthin (ASX), which is known to be a potent antioxidant, on oxidative stress in overweight and obese adults in Korea. Twenty-three adults with BMI > 25.0 kg/m² enrolled in this study and were randomly assigned to two dose groups: ASX 5 mg and 20 mg once daily for 3 weeks. Malondialdehyde (MDA), isoprostane (ISP), superoxide dismutase (SOD) and total antioxidant capacity (TAC), as oxidative stress biomarkers, were measured at baseline and 1, 2 and 3 weeks after ASX administration. Compared with baseline, the MDA (by 34.6% and 35.2%) and ISP (by 64.9% and 64.7%) levels were significantly lowered, whereas SOD (by 193% and 194%) and TAC (by 121% and 125%) levels were significantly increased in two dose groups after the 3 week intervention.

This study revealed that supplemental ASX for 3 weeks improved oxidative stress biomarkers by suppressing lipid peroxidation and stimulating the activity of the antioxidant defense system.

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PMID:

21480416

[PubMed - indexed for MEDLINE]

Astaxanthin decreases heart rate in endurance athletes in double-blind, placebo-controlled human clinical trial.

[EC Nutr](#) 11.6 (2016) 253-259.

Effect of Astaxanthin Supplementation on Cardiorespiratory Function in Runners

Talbott, S., Hantla, D., Capelli, B., Ding, L., Li, Y., Artaria, C.

Abstract

Purpose: Marine microalgae is the predominant source of natural astaxanthin (NAX), a red-orange carotenoid with powerful antioxidant and anti-inflammatory properties. Studies in both rodents and humans suggest that NAX supplementation improves antioxidant capacity and reduces oxidative stress, while also improving fat utilization and exercise endurance. The purpose of this study was to assess the effects of a moderate dose of NAX supplementation (12mg/day for 8 weeks) on cardiorespiratory function during both higher and lower intensity exercise in recreational runners.

Patients and Methods: Using a double-blind parallel design, 28 recreational runners (male = 14, female = 14, age = 42) were supplemented with NAX (*Haematococcus pluvialis* algal extract) or a placebo. Before and after the supplementation period, subjects performed a maximal running test (VO₂max on treadmill) and a maximal cycling test (watts on cycle ergometer).

Results: There was no improvement in maximal oxygen uptake (running VO₂ max) or maximal power output (cycling watts) with NAX supplementation. However, subjects in the NAX group showed a significant ~10% lower average heart rate at submaximal running intensities compared to placebo (aerobic threshold, AeT; NAX 130+17 v. PL 145+14; and anaerobic threshold, AT; NAX 139+20 v. PL 154+11, $p < 0.05$).

Conclusion: Supplementation with 12 mg/day of NAX for 8 weeks reduced average heart rate at submaximal endurance intensities (AeT and AT), but not at higher “peak” intensities. These results suggest that NAX may be a beneficial ergogenic aid for long/ultradistance endurance athletes, but not necessarily for athletes competing in shorter higher intensity efforts. In addition, these data are also suggestive of a general “cardiotonic” effect of NAX, that should be investigated in non-athletic populations including elderly subjects and those with cardiac complications including post-myocardial infarction, heart failure, statin usage, mitochondrial dysfunction, chronic fatigue, and related conditions.

Astaxanthin improves mood state in double-blind, placebo-controlled human clinical study.

Published as a poster at American College of Lifestyle Medicine and to be published as a full manuscript in 2019.

Natural Astaxanthin Supplementation Improves Mental Wellness

Talbott, S., Hantla, D., Capelli, B., Ding, L., Li, Y., Artaria, C.

Introduction: Nutrition plays a major role in the pathophysiology of many “physical” disease states, including cardiovascular disease, cancer, obesity, and diabetes. The role of nutrition is less well-known with respect to “mental” disease states, including depression, anxiety, attention deficit disorder, psychological burnout and chronic pain. Diet-related changes in psychological mood state and mental wellness may be due to cellular, biochemical, and behavioral factors – and may be mediated by lifestyle factors including diet and exercise.

Purpose: Our objective was to assess changes in mental wellness by assessing psychological mood state in response to dietary supplementation with natural astaxanthin (12mg/day for 8 weeks). Marine microalgae is the predominant source of natural astaxanthin (NAX), a red-orange carotenoid with powerful antioxidant and anti-inflammatory properties. Studies in both rodents and humans suggest that NAX supplementation improves antioxidant capacity and reduces oxidative stress – effects which may be related to mental wellness.

Methods: Using a double-blind parallel design, 28 recreational runners (male = 14, female = 14, age = 42) were supplemented with NAX (*Haematococcus pluvialis* algal extract) or a placebo. Before and after the supplementation period, subjects completed the validated Profile of Mood States (POMS) survey to assess mental wellness parameters including global mood state (GM) and related subscales: Vigor (V), Tension (T), Depression (D), Anger (A), Fatigue (F), and Confusion (C).

Results & Conclusions: Significant changes (all, $p < 0.05$) were found for improvements in positive mood state parameters: GM (+11%) & V (+5%); as well as reductions in negative mood state parameters: T (-20%), D (-57%), A (-12%), F (-36%), and C (-28%). Previous studies have shown astaxanthin supplementation to be associated with improvements in fatigue, attention, and memory – with suggestions that it may also play a role in prevention of dementia and age-related memory loss. These data are the first to suggest that astaxanthin supplementation improves mental wellness parameters associated with improvements in mood state and depression.

Astaxanthin taken internally improves the beauty of the skin in human clinical trial.

[Acta Biochim Pol.](#) 2012;59(1):43-7. Epub 2012 Mar 17.

Cosmetic benefits of astaxanthin on humans subjects.

[Tominaga K¹](#), [Hongo N](#), [Karato M](#), [Yamashita E](#).

Author information

Abstract

Two human clinical studies were performed. One was an open-label non-controlled study involving 30 healthy female subjects for 8 weeks. Significant improvements were observed by combining 6 mg per day oral supplementation and 2 ml (78.9 µM solution) per day topical application of astaxanthin. Astaxanthin derived from the microalgae, *Haematococcus pluvialis* showed improvements in skin wrinkle (crow's feet at week-8), age spot size (cheek at week-8), elasticity (crow's feet at week-8), skin texture (cheek at week-4), moisture content of corneocyte layer (cheek in 10 dryskin subjects at week-8) and corneocyte condition (cheek at week-8). It may suggest that astaxanthin derived from *H. pluvialis* can improve skin condition in all layers such as corneocyte layer, epidermis, basal layer and dermis by combining oral supplementation and topical treatment. Another was a randomized double-blind placebo controlled study involving 36 healthy male subjects for 6 weeks. Crow's feet wrinkle and elasticity; and transepidermal water loss (TEWL) were improved after 6 mg of astaxanthin (the same as former study) daily supplementation. Moisture content and sebum oil level at the cheek zone showed strong tendencies for improvement. These results suggest that astaxanthin derived from *Haematococcus pluvialis* may improve the skin condition in not only in women but also in men.

PMID:

22428137

[PubMed - indexed for MEDLINE]

Free full text

Astaxanthin with collagen improves photo-aged skin in placebo-controlled human clinical study.

[J Med Food](#). 2014 Jul;17(7):810-6. doi: 10.1089/jmf.2013.3060. Epub 2014 Jun 23.

Supplementing with dietary astaxanthin combined with collagen hydrolysate improves facial elasticity and decreases matrix metalloproteinase-1 and -12 expression: a comparative study with placebo.

[Yoon HS¹](#), [Cho HH](#), [Cho S](#), [Lee SR](#), [Shin MH](#), [Chung JH](#).

Author information

Abstract

Photoaging accounts for most age-related changes in skin appearance. It has been suggested that both astaxanthin, a potent antioxidant, and collagen hydrolysate can be used as antiaging modalities in photoaged skin. However, there is no clinical study using astaxanthin combined with collagen hydrolysate. We investigated the effects of using a combination of dietary astaxanthin and collagen hydrolysate supplementation on moderately photoaged skin in humans. A total of 44 healthy subjects were recruited and treated with astaxanthin (2 mg/day) combined with collagen hydrolysate (3 g/day) or placebos, which were identical in appearance and taste to the active supplementation for 12 weeks. The elasticity and hydration properties of facial skin were evaluated using noninvasive objective devices. In addition, we also evaluated the expression of procollagen type I, fibrillin-1, matrix metalloproteinase-1 (MMP-1) and -12, and ultraviolet (UV)-induced DNA damage in artificially UV-irradiated buttock skin before and after treatment. The supplement group showed significant improvements in skin elasticity and transepidermal water loss in photoaged facial skin after 12 weeks compared with the placebo group. In the supplement group, expression of procollagen type I mRNA increased and expression of MMP-1 and -12 mRNA decreased compared with those in the placebo group. In contrast, there was no significant difference in UV-induced DNA damage between groups. These results demonstrate that dietary astaxanthin combined with collagen hydrolysate can improve elasticity and barrier integrity in photoaged human facial skin, and such treatment is well tolerated.

KEYWORDS:

anti-aging; astaxanthin; collagen hydrolysate; photoaging

PMID: 24955642

DOI: [10.1089/jmf.2013.3060](https://doi.org/10.1089/jmf.2013.3060)

Astaxanthin reduces wrinkles and improves skin moisture and elasticity in double-blind, randomized study.

[Clin Interv Aging](#). 2015 Nov 19;10:1849-56. doi: 10.2147/CIA.S90092. eCollection 2015.

The effectiveness of a standardized rose hip powder, containing seeds and shells of *Rosa canina*, on cell longevity, skin wrinkles, moisture, and elasticity.

[Phetcharat L](#)¹, [Wongsuphasawat K](#)¹, [Winther K](#)².

Author information

Abstract

OBJECTIVE: To evaluate the effects of a rose hip powder (Hyben Vital®) made from seeds and shells on cell senescence, skin wrinkling, and aging.

METHODS: A total of 34 healthy subjects, aged 35-65 years, with wrinkles on the face (crow's-feet) were subjected to a randomized and double-blinded clinical study of the effects of the rose hip powder, as compared to astaxanthin, a well-known remedy against wrinkles. During the 8-week study, half of the participants ingested the standardized rose hip product, while the other half ingested astaxanthin. Objective measurements of facial wrinkles, skin moisture, and elasticity were made by using Visioscan, Corneometer, and Cutometer at the beginning of the study, after 4 weeks, and after 8 weeks. Evaluation of participant satisfaction of both supplements was assessed using questionnaires. In addition, the effect of the rose hip preparation on cell longevity was measured in terms of leakage of hemoglobin through red cell membranes (hemolytic index) in blood samples kept in a blood bank for 5 weeks. Significance of all values was attained with $P \leq 0.05$.

RESULTS: In the double-blinded study, the rose hip group showed statistically significant improvements in crow's-feet wrinkles ($P < 0.05$), skin moisture ($P < 0.05$), and elasticity ($P < 0.05$) after 8 weeks of treatment. A similar improvement was observed for astaxanthin, with P -values 0.05, 0.001, and 0.05. Likewise, both groups expressed equal satisfaction with the results obtained in their self-assessment. The rose hip powder further resulted in increased cell longevity of erythrocyte cells during storage for 5 weeks in a blood bank.

CONCLUSION: Results suggest that intake of the standardized rose hip powder (Hyben Vital®) improves aging-induced skin conditions. The apparent stabilizing effects of the rose hip product on cell membranes of stored erythrocyte cells observed in this study may contribute to improve the cell longevity and obstructing skin aging.

PMID: 26604725 PMCID: [PMC4655903](#) DOI: [10.2147/CIA.S90092](#) [Indexed for MEDLINE] [Free PMC Article](#)

Astaxanthin is effective against UV-induced skin deterioration in double-blind, placebo-controlled human clinical study.

Nutrients **2018**, *10*(7), 817; doi:[10.3390/nu10070817](https://doi.org/10.3390/nu10070817)

Article

The Protective Role of Astaxanthin for UV-Induced Skin Deterioration in Healthy People—A Randomized, Double-Blind, Placebo-Controlled Trial

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Abstract

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Skin is a major safeguard tissue in humans. Because biological barrier function is deteriorated by several kinds of stresses including exposure to ultra-violet (UV) rays, the protection and treatment of skin conditions by dietary supplements are important. We therefore evaluated the effects of dietary supplementation with an algal food-derived antioxidant, astaxanthin, on UV-induced skin deterioration. Twenty-three healthy Japanese participants were recruited to a 10-week double-blind placebo-controlled study. They were assigned to the astaxanthin group supplemented with a capsule containing 4 mg of astaxanthin or the placebo group. To assess the protective role of astaxanthin for UV-induced skin deterioration, we determined the minimal erythema dose (MED) and analyzed UV-induced changes of moisture and transepidermal water loss (TEWL) at baseline and after 9 weeks of supplementation. Subjective skin conditions were assessed by the visual analog scale. The astaxanthin group showed increased MED compared with placebo. In addition, the astaxanthin group had a reduced loss of skin moisture in the irradiated area compared with placebo. Subjective skin conditions for “improvement of rough skin” and “texture” in non-irradiated areas were significantly improved by astaxanthin. Astaxanthin seems protective against UV-induced skin deterioration and helps maintain healthy skin in healthy people.

Keywords:

astaxanthin; antioxidant; skin; ultra-violet; UV; MED; moisture

ASTAXANTHIN DECREASES MALONDIALDEHYDE (MARKER FOR DIABETES); DECREASES INFLAMMATORY MARKER INTERLEUKIN-6; AND DECREASES THE EXPRESSION OF DIABETES-RELATED COMPOUND MIR-126 IN RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED HUMAN CLINICAL TRIAL.

Int J Clin Pract. 2021 Jan 14;e14022.

doi: 10.1111/ijcp.14022. Online ahead of print.

The antioxidant and anti-inflammatory effects of astaxanthin supplementation on the expression of miR-146a and miR-126 in patients with type 2 diabetes mellitus: A randomised, double-blind, placebo-controlled clinical trial

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PMID: 33445213 DOI: [10.1111/ijcp.14022](https://doi.org/10.1111/ijcp.14022)

Abstract

Background: The pathogenesis of type 2 diabetes mellitus (T2DM) is associated with chronic oxidative stress and inflammation. It is well known that the expression of some miRNAs such as miRNA-146a is upregulated in diabetic and hyperglycaemic patients, whereas circulating miRNA-126 is reduced. Therefore, we aimed to determine the effects of astaxanthin (AST) supplementation on the circulating malondialdehyde (MDA) and interleukin 6 (IL-6) levels, and the expression of miR-146a and miR-126 in patients with T2DM.

Methods: This randomised, double-blind, placebo-controlled clinical trial was conducted in 44 patients with T2DM randomly receiving 8 mg/d of oral AST (n = 22) or placebo (n = 22) for 8 weeks.

Results: We observed that AST supplementation could decrease plasma levels of MDA and IL-6 (P < .05) and decrease the expression level of miR-146a over time (fold change: -1/388) (P < .05).

Conclusion: AST supplementation might be beneficial for improving circulating MDA and IL-6 and the down-regulation of miR-146a. However, future investigations are suggested to confirm these results.

ASTAXANTHIN IMPROVES PERFORMANCE; ENHANCES WHOLE-BODY FAT OXIDATION RATES; AND REDUCES RESPIRATORY EXCHANGE RATIO IN RECREATIONAL CYCLISTS IN ONLY SEVEN DAYS OF SUPPLEMENTATION IN HUMAN CLINICAL TRIAL.

J Sci Med Sport. 2021 Jan;24(1):92-97.

doi: 10.1016/j.jsams.2020.06.017. Epub 2020 Jul 3.

The effect of astaxanthin supplementation on performance and fat oxidation during a 40 km cycling time trial

[Daniel R Brown](#)¹, [Ashley R Warner](#)², [Sanjoy K Deb](#)³, [Lewis A Gough](#)⁴, [S Andy Sparks](#)⁵, [Lars R McNaughton](#)⁶

PMID: 32660833 DOI: [10.1016/j.jsams.2020.06.017](https://doi.org/10.1016/j.jsams.2020.06.017)

Abstract

Objectives: This study aimed to investigate whether supplementation with 12 mg·day⁻¹ astaxanthin for 7 days can improve exercise performance and metabolism during a 40 km cycling time trial.

Design: A randomised, double-blind, crossover design was employed.

Methods: Twelve recreationally trained male cyclists (VO_{2peak} : 56.5 ± 5.5 mL·kg⁻¹·min⁻¹, W_{max} : 346.8 ± 38.4 W) were recruited. Prior to each experimental trial, participants were supplemented with either 12 mg·day⁻¹ astaxanthin or an appearance-matched placebo for 7 days (separated by 14 days of washout). On day 7 of supplementation, participants completed a 40 km cycling time trial on a cycle ergometer, with indices of exercise metabolism measured throughout.

Results: Time to complete the 40 km cycling time trial was improved by $1.2 \pm 1.7\%$ following astaxanthin supplementation, from 70.76 ± 3.93 min in the placebo condition to 69.90 ± 3.78 min in the astaxanthin condition (mean improvement = 51 ± 71 s, $p = 0.029$, $g = 0.21$). Whole-body fat oxidation rates were also greater ($+0.09 \pm 0.13$ g·min⁻¹, $p = 0.044$, $g = 0.52$), and the respiratory exchange ratio lower (-0.03 ± 0.04 , $p = 0.024$, $g = 0.60$) between 39-40 km in the astaxanthin condition.

Conclusions: Supplementation with 12 mg·day⁻¹ astaxanthin for 7 days provided an ergogenic benefit to 40 km cycling time trial performance in recreationally trained male cyclists and enhanced whole-body fat oxidation rates in the final stages of this endurance-type performance event.

ASTAXANTHIN-CONTAINING FORMULA INCREASES RESTING OXYGEN CONSUMPTION; DECREASES OXIDATION MARKER AFTER EXERCISE; AND INCREASES MAXIMAL VOLUNTARY CONTRACTION, LEADING TO CONCLUSION THAT THE FORMULA SUPPORTS RESISTANCE TRAINING-INDUCED STRENGTH AND METABOLIC APPLICATIONS IN HUMAN CLINICAL TRIAL.

Antioxidants (Basel). 2021 Jan 14;10(1):113.
doi: 10.3390/antiox10010113.

Astaxanthin-, β -Carotene-, and Resveratrol-Rich Foods Support Resistance Training-Induced Adaptation

[Aki Kawamura](#)^{1,2}, [Wataru Aoi](#)¹, [Ryo Abe](#)^{1,3}, [Yukiko Kobayashi](#)¹, [Masashi Kuwahata](#)¹, [Akane Higashi](#)¹

PMID: 33466842 PMCID: [PMC7830030](#) DOI: [10.3390/antiox10010113](#) [Free PMC article](#)

Abstract

Resistance training adaptively increases the muscle strength associated with protein anabolism. Previously, we showed that the combined intake of astaxanthin, β -carotene, and resveratrol can accelerate protein anabolism in the skeletal muscle of mice. The purpose of this study was to investigate the effect of anabolic nutrient-rich foods on muscle adaptation induced by resistance training. Twenty-six healthy men were divided into control and intervention groups. All participants underwent a resistance training program twice a week for 10 weeks. Astaxanthin-, β -carotene-, and resveratrol-rich foods were provided to the intervention group. Body composition, nutrient intake, maximal voluntary contraction of leg extension, oxygen consumption, and serum carbonylated protein level were measured before and after training. The skeletal muscle mass was higher after training than before training in both groups ($p < 0.05$). Maximal voluntary contraction was increased after training in the intervention group ($p < 0.05$), but not significantly increased in the control group. Resting oxygen consumption was higher after training in the intervention group only ($p < 0.05$). As an oxidative stress marker, serum carbonylated protein level tended to be lower immediately after exercise than before exercise in the intervention group only ($p = 0.056$). Intake of astaxanthin-, β -carotene-, and resveratrol-rich foods supported resistance training-induced strength and metabolic adaptations

Astaxanthin rejuvenates facial skin and reduces oxidative stress in skin in human clinical study.

[Nutr Res.](#) 2017 Dec;48:40-48. doi: 10.1016/j.nutres.2017.10.006. Epub 2017 Oct 10.

Continuous astaxanthin intake reduces oxidative stress and reverses age-related morphological changes of residual skin surface components in middle-aged volunteers.

[Chalyk NE](#)¹, [Klochkov VA](#)¹, [Bandaletova TY](#)², [Kyle NH](#)³, [Petyaev IM](#)⁴.

Author information

Abstract

Oxidative stress accelerates skin aging, and dietary supplementation with antioxidants may alleviate it. Morphological analysis of the residual skin surface components (RSSCs) allows detecting age-related changes in corneocyte desquamation, microbial presence, and lipid droplet size. We hypothesized that continuous ingestion of carotenoid antioxidant astaxanthin (4 mg/d) for 4 weeks could influence RSCC morphology and evaluated RSCC samples taken from middle-aged subjects before and after this dietary intervention. The study included 31 volunteers (17 men and 14 women) over the age of 40. RSCC samples were collected from the surface of the facial skin at the beginning (day 0) and end (day 29) of the study. In addition, blood samples were taken on days 0, 15, and 29 for measuring plasma levels of malondialdehyde that allowed assessing systemic oxidative stress. The results demonstrated that plasma malondialdehyde consistently decreased during astaxanthin consumption (by 11.2% on day 15 and by 21.7% on day 29). The analysis of RSCC samples has revealed significantly decreased levels of corneocyte desquamation ($P=.0075$) and microbial presence ($P=.0367$) at the end of the study. These phenomena as well as a significant ($P=.0214$) increase in lipid droplet size were more strongly manifested among obese (body mass index >30 kg/m²) subjects. All described RSCC changes correspond to a shift toward characteristics of skin associated with a younger age. The results confirm our hypothesis by demonstrating that continuous astaxanthin consumption produces a strong antioxidant effect resulting in facial skin rejuvenation which is especially pronounced in obese subjects.

KEYWORDS:

Antiaging effect; Antioxidant; Astaxanthin; Corneocyte desquamation; Malondialdehyde; Skin surface

PMID: 29246280

DOI: [10.1016/j.nutres.2017.10.006](https://doi.org/10.1016/j.nutres.2017.10.006)

[Indexed for MEDLINE]

ASTAXANTHIN INCREASES PHYSICAL ACTIVITY AND IMPROVES BOTH PHYSICAL AND MENTAL QUALITY-OF-LIFE SELF-ASSESSMENT IN PATIENTS WITH HEART FAILURE IN HUMAN CLINICAL TRIAL.

Ann Palliat Med. 2020 Nov 10;apm-20-1378.

doi: 10.21037/apm-20-1378. Online ahead of print.

Changes in self-reported physical activity and health-related quality of life following 3-month astaxanthin supplementation in patients with heart failure: results from a pilot study

[Sayaki Ishiwata¹](#), [Takao Kato²](#), [Takatoshi Kasai³](#), [Akihiro Sato¹](#), [Shoichiro Yatsu²](#), [Hiroki Matsumoto²](#), [Jun Shitara²](#), [Azusa Murata²](#), [Megumi Shimizu²](#), [Shoko Suda²](#), [Yuya Matsue¹](#), [Ryo Naito¹](#), [Masaru Hiki²](#), [Hiroyuki Daida²](#)

- PMID: 33183036
- DOI: [10.21037/apm-20-1378](https://doi.org/10.21037/apm-20-1378)

Free article

Abstract

Background: Astaxanthin has a strong antioxidant effect. We recently demonstrated that following 3-month astaxanthin supplementation, cardiac contractility and exercise tolerance improved, possibly through the suppression of oxidative stress in a small pilot study involving patients with heart failure with left ventricular systolic dysfunction. This is a sub-study of our pilot study to investigate whether improvements of self-reported physical activity and health-related quality of life were observed following 3-month astaxanthin supplementation.

Methods: We investigated the changes in physical activity by the Specific Activity Scale score and health-related quality of life by physical and mental component summary scores in Short Form-8 at baseline and after 3-month astaxanthin supplementation.

Results: Data from 17 patients with heart failure were assessed. Following 3-month astaxanthin supplementation, the Specific Activity Scale score increased from the median of 4.5 (interquartile range, 2.0) to 6.5 (interquartile range, 1.1) metabolic equivalent ($P=0.001$), and the physical and mental component summary scores increased from 46.1 ± 9.2 to 50.8 ± 6.8 ($P=0.015$) and from 48.9 ± 9.1 to 53.8 ± 4.8 ($P=0.022$), respectively. There was a linear relationship of the baseline heart rate, or mental component summary score with the percent change in the Specific Activity Scale score ($r=0.523$, $P=0.031$ and $r=-0.505$, $P=0.039$, respectively). In addition, there was a direct relationship of ischemic etiology with the percent change in the physical component summary score ($r=0.483$, $P=0.049$, respectively). Finally, there was a linear relationship between the percent change in the Specific Activity Scale score and that in the mental component summary score ($r=0.595$, $P=0.012$).

Conclusions: Following 3-month astaxanthin supplementation, improvements of the self-reported physical activity level and health-related quality of life in both mental and physical components were observed. In patients with heart failure, those with higher baseline heart rate, ischemic etiology, and poorer baseline health-related quality of life have potentials to have greater improvement of physical activity and/or health-related quality of life.

Astaxanthin prevents skin deterioration due to environmental factors such as UV and dehydration in placebo-controlled human clinical study.

[J Clin Biochem Nutr.](#) 2017 Jul;61(1):33-39. doi: 10.3164/jcbn.17-35. Epub 2017 Jun 20.

Protective effects of astaxanthin on skin deterioration.

[Tominaga K¹](#), [Hongo N¹](#), [Fujishita M¹](#), [Takahashi Y¹](#), [Adachi Y¹](#).

Author information

Abstract

Astaxanthin is a carotenoid with potent antioxidant and anti-inflammatory activity. To evaluate the anti-inflammatory effect of astaxanthin on skin deterioration, we confirmed its role in epidermal-dermal interactions *in vitro*. Astaxanthin treatment suppressed ultraviolet B (UVB)-induced inflammatory cytokine secretion in keratinocytes, and matrix metalloproteinase-1 secretion by fibroblasts cultured in UVB-irradiated keratinocyte medium. To verify these findings, we conducted a 16-week clinical study with 65 healthy female participants. Participants were orally administered either a 6 mg or 12 mg dose of astaxanthin or a placebo. Wrinkle parameters and skin moisture content significantly worsened in the placebo group after 16 weeks. However, significant changes did not occur in the astaxanthin groups. Interleukin-1 α levels in the stratum corneum significantly increased in the placebo and low-dose groups but not in the high-dose group between weeks 0 and 16. This study was performed in Japan from August to December, when changing environmental factors, such as UV and dryness, exacerbate skin deterioration. In conclusion, our study suggests that long-term prophylactic astaxanthin supplementation may inhibit age-related skin deterioration and maintain skin conditions associated with environmentally induced damage via its anti-inflammatory effect. (UMIN Clinical Trials Registry ID: UMIN000018550).

KEYWORDS:

astaxanthin; inflammatory cytokines; interleukin-1 α ; skin elasticity; wrinkle formation

PMID: 28751807

PMCID: [PMC5525019](#)

DOI: [10.3164/jcbn.17-35](#)

[Free PMC Article](#)

Astaxanthin reduces blood pressure, improves glucose metabolism and reduces visceral body fat mass in placebo-controlled randomized study on patients with Type-2 diabetes.

[Asia Pac J Clin Nutr.](#) 2018;27(2):341-346. doi: 10.6133/apjcn.052017.11.

Astaxanthin improves glucose metabolism and reduces blood pressure in patients with type 2 diabetes mellitus.

[Mashhadi NS](#)¹, [Zakerkish M](#)², [Mohammadiasl J](#)³, [Zarei M](#)⁴, [Mohammadshahi M](#)⁵, [Haghighizadeh MH](#)⁶.

Author information

Abstract

BACKGROUND AND OBJECTIVES:

This randomized, placebo-controlled trial was performed for 8 weeks to investigate the potential effects of astaxanthin (AST) supplementation on the adiponectin concentration, lipid peroxidation, glycemic control, insulin sensitivity, and anthropometric indices in participants with type 2 diabetes mellitus.

METHODS AND STUDY DESIGN:

We enrolled 44 participants with type 2 diabetes who met our inclusion criteria. Eight milligrams of AST supplementation or a placebo were randomly administered once daily for 8 weeks to these participants.

RESULTS:

The 8-week administration of AST supplementation increased the serum adiponectin concentration and reduced visceral body fat mass ($p < 0.01$), serum triglyceride and very-low-density lipoprotein cholesterol concentrations, and systolic blood pressure ($p < 0.05$). Furthermore, AST significantly reduced the fructosamine concentration ($p < 0.05$) and marginally reduced the plasma glucose concentration ($p = 0.057$).

CONCLUSIONS:

We demonstrated that because participants with type 2 diabetes often have hypertriglycemia and uncontrolled glucose metabolism; our findings of dual beneficial effects are clinically valuable. Our results may provide a novel complementary treatment with potential impacts on diabetic complications without adverse effects.

PMID: 29384321

DOI: [10.6133/apjcn.052017.11](#)

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Astaxanthin decreases blood pressure and improves oxidative stress in human clinical trial.

Anti-Aging Med

Anti-Aging Med 6(4), 15-21, 2009

Japanese Society of Anti-Aging Medicine

Efficacy and safety of eight-week treatment with astaxanthin in individuals screened for increased oxidative stress burden

- **Iwabayashi Masaaki, Fujioka Noriko, Nomoto Keitaro, Miyazaki Ryo, Takahashi Hozumi, Hibino Sawako, Takahashi Yoko, Nishikawa Koji, Nishida Mitsunori, Yonei Yoshikazu,**
- **Abstract**

Objective: An open-label noncontrolled study was conducted in subjects with increased oxidative stress burden to evaluate the mental and physical effects of antioxidant astaxanthin. **Methods:** Of 35 healthy postmenopausal women, 21 with high oxidative stress (diacron-reactive oxygen metabolites; d-ROM) were selected, and 20 (55.7±4.8 years old, BMI 22.1±3.9) were included in the study, after excluding 1 dropout. In subjects orally treated with astaxanthin (Fuji Chemical Industry) at a daily dose of 12 mg for eight weeks, Anti-Aging QOL Common Questionnaire, somatometry, hematological examination/urinalysis, oxidative stress test, and vascular function tests (cardio ankle vascular index, CAVI; ankle brachial pressure index, ABI; fingertip acceleration pulse wave; flow-mediated dilation FMD) were performed before and four and eight weeks after the start of the study. **Results:** After eight-week treatment with astaxanthin, significant improvement was observed in 5 of 34 physical symptoms listed in the common questionnaire, including "tired eyes", "stiff shoulders", "constipation", "gray hair", and "cold skin", and in 3 of 21 mental symptoms, including "daily life is not enjoyable", "difficulty in falling asleep", and "a sense of tension". In addition, systolic (118.0±16.4 mmHg at baseline, -4.6%, p=0.021) and diastolic blood pressure (74.1±11.7 mmHg at baseline, -6.9%, p<0.001) significantly decreased. In the vascular function test, CAVI, fingertip acceleration pulse wave, and FMD did not change, but ABI significantly increased from 1.06±0.10 at baseline to 1.10±0.06 at Week 8 (+3.7%, p=0.030). In the oxidative stress test, d-ROM did not change, but BAP significantly increased (+4.6%, p=0.030). In biochemical examination, AST (-19.2%, p=0.044), LDH (-6.4%, p=0.006), and HbA1c (-3.2%, p<0.001) significantly improved. Although IGF-I and insulin did not change, DHEA-s (-15.1%, p<0.001), cortisol (-22.8%, p=0.002), and adiponectin (-14.1%, p=0.003) decreased. No serious adverse event occurred during or after the study. **Conclusion:** Results show that astaxanthin may enhance antioxidant capacity (increase BAP), reduce lower limb vascular resistance (increase ABI), decrease blood pressure, and improve physical symptoms in women with high oxidative stress.

Astaxanthin combined with Sesamin improves recovery from mental fatigue in double-blind, placebo-controlled crossover human clinical trial.

[Nutrients](#). 2018 Feb 28;10(3). pii: E281. doi: 10.3390/nu10030281.

Effects of Dietary Supplementation of Astaxanthin and Sesamin on Daily Fatigue: A Randomized, Double-Blind, Placebo-Controlled, Two-Way Crossover Study.

[Imai A](#)¹, [Oda Y](#)², [Ito N](#)³, [Seki S](#)⁴, [Nakagawa K](#)⁵, [Miyazawa T](#)^{6,7}, [Ueda F](#)⁸.

Author information

Abstract

Severe fatigue can negatively affect quality of life, and oxidative stress may play a role in its mechanism. The aim of this study was to evaluate the effect of dietary supplementation of astaxanthin and sesamin (AS), strong food-derived antioxidants, on fatigue. Twenty-four healthy volunteers were supplemented with AS and placebo, each for four weeks. After each supplementation period, participants underwent tasks inducing mental and physical fatigue (visual display terminal task and ergometer task, respectively). Subjective fatigue was evaluated using a visual analogue scale during and after the mental and physical tasks, and daily subjective fatigue was evaluated by the Chalder fatigue questionnaire. Secondary outcomes included other subjective feelings, work efficiency, autonomic nerve activity, levels of an oxidative stress marker (plasma phosphatidylcholine hydroperoxide (PCOOH)) and safety. AS supplementation was associated with significantly improved recovery from mental fatigue compared with placebo. Increased PCOOH levels during mental and physical tasks were attenuated by AS supplementation. No differences between AS and placebo were detected in secondary outcomes, and no adverse effects of AS supplementation were observed. In conclusion, AS supplementation may be a candidate to promote recovery from mental fatigue which is experienced by many healthy people.

KEYWORDS:

astaxanthin; fatigue; phosphatidylcholine hydroperoxide; sesame seed extract; sesamin; visual analogue scale

PMID: 29495607

PMCID: [PMC5872699](#)

DOI: [10.3390/nu10030281](#)

[Indexed for MEDLINE]

[Free PMC Article](#)

Astaxanthin decreases mental and physical fatigue in double-blind, placebo-controlled human clinical trial.

J. Clin. Thera & Med 32.7 (2016):277-91 (Japanese)

Randomized Controlled Trial of the Anti-Fatigue Effects of Astaxanthin on Mental and Physical Loads Simulating Daily Life.

Hongo, N. et al.

In a study designed to induce fatigue and stress encountered in daily life, natural astaxanthin from *Haematococcus pluvialis* microalgae was administered over eight weeks to the treatment group in a double-blind, placebo-controlled study. A mental challenge comprised of a number of timed calculations (the Uchida-Kraepelin test) and a physical test on a bicycle ergometer were assessed in both the placebo and treatment groups before and after the eight-week supplementation period. Participants consisted of 39 healthy subjects who were divided into two groups. The treatment group received 12mg per day of natural astaxanthin combined with 20mg of tocotrienols while the control group received 20mg of tocotrienols without any astaxanthin. A Visual Analogue Scale analysis showed that astaxanthin significantly reduced perceived symptoms of mental and physical fatigue compared to placebo. Results included improvements in clarity of thinking, concentration, motivation and mood. Irritation and feelings of body heaviness were reduced. In the mental challenge test, an increase in errors observed in the placebo group was almost eliminated in the astaxanthin group. Salivary cortisol (a marker for stress) was significantly reduced in the astaxanthin group. These results suggest that astaxanthin supplementation has beneficial effects on fatigue encountered in daily life.

Astaxanthin affects various markers in patients with sickle cell disease in human trial.

Free Radicals and Antioxidants (2013). <http://dx.doi.org/10.1016/j.fra.2013.10.1003>

Supplementation of patients with sickle cell disease with astaxanthin increases plasma- and erythrocyte-astaxanthin and may improve the hemolytic component of the disease

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<https://doi.org/10.1016/j.fra.2013.10.1003>Get rights and content

Aim & background: [Sickle cell disease](#) (SCD) is characterized by hemolytic and vaso-occlusive components. [Astaxanthin](#) is a [carotenoid](#) of marine origin, without [pro-oxidant](#) properties.

Methods: In this open label pilot study, we investigated whether orally administered astaxanthin incorporates into erythrocytes (RBC) of SCD patients and studied the effect on hematological and clinical chemical parameters. Ten SCD patients (6–52 years) in Sint Maarten received 8–12 mg astaxanthin during 3 months.

Results: Baseline plasma- (33 nmol/L) and RBC- (11 nmol/L packed RBC) astaxanthin increased to 225, 174, 167 nmol/L (plasma) and 149, 100, 71 nmol/L packed RBC at 1–3 months, respectively. [Reticulocytes](#) decreased from baseline and 2 months (9.5 and 8.8%) to 3 months (5.6%), [MCV](#) from 2 to 3 months (88–86 fL), MCH from baseline to 3 months (30–28 pg) and RDW from baseline and 2 months (19.2 and 19.0%) to 3 months (16.7%). Plasma [arginine](#) decreased from 2 to 3 months (46.6–39.4 μmol/L). [Asymmetric dimethylarginine](#) (ADMA) did not change. Reticulocytes at baseline correlated with relative changes in reticulocytes from baseline to 3 months. Relative changes in reticulocytes correlated with relative changes in RBC, RDW, [LDH](#), ALAT, but not [hematocrit](#), within the same period.

Conclusion: Astaxanthin incorporates into SCD RBC and may favorably affect the hemolytic component. A larger randomized controlled trial is indicated, using similar or [higher dose](#), preferably during more than 3 months, concomitant with (other) [low dose antioxidants](#) (vitamin E, [beta-carotene](#), [vitamin C](#), folic acid), minerals (zinc, if necessary, selenium), arginine, [fish oil](#) and [vitamin D](#).

Astaxanthin reduces body fat percentage versus placebo in individuals doing moderate exercise over six weeks in placebo-controlled human clinical trial.

Fukumauchi M. Food Style 21. 2007;11:1-4. ?15

Astaxanthin increases fat utilisation during exercise

A randomised, double-blind study on humans has confirmed that natural astaxanthin increases fat utilisation during exercise.¹⁵ In the study, 32 individuals were supplemented with 2 x 6mg of astaxanthin per day, or placebo, for six weeks. The participants were instructed to undertake 40 minutes of continuous exercise three times per week during the 6-week period. After six weeks, the astaxanthin group had a significant reduction in body fat percentage, whereas there was no difference in the placebo group. These results indicate that astaxanthin increases muscle endurance and reduces lactic acid during intensive training by promoting the use of fat compared with glycogen stores.

Astaxanthin with Saw Palmetto affects testosterone levels in men in human clinical trial.

[J Int Soc Sports Nutr.](#) 2014 Aug 23;11:43. doi: 10.1186/s12970-014-0043-x. eCollection 2014.

Evaluation of Resettin® on serum hormone levels in sedentary males.

[Anderson ML](#)¹.

Author information

Abstract

BACKGROUND: Comparisons of hormones such as dihydrotestosterone (DHT), estradiol (E2), and testosterone indicate their impact on metabolism and body composition. While less is known regarding DHT and E2, testosterone is an androgenic metabolic hormone capable of positively regulating a variety of anabolic and androgenic processes in the body. Accordingly, it has been postulated that the age-related reduction in serum testosterone levels leads to reductions in lean muscle mass, bone mineral density, and other physical conditions that impair physical performance and decrease quality of life. Preliminary studies suggest that key ingredients found in Resettin®/MyTosterone™, a natural supplement containing the carotenoid astaxanthin from *Haematococcus pluvialis* and Saw Palmetto berry lipid extract from *Serenoa repens*, could positively impact testosterone levels. To investigate the clinical efficacy of Resettin®, the serum profiles of testosterone, E2 and DHT in healthy sedentary males before and after Resettin® treatment were evaluated in a randomized, placebo controlled clinical trial.

METHOD: Twenty healthy, sedentary men between the ages of 21 and 70 were randomized into either an 800 mg/day or 1200 mg/day Resettin®/MyTosterone™ treatment group or lecithin, which was used as the placebo. After a 14-day treatment period, there was a 14-day washout period. After the wash-out period, participants were crossed over within their respective group to either Resettin®/MyTosterone™ or the lecithin placebo for 14 days.

RESULTS: After 14 days, participants receiving 800 mg per day of Resettin® had significantly reduced baseline-subtracted serum DHT levels in comparison to the placebo control group. While after 14 days, participants receiving 1200 mg per day of Resettin® had significantly reduced baseline-subtracted serum DHT and E2 levels in comparison to the placebo control group. Moreover, participants receiving 1200 mg per day of Resettin® experienced a 38% increase in serum testosterone levels in comparison to the placebo control group, but the effect did not reach statistical significance.

CONCLUSION: Although additional studies will be required to evaluate how Resettin® may promote proper testosterone regulation, these findings indicate that Resettin® can favorably influence serum hormone profiles in men.

PMID: 25183955 PMCID: [PMC4151021](#) DOI: [10.1186/s12970-014-0043-x](#) [Free PMC Article](#)

Astaxanthin combined with Saw Palmetto increases Testosterone in men in human clinical trial.

[J Int Soc Sports Nutr](#). 2008 Aug 12;5:12. doi: 10.1186/1550-2783-5-12.

An open label, dose response study to determine the effect of a dietary supplement on dihydrotestosterone, testosterone and estradiol levels in healthy males.

[Angwafor F 3rd^{#1}](#), [Anderson ML^{#2}](#).

Author information

Abstract

BACKGROUND:

Maintaining endogenous testosterone (T) levels as men age may slow the symptoms of sarcopenia, andropause and decline in physical performance. Drugs inhibiting the enzyme 5alpha-reductase (5AR) produce increased blood levels of T and decreased levels of dihydrotestosterone (DHT). However, symptoms of gynecomastia have been reported due to the aromatase (AER) enzyme converting excess T to estradiol (ES). The carotenoid astaxanthin (AX) from *Haematococcus pluvialis*, Saw Palmetto berry lipid extract (SPLE) from *Serenoa repens* and the precise combination of these dietary supplements, Alphastat(R) (Mytosterone(trade mark)), have been reported to have inhibitory effects on both 5AR and AER in-vitro. Concomitant regulation of both enzymes in-vivo would cause DHT and ES blood levels to decrease and T levels to increase. The purpose of this clinical study was to determine if patented Alphastat(R) (Mytosterone(trade mark)) could produce these effects in a dose dependent manner.

METHODS:

To investigate this clinically, 42 healthy males ages 37 to 70 years were divided into two groups of twenty-one and dosed with either 800 mg/day or 2000 mg/day of Alphastat(R) (Mytosterone(trade mark)) for fourteen days. Blood samples were collected on days 0, 3, 7 and 14 and assayed for T, DHT and ES. Body weight and blood pressure data were collected prior to blood collection. One-way, repeated measures analysis of variance (ANOVA-RM) was performed at a significance level of $\alpha = 0.05$ to determine differences from baseline within each group. Two-way analysis of variance (ANOVA-2) was performed after baseline subtraction, at a significance level of $\alpha = 0.05$ to determine differences between dose groups. Results are expressed as means +/- SEM.

RESULTS:

ANOVA-RM showed significant within group increases in serum total T and significant decreases in serum DHT from baseline in both dose groups at a significance level of $\alpha = 0.05$. Significant decreases in serum ES are reported for the 2000 mg/day dose group and not the 800 mg/day dose

group. Significant within group effects were confirmed using ANOVA-2 analyses after baseline subtraction. ANOVA-2 analyses also showed no significant difference between dose groups with regard to the increase of T or the decrease of DHT. It did show a significant dose dependant decrease in serum ES levels.

CONCLUSION:

Both dose groups showed significant ($p = 0.05$) increases in T and decreases in DHT within three days of treatment with Alphastat(R) (Mystosterone(trade mark)). Between group statistical analysis showed no significant ($p = 0.05$) difference, indicating the effect was not dose dependent and that 800 mg/per day is equally effective as 2000 mg/day for increasing T and lowering DHT. Blood levels of ES however, decreased significantly ($p = 0.05$) in the 2000 mg/day dose group but not in the 800 mg/day dose group indicating a dose dependant decrease in E levels.

PMID: 18700016

PMCID: [PMC2525623](#)

DOI: [10.1186/1550-2783-5-12](#)

[Free PMC Article](#)

ASTAXANTHIN IMPROVES METABOLIC ADAPTATION AND IMPROVES MUSCLE ENDURANCE IN ELDERLY SUBJECTS DURING AEROBIC TRAINING IN RANDOMIZED, PLACEBO-CONTROLLED HUMAN CLINICAL STUDY.

Physiol Rep. 2021 Jun;9(11):e14887.

doi: 10.14814/phy2.14887.

Astaxanthin supplementation enhances metabolic adaptation with aerobic training in the elderly

[Sophia Z Liu](#)¹, [Ana P Valencia](#)¹, [Matt P VanDoren](#)², [Eric G Shankland](#)¹, [Baback Roshanravan](#)³, [Kevin E Conley](#)^{1,4,5}, [David J Marcinek](#)^{1,5,6}

- PMID: 34110707 PMCID: [PMC8191397](#) DOI: [10.14814/phy2.14887](#) [Free PMC article](#)

Abstract

Endurance training (ET) is recommended for the elderly to improve metabolic health and aerobic capacity. However, ET-induced adaptations may be suboptimal due to oxidative stress and exaggerated inflammatory response to ET. The natural antioxidant and anti-inflammatory dietary supplement astaxanthin (AX) has been found to increase endurance performance among young athletes, but limited investigations have focused on the elderly. We tested a formulation of AX in combination with ET in healthy older adults (65-82 years) to determine if AX improves metabolic adaptations with ET, and if AX effects are sex-dependent. Forty-two subjects were randomized to either placebo (PL) or AX during 3 months of ET. Specific muscle endurance was measured in ankle dorsiflexors. Whole body exercise endurance and fat oxidation (FATox) was assessed with a graded exercise test (GXT) in conjunction with indirect calorimetry. Results: ET led to improved specific muscle endurance only in the AX group (Pre 353 ± 26 vs. Post 472 ± 41 contractions), and submaximal GXT duration improved in both groups (PL 40.8 ± 9.1% and AX 41.1 ± 6.3%). The increase in FATox at lower intensity after ET was greater in AX (PL 0.23 ± 0.15 g vs. AX 0.76 ± 0.18 g) and was associated with reduced carbohydrate oxidation and increased exercise efficiency in males but not in females.

Astaxanthin improves processing speed and psychomotor speed in patients with mild cognitive impairment in double-blind, placebo-controlled study.

Journal of Alzheimer's Disease 62 (2018) 1767–1775

DOI 10.3233/JAD-170969

IOS Press 1767

Effects of Composite Supplement Containing Astaxanthin and Sesamin on Cognitive Functions in People with Mild Cognitive Impairment: A Randomized, Double-Blind, Placebo-Controlled Trial

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Accepted 11 January 2018

Abstract.

Background: Dementia and its first or transitional stage, mild cognitive impairment (MCI), is a major concern for the aging Japanese society. Thus, the use of dietary supplements to improve or maintain cognitive function has become a topic of public interest.

Objective: In this study, we evaluated the effects of a composite supplement containing food-derived antioxidants, specifically astaxanthin and sesamin (AS), on cognitive function in people with MCI.

Method: Twenty-one healthy participants with MCI were recruited in our double-blind placebo-controlled pilot study. They were assigned to either an AS group, who received ingestible capsules containing AS, or a placebo group, who received identical placebo capsules. To assess cognitive functions, we performed the Japanese version of the Central Nervous System Vital Signs (CNSVS) test and the Alzheimer's Disease Assessment Scale-Cog test at baseline, after 6 weeks, and after 12 weeks of dietary supplementation.

Results: The CNSVS test revealed significant improvements in psychomotor speed and processing speed in the AS group compared with the placebo group, suggesting that the daily supplementation of AS improved cognitive functions related to the ability to comprehend, and perform complex tasks quickly and accurately.

Conclusion: Our results provide support for the use of AS as a dietary supplementation for improving cognitive functions.

Astaxanthin increases oxygen scavenging activity and decreases peroxide production in human clinical trial.

[J Clin Biochem Nutr.](#) 2016 Jul;59(1):10-5. doi: 10.3164/jcfn.15-137. Epub 2016 May 21.

The effect of astaxanthin on vascular endothelial growth factor (VEGF) levels and peroxidation reactions in the aqueous humor.

[Hashimoto H¹](#), [Arai K²](#), [Hayashi S³](#), [Okamoto H⁴](#), [Takahashi J⁵](#), [Chikuda M²](#).

Author information

Abstract

We explored the effect of astaxanthin on vascular endothelial growth factor in the aqueous humor, by measuring vascular endothelial growth factor levels and oxidation-related parameters, including O₂ (•-) scavenging activity, H₂O₂ level, and total hydroperoxide level in the aqueous humor, obtained from 35 patients before and after astaxanthin administration. We evaluated the relationship between vascular endothelial growth factor and the oxidation-related parameters as well as the patient's diabetic status, age, and sex. Vascular endothelial growth factor levels did not change significantly but O₂ (•-) scavenging activity and total hydroperoxide level significantly ($p < 0.05$) increased and decreased, respectively. Both pre- and post- astaxanthin intake, vascular endothelial growth factor and total hydroperoxide levels were positively correlated (Pearson: $r = 0.42$, $p < 0.05$; $r = 0.55$, $p < 0.01$, respectively). Analysis of vascular endothelial growth factor levels and O₂ (•-) scavenging activities gave a negative correlation but only pre-astaxanthin intake ($r = -0.37$, $p < 0.05$). Differences in levels pre- and post-astaxanthin only showed association between vascular endothelial growth factor and total hydroperoxide ($r = 0.49$, $p < 0.01$) analyzed by multiple linear regression. Using multivariate analysis, pre-astaxanthin vascular endothelial growth factor level was associated with two factors of total hydroperoxide and O₂ (•-) scavenging activity ($r = 0.49$, $p < 0.05$), and post-astaxanthin vascular endothelial growth factor level with two factors of total hydroperoxide and sex ($r = 0.60$, $p < 0.01$). Astaxanthin intake may have affected vascular endothelial growth factor level through its antioxidant effects by increasing O₂ (•-) scavenging activity and suppressing peroxide production.

KEYWORDS: aqueous humor; astaxanthin; oxidation; superoxide; vascular endothelial growth factor

PMID: 27499573

PMCID: [PMC4933686](#)

DOI: [10.3164/jcfn.15-137](#)

[Free PMC Article](#)

Astaxanthin reduces inflammation and injury to vocal fold in human volunteers after 60 minutes vocal loading in human clinical trial.

[J Voice](#). 2017 May;31(3):352-358. doi: 10.1016/j.jvoice.2016.06.017. Epub 2016 Oct 26.

Protective Effect of Astaxanthin on Vocal Fold Injury and Inflammation Due to Vocal Loading: A Clinical Trial.

[Kaneko M](#)¹, [Kishimoto Y](#)¹, [Suzuki R](#)¹, [Kawai Y](#)¹, [Tateya I](#)¹, [Hirano S](#)².

Author information

Abstract

OBJECTIVES: Professional voice users, such as singers and teachers, are at greater risk of developing vocal fold injury from excessive use of voice; thus, protection of the vocal fold is essential. One of the most important factors that aggravates injury is the production of reactive oxygen species at the wound site. The purpose of the current study was to assess the effect of astaxanthin, a strong antioxidant, on the protection of the vocal fold from injury and inflammation due to vocal loading.

STUDY DESIGN: This study is an institutional review board-approved human clinical trial.

METHODS: Ten male subjects underwent a 60-minute vocal loading session and received vocal assessments prior to, immediately after, and 30 minutes postvocal loading (AST(-) status). All subjects were then prescribed 24 mg/day of astaxanthin for 28 days, after which they received the same vocal task and assessments (AST(+) status). Phonatory parameters were compared between both groups.

RESULTS: Aerodynamic assessment, acoustic analysis, and GRBAS scale (grade, roughness, breathiness, asthenia, and strain) were significantly worse in the AST(-) status immediately after vocal loading, but improved by 30 minutes after loading. In contrast, none of the phonatory parameters in the AST(+) status were statistically worse, even when measured immediately after vocal loading. No allergic responses or adverse effects were observed after administration of astaxanthin.

CONCLUSIONS: The current results suggest that astaxanthin can protect the vocal fold from injury and inflammation caused by vocal loading possibly through the regulation of oxidative stress.

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KEYWORDS: Astaxanthin; Clinical trial; Reactive oxygen species; Vocal fold; Vocal loading

PMID: 27481232 DOI: [10.1016/j.jvoice.2016.06.017](https://doi.org/10.1016/j.jvoice.2016.06.017) [Indexed for MEDLINE]

ASTAXANTHIN IN COMBINATION WITH TOCOTRIENOLS LEADS TO COGNITIVE IMPROVEMENT IN ELDERLY SUBJECTS WITH MILD FORGETFULNESS IN BGG-SPONSORED HUMAN CLINICAL TRIAL.

J Clin Biochem Nutr. 2020 Nov;67(3):307-316.

doi: 10.3164/jcfn.19-116. Epub 2020 Jun 19.

Cognitive function improvement with astaxanthin and tocotrienol intake: a randomized, double-blind, placebo-controlled study

[Takahiro Sekikawa](#)¹, [Yuki Kizawa](#)¹, [Yanmei Li](#)², [Tsuyoshi Takara](#)³

PMID: 33293773 PMCID: [PMC7705074](#) DOI: [10.3164/jcfn.19-116](#) [Free PMC article](#)

Abstract

We examined the effects of the mixed ingestion of astaxanthin derived from *Haematococcus pluvialis* and tocotrienols on the cognitive function of healthy Japanese adults who feel a memory decline. Forty-four subjects were randomly but equally assigned to the astaxanthin-tocotrienols or placebo group. An astaxanthin-tocotrienols or placebo capsule was taken once daily before or after breakfast for a 12-week intervention period. The primary outcome was composite memory from the Cognitrix cognitive test, and the secondary outcomes were other cognitive functions and subjective symptoms for memory. Each group included 18 subjects in the efficacy analysis (astaxanthin-tocotrienols group, 55.4 ± 7.9 years; placebo group, 54.6 ± 6.9 years). The astaxanthin-tocotrienols group showed a significant improvement in composite memory and verbal memory in Cognitrix at Δ12 weeks compared with the placebo group. Additionally, the astaxanthin-tocotrienols group showed a significant improvement in the subjective symptom of "During the last week, have you had trouble remembering people's names or the names of things?" compared with the placebo group after 12 weeks. No adverse events were observed in this study. The results demonstrated that taking an astaxanthin-tocotrienols combination improves the composite memory and verbal memory of Japanese adults who feel a memory decline (UMIN 000031758).

Astaxanthin formula may provide therapeutic benefit to patients suffering from dry eye syndrome in double-blind, placebo-controlled human clinical trial.

[Clin Ophthalmol.](#) 2016 May 9;10:813-20. doi: 10.2147/OPTH.S106455. eCollection 2016.

A randomized, double-blind, placebo-controlled study of oral antioxidant supplement therapy in patients with dry eye syndrome.

[Huang JY¹](#), [Yeh PT¹](#), [Hou YC¹](#).

Author information

Abstract

PURPOSE: To evaluate the efficacy of oral antioxidant supplementation in the treatment of patients with dry eye syndrome (DES).

METHODS: A prospective, randomized, double-blinded study compared the effects of an antioxidant supplement (containing anthocyanosides, astaxanthin, vitamins A, C, and E, and several herbal extracts, including *Cassiae semen* and *Ophiopogonis japonicus*) with placebo on patients with DES. We assessed dry eye symptoms, visual acuity, Schirmer's test, tear film breakup time, cornea and conjunctiva fluorescein staining, serum anti-SSA/anti-SSB antibodies, and the level of reactive oxygen species (ROS) in tears. The supplementation period was 8 weeks and patients were followed up every 4 weeks for 16 weeks. A linear mixed model was used to compare the groups, while within-group differences were tested by repeated-measures analysis of variance.

RESULTS: Forty-three patients, 20 and 23 in treatment and placebo groups, respectively, completed the study. Liver and renal functions were normal. Diastolic blood pressure decreased in the treatment group. There were no significant differences in systolic blood pressure, dry eye symptoms, serum anti-SSA and anti-SSB, visual acuity, intraocular pressure, or fluorescein corneal staining between the groups. Tear film breakup time scores and Schirmer's test without topical anesthesia significantly improved in the treatment group. Tear ROS level differed between the groups and decreased after treatment. Overall subjective impression revealed a significant improvement with treatment compared with placebo.

CONCLUSION: Oral antioxidant supplementations may increase tear production and improve tear film stability by reducing tear ROS. The vegetable-based antioxidant supplement used in this study is safe and can be utilized as an adjuvant therapy to conventional artificial tear therapy for patients with DES.

KEYWORDS: blood pressure; dry eye; herbal extracts; reactive oxygen species; tear

PMID: 27274185 PMCID: [PMC4869783](#) DOI: [10.2147/OPTH.S106455](#)

[Free PMC Article](#)

Astaxanthin formula reduces blood lipids in patients with heart disease in human clinical trial.

[Am J Cardiol.](#) 2015 Dec 15;116(12):1798-801. doi: 10.1016/j.amjcard.2015.09.023. Epub 2015 Oct 3.

Usefulness of Nutraceuticals (Armolid Plus) Versus Ezetimibe and Combination in Statin-Intolerant Patients With Dyslipidemia With Coronary Heart Disease.

[Marazzi G](#)¹, [Pelliccia F](#)², [Campolongo G](#)³, [Quattrino S](#)³, [Cacciotti L](#)⁴, [Volterrani M](#)³, [Gaudio C](#)², [Rosano G](#)³.

Author information

Abstract

Statins are extensively used to treat dyslipidemia, but, because of their low tolerability profile, they are discontinued in a significant proportion of patients. Ezetimibe and nutraceuticals have been introduced as alternative therapies and have proved to be effective and well tolerated. A single-blind, single-center, randomized, prospective, and parallel group trial comparing a combination of nutraceuticals (red yeast rice, policosanol, berberine, folic acid, coenzyme Q10 and astaxanthin), called Armolid Plus, and ezetimibe for 3 months in terms of efficacy and tolerability. Patients who did not achieve their therapeutic target (low-density lipoprotein cholesterol <100 mg/dl) could add the alternative treatment on top of randomized treatment for another 12 months: 100 patients who are dyslipidemic with ischemic heart disease treated with percutaneous coronary intervention were enrolled (ezetimibe n = 50, nutraceutical n = 50). Efficacy (lipid profile) and tolerability (adverse events, transaminases, and creatine kinase) were assessed after 3 and 12 months. After 3 months, 14 patients in the nutraceutical group achieved their therapeutic target, whereas none of the patients in the ezetimibe group did. At 1-year follow-up, 58 patients (72.5%) of the combined therapy group (n = 86) and 14 (100%) of the nutraceutical group reached the therapeutic goal. No patients experienced important undesirable effects. In conclusion, nutraceuticals alone or in combination with ezetimibe are well tolerated and improve the lipid profile in statin-intolerant patients with coronary heart disease. Further studies are needed to assess long-term effects of nutraceuticals on mortality.

PMID: 26611120

DOI: [10.1016/j.amjcard.2015.09.023](https://doi.org/10.1016/j.amjcard.2015.09.023)

[Indexed for MEDLINE]

Astaxanthin formula reduces LDL and total cholesterol similar to statin drug pravastatin in patients with high blood lipids in double-blind, placebo-controlled randomized crossover human clinical trial.

J Clin Lipidol. 2014 Jan-Feb;8(1):61-8. doi: 10.1016/j.jacl.2013.11.003. Epub 2013 Nov 11.

Nutraceutical approach to moderate cardiometabolic risk: results of a randomized, double-blind and crossover study with Armolipid Plus.

[Ruscica M¹](#), [Gomaschi M¹](#), [Mombelli G²](#), [Macchi C³](#), [Bosisio R²](#), [Pazzucconi F¹](#), [Pavanello C²](#), [Calabresi L¹](#), [Arnoldi A⁴](#), [Sirtori CR⁵](#), [Magni P¹](#).

Author information

Abstract

BACKGROUND: Primary cardiovascular prevention may be achieved by lifestyle/nutrition improvements and specific drugs, although a relevant role is now emerging for specific functional foods and nutraceuticals.

OBJECTIVES: The aim of this study was to evaluate the usefulness of a nutraceutical multitarget approach in subjects with moderate cardiovascular risk and to compare it with pravastatin treatment.

SUBJECTS: Thirty patients with moderate dyslipidemia and metabolic syndrome (according to the Third Report of the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults) were included in an 8-week randomized, double-blind crossover study and took either placebo or a nutraceutical combination that contained red yeast rice extract, berberine, policosanol, astaxanthin, coenzyme Q10, and folic acid (Armolipid Plus). Subsequently, they were subjected to another 8-week treatment with pravastatin 10 mg/d. This dosage was selected on the basis of its expected -20% efficacy in reducing low-density lipoprotein-cholesterol.

RESULTS: Treatment with Armolipid Plus led to a significant reduction of total cholesterol (-12.8%) and low-density lipoprotein-cholesterol (-21.1%), similar to pravastatin (-16% and -22.6%, respectively), and an increase of high-density lipoprotein-cholesterol (4.8%). Armolipid Plus improved the leptin-to-adiponectin ratio, whereas adiponectin levels were unchanged.

CONCLUSIONS: These results indicate that this nutraceutical approach shows a lipid-lowering activity comparable to pravastatin treatment. Hence, it may be a safe and useful option, especially in conditions of moderate cardiovascular risk, in which a pharmacologic intervention may not be appropriate.

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KEYWORDS: Berberine; Cardiovascular risk; HDL-cholesterol; LDL-cholesterol; Monacolin K

PMID: 24528686 DOI: [10.1016/j.jacl.2013.11.003](https://doi.org/10.1016/j.jacl.2013.11.003) [Indexed for MEDLINE]

Astaxanthin formula counteracts cognitive impairment in subjects with mild cognitive impairment in human clinical trial.

[Neuropsychiatr Dis Treat.](#) 2014 Feb 3;10:225-30. doi: 10.2147/NDT.S51092. eCollection 2014.

Cognitive effects of a dietary supplement made from extract of *Bacopa monnieri*, astaxanthin, phosphatidylserine, and vitamin E in subjects with mild cognitive impairment: a noncomparative, exploratory clinical study.

[Zanotta D¹](#), [Puricelli S¹](#), [Bonoldi G¹](#).

Author information

Abstract

A prospective cohort, noncomparative, multicenter trial was conducted to explore the potential of a phytotherapeutic compound, available as a dietary supplement and containing extracts of *Bacopa monnieri* and *Haematococcus pluvialis* (astaxanthin) plus phosphatidylserine and vitamin E, in improving cognition in subjects diagnosed with mild cognitive impairment. Enrolled subjects (n=104) were aged 71.2±9.9 years and had a mini-mental state examination score of 26.0±2.0 (mean ± standard deviation). They underwent the Alzheimer's Disease Assessment Scale-cognitive subscale (ADAS-cog) test and the clock drawing test at baseline and upon completion of a 60-day period of dietary supplementation with one tablet daily of the tested compound. In 102 assessable subjects, total ADAS-cog scores improved from 13.7±5.8 at baseline to 9.7±4.9 on day 60, and the clock drawing test scores improved from 8.5±2.3 to 9.1±1.9. Both changes were statistically significant (P<0.001). Memory tasks were the individual components of ADAS-cog showing the largest improvements. In a multivariate analysis, larger improvements in total ADAS-cog score were associated with less compromised baseline mini-mental state examination scores. Perceived efficacy was rated as excellent or good by 62% of study subjects. The tested compound was well tolerated; one nonserious adverse event was reported in the overall study population, and perceived tolerability was rated excellent or good by 99% of the subjects. In conclusion, dietary supplementation with the tested compound shows potential for counteracting cognitive impairment in subjects with mild cognitive impairment and warrants further investigation in adequately controlled, longer-term studies.

KEYWORDS: ADAS-cog test; *Bacopa monnieri*; astaxanthin; clock drawing test; dietary supplement; mild cognitive impairment

PMID: 24523587 PMCID: [PMC3921088](#) DOI: [10.2147/NDT.S51092](#) [Free PMC Article](#)

Astaxanthin shows therapeutic potential for salivary secretion in human clinical trial and reduces the level of an oxidative stress marker in the subjects' saliva.

[J Clin Biochem Nutr.](#) 2010 Sep;47(2):130-7. Epub 2010 Jun 22.

Evaluation of therapeutic effects of astaxanthin on impairments in salivary secretion.

[Yamada T](#), [Ryo K](#), [Tai Y](#), [Tamaki Y](#), [Inoue H](#), [Mishima K](#), [Tsubota K](#), [Saito I](#).

Source

Department of Pathology, Tsurumi University School of Dental Medicine, 2-1-3, Tsurumi, Tsurumi-ku, Yokohama 230-8501, Japan.

Abstract

The involvement of reactive oxygen species (ROS) in the pathophysiology of Sjögren's syndrome (SS), an autoimmune disorder, and irradiation-induced impairments in salivary secretion has been reported. Meanwhile, the strong antioxidant astaxanthin (Ast) has been suggested to have therapeutic effects on various diseases. In the present study, we examined the ROS scavenging capacity of Ast using a human salivary gland epithelial cell line (HSY) and investigated the effects of Ast on salivary secretion in a mouse model of irradiation-induced salivary gland dysfunction. Furthermore, we performed a clinical study of Ast in six SS patients and six normal individuals, quantifying the volume of saliva secretion and the level of oxidative stress markers in the saliva. Ast partially suppressed hydrogen peroxide-induced ROS in HSY cells. The mouse model demonstrated that the pre-administration of Ast resulted in the suppression of irradiation-induced hyposalivation. Furthermore, the administration of Ast appeared to increase salivary output in both the SS and normal groups. The level of oxidative stress marker, hexanoyl-lysine, in the saliva was reduced after Ast intake. These results suggest that Ast might act as an ROS scavenger, providing benefits to SS patients with impaired salivary secretion.

PMID: 20838568 [PubMed]

PMCID: PMC2935153

ASTAXANTHIN SHOWS POTENTIAL TO WORK AS EYE ANTIOXIDANT DURING CATARACT SURGERY IN FEMALES IN HUMAN CLINICAL STUDY.

J Clin Biochem Nutr. 2019 Jul;65(1):47-51.

doi: 10.3164/jcfn.18-110. Epub 2019 Apr 18.

Effects of astaxanthin on VEGF level and antioxidation in human aqueous humor: difference by sex

[Hirotaka Hashimoto](#)¹, [Kiyomi Arai](#)², [Jiro Takahashi](#)³, [Makoto Chikuda](#)²

- PMID: **31379413**
- PMCID: [PMC6667389](#)
- DOI: [10.3164/jcfn.18-110](#)

Free PMC article

Abstract

In our previous report, we showed the effect of astaxanthin intake on VEGF level in the aqueous humor and the relationship between VEGF level and reactive oxygen species-related parameters and other relevant factors. VEGF level is associated with total hydroperoxide level, and a multivariate analysis identified sex as a secondary factor affecting these relationships. Here, we analyzed the effects of astaxanthin on the relationship between VEGF level and reactive oxygen species-related parameters by sex. Patients (16 males and 19 females, aged 71.3 and 70.6, respectively) underwent bilateral cataract surgery on one side before and the other side after astaxanthin treatment (6 mg/day for 2 weeks). Levels of VEGF, hydrogen peroxide, and total hydroperoxide, and O₂^{-•} scavenging activity, were measured in the aqueous humor. In females only, VEGF level was negatively correlated with O₂^{-•} scavenging activity before the astaxanthin intake ($r = -0.6$, $p < 0.01$) and positively correlated with total hydroperoxide level before and after the astaxanthin intake ($r = 0.7$ and 0.8 , respectively, $p < 0.01$). In conclusion, astaxanthin appears to affect O₂^{-•} scavenging activity in the aqueous humor in females, and is likely to be involved in the control of VEGF levels in the anterior eye.

ASTAXANTHIN REVIEWED FOR POTENTIAL TO TREAT A VARIETY OF OCULAR DISEASES IN HUMAN AND ANIMALS.

Mar Drugs. 2020 May 1;18(5):239.

doi: 10.3390/md18050239.

Clinical Applications of Astaxanthin in the Treatment of Ocular Diseases: Emerging Insights

[Giuseppe Giannaccare](#)¹, [Marco Pellegrini](#)², [Carlotta Senni](#)², [Federico Bernabei](#)², [Vincenzo Scordia](#)¹, [Arrigo Francesco Giuseppe Cicero](#)³

- PMID: [32370045](#)
- PMCID: [PMC7281326](#)
- DOI: [10.3390/md18050239](#)

[Free PMC article](#)

Abstract

Astaxanthin is a naturally occurring red carotenoid pigment belonging to the family of xanthophylls, and is typically found in marine environments, especially in microalgae and seafood such as salmonids, shrimps and lobsters. Due to its unique molecular structure, astaxanthin features some important biologic properties, mostly represented by strong antioxidant, anti-inflammatory and antiapoptotic activities. A growing body of evidence suggests that astaxanthin is efficacious in the prevention and treatment of several ocular diseases, ranging from the anterior to the posterior pole of the eye. Therefore, the present review aimed at providing a comprehensive evaluation of current clinical applications of astaxanthin in the management of ocular diseases. The efficacy of this carotenoid in the setting of retinal diseases, ocular surface disorders, uveitis, cataract and asthenopia is reported in numerous animal and human studies, which highlight its ability of modulating several metabolic pathways, subsequently restoring the cellular homeostatic balance. To maximize its multitarget therapeutic effects, further long-term clinical trials are warranted in order to define appropriate dosage, route of administration and exact composition of the final product.

ASTAXANTHIN IMPROVES AEROBIC EXERCISE RECOVERY IN HUMAN CLINICAL TRIAL.

Front Sports Act Living. 2019 Sep 4;1:17.
doi: 10.3389/fspor.2019.00017. eCollection 2019.

Astaxanthin Improves Aerobic Exercise Recovery Without Affecting Heat Tolerance in Humans

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PMID: 33344941 PMCID: [PMC7739736](#) DOI: [10.3389/fspor.2019.00017](#) [Free PMC article](#)

Abstract

Objectives: To examine the supplementation effects of the xanthophyll carotenoid Astaxanthin on physical performance and exertional heat strain in humans. **Design:** A randomized double blind placebo controlled trial. **Methods:** Twenty two male participants (Age: 23.14 ± 3.5 y, height: 175 ± 6 cm, body mass: 69.6 ± 8.7 kg, % body fat: 16.8 ± 3.8) received placebo (PLA, $n = 10$) or Astaxanthin (ATX, $n = 12$) 12 mg/day Per os (P.O), for 30 days, and were tested pre and post-supplementation with a maximal oxygen uptake (VO_2 Max) test and the heat tolerance test (HTT) (2 h walk at 40°C , 40% relative humidity (RH), 5 kph, 2% incline). NIH database registration no. [NCT02088242](#). Gas exchange, Heart rate (HR), Relative perceived exertion (RPE), and blood lactate were measured during the VO_2 Max test. Heart rate (HR), rectal (T_{rec}), and skin (T_{skin}) temperatures, RPE, and sweat rate (SR) were monitored in the HTT. Serum heat shock protein 72 (HSP72), Creatine phospho-kinase (CPK), C-reactive protein (CRP), and lipid profile were measured before and after the test. **Results:** The rise in blood lactate caused by the VO_2 Max test was significantly diminished in the ATX group (9.4 ± 3.1 and 13.0 ± 3.1 $\text{mmole}\cdot\text{l}^{-1}$ in the ATX and PLA groups, respectively $P < 0.02$), as was the change in oxygen uptake during recovery (-2.02 ± 0.64 and $0.83 \pm 0.79\%$ of VO_2 Max in the ATX and PLA group, respectively, $p = 0.001$). No significant differences were observed in the anaerobic threshold or VO_2 Max. In the HTT, no significant physiological or biochemical differences were observed (HR < 120 bpm, T_{rec} rose by $\sim 1^\circ\text{C}$ to $< 38^\circ\text{C}$, no difference in SR). **Conclusions:** Astaxanthin supplementation improved exercise recovery. No benefit was observed for ATX over PLA in response to heat stress. Further examination of Astaxanthin in higher exertional heat strain is required.

ASTAXANTHIN-CONTAINING FORMULA MAY BE EFFECTIVE FOR COMBATING AGE-RELATED COGNITIVE DECLINE IN HUMAN CLINICAL STUDY.

Nutrients. 2020 Dec 27;13(1):56.
doi: 10.3390/nu13010056.

Improvement of Executive Function after Short-Term Administration of an Antioxidants Mix Containing Bacopa, Lycopene, Astaxanthin and Vitamin B12: The BLAtwelve Study

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PMID: [33375429](#) PMCID: [PMC7824614](#) DOI: [10.3390/nu13010056](#) [Free PMC article](#)

Abstract

During the last few years increasing interest has been focused on antioxidants as potentially useful agents in the prevention of the onset and progression of cognitive dysfunction. In this randomized, double-blind, controlled, parallel arm study, the effects of daily consumption of an antioxidant mix on cognitive function in healthy older adults were evaluated. After a 1 week run-in period, 80 subjects aged 60 years or more, and with no evidence of cognitive dysfunction, were randomly allocated to a mix of four bioactive compounds (bacopa, lycopene, astaxanthin, and vitamin B12) or matched placebo, taken orally once a day for 8 weeks. The primary objective of the study was to evaluate the changes in trail making test (TMT) scores from baseline to 8 weeks of treatment, analyzed in the following hierarchical order: TMT-B, TMT-A, and TMT-B minus TMT-A. TMT-B increased in the control group (+3.46 s) and decreased in the active group (-17.63 s). The treatment difference was -21.01 s in favor of the active group (95% C.I. -26.80 to -15.2, $p < 0.0001$). The decrease in TMT-A was significantly higher in the active group (-6.86 s) than in the control group (-0.37 s). TMT-B minus TMT-A increased in the control group (+3.84 s) and decreased in the active group (-10.46 s). The increase in letter fluency in the verbal fluency test (VFT) was also significantly higher in the active group and statistically significant (+5.28 vs. +1.07 words; $p < 0.001$). Our findings provide encouraging evidence that regular dietary supplementation with bacopa, lycopene, astaxanthin, and vitamin B12 may be an effective dietary approach for counteracting cognitive changes associated with brain aging.

ASTAXANTHIN FORMULA MODULATES TRAINING-INDUCED AEROBIC METABOLISM OF CARBS AND FAT DURING REST AND EXERCISE IN HEALTHY YOUNG MEN IN HUMAN CLINICAL TRIAL.

J Clin Biochem Nutr. 2019 Jan;64(1):79-85.

doi: 10.3164/jcbn.18-40. Epub 2018 Aug 8.

Effect of dietary antioxidant-rich foods combined with aerobic training on energy metabolism in healthy young men

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PMID: 30705516 PMCID: [PMC6348409](#) DOI: [10.3164/jcbn.18-40](#) [Free PMC article](#)

Abstract

Although supplementation with several antioxidants has been suggested to improve aerobic metabolism during exercise, whether dietary foods containing such antioxidants can exert the metabolic modulation is unclear. This study aimed to investigate the effect of intake of the specific antioxidant-rich foods coupled with exercise training on energy metabolism. Twenty young healthy, untrained men were assigned to antioxidant and control groups: participants in the antioxidant group were encouraged to consume foods containing catechin, astaxanthin, quercetin, glutathione, and anthocyanin. All participants performed cycle training at 60% maximum oxygen consumption for 30 min, 3 days per week for 4 weeks. Maximum work load was significantly increased by training in both groups, while oxygen consumption during exercise was significantly increased in the antioxidant group only. There were positive correlations between maximum work load and fat/carbohydrate oxidations in the antioxidant group. Carbohydrate oxidation during rest was significantly higher in the post-training than that in the pre-training only in the antioxidant group. More decreased levels of serum insulin and HOMA-IR after training were observed in the antioxidant group than in the control group. This study suggests that specific antioxidant-rich foods could modulate training-induced aerobic metabolism of carbohydrate and fat during rest and exercise.

ASTAXANTHIN-CONTAINING FORMULA REDUCES SYSTOLIC BLOOD PRESSURE; REDUCES HIGH-SENSITIVITY C-REACTIVE PROTEIN AND INTERLEUKIN-6 INFLAMMATORY MARKERS; AND IMPROVES ENDOTHELIAL FUNCTION IN HUMAN CLINICAL STUDY.

Clin Nutr ESPEN. 2020 Feb;35:174-179.
doi: 10.1016/j.clnesp.2019.09.011. Epub 2019 Oct 24.

A combined effect of Cavacurcumin, Eicosapentaenoic acid (Omega-3s), Astaxanthin and Gamma -linoleic acid (Omega-6) (CEAG) in healthy volunteers- a randomized, double-blind, placebo-controlled study

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- PMID: 31987113
- DOI: [10.1016/j.clnesp.2019.09.011](https://doi.org/10.1016/j.clnesp.2019.09.011)

Abstract

Background: Inflammation plays a key role and is one of the early steps in the pathogenesis of endothelial function, thereby increasing the risk of hypertension (HTN), coronary artery disease (CAD), stroke and several other risk factors of cardiovascular disease (CVD). We assessed the efficacy for improving cardiovascular health (blood pressure, inflammation and endothelial reactivity) over a 4-week intervention period in healthy individuals.

Methods: We performed a randomized, double-blinded, placebo-controlled, randomized clinical trial to investigate Curcumin, Eicosapentaenoic acid (EPA), Astaxanthin and Gamma -linoleic acid (GLA) (CEAG) supplements with 80 individuals (30 men and 50 women). The mean age of participants was 48.8 ± 16.0 years. Participants were enrolled and randomized to active or placebo and followed for 4 weeks. Paired

and Independent T-tests were used to analyze the mean differences between and within groups.

Results: The primary endpoints of the study were the effect on inflammatory markers (IL-6, CRP), endothelial function and blood pressure at 4 weeks. There was a significant reduction in mean SBP at 4 weeks in the CEAG group compared to placebo [mean \pm SD 4.7 ± 6.8 ($p = 0.002$)]. Relative to placebo, active group showed a significant decrease in High sensitivity C Reactive Protein (hsCRP) (-0.49 ± 1.9 vs $+ 0.51 \pm 2.5$, $p = 0.059$) and blunted increase in IL-6 ($+0.2$ vs $+ 0.4$ in placebo, $p = 0.60$).

Conclusion: Inflammatory markers were reduced or blunted by CEAG, with a robust increase in both EPA levels and the fatty acid index. Furthermore, systolic BP was reduced over 4 weeks with concurrent improvement in endothelial function.

Astaxanthin increases the lifespan of *C. elegans* (a model organism used in aging research) by 16% to 30%.

[Oxid Med Cell Longev](#). 2011;2011:596240. Epub 2011 Oct 12.

Supplemental Cellular Protection by a Carotenoid Extends Lifespan via Ins/IGF-1 Signaling in *Caenorhabditis elegans*.

[Yazaki K](#), [Yoshikoshi C](#), [Oshiro S](#), [Yanase S](#).

Source

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Abstract

Astaxanthin (AX), which is produced by some marine animals, is a type of carotenoid that has antioxidative properties. In this study, we initially examined the effects of AX on the aging of a model organism *C. elegans* that has the conserved intracellular pathways related to mammalian longevity. The continuous treatments with AX (0.1 to 1 mM) from both the prereproductive and young adult stages extended the mean lifespans by about 16-30% in the wild-type and long-lived mutant *age-1* of *C. elegans*. In contrast, the AX-dependent lifespan extension was not observed even in a *daf-16* null mutant. Especially, the expression of genes encoding superoxide dismutases and catalases increased in two weeks after hatching, and the DAF-16 protein was translocated to the nucleus in the AX-exposed wild type. These results suggest that AX protects the cell organelle mitochondria and nucleus of the nematode, resulting in a lifespan extension via an Ins/IGF-1 signaling pathway during normal aging, at least in part.

PMID: 22013497 [PubMed - in process]

PMCID: PMC3195502

Astaxanthin shows anti-aging properties by significantly increasing the lifespan of fruit flies under oxidative stress and improving their age-related decline in locomotor function.

[J Agric Food Chem](#). 2013 Aug 14;61(32):7800-4. doi: 10.1021/jf402224w. Epub 2013 Aug 6.

Antiaging effects of astaxanthin-rich alga *Haematococcus pluvialis* on fruit flies under oxidative stress.

[Huangfu J¹](#), [Liu J](#), [Sun Z](#), [Wang M](#), [Jiang Y](#), [Chen ZY](#), [Chen F](#).

Author information

Abstract

The microalga *Haematococcus pluvialis* (HP) is the best natural producer of astaxanthin (AX), which is a potent antioxidant with broad health benefits. The present study investigated the antiaging potential of HP biomass using the fruit fly *Drosophila melanogaster* as the animal model. The results showed that in wild-type flies the treatment of HP induced the early mortality at a concentration of 20 mg/mL, which was associated with the decreased enzymatic activities of CuZn-superoxide dismutase (SOD1) and Mn-superoxide dismutase (SOD2) as well as the down-regulation of SOD1, SOD2, and catalase (CAT) at the transcriptional level. In SOD(n108) mutant flies, the supplementation of HP (10 or 20 mg/mL) significantly extended their lifespan and ameliorated the age-related decline in locomotor function. Further studies suggested that HP may play a role as a complement to the defective endogenous antioxidant system to exert such lifespan elongation effects. These results, taken together, strongly support the antiaging properties of HP and its therapeutic rather than preventive potential against aging-related diseases.

PMID:

23879808

[PubMed - indexed for MEDLINE]

Astaxanthin shown to be 75X to 6000X stronger than other common natural antioxidants.

Carotenoid Science, Vol.11, 2007, 16-20

Quenching Activities of Common Hydrophilic and Lipophilic Antioxidants against Singlet Oxygen Using Chemiluminescence Detection System

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The singlet oxygen quenching activities among common hydrophilic and lipophilic antioxidants such as polyphenols, tocopherols, carotenoids, ascorbic acid, coenzyme Q10 and α -lipoic acid were recorded under the same test condition: the chemiluminescence detection system for direct 1O_2 counting using the thermodissociable endoperoxides of 1,4-dimethylnaphthalene as 1O_2 generator in DMF : $CDCl_3$ (9 : 1). Carotenoids exhibited larger total quenching rate constants than other antioxidants, with astaxanthin showing the strongest activity. α -Tocopherol and α -lipoic acid showed considerable activities, whereas the activities of ascorbic acid, CoQ10 and polyphenols were only slight; these included capsaicin, probucol, edaravon, BHT and Trolox. This system has the potential of being a powerful tool to evaluate the quenching activity against singlet oxygen for various hydrophilic and lipophilic compounds.

Summary of Above Abstract.

**From Nishida, Yamashita, Miki, Carotenoid Science, Vol. 11, 2007, 16-20
(in Japanese)**

Astaxanthin has exceptional antioxidant activity to combat singlet oxygen when compared to other antioxidants. In particular, Astaxanthin can be used to defend against singlet oxygen damage for eye and skin health, which are especially susceptible to UV damage and aging effects.

Singlet oxygen is an active oxygen species generated in human skin by exposure to ultraviolet radiation (UV) that causes skin damage and eye damage. In this study, Astaxanthin extracted from *Haematococcus* microalgae powerfully quenched singlet oxygen. Results show that the quenching effect of Astaxanthin is 800 times greater than coenzyme Q10. Astaxanthin was also about 75 times greater than alpha lipoic acid, about 550 times greater than green tea catechins and about 6000 times greater than Vitamin C.

Astaxanthin 550 times stronger than Vitamin E and 11 times stronger than Beta-Carotene in singlet oxygen quenching.

Carotenoids as Singlet Oxygen Quenchers in Marine Organisms

Shimidzu, Goto, Miki, 1996. Fisheries Science 62(1), 134-137

To understand the roles of carotenoids as singlet oxygen quenchers in marine organisms, quenching activities of eight major carotenoids, astaxanthin, canthaxanthin, β -carotene, zeaxanthin, lutein, tunaxanthin, fucoxanthin and halocynthiaxanthin were examined according to the method using a thermodissociable endoperoxide of 1,4-dimethylnaphthalene as a singlet oxygen generator. The second-order rate constant for the singlet oxygen quenching activity by each carotenoid was determined, suggesting that an increasing number of conjugated double bonds in carotenoid was proportional to greater quenching activity. The quenching activity of each carotenoid was found to be approximately 40 to 600 times greater than that of α -tocopherol. The potency of these carotenoids suggests that they may play a role in protecting marine organisms from active oxygen species.

Summary: Results indicated that Astaxanthin was significantly stronger than all other antioxidants tested as singlet oxygen quenchers. Among the results Astaxanthin was shown to be 550X stronger than Vitamin E; 11X stronger than Beta-Carotene; 2.75X stronger than Lutein.

Astaxanthin is 14 to 65 times stronger than other common antioxidants in free radical scavenging and Natural Astaxanthin is 20 times stronger than Synthetic Astaxanthin in free radical scavenging.

Nutrafoods (2013)

DOI 10.1007/s13749-013-0051-5

Synthetic astaxanthin is significantly inferior to algal-based astaxanthin as an antioxidant and may not be suitable as a human nutraceutical supplement

Bob Capelli, Debasis Bagchi, Gerald R. Cysewski

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Abstract

Synthetic astaxanthin (S-AX) was tested against natural astaxanthin from *Haematococcus pluvialis* microalgae (N-AX) for antioxidant activity. *In vitro* studies conducted at Creighton University and Brunswick Laboratories showed N-AX to be over 50 times stronger than S-AX in singlet oxygen quenching and approximately 20 times stronger in free radical elimination. N-AX has been widely used over the last 15 years as a human nutraceutical supplement after extensive safety data and several health benefits were established. S-AX, which is synthesised from petrochemicals, has been used as a feed ingredient, primarily to pigment the flesh of salmonids. S-AX has never been demonstrated to be safe for use as a human nutraceutical supplement and has not been tested for health benefits in humans. Due to safety concerns with the use of synthetic forms of other carotenoids such as canthaxanthin and beta-carotene in humans, the authors recommend against the use of S-AX as a human nutraceutical supplement until extensive, long-term safety parameters have been established and human clinical trials have been conducted showing potential health benefits. Additionally, differences in various other properties between S-AX and N-AX such as stereochemistry, esterification and the presence of supporting naturally occurring carotenoids in N-AX are discussed, all of which elicit further questions as to the safety and potential health benefits of S-AX. Ultimately, should S-AX prove safe for direct human consumption, dosage levels roughly 20–30 times greater than N-AX should be used as a result of the extreme difference in antioxidant activity between the two forms.

Astaxanthin's Anti-Inflammatory mechanisms found to be broad-spectrum.

[Mol Cells](#). 2003 Aug 31;16(1):97-105.

Astaxanthin inhibits nitric oxide production and inflammatory gene expression by suppressing I(kappa)B kinase-dependent NF-kappaB activation.

[Lee SJ](#), [Bai SK](#), [Lee KS](#), [Namkoong S](#), [Na HJ](#), [Ha KS](#), [Han JA](#), [Yim SV](#), [Chang K](#), [Kwon YG](#), [Lee SK](#), [Kim YM](#).

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Astaxanthin, a carotenoid without vitamin A activity, has shown anti-oxidant and anti-inflammatory activities; however, its molecular action and mechanism have not been elucidated. We examined in vitro and in vivo regulatory function of astaxanthin on production of nitric oxide (NO) and prostaglandin E2 (PGE2) as well as expression of inducible NO synthase (iNOS), cyclooxygenase-2, tumor necrosis factor-alpha (TNF-alpha), and interleukin-1beta (IL-1beta). Astaxanthin inhibited the expression or formation production of these proinflammatory mediators and cytokines in both lipopolysaccharide (LPS)-stimulated RAW264.7 cells and primary macrophages. Astaxanthin also suppressed the serum levels of NO, PGE2, TNF-alpha, and IL-1beta in LPS-administrated mice, and inhibited NF-kappaB activation as well as iNOS promoter activity in RAW264.7 cells stimulated with LPS. This compound directly inhibited the intracellular accumulation of reactive oxygen species in LPS-stimulated RAW264.7 cells as well as H2O2-induced NF-kappaB activation and iNOS expression. Moreover, astaxanthin blocked nuclear translocation of NF-kappaB p65 subunit and I(kappa)B(alpha) degradation, which correlated with its inhibitory effect on I(kappa)B kinase (IKK) activity. These results suggest that astaxanthin, probably due to its antioxidant activity, inhibits the production of inflammatory mediators by blocking NF-kappaB activation and as a consequent suppression of IKK activity and I(kappa)B-alpha degradation.

Publication Types:

- [Research Support, Non-U.S. Gov't](#)

PMID: 14503852 [PubMed - indexed for MEDLINE]

ASTAXANTHIN PROTECTS THE MITOCHONDRIA AGAINST HEAT-INDUCED DAMAGE IN MICE.

Neuroscience 2021 Sep 17;S0306-4522(21)00477-2. doi: 10.1016/j.neuroscience.2021.09.010. Online ahead of print.

Astaxanthin protects against heat-induced mitochondrial alterations in mouse hypothalamus

[Yifan Chen](#)¹, [Tianzheng Yu](#)², [Patricia Deuster](#)³

- PMID: 34543676 DOI: [10.1016/j.neuroscience.2021.09.010](https://doi.org/10.1016/j.neuroscience.2021.09.010)

Abstract

The hypothalamus plays an essential role in regulating whole-body energy and temperature homeostasis when adapting to environmental changes. We previously reported that heat exposure causes mitochondrial dysfunction and apoptosis in mouse skeletal muscle, and pretreatment with astaxanthin (AST), an antioxidant, prevents this effect. How the hypothalamus responds to heat stress remains largely unexplored. In this study, we investigated the effects of heat exposure on hypothalamic mitochondria in mice with and without AST pretreatment. During heat exposure, both vehicle and AST-treated mice had a hyperthermic response though no significant differences in peak core body temperature were noted between the two groups. Heat exposure induced mitochondrial fission in the hypothalamus, as manifested by increased mitochondrial fragmentation and expression of both total and phosphorylated dynamin-related protein 1. In addition, transmission electron microscopy revealed damaged and degraded mitochondria in the hypothalamus of heat-exposed mice. Heat induced apoptosis and mitophagy were further confirmed by increased formation of reactive oxygen species, activation of caspase 3/7 and expression of LC3 proteins. Moreover, heat exposure increased the expression of PINK1 and Parkin in mouse hypothalamus. In contrast, pretreatment with AST reduced these effects. These results demonstrate that heat stress-induced hypothalamic apoptosis is associated with altered mitochondrial dynamics favoring fission and mitophagy. AST protects the hypothalamus against heat-induced injury by preserving redox homeostasis and mitochondrial integrity.

Astaxanthin shows potential against osteoporosis in mouse and in-vitro studies.

[Int J Mol Sci](#). 2018 Mar 19;19(3). pii: E912. doi: 10.3390/ijms19030912.

Suppression Effect of Astaxanthin on Osteoclast Formation In Vitro and Bone Loss In Vivo.

[Hwang YH¹](#), [Kim KJ²](#), [Kim SJ³](#), [Mun SK⁴](#), [Hong SG⁵](#), [Son YJ⁶](#), [Yee ST⁷](#).

Author information

Abstract

Osteoporosis is characterized by a reduction of the bone mineral density (BMD) and microarchitectural deterioration of the bone, which lead to bone fragility and susceptibility to fracture. Astaxanthin (AST) has a variety of biological activities, such as a protective effect against asthma or neuroinflammation, antioxidant effect, and decrease of the osteoclast number in the right mandibles in the periodontitis model. Although treatment with AST is known to have an effect on inflammation, no studies on the effect of AST exposure on bone loss have been performed. Thus, in the present study, we examined the antiosteoporotic effect of AST on bone mass in ovariectomized (OVX) mice and its possible mechanism of action. The administration of AST (5, 10 mg/kg) for 6 weeks suppressed the enhancement of serum calcium, inorganic phosphorus, alkaline phosphatase, total cholesterol, and tartrate-resistant acid phosphatase (TRAP) activity. The bone mineral density (BMD) and bone microarchitecture of the trabecular bone in the tibia and femur were recovered by AST exposure. Moreover, in the in vitro experiment, we demonstrated that AST inhibits osteoclast formation through the expression of the nuclear factor of activated T cells (NFAT) c1, dendritic cell-specific transmembrane protein (DC-STAMP), TRAP, and cathepsin K without any cytotoxic effects on bone marrow-derived macrophages (BMMs). Therefore, we suggest that AST may have therapeutic potential for the treatment of postmenopausal osteoporosis.

KEYWORDS:

Astaxanthin (AST); bone mineral density (BMD); nuclear factor of activated T cells c1 (NFATc1); osteoclast; osteoporosis

PMID: 29562730

PMCID: [PMC5877773](#)

DOI: [10.3390/ijms19030912](#) [Indexed for MEDLINE] [Free PMC Article](#)

Astaxanthin inhibits a variety of pro-inflammatory cytokines in cells.

[Eur J Nutr.](#) 2010 Mar;49(2):119-26. Epub 2009 Sep 26.

Astaxanthin suppresses scavenger receptor expression and matrix metalloproteinase activity in macrophages.

[Kishimoto Y](#), [Tani M](#), [Uto-Kondo H](#), [Iizuka M](#), [Saita E](#), [Sone H](#), [Kurata H](#), [Kondo K](#).

Source

Institute of Environmental Science for Human Life, Ochanomizu University, Tokyo, Japan.

Abstract

BACKGROUND: *Astaxanthin is a red carotenoid pigment which has significant potential for antioxidant activity. The macrophages in atherosclerotic lesions, known as activated macrophages, express scavenger receptors responsible for the clearance of pathogenic lipoproteins. In addition, the expression and secretion of proteolytic enzymes, matrix metalloproteinases (MMPs), and pro-inflammatory cytokines are remarkably promoted in activated macrophages.*

AIM OF THE STUDY: *In this study, we investigated the effects of astaxanthin on the expression of scavenger receptors, MMPs, and pro-inflammatory cytokines in macrophages.*

METHODS: *THP-1 macrophages were incubated with 5-10 microM astaxanthin for 24 h. The expression levels of scavenger receptors, MMPs, and pro-inflammatory cytokines were determined by Western blot analysis or real-time RT-PCR. The MMP-9 and -2 activities were examined by gelatin zymography and total MMP activity was measured by fluorometry.*

RESULTS: *We found that astaxanthin remarkably decreased the class A scavenger receptor and CD36 expression in the protein and mRNA levels. Astaxanthin also reduced MMP-1, -2, -3, -9, -12, and -14 activity and expression. The mRNA expression of tumor necrosis factor-alpha, interleukin-1beta, interleukin-6, inducible nitric oxide synthase, and cyclooxygenase-2 were significantly suppressed by astaxanthin. Furthermore, astaxanthin inhibited the phosphorylation of nuclear factor-kappaB.*

CONCLUSIONS: *These results indicate that astaxanthin has inhibitory effects on macrophage activation, such as scavenger receptors up-regulation, MMPs activation, and pro-inflammatory cytokines secretion.*

PMID: 19784539 [PubMed - indexed for MEDLINE]

Astaxanthin found to be a multi-faceted anti-inflammatory with various mechanisms of action.

[Invest Ophthalmol Vis Sci](#). 2003 Jun;44(6):2694-701.

Effects of astaxanthin on lipopolysaccharide-induced inflammation in vitro and in vivo.

[Ohgami K](#), [Shiratori K](#), [Kotake S](#), [Nishida T](#), [Mizuki N](#), [Yazawa K](#), [Ohno S](#).

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PURPOSE: Astaxanthin (AST) is a carotenoid that is found in marine animals and vegetables. Several previous studies have demonstrated that AST exhibits a wide variety of biological activities including antioxidant, antitumor, and anti-Helicobacter pylori effects. In this study, attention was focused on the antioxidant effect of AST. The object of the present study was to investigate the efficacy of AST in endotoxin-induced uveitis (EIU) in rats. In addition, the effect of AST on endotoxin-induced nitric oxide (NO), prostaglandin E2 (PGE2), and tumor necrosis factor (TNF)-alpha production in a mouse macrophage cell line (RAW 264.7) was studied in vitro. **METHODS:** EIU was induced in male Lewis rats by a footpad injection of lipopolysaccharide (LPS). AST or prednisolone was administered intravenously at 30 minutes before, at the same time as, or at 30 minutes after LPS treatment. The number of infiltrating cells and protein concentration in the aqueous humor collected at 24 hours after LPS treatment was determined. RAW 264.7 cells were pretreated with various concentrations of AST for 24 hours and subsequently stimulated with 10 microg/mL of LPS for 24 hours. The levels of PGE2, TNF-alpha, and NO production were determined in vivo and in vitro. **RESULTS:** AST suppressed the development of EIU in a dose-dependent fashion. The anti-inflammatory effect of 100 mg/kg AST was as strong as that of 10 mg/kg prednisolone. AST also decreased production of NO, activity of inducible nitric oxide synthase (NOS), and production of PGE2 and TNF-alpha in RAW264.7 cells in vitro in a dose-dependent manner. **CONCLUSIONS:** This study suggests that AST has a dose-dependent ocular anti-inflammatory effect, by the suppression of NO, PGE2, and TNF-alpha production, through directly blocking NOS enzyme activity.

Publication Types:

- [Comparative Study](#)
- [Research Support, Non-U.S. Gov't](#)

PMID: 12766075 [PubMed - indexed for MEDLINE]

Astaxanthin inhibits the production of inflammatory markers by blocking nitric oxide and Cox-2.

[J Microbiol Biotechnol.](#) 2008 Dec;18(12):1990-6.

Effects of astaxanthin on the production of NO and the expression of COX-2 and iNOS in LPS-stimulated BV2 microglial cells.

[Choi SK](#), [Park YS](#), [Choi DK](#), [Chang HI](#).

Department of Biotechnology, School of Life Sciences and Biotechnology, Korea University, Seoul 136-701, Korea.

Astaxanthin has shown antioxidant, antitumor, and antiinflammatory activities; however, its molecular action and mechanism in the nervous system have yet to be elucidated. We examined the in vitro effects of astaxanthin on the production of nitric oxide (NO), as well as the expression of inducible NO synthase (iNOS) and cyclooxygenase-2 (COX-2) in lipopolysaccharide (LPS)-stimulated BV2 microglial cells. Astaxanthin inhibited the expression or formation of nitric oxide (NO), iNOS and COX-2 in lipopolysaccharide (LPS)-stimulated BV-2 microglial cells. Astaxanthin also suppressed the protein levels of iNOS and COX-2 in LPS-stimulated BV2 microglial cells. These results suggest that astaxanthin, probably due to its antioxidant activity, inhibits the production of inflammatory mediators by blocking iNOS and COX-2 activation or by the suppression of iNOS and COX-2 degradation.

PMID: 19131704 [PubMed - in process]

Astaxanthin much more potent than curcumin and its derivatives in scavenging nitric oxide.

[Biol Pharm Bull.](#) 2004 Feb;27(2):170-3.

Evaluation of the nitric oxide radical scavenging activity of manganese complexes of curcumin and its derivative.

[Sumanont Y](#), [Murakami Y](#), [Tohda M](#), [Vajragupta O](#), [Matsumoto K](#), [Watanabe H](#).

Department of Pharmacology, Institute of Natural Medicine, Toyama Medical and Pharmaceutical University, 2630 Sugitani, Toyama 930-0194, Japan.

Curcumin manganese complex (CpCpx) and diacetylcurcumin manganese complex (AcylCpCpx) were determined as to their effect on the nitric oxide (NO) radical scavenging in vitro method using a sodium nitroprusside generating NO system compared with their parent compound and astaxanthin, an extreme antioxidant. All compounds effectively reduced the generation of NO radicals in a dose dependent manner. They exhibited strong NO radical scavenging activity with low IC(50) values. The IC(50) values of curcumin, diacetylcurcumin, CpCpx and AcylCpCpx obtained are 20.39 \pm 4.10 microM, 28.76 \pm 1.48 microM, 9.79 \pm 1.50 microM and 8.09 \pm 0.99 microM, respectively. CpCpx and AcylCpCpx show greater NO radical scavenging than their parent compounds, curcumin and acetylcurcumin, respectively. However, the IC(50) values of curcumin and related compounds were found to be less than astaxanthin, an extreme antioxidant, with the lower IC(50) value of 3.42 \pm 0.50 microM.

Publication Types:

- [Research Support, Non-U.S. Gov't](#)

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Astaxanthin effective in reducing pain and increasing satisfaction in patients suffering from rheumatoid arthritis in double-blind, placebo-controlled human clinical trial.

EFFECT OF AN ASTAXANTHIN-CONTAINING PRODUCT ON RHEUMATOID ARTHRITIS

Nir, Y., Spiller, G., Multz, C.

Health Research and Studies Center, Los Altos, CA

Study Report, May 2002

Journal of the American College of Nutrition (October 2002) Volume 21, Number 5.

ABSTRACT

Rheumatoid arthritis (RA) is a chronic destructive disorder requiring aggressive treatment. Conventional treatments present problems in terms of safety and efficacy, and the alternative therapies so far investigated have not yielded consistent results. We investigated the effect of an extract of *Haematococcus* algae grown in Hawaii, taken three times a day, each dose supplying 4 mg of astaxanthin, 40 ug lutein, 65 IU vitamin A as beta-carotene, and 50 IU of vitamin E, on the symptoms of RA in a double-blind, placebo-controlled, parallel design study. Twenty-one subjects were randomized to receive either the extract (14 subjects) or a placebo (7 subjects) for eight weeks. Pain and satisfaction with the ability to perform daily activities were measured at the beginning of the study, and after 4 and 8 weeks of treatment. The results showed a significant difference ($P < 0.05$) both in pain and satisfaction scores between the treatment and control groups at the end of the study. Pain scores (mean \pm SD, VAS scale) at 0, 4, and 8 weeks were respectively, 0.42 \pm 0.22, 0.38 \pm 0.21, and 0.27 \pm 0.25 for the treatment group, and 0.48 \pm 0.23, 0.42 \pm 0.16, and 0.45 \pm 0.14 for the control group. Satisfaction scores were 1.75 \pm 0.72, 1.50 \pm 0.76, and 1.00 \pm 0.60 for the treatment group, and 1.83 \pm 0.69, 1.50 \pm 0.96, and 1.67 \pm 0.94 for the control group. Astaxanthin-based supplements appear to be an effective addition in the treatment of RA and further studies should be carried out with a larger population.

Astaxanthin decreases pain rate and pain duration in subjects suffering from carpal tunnel syndrome in double blind, placebo controlled human clinical study.

EFFECT OF AN ASTAXANTHIN-CONTAINING PRODUCT ON CARPAL TUNNEL SYNDROME

Nir, Y., Spiller, G., Multz, C.

Health Research and Studies Center, Los Altos, CA,

Study Report, May, 2002

Journal of the American College of Nutrition, Oct 2002, Volume 21, Number 5

ABSTRACT

Carpal Tunnel Syndrome (CTS) is a debilitating disease often requiring surgery. Because not all patients respond to surgery and current non-surgical treatments provide limited benefits, investigations into alternative techniques are necessary. We investigated the effect of an extract of *Haematococcus* algae grown in Hawaii, taken three times a day, each dose supplying 4 mg of astaxanthin, 40 ug lutein, 65 IU vitamin A as beta-carotene, and 50 IU of vitamin E, on the symptoms of CTS in a double-blind, placebo-controlled, parallel design study. Twenty participants were randomized to receive either the extract (13 subjects) or a placebo (7 subjects) for eight weeks. Daytime pain rate and duration were measured at the beginning of the study, and after 4 and 8 weeks of treatment, with the use of questionnaires. Results showing a trend towards decreasing pain rate and duration in the subjects receiving the extract, but because of the small number of subjects the results did not reach statistical significance ($P>0.05$). The daytime pain rates (mean \pm SD) at 0, 4 and 8 weeks were, respectively, 1.69 ± 0.99 , 1.23 ± 0.70 , and 1.00 ± 0.88 for the treatment group, and 1.67 ± 0.47 , 1.83 ± 0.37 , and 1.50 ± 0.50 for the control group. Similarly, the duration of daytime pain was 2.15 ± 1.23 , 1.69 ± 1.13 , and 1.38 ± 1.44 for the treatment group, and 2.17 ± 1.07 , 2.67 ± 1.10 , and 2.17 ± 1.34 for the control group. The positive trend observed in this pilot study suggests that an astaxanthin-containing product may be effective in treating symptoms of CTS. Further investigations in a larger-scale study are needed.

Astaxanthin decreases C-reactive protein levels by 20% on average in double-blind, placebo-controlled human clinical study.

Effect of daily use natural astaxanthin on C-reactive protein.

Gene A. Spiller, PhD, Antonella Dewell, MS, RD, Sally Chaves, RN, Zaga Rakidzich
Health Research & Studies Center, Los Altos, CA

Study Report, January, 2006

Unpublished study referenced in *The Medical Research of Astaxanthin* by Capelli, B., Keily, S., Linhart, J., and Cysewski, G. (2013) and in *The World's Best Kept Health Secret: Natural Astaxanthin* by Capelli, B., and Cysewski, G. (2014).

ABSTRACT

Previous studies have provided data suggesting that daily use of natural astaxanthin can positively address inflammatory conditions such as rheumatoid arthritis and carpal tunnel syndrome. In this study, the effect of daily use of a microalgae extract containing natural astaxanthin, on C-reactive protein was evaluated. It was found that after daily use for eight weeks C-reactive protein (CRP) was significantly lowered in the treatment group as compared to the placebo group. The average decrease in patients receiving natural astaxanthin was 20%. This correlation of reduced CRP and use of astaxanthin may suggest that daily use can help reduce CRP and possibly lower inflammation levels in the body.

Astaxanthin use leads to increase in grip strength by 93% in eight weeks by patients suffering from tendonitis (tennis elbow) in double-blind, placebo-controlled human clinical trial.

Effect of daily use of natural astaxanthin on symptoms associated with Tennis Elbow (lateral humeral epicondylitis)

Gene A. Spiller, PhD, CNS, Antonella Dewell, MS, RD, Sally Chaves, RN, Zaga Rakidzich, Health Research & Studies Center, Los Altos, CA
Study Report, January, 2006

Unpublished study referenced in *The Medical Research of Astaxanthin* by Capelli, B., Keily, S., Linhart, J., and Cysewski, G. (2013) and in *The World's Best Kept Health Secret: Natural Astaxanthin* by Capelli, B., and Cysewski, G. (2014).

ABSTRACT

Previous studies have provided data suggesting that daily use of a microalgal extract containing natural astaxanthin can help alleviate pain associated with joint damage, specifically that seen in rheumatoid arthritis and carpal tunnel syndrome. For this study, the benefits of daily use natural astaxanthin for the purpose of alleviating pain associated with Tennis Elbow (lateral humeral epicondylitis) was evaluated. It was found that grip strength measurements (GSM) for those on the active product were significantly improved by the end of the study. The average grip strength improved by 93% in subjects supplementing with 12mg per day of natural astaxanthin in a period of 8 weeks. This correlation of improved GSM and use of natural astaxanthin may suggest that daily use can help alleviate pain associated with Tennis Elbow, and increase mobility. This improvement may greatly improve the standard of living for those who suffer from such joint disorders.

Astaxanthin inhibits LDL oxidation in human clinical study and may contribute to the prevention of atherosclerosis. Results were best at 14.4mg per day as compared to 3.6mg per day and 21.6mg per day.

[J Atheroscler Thromb.](#) 2000;7(4):216-22.

Inhibition of low-density lipoprotein oxidation by astaxanthin.

[Iwamoto T¹](#), [Hosoda K](#), [Hirano R](#), [Kurata H](#), [Matsumoto A](#), [Miki W](#), [Kamiyama M](#), [Itakura H](#), [Yamamoto S](#), [Kondo K](#).

Author information

Abstract

Marine animals produce astaxanthin which is a carotenoid and antioxidant. In this study we determined the in vitro and ex vivo effects of astaxanthin on LDL oxidation. The oxidation of LDL was measured in a 1 ml reaction system consisting of increasing concentrations of astaxanthin (12.5, 25.0, 50.0 microg/ml), 400 microM V-70 (2, 2'-azobis(4-methoxy-2, 4-dimethylvaleronitrile)), and LDL (70 microg/ml protein). Astaxanthin dose, dependently significantly prolonged the oxidation lag time (31.5, 45.4, 65.0 min) compared with the control (19.9 min). For the ex vivo study 24 volunteers (mean age 28.2 [SD 7.8] years) consumed astaxanthin at doses of 1.8, 3.6, 14.4 and 21.6 mg per day for 14 days. No other changes were made in the diet. Fasting venous blood samples were taken at days 0, +14. LDL lag time was longer (5.0, 26.2, 42.3 and 30.7% respectively) compared with day 0 after consuming astaxanthin at doses of 1.8, 3.6, 14.4 and 21.6 mg for 14 days compared with day 0, but there was no difference in oxidation of LDL between day 0 (lag time 59.9+/-7.2 min) and day 14 (57.2+/-6.0 min) in the control group. Our results provide evidence that consumption of marine animals producing astaxanthin inhibits LDL oxidation and possibly therefore contributes to the prevention of atherosclerosis.

PMID:

11521685

[PubMed - indexed for MEDLINE]

Astaxanthin increases HDL (good) cholesterol and adiponectin in patients with mild hyperlipidemia in randomized placebo-controlled human clinical study.

[Atherosclerosis](#). 2010 Apr;209(2):520-3. Epub 2009 Oct 14.

Administration of natural astaxanthin increases serum HDL-cholesterol and adiponectin in subjects with mild hyperlipidemia.

[Yoshida H](#), [Yanai H](#), [Ito K](#), [Tomono Y](#), [Koikeda T](#), [Tsukahara H](#), [Tada N](#).

Department of Laboratory Medicine, Jikei University Kashiwa Hospital, Chiba, Japan.

hyoshida@jikei.ac.jp

Abstract

BACKGROUND: Astaxanthin has been reported to improve dyslipidemia and metabolic syndrome in animals, but such effects in humans are not well known.

METHODS: Placebo-controlled astaxanthin administration at doses of 0, 6, 12, 18 mg/day for 12 weeks was randomly allocated to 61 non-obese subjects with fasting serum triglyceride of 120-200mg/dl and without diabetes and hypertension, aged 25-60 years.

RESULTS: In before and after tests, body mass index (BMI) and LDL-cholesterol were unaffected at all doses, however, triglyceride decreased, while HDL-cholesterol increased significantly. Multiple comparison tests showed that 12 and 18 mg/day doses significantly reduced triglyceride, and 6 and 12 mg doses significantly increased HDL-cholesterol. Serum adiponectin was increased by astaxanthin (12 and 18 mg/day), and changes of adiponectin correlated positively with HDL-cholesterol changes independent of age and BMI.

CONCLUSIONS: This first-ever randomized, placebo-controlled human study suggests that astaxanthin consumption ameliorates triglyceride and HDL-cholesterol in correlation with increased adiponectin in humans.

PMID: 19892350 [PubMed - indexed for MEDLINE]

Astaxanthin decreases lipid peroxidation in double-blind, placebo controlled human clinical trial.

[Int J Vitam Nutr Res.](#) 2007 Jan;77(1):3-11.

Effects of astaxanthin supplementation on lipid peroxidation.

[Karppi J¹](#), [Rissanen TH](#), [Nyyssönen K](#), [Kaikkonen J](#), [Olsson AG](#), [Voutilainen S](#), [Salonen JT](#).

Author information

Abstract

Astaxanthin, the main carotenoid pigment in aquatic animals, has greater antioxidant activity in vitro (protecting against lipid peroxidation) and a more polar configuration than other carotenoids. We investigated the effect of three-month astaxanthin supplementation on lipid peroxidation in healthy non-smoking Finnish men, aged 19-33 years by using a randomized double-blind study design. Also absorption of astaxanthin from capsules into bloodstream and its safety were evaluated. The intervention group received two 4-mg astaxanthin (Astaxin) capsules daily, and the control group two identical-looking placebo capsules. Astaxanthin supplementation elevated plasma astaxanthin levels to 0.032 pmol/L ($p < 0.001$ for the change compared with the placebo group). We observed that levels of plasma 12- and 15-hydroxy fatty acids were reduced statistically significantly in the astaxanthin group ($p = 0.048$ and $p = 0.047$ respectively) during supplementation, but not in the placebo group and the change of 15-hydroxy fatty acid was almost significantly greater ($p = 0.056$) in the astaxanthin group, as compared with the placebo group. The present study suggests that intestinal absorption of astaxanthin delivered as capsules is adequate, and well tolerated. Supplementation with astaxanthin may decrease in vivo oxidation of fatty acids in healthy men.

PMID:

17685090

[PubMed - indexed for MEDLINE]

Astaxanthin has superior photo-aging preventive properties than other carotenoids.

[Exp Dermatol.](#) 2009 Mar;18(3):222-31. doi: 10.1111/j.1600-0625.2008.00790.x. Epub 2008 Sep 18.

Astaxanthin, canthaxanthin and beta-carotene differently affect UVA-induced oxidative damage and expression of oxidative stress-responsive enzymes.

[Camera E¹](#), [Mastrofrancesco A](#), [Fabbri C](#), [Daubrawa F](#), [Picardo M](#), [Sies H](#), [Stahl W](#).

Author information

Abstract

Carotenoids are used for systemic photoprotection in humans. Regarding mechanisms underlying photoprotective effects of carotenoids, here we compared the modulation of UVA-related injury by carotenoids. Human dermal fibroblasts (HDF) were exposed to moderate doses of UVA, which stimulated apoptosis, increased levels of reactive oxygen species and thiobarbituric acid reactive substances, decreased antioxidant enzymes activities, promoted membrane perturbation, and induced the expression of heme oxygenase-1 (HO-1). The carotenoids astaxanthin (AX), canthaxanthin (CX) and beta-carotene (betaC) were delivered to HDF 24 h before exposure to UVA. Astaxanthin exhibited a pronounced photoprotective effect and counteracted all of the above-mentioned UVA-induced alterations to a significant extent. beta-Carotene only partially prevented the UVA-induced decline of catalase and superoxide dismutase activities, but it increased membrane damage and stimulated HO-1 expression. Moreover, betaC dose-dependently induced caspase-3 activity following UVA exposure. In contrast, CX had no effect on oxidative damage, except for HO-1 expression, which was augmented. Uptake of AX by fibroblasts was higher than that of the other two carotenoids. The photostability of the three compounds in fibroblasts was AX > CX >> betaC. The data indicate that the oxo-carotenoid AX has a superior preventive effect towards photo-oxidative changes in cell culture.

PMID:

18803658

[PubMed - indexed for MEDLINE]

Astaxanthin may have protective effect against photo-aging, wrinkles and sagging.

[J Dermatol Sci](#). 2010 May;58(2):136-42. doi: 10.1016/j.jdermsci.2010.02.009. Epub 2010 Feb 18.

Astaxanthin attenuates the UVA-induced up-regulation of matrix-metalloproteinase-1 and skin fibroblast elastase in human dermal fibroblasts.

[Suganuma K](#)¹, [Nakajima H](#), [Ohtsuki M](#), [Imokawa G](#).

Author information

Abstract

BACKGROUND:

Repetitive exposure of the skin to UVA radiation elicits sagging more frequently than wrinkling, which is mainly attributed to its biochemical mechanism to up-regulate the expression of matrix-metalloproteinase (MMP)-1 and skin fibroblast elastase (SFE)/neutral endopeptidase (NEP), respectively.

OBJECTIVE:

In this study, we examined the effects of a potent antioxidant, astaxanthin (AX), on the induction of MMP-1 and SFE by UVA treatment of cultured human dermal fibroblasts.

METHODS:

Those effects were assessed by real-time RT-PCR, Western blotting and enzymic activity assays.

RESULTS:

UVA radiation elicited a significant increase in the gene expression of MMP-1 as well as SFE/NEP (to a lesser extent) which was followed by distinct increases in their protein and enzymatic activity levels. The addition of AX at concentrations of 4-8 microM immediately after UVA exposure significantly attenuated the induction of MMP-1 and SFE/NEP expression elicited by UVA at the gene, protein and activity levels although both the UVA stimulation and the subsequent AX inhibition were greater for MMP-1 than for SFE/NEP. Analysis of the UVA-induced release of cytokines revealed that UVA significantly stimulated only the secretion of IL-6 among the cytokines tested and that AX significantly diminished only the IL-6 secretion.

CONCLUSION:

These findings indicate that, based on different effective concentrations of AX, a major mode of action leading to the inhibition elicited by AX depends on inhibition of UVA effects of the reactive oxygen species-directed signaling cascade, but not on interruption of the IL-6-mediated signaling cascade. We hypothesize that AX would have a significant benefit on protecting against UVA-induced skin photo-aging such as sagging and wrinkles.

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PMID:

20219323

[PubMed - indexed for MEDLINE]

ASTAXANTHIN SHOWS PROTECTIVE POTENTIAL IN RAT MODEL OF MULTIPLE SCLEROSIS.

Cell J. 2021 Jan;22(4):565-571.

doi: 10.22074/cellj.2021.6999. Epub 2020 Apr 22.

Astaxanthin Reduces Demyelination and Oligodendrocytes Death in A Rat Model of Multiple Sclerosis

[Alireza Lotfi](#)¹, [Mitra Soleimani](#)¹, [Nazem Ghasemi](#)²

PMID: 32347051 PMCID: [PMC7211289](#) DOI: [10.22074/cellj.2021.6999](#) [Free PMC article](#)

Abstract

Objective: Astaxanthin (AST) is a carotenoid with anti-oxidative, anti-inflammatory, and anti-apoptotic properties. It has also been reported that AST exerts protective effects against neurodegenerative diseases and reduces oxidative stress-induced the central nervous system (CNS) injury. In this study, we aimed to evaluate the protective potential of AST in inhibiting demyelination and oligodendrocyte death in a rat model of multiple sclerosis (MS).

Materials and Methods: In this experimental study, forty Wistar rats were randomly assigned to four experimental groups: control group (with normal feeding), cuprizone (CPZ group) that daily received 0.6% CPZ for 4 weeks, sham group that daily received 0.6% CPZ plus dimethyl sulfoxid (DMSO) for 4 weeks, and AST group that daily received 0.6% CPZ and after 12 hours were treated with AST (3 mg/kg), for 4 weeks. Muscle strength was evaluated by the behavioral basket test at the end of every week for 4 weeks. Luxol Fast Blue (LFB) staining was utilized for the identification of myelination and demyelination. Myelin density was evaluated by the ImageJ software. The expression of A2B5 (oligodendrocyte precursor protein) and myelin oligodendrocyte protein (MOG) were assessed by immunohistochemistry (IHC) and the expression of myelin basic protein (*MBP*), MOG, and platelet-derived growth factor-alpha (*PDGFR- α*) genes was examined by the real-time polymerase chain reaction (RT-PCR) technique.

Results: The administration of AST reduced the oligodendrocyte damage and myelin sheath disruption in a rat model of MS. The basket behavioral test showed the improvement of muscle strength in the AST group compared with CPZ and sham

groups. Besides, the results of real-time PCR and IHC indicated the beneficial effects of AST in declining demyelination and oligodendrocyte death in a rat model of MS.

Conclusion: AST reduces damages to the myelin sheath and oligodendrocyte death in a rat model of MS.

Astaxanthin shows therapeutic potential for salivary secretion in human clinical trial and reduces the level of an oxidative stress marker in the subjects' saliva.

[J Clin Biochem Nutr.](#) 2010 Sep;47(2):130-7. Epub 2010 Jun 22.

Evaluation of therapeutic effects of astaxanthin on impairments in salivary secretion.

[Yamada T](#), [Ryo K](#), [Tai Y](#), [Tamaki Y](#), [Inoue H](#), [Mishima K](#), [Tsubota K](#), [Saito I](#).

Source

Department of Pathology, Tsurumi University School of Dental Medicine, 2-1-3, Tsurumi, Tsurumi-ku, Yokohama 230-8501, Japan.

Abstract

The involvement of reactive oxygen species (ROS) in the pathophysiology of Sjögren's syndrome (SS), an autoimmune disorder, and irradiation-induced impairments in salivary secretion has been reported. Meanwhile, the strong antioxidant astaxanthin (Ast) has been suggested to have therapeutic effects on various diseases. In the present study, we examined the ROS scavenging capacity of Ast using a human salivary gland epithelial cell line (HSY) and investigated the effects of Ast on salivary secretion in a mouse model of irradiation-induced salivary gland dysfunction. Furthermore, we performed a clinical study of Ast in six SS patients and six normal individuals, quantifying the volume of saliva secretion and the level of oxidative stress markers in the saliva. Ast partially suppressed hydrogen peroxide-induced ROS in HSY cells. The mouse model demonstrated that the pre-administration of Ast resulted in the suppression of irradiation-induced hyposalivation. Furthermore, the administration of Ast appeared to increase salivary output in both the SS and normal groups. The level of oxidative stress marker, hexanoyl-lysine, in the saliva was reduced after Ast intake. These results suggest that Ast might act as an ROS scavenger, providing benefits to SS patients with impaired salivary secretion.

PMID: 20838568 [PubMed]

PMCID: PMC2935153

Natural Astaxanthin 90 times stronger than Synthetic Astaxanthin in intracellular antioxidant activity.

[Mar Drugs](#). 2015 May 7;13(5):2857-74. doi: 10.3390/md13052857.

Astaxanthin from *Haematococcus pluvialis* Prevents Oxidative Stress on Human Endothelial Cells without Toxicity.

[Régnier P](#)¹, [Bastias J](#)², [Rodriguez-Ruiz V](#)³, [Caballero-Casero N](#)⁴, [Caballo C](#)⁵, [Sicilia D](#)⁶, [Fuentes A](#)⁷, [Maire M](#)⁸, [Crepin M](#)⁹, [Letourneur D](#)¹⁰, [Guequen V](#)¹¹, [Rubio S](#)¹², [Pavon-Djavid G](#)¹³.

Author information

Abstract

Astaxanthin, a powerful antioxidant, is a good candidate for the prevention of intracellular oxidative stress. The aim of the study was to compare the antioxidant activity of astaxanthin present in two natural extracts from *Haematococcus pluvialis*, a microalgae strain, with that of synthetic astaxanthin. Natural extracts were obtained either by solvent or supercritical extraction methods. UV, HPLC-DAD and (HPLC-(atmospheric pressure chemical ionization (APCI)+)/ion trap-MS) characterizations of both natural extracts showed similar compositions of carotenoids, but different percentages in free astaxanthin and its ester derivatives. The Trolox equivalent antioxidant capacity (TEAC) assay showed that natural extracts containing esters displayed stronger antioxidant activities than free astaxanthin. Their antioxidant capacities to inhibit intracellular oxidative stress were then evaluated on HUVEC cells. The intracellular antioxidant activity in natural extracts was approximately 90-times higher than synthetic astaxanthin (5 μM). No modification, neither in the morphology nor in the viability, of vascular human cells was observed by in vitro biocompatibility study up to 10 μM astaxanthin concentrations. Therefore, these results revealed the therapeutic potential of the natural extracts in vascular human cell protection against oxidative stress without toxicity, which could be exploited in prevention and/or treatment of cardiovascular diseases.

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PMCID: [PMC4446609](#)

DOI: [10.3390/md13052857](#)

[PubMed - indexed for MEDLINE]

[Free PMC Article](#)

Natural Astaxanthin superior to Synthetic in prolonging the life of investigational worms by reducing reactive oxygen species more effectively.

[J Food Sci.](#) 2016 Sep;81(9):H2280-7. doi: 10.1111/1750-3841.13417. Epub 2016 Aug 16.

Mechanism of Different Stereoisomeric Astaxanthin in Resistance to Oxidative Stress in *Caenorhabditis elegans*.

[Liu X¹](#), [Luo Q²](#), [Cao Y²](#), [Goulette T³](#), [Liu X³](#), [Xiao H⁴](#).

Author information

Abstract

As a potent antioxidant in human diet, astaxanthin (AST) may play important roles in alleviating oxidative stress-driven adverse physiological effects. This study examined the effects of different stereoisomers of AST in protecting *Caenorhabditis elegans* from chemically induced oxidative stress. Three stereoisomers of AST investigated herein included 3S,3'S (S) AST, 3R,3'R (R) AST, and a statistical mixture (S: meso: R = 1:2:1) (M) AST. Under paraquat-induced oxidative conditions, all three types of AST significantly enhanced survival rate of *C. elegans*. The accumulation levels of ROS in the worms were reduced by 40.12%, 30.05%, and 22.04% by S, R, and M AST, respectively ($P < 0.05$). Compared with R and M AST, S significantly enhanced the expression levels of SOD-3. The results of RNA-Seq analysis demonstrated that AST protected *C. elegans* from oxidative damage potentially by modulating genes involved in the insulin/insulin-like growth factor (IGF) signaling (IIS) pathway and the oxidoreductase system. It is noteworthy that different stereoisomers of AST showed different effects on the expression levels of various genes related with oxidative stress. This study revealed important information on the *in vivo* antioxidative effects of AST stereoisomers, which might provide useful information for better utilization of AST.

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KEYWORDS:

Caenorhabditis elegans; RNA-seq; astaxanthin; oxidative stress; stereoisomeric

PMID:

27527357

DOI: [10.1111/1750-3841.13417](https://doi.org/10.1111/1750-3841.13417)

[PubMed - in process]

Astaxanthin prevents lipid and protein oxidation and increases the activity of antioxidant enzymes in human cells.

[Phytother Res.](#) 2009 Jun 22. [Epub ahead of print]

Cytoprotective role of astaxanthin against glycated protein/iron chelate-induced toxicity in human umbilical vein endothelial cells.

[Nishigaki I](#), [Rajendran P](#), [Venugopal R](#), [Ekambaram G](#), [Sakthisekaran D](#), [Nishigaki Y](#).

NPO International Laboratory of Biochemistry, 1-166 Uchide, Nakagawa-ku Nagoya 454-0926, Japan.

Astaxanthin (ASX), a red carotenoid pigment with no pro-vitamin A activity, is a biological antioxidant that occurs naturally in a wide variety of plants, algae and seafoods. This study investigated whether ASX could inhibit glycated protein/iron chelate-induced toxicity in human umbilical-vein endothelial cells (HUVEC) by interfering with ROS generation in these cells. Glycated fetal bovine serum (GFBS) was prepared by incubating fetal bovine serum (FBS) with high-concentration glucose. Stimulation of cultured HUVECs with 50 mm 1 mL of GFBS significantly enhanced lipid peroxidation and decreased antioxidant enzyme activities and levels of phase II enzymes. However, preincubation of the cultures with ASX resulted in a marked decrease in the level of lipid peroxide (LPO) and an increase in the levels of antioxidant enzymes in an ASX concentration-dependent manner. These results demonstrate that ASX could inhibit LPO formation and enhance the antioxidant enzyme status in GFBS/iron chelate-exposed endothelial cells by suppressing ROS generation, thereby limiting the effects of the AGE-RAGE interaction. The results indicate that ASX could have a beneficial role against glycated protein/iron chelate-induced toxicity by preventing lipid and protein oxidation and increasing the activity of antioxidant enzymes.

PMID: 19548280 [PubMed - as supplied by publisher]

Astaxanthin improves liver oxidative stress in diabetic rats.

[Pharmacol Rep.](#) 2015 Apr;67(2):310-6. doi: 10.1016/j.pharep.2014.09.012. Epub 2014 Oct 7.

Ability of natural astaxanthin from shrimp by-products to attenuate liver oxidative stress in diabetic rats.

[Sila A¹](#), [Kamoun Z²](#), [Ghliissi Z³](#), [Makni M²](#), [Nasri M⁴](#), [Sahnoun Z³](#), [Nedjar-Arroume N⁵](#), [Bougatef A⁶](#).

Author information

Abstract

BACKGROUND:

Reactive oxygen species play a crucial role in the pathogenesis of diabetes and its complications. The present study was undertaken, in vivo, to examine the protective effect of astaxanthin extracted from the shell waste of deep-water pink shrimp (*Parapenaeus longirostris*) against oxidative stress of alloxanic adult male rats.

RESULTS:

Alloxan treatment revealed a significant elevation in plasma glycemia and lipid parameters such as total lipid, total cholesterol and triglycerides compared to the control group (C). In addition, liver malonaldehyde levels (MDA), an index of lipid peroxidation, significantly increased compared to control group. The activities of antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx) and glutathione reductase (GR) and reduced glutathione (GSH) levels decreased significantly compared to control group. Moreover, diabetic rats presented a significant increase in the activities of aspartate transaminase (AST) alanine transaminase (ALT) and alkaline phosphatase (ALP) in plasma, indicating considerable hepatocellular injury. Astaxanthin treatment restores these parameters near to control values. Histological studies on the liver tissue of alloxan and astaxanthin treated rats confirmed the protective effects of astaxanthin.

CONCLUSIONS:

The results revealed that astaxanthin may be helpful in preventing diabetic complications in adult rats by reversing hepatotoxicity. It can be one of the ingredients in a number of healthy products.

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KEYWORDS:

Astaxanthin; Diabetes; Liver; Oxidative stress; Rats

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25712656

[PubMed - in process]

ASTAXANTHIN'S MECHANISM FOR PREVENTING MITOCHONDRIAL DYSFUNCTION ELICITED IN CELL STUDY.

Eur J Pharmacol 2021 Oct 5;908:174336. doi: 10.1016/j.ejphar.2021.174336. Epub 2021 Jul 13.

Astaxanthin prevents mitochondrial impairment in the dopaminergic SH-SY5Y cell line exposed to glutamate-mediated excitotoxicity: Role for the Nrf2/HO-1/CO-BR axis

[Flávia Bittencourt Brasil](#)¹, [Fhelipe Jolner Souza de Almeida](#)², [Matheus Dargesso Luckachaki](#)³, [Evandro Luiz Dall'Oglio](#)³, [Marcos Roberto de Oliveira](#)⁴

- PMID: 34265290 DOI: [10.1016/j.ejphar.2021.174336](https://doi.org/10.1016/j.ejphar.2021.174336)

Abstract

Mitochondrial dysfunction has been viewed in several diseases, including neurological disorders. In the glutamate (GLU)-mediated excitotoxicity, it has been described mitochondrial impairment, disrupted redox environment, and increased rates of cell death in the affected brain areas. Astaxanthin (AST) is a potent antioxidant and anti-inflammatory xanthophyll that also promotes beneficial mitochondria-related effects in brain cells. However, it is not completely clear how AST would be able to promote mitochondrial protection in those cell types. Thus, we investigated here how AST would protect mitochondria in the dopaminergic SH-SY5Y cell line exposed to GLU. AST was administrated to the cells at 1-40 μ M for 24 h prior to the exposure to GLU at 80 mM for additional 24 h. AST prevented the GLU-induced impairment in the activity of the Complexes I and V, the loss in mitochondrial membrane potential (MMP), and the decline in the synthesis of ATP. AST also induced an antioxidant effect in the membranes of mitochondria obtained from the GLU-treated SH-SY5Y cells. Inhibition of the enzyme heme oxygenase-1 (HO-1) or silencing of the transcription factor nuclear factor erythroid 2-related factor 2 (Nrf2) suppressed the AST-promoted cellular and mitochondrial protection. Either tricarbonyldichlororuthenium(II) dimer (CORM-2, a source of carbon monoxide - CO) or bilirubin (BR), that are products of the HO-1-biliverdin reductase (BVR) axis, blocked some of the effects caused by GLU in the SH-SY5Y cells. Overall, our data demonstrate that AST prevented mitochondrial dysfunction by a mechanism related to the Nrf2/HO-1 axis in GLU-challenged cells.

Astaxanthin shows anti-aging effects in fruit flies under oxidative stress.

[J Agric Food Chem](#). 2013 Aug 14;61(32):7800-4. doi: 10.1021/jf402224w. Epub 2013 Aug 6.

Antiaging effects of astaxanthin-rich alga *Haematococcus pluvialis* on fruit flies under oxidative stress.

[Huangfu J¹](#), [Liu J](#), [Sun Z](#), [Wang M](#), [Jiang Y](#), [Chen ZY](#), [Chen F](#).

Author information

Abstract

The microalga *Haematococcus pluvialis* (HP) is the best natural producer of astaxanthin (AX), which is a potent antioxidant with broad health benefits. The present study investigated the antiaging potential of HP biomass using the fruit fly *Drosophila melanogaster* as the animal model. The results showed that in wild-type flies the treatment of HP induced the early mortality at a concentration of 20 mg/mL, which was associated with the decreased enzymatic activities of CuZn-superoxide dismutase (SOD1) and Mn-superoxide dismutase (SOD2) as well as the down-regulation of SOD1, SOD2, and catalase (CAT) at the transcriptional level. In SOD(n108) mutant flies, the supplementation of HP (10 or 20 mg/mL) significantly extended their lifespan and ameliorated the age-related decline in locomotor function. Further studies suggested that HP may play a role as a complement to the defective endogenous antioxidant system to exert such lifespan elongation effects. These results, taken together, strongly support the antiaging properties of HP and its therapeutic rather than preventive potential against aging-related diseases.

PMID:

23879808

[PubMed - indexed for MEDLINE]

Astaxanthin and Vitamin C shown in-vitro that they may be helpful to improve the immune function of patients with exacerbated production of reactive oxygen species.

[Int Immunopharmacol.](#) 2012 Dec;14(4):690-7. doi: 10.1016/j.intimp.2012.10.003. Epub 2012 Oct 17.

Changes in lymphocyte oxidant/antioxidant parameters after carbonyl and antioxidant exposure.

[Bolin AP](#)¹, [Guerra BA](#), [Nascimento SJ](#), [Otton R](#).

Author information

Abstract

During normal B- and T-cell life, processes including activation, proliferation, signaling pathways and apoptosis are markedly dependent on ROS generation. However, these cells can also suffer the effect of oxidant overproduction. Thus, the purpose of the present study was to examine the possible pro-oxidant effects of MGO/high glucose and antioxidant effects of astaxanthin associated with vitamin C on some oxidative and antioxidant parameters of human lymphocytes in vitro. Lymphocytes from healthy subjects were treated with 20mM of glucose and 30 μ M MGO followed or not by the addition of the antioxidants astaxanthin (2 μ M) and vitamin C (100 μ M) for up to 24h. We examined superoxide dismutase (SOD), catalase, glutathione peroxidase, glutathione reductase, and glucose-6-phosphate dehydrogenase (G6PDH) activities, GSH/GSSG ratio and total thiol and carbonyl content. Oxidative parameters included superoxide anion, hydrogen peroxide and nitric oxide production. The association of astaxanthin and vitamin C proved to be a powerful antioxidant in human lymphocytes as showed by the marked reduction in superoxide anion, and hydrogen peroxide production as well as increased GSH content, GSH/GSSG ratio, GPx and GR activities. The antioxidant association showed to be more potent than their individual application. High glucose and methylglyoxal did not promote oxidative stress in human lymphocytes, since neither the oxidative parameters nor the antioxidant defense system was altered. According to these results, new therapies with the association of astaxanthin and vitamin C may be helpful to improve the immune function of patients with exacerbated production of ROS.

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PMID:

23085288

[PubMed - indexed for MEDLINE]

Free full text

Astaxanthin may prevent age-related decrease in saliva secretion and decreases oxidative stress in aging mice.

[J Clin Biochem Nutr.](#) 2016 Sep;59(2):79-85. Epub 2016 Jul 16.

Astaxanthin affects oxidative stress and hyposalivation in aging mice.

[Kuraji M](#)¹, [Matsuno T](#)¹, [Sato T](#)¹.

Author information

Abstract

Oral dryness, a serious problem for the aging Japanese society, is induced by aging-related hyposalivation and causes dysphagia, dysgeusia, inadaptation of dentures, and growth of oral *Candida albicans*. Oxidative stress clearly plays a role in decreasing saliva secretion and treatment with antioxidants such as astaxanthin supplements may be beneficial. Therefore, we evaluated the effects of astaxanthin on the oral saliva secretory function of aging mice. The saliva flow increased in astaxanthin-treated mice 72 weeks after administration while that of the control decreased by half. The plasma d-ROMs values of the control but not astaxanthin-treated group measured before and 72 weeks after treatment increased. The diacron-reactive oxygen metabolites (d-ROMs) value of astaxanthin-treated mice 72 weeks after treatment was significantly lower than that of the control group was. The plasma biological antioxidative potential (BAP) values of the control but not astaxanthin-treated mice before and 72 weeks after treatment decreased. Moreover, the BAP value of the astaxanthin-treated group 72 weeks after treatment was significantly higher than that of the control was. Furthermore, the submandibular glands of astaxanthin-treated mice had fewer inflammatory cells than the control did. Specifically, immunofluorescence revealed a significantly large aquaporin-5 positive cells in astaxanthin-treated mice. Our results suggest that astaxanthin treatment may prevent age-related decreased saliva secretion.

KEYWORDS:

aquaporin-5; astaxanthin; hyposalivation; inflammation; oral dryness

PMID: 27698533

PMCID: [PMC5018570](#)

DOI: [10.3164/jcbn.15-150](#) PubMed - in process]

Free PMC Article

Astaxanthin has a neuroprotective effect in rat ganglion cells subjected to oxidative stress and other insults.

[Mol Vis.](#) 2014 Dec 31;20:1796-805. eCollection 2014.

Neuroprotective effect of astaxanthin against rat retinal ganglion cell death under various stresses that induce apoptosis and necrosis.

[Yamaqishi R](#)¹, [Aihara M](#)².

Author information

Abstract

PURPOSE:

Astaxanthin is a type of carotenoid known to have strong antioxidant effects. The purpose of this study was to investigate whether astaxanthin confers a neuroprotective effect against glutamate stress, oxidative stress, and hypoxia-induced apoptotic or necrotic cell death in primary cultures of rat retinal ganglion cells (RGCs).

METHODS:

Purified rat RGCs were exposed to three kinds of stressors induced by 25 μ M glutamate for 72 h, B27 medium without an antioxidant for 4 h, and a reduced oxygen level of 5% for 12 h. Each assay was repeated 12 times, with or without 1 nM, 10 nM, and 100 nM astaxanthin. The number of live RGCs was then counted using a cell viability assay. RGC viability in each condition was evaluated and compared with controls. In addition, we measured apoptosis and DNA damage.

RESULTS:

We found that under glutamate stress, RGC viability was reduced to 58%. Cultures with 1 nM, 10 nM, and 100 nM astaxanthin showed an increase in RGC viability of 63%, 74%, and 84%, respectively. Under oxidative stress, RGC viability was reduced to 40%, and astaxanthin administration resulted in increased viability of 43%, 50%, and 67%, respectively. Under hypoxia, RGC viability was reduced to 66%, and astaxanthin administration resulted in a significant increase in viability to 67%, 77%, and 93%, respectively. These results indicate that 100 nM astaxanthin leads to a statistically significant increase in RGC viability under the three kinds of stressors tested, compared to controls (Dunnett's test, $p < 0.05$). The apoptotic activity of RGCs under glutamate stress increased to 32%, but was reduced to 15% with 100 nM astaxanthin administration. Glutamate stress led to a 58% increase in DNA damage, which was reduced to 43% when cultured with 100 nM astaxanthin. Thus, 100 nM astaxanthin showed a statistically significant reduction in apoptosis and DNA damage in RGCs (Wilcoxon rank-sum test, $p < 0.05$).

CONCLUSIONS:

Our results suggest that astaxanthin has a neuroprotective effect against RGC death induced by glutamate stress, oxidative stress, and hypoxia, which induce apoptotic and necrotic cell death.

PMID:

25593507 [PubMed - in process] PMID: PMC4287717

[Free PMC Article](#)

Astaxanthin inhibits colonic lesions in mice in obesity-related colorectal carcinogenesis model by reducing oxidative stress and reducing chronic inflammation.

[BMC Gastroenterol.](#) 2014 Dec 17;14:212. doi: 10.1186/s12876-014-0212-z.

Inhibitory effects of astaxanthin on azoxymethane-induced colonic preneoplastic lesions in C57/BL/KsJ-db/db mice.

[Kochi T](#)¹, [Shimizu M](#)², [Sumi T](#)³, [Kubota M](#)⁴, [Shirakami Y](#)⁵, [Tanaka T](#)⁶, [Moriwaki H](#)⁷.

Author information

Abstract

BACKGROUND:

Obesity and related metabolic abnormalities, including excess oxidative stress and chronic inflammation, are associated with colorectal carcinogenesis. Astaxanthin, a xanthophyll carotenoid found in aquatic animals, is known to possess antioxidant, anti-inflammatory, and antineoplastic properties. The present study examined the effects of astaxanthin on the development of azoxymethane (AOM)-induced colonic premalignant lesions in C57BL/KsJ-db/db (db/db) obese mice.

METHOD:

Male db/db mice were administered 4 weekly subcutaneous injections of AOM (15 mg/kg body weight) from 5 weeks of age and subsequently, from 1 week after the last injection of AOM, were fed a diet containing 200 ppm astaxanthin throughout the experiment (8 weeks).

RESULT:

The development of colonic premalignant lesions, i.e., aberrant crypt foci and β -catenin accumulated crypts, was significantly inhibited in mice treated with astaxanthin than in mice fed the basal diet. Astaxanthin administration markedly reduced urinary levels of 8-OHdG and serum levels of d-ROMs, which are oxidative stress markers, while increasing the expression of mRNA for the antioxidant enzymes GPx1, SOD1, and CAT in the colonic mucosa of AOM-treated db/db mice. The expression levels of IL-1 β , IL-6, F4/80, CCL2, and CXCL2 mRNA in the colonic mucosa of AOM-treated mice were significantly decreased by astaxanthin. Dietary feeding with astaxanthin also resulted in a reduction in the numbers of NF- κ B- and PCNA-positive cells that were increased by AOM exposure, in the colonic epithelium.

CONCLUSION:

These findings suggest that astaxanthin inhibits the development of colonic premalignant lesions in an obesity-related colorectal carcinogenesis model by reducing oxidative stress, attenuating chronic inflammation, and inhibiting NF- κ B activation and cell proliferation in the colonic mucosa. Astaxanthin, therefore, may be a potential candidate as a chemoprevention agent against colorectal carcinogenesis in obese individuals.

PMID: 25515685

[PubMed - indexed for MEDLINE]

PMCID: PMC4273491

[Free PMC Article](#)

Astaxanthin increases endurance and limits oxidative stress in mice during exercise.

[Nutrients](#). 2014 Dec 12;6(12):5819-38. doi: 10.3390/nu6125819.

Astaxanthin supplementation delays physical exhaustion and prevents redox imbalances in plasma and soleus muscles of Wistar rats.

[Polotow TG](#)¹, [Vardaris CV](#)², [Mihaliuc AR](#)³, [Gonçalves MS](#)⁴, [Pereira B](#)⁵, [Ganini D](#)⁶, [Barros MP](#)⁷.

Author information

Abstract

Astaxanthin (ASTA) is a pinkish-orange carotenoid commonly found in marine organisms, especially salmon. ASTA is a powerful antioxidant and suggested to provide benefits for human health, including the inhibition of LDL oxidation, UV-photoprotection, and prophylaxis of bacterial stomach ulcers. Exercise is associated to overproduction of free radicals in muscles and plasma, with pivotal participation of iron ions and glutathione (GSH). Thus, ASTA was studied here as an auxiliary supplement to improve antioxidant defenses in soleus muscles and plasma against oxidative damage induced by exhaustive exercise. Long-term 1 mg ASTA/kg body weight (BW) supplementation in Wistar rats (for 45 days) significantly delayed time to exhaustion by 29% in a swimming test. ASTA supplementation increased scavenging/iron-chelating capacities (TEAC/FRAP) and limited exercise-induced iron overload and its related pro-oxidant effects in plasma of exercising animals. On the other hand, ASTA induced significant mitochondrial Mn-dependent superoxide dismutase and cytosolic glutathione peroxidase antioxidant responses in soleus muscles that, in turn, increased GSH content during exercise, limited oxidative stress, and delayed exhaustion. We also provided significant discussion about a putative "mitochondrial-targeted" action of ASTA based on previous publications and on the positive results found in the highly mitochondrial populated (oxidative-type) soleus muscles here.

PMID:

25514562

[PubMed - in process]

PMCID:

PMC4277001

[Free PMC Article](#)

Astaxanthin effective in free radical scavenging and protects against nitrite stress in shrimp.

[J Agric Food Chem](#). 2014 Dec 24;62(51):12326-31. doi: 10.1021/jf503754q. Epub 2014 Dec 10.

Effect of dietary astaxanthin on free radical scavenging capacity and nitrite stress tolerance of postlarvae shrimp, *Pleoticus muelleri*.

[Díaz AC¹](#), [Velurtas SM](#), [Espino ML](#), [Fenucci JL](#).

Author information

Abstract

The aim of this study was to investigate the effect of astaxanthin feed supplementation and environmental nitrite stress in postlarvae of *Pleoticus muelleri* (15 ± 0.004 mg initial weight) under culture conditions. Diets containing three levels of astaxanthin, 0 mg kg⁻¹ of diet (C0), 100 mg kg⁻¹ of diet (C(100)), and 300 mg kg⁻¹ of diet (C(300)), were used. Postlarvae fed with each diet were exposed to different concentrations of nitrite (NO(2)Na) (0-200 mg L⁻¹). The 96 h median lethal concentration (LC50) values of nitrite N were 76.3, 89.7, and 157 mg L⁻¹ for shrimps fed to C0, C(100), and C(300). The scavenging properties were evaluated against the stable 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical by electron resonance spectroscopy (EPR). For all feed treatments, the extracts exhibited strong DPPH scavenging activity; however, shrimp fed with C(100) and C(300) showed the greatest activity to quench DPPH (62 and 59%, respectively) with respect to C0 (43%). It can be concluded that astaxanthin acts as a protector of nitrite stress in *P. muelleri*.

KEYWORDS:

Pleoticus muelleri; astaxanthin; histopathology; nitrite; scavenging capacity

PMID:

25427235

[PubMed - indexed for MEDLINE]

Astaxanthin inhibits apoptosis in-vivo and in-vitro due to its antioxidant activity and may be of therapeutic value in lung fibrosis treatment.

[J Cell Mol Med.](#) 2014 Nov;18(11):2198-212. doi: 10.1111/jcmm.12347. Epub 2014 Sep 12.

Astaxanthin inhibits apoptosis in alveolar epithelial cells type II in vivo and in vitro through the ROS-dependent mitochondrial signalling pathway.

[Song X¹](#), [Wang B](#), [Lin S](#), [Jing L](#), [Mao C](#), [Xu P](#), [Lv C](#), [Liu W](#), [Zuo J](#).

Author information

Abstract

Oxidative stress is an important molecular mechanism underlying lung fibrosis. The mitochondrion is a major organelle for oxidative stress in cells. Therefore, blocking the mitochondrial signalling pathway may be the best therapeutic manoeuvre to ameliorate lung fibrosis. Astaxanthin (AST) is an excellent antioxidant, but no study has addressed the pathway of AST against pulmonary oxidative stress and free radicals by the mitochondrion-mediated signalling pathway. In this study, we investigated the antioxidative effects of AST against H₂O₂ - or bleomycin (BLM)-induced mitochondrial dysfunction and reactive oxygen species (ROS) production in alveolar epithelial cells type II (AECs-II) in vivo and in vitro. Our data show that AST blocks H₂O₂ - or BLM-induced ROS generation and dose-dependent apoptosis in AECs-II, as characterized by changes in cell and mitochondria morphology, translocation of apoptotic proteins, inhibition of cytochrome c (Cyt c) release, and the activation of caspase-9, caspase-3, Nrf-2 and other cytoprotective genes. These data suggest that AST inhibits apoptosis in AECs-II cells through the ROS-dependent mitochondrial signalling pathway and may be of potential therapeutic value in lung fibrosis treatment.

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KEYWORDS:

ROS; astaxanthin; lung fibrosis; mitochondrial signalling pathway; oxidative stress

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25215580

[PubMed - indexed for MEDLINE]

PMCID:

PMC4224554

Free PMC Article

Astaxanthin improves age-associated changes of vocal folds in rats which may be due to its ability to prevent reactive oxygen species-induced diseases.

[Laryngoscope](#). 2014 Oct;124(10):E411-7. doi: 10.1002/lary.24733. Epub 2014 May 27.

Effect of AST on age-associated changes of vocal folds in a rat model.

[Mizuta M¹](#), [Hirano S](#), [Hiwatashi N](#), [Kobayashi T](#), [Tateya I](#), [Kanemaru S](#), [Nakamura T](#), [Ito J](#).

Author information

Abstract

OBJECTIVES/HYPOTHESIS:

Reactive oxygen species (ROS) are associated with aging. Astaxanthin (AST) is a strong antioxidant and has been reported to prevent various ROS-induced diseases. In the current study, we investigated the effect of AST on age-associated histological and mRNA changes of vocal folds.

STUDY DESIGN:

Prospective animal experiment with control.

METHODS:

Six-month-old Sprague-Dawley rats were fed on a normal powder diet with 0.01% (w/w) AST (aged AST-treated group) or without AST (aged sham-treated group). After 12 months of feeding, the larynges were harvested for histology, immunohistochemical detection of 4-hydroxy-2-nonenal (4-HNE), and quantitative real-time polymerase chain reaction for basic fibroblast growth factor (bFGF) and hepatocyte growth factor (HGF). Thirteen-week-old rats were used as a young control group (young group).

RESULTS:

The expression of 4-HNE, an oxidative stress marker, significantly increased in the two aged groups compared with the young group. Histological examination showed that the deposition of hyaluronic acid in the lamina propria (LP) was significantly reduced in the aged sham-treated group compared with the young group, but no significant difference was observed between the aged AST-treated group and the young group. There were no significant differences in the mRNA expression of bFGF and HGF between the aged AST-treated group and the young group, although the expression of these genes was significantly reduced in the aged sham-treated group as compared with the young group.

CONCLUSIONS:

These results suggest that AST has the potential to attenuate age-associated changes of vocal folds.

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KEYWORDS:

AST; age-associated changes; reactive oxygen species; vocal folds

PMID:

24764173

[PubMed - indexed for MEDLINE]

Astaxanthin protects against light-induced retinal damage in mice via the mechanism of its antioxidant effect.

[J Pharmacol Sci.](#) 2013;123(3):209-18. Epub 2013 Oct 22.

Protective effects of a dietary carotenoid, astaxanthin, against light-induced retinal damage.

[Otsuka T¹](#), [Shimazawa M](#), [Nakanishi T](#), [Ohno Y](#), [Inoue Y](#), [Tsuruma K](#), [Ishibashi T](#), [Hara H](#).

Author information

Abstract

Dietary carotenoids exhibit various biological activities, including antioxidative activity. In particular, astaxanthin, a type of carotenoid, is well known as a powerful antioxidant. We investigated whether astaxanthin would protect against light-induced retinal damage. In an in vivo study, ddY male mice were exposed to white light at 8,000 lux for 3 h to induce retinal damage. Five days after light exposure, retinal damage was evaluated by measuring electroretinogram (ERG) amplitude and outer nuclear layer (ONL) thickness. Furthermore, expression of apoptotic cells, 8-hydroxy-deoxyguanosine (8-OHdG), was measured. In an in vitro study, retinal damage was induced by white light exposure at 2,500 lux for 24 h, and propidium iodide (PI)-positive cells was measured and intracellular reactive oxygen species (ROS) activity was examined. Astaxanthin at 100 mg/kg inhibited the retinal dysfunction in terms of ERG and ONL loss and reduced the expression of apoptotic and 8-OHdG-positive cells induced by light exposure. Furthermore, astaxanthin protected against increases of PI-positive cells and intracellular reactive oxygen species (ROS) activity in 661W cells. These findings suggest that astaxanthin has protective effects against light-induced retinal damage via the mechanism of its antioxidative effect.

PMID:

24152963

[PubMed - indexed for MEDLINE]

Free full text

Astaxanthin shows anti-inflammatory, anti-coagulatory and antioxidant effects in diabetic rats.

[J Food Sci.](#) 2012 Feb;77(2):H76-80. doi: 10.1111/j.1750-3841.2011.02558.x. Epub 2012 Feb 6.

Anticoagulatory and antiinflammatory effects of astaxanthin in diabetic rats.

[Chan KC¹](#), [Pen PJ](#), [Yin MC](#).

Author information

Abstract

Astaxanthin at 0.01 or 0.05% of the diet was supplied to diabetic rats for 12 wk. Astaxanthin intake significantly increased its deposit in plasma, and retained glutathione content, reduced the production of reactive oxygen species, interleukin-6, tumor necrosis factor- α , and monocyte chemoattractant protein-1 in blood and kidney of diabetic rats ($P < 0.05$). Astaxanthin treatments also significantly decreased plasma levels of C-reactive protein and von Willebrand factor in diabetic rats ($P < 0.05$). Astaxanthin intake at 0.05% significantly diminished plasminogen activator inhibitor-1 and factor VII activities, enhanced antithrombin-III and protein C activities in circulation ($P < 0.05$). These results support that astaxanthin could attenuate diabetes associated coagulatory, oxidative, and inflammatory stress.

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PMID:

22309505

[PubMed - indexed for MEDLINE]

Astaxanthin inhibits thrombosis in cerebral vessels of stroke prone, hypertensive rats which may be attributed to decreased inactivation of nitric oxide by reactive oxygen species.

[Nutr Res.](#) 2011 Oct;31(10):784-9. doi: 10.1016/j.nutres.2011.09.010.

Astaxanthin inhibits thrombosis in cerebral vessels of stroke-prone spontaneously hypertensive rats.

[Sasaki Y¹](#), [Kobara N](#), [Higashino S](#), [Giddings JC](#), [Yamamoto J](#).

Author information

Abstract

It is known that vitamin E and some carotenoids have antioxidant activities that alleviate endothelial dysfunction and play a protective role against cardiovascular disease. The current study was designed to examine the hypothesis that astaxanthin, a red pigment carotenoid found in salmonid and crustacean aquaculture, protects stroke-prone spontaneously hypertensive rats (SHRSP) from vascular oxidative damage, hypertension, and cerebral thrombosis. Male 6-week-old SHRSP were classified into 4 groups: a control group, 2 astaxanthin groups, and a vitamin E group. The treated animals were given either astaxanthin or vitamin E for 3 weeks. Body weights in each group were not significantly different from control group during the treatment period, but the usual increase in systolic blood pressure in SHRSP observed with age was significantly suppressed by treatment. Thrombogenesis, assessed using a helium-neon (He-Ne) laser technique in pial blood vessels, together with antioxidant activity, assessed by measuring urinary 8-OHdG levels, were significantly moderated. Urinary nitric oxide (NO) metabolites were increased after treatment. These results supported our hypothesis and strongly suggested that the antithrombotic and antihypertensive effects of astaxanthin or vitamin E may be related to an increase in bioavailable NO, possibly mediated by decreased inactivation of NO by reactive oxygen species.

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PMID:

22074803

[PubMed - indexed for MEDLINE]

Astaxanthin may have protective effects against oxidative damage and DNA damage induced by gamma rays.

[Wei Sheng Yan Jiu](#). 2011 Sep;40(5):551-4.

[Protective effects of astaxanthin against oxidative damage induced by 60Co gamma-ray irradiation].

[Article in Chinese]

[Zhao W](#)¹, [Jing X](#), [Chen C](#), [Cui J](#), [Yang M](#), [Zhang Z](#).

Author information

Abstract

OBJECTIVE:

To investigate the protection effect of haematococcus pluvialis (containing astaxanthin) against the impairment of anti-oxidative system and DNA damage in mice induced by 60Co gamma-rays.

METHODS:

Fifty mice were randomly divided into five groups, i.e. three haematococcus pluvialis groups (41.7, 83.3 and 166.7 mg/kg in vegetable oil, respectively), control group and model group (vegetable oil only). All mice except control group were irradiated by 8 Gy 60Co gamma-rays 30 days later, and executed in the 4th day after irradiation. Liver cells were collected for the analysis of the integrity of DNA by comet assay, as well as MDA contents, SOD and GSH-Px activities in liver by commercial kits. Peripheral granulocyte and bone marrow nucleated cells were counted by hematocyte counter.

RESULTS:

MDA contents of model group were higher than those of control group ($P < 0.01$), and SOD, GSH-Px activities of model group were lower than those of control group ($P < 0.01$). Compared with the model group, MDA contents were decreased ($P < 0.01$), and SOD and GSH-Px activities were increased ($P < 0.01$) in all haematococcus pluvialis groups, especially in the high haematococcus pluvialis group, and the more haematococcus pluvialis in the diet of mice, the lower rate of comet tail and OTM value were shown ($P < 0.01$). Furthermore, the counts of peripheral granulocyte and bone marrow nucleated cells of model group were lower than those of the control group, while the counts of peripheral granulocyte and bone marrow nucleated cells of medium and high haematococcus pluvialis groups were increased significantly when compared with the model group ($P < 0.01$).

CONCLUSION:

Astaxanthin might have some protective effect against oxidative impairment and DNA damage induced by 60Co gamma-rays in mice.

PMID:

22043699

[PubMed - indexed for MEDLINE]

Astaxanthin more effective than other carotenoids as a neuroprotectant in rats due to its reactive oxygen species scavenging activities.

[Kaohsiung J Med Sci](#). 2013 Aug;29(8):412-21. doi: 10.1016/j.kjms.2012.12.002. Epub 2013 Feb 8.

Reactive oxygen species scavenging activities in a chemiluminescence model and neuroprotection in rat pheochromocytoma cells by astaxanthin, beta-carotene, and canthaxanthin.

[Chang CS](#)¹, [Chang CL](#), [Lai GH](#).

Author information

Abstract

The objective of this study was to determine chemiluminescence (CL) antioxidant activities and neuroprotective effects of astaxanthin, beta-carotene (β -carotene), and canthaxanthin on undifferentiated rat pheochromocytoma (PC12) cells. We performed three CL antioxidant assays, and the three carotenoids showed varying degrees of antioxidant activity, with astaxanthin exhibiting the highest antioxidant activity than the other two samples. Results of a pyrogallol-luminol assay revealed β -carotene to have higher antioxidant activity than canthaxanthin, whereas cupric sulfate-Phen-Vc-hydrogen peroxide (H_2O_2) assay showed canthaxanthin to have higher antioxidant activity than β -carotene. Luminol- H_2O_2 assay showed the antioxidant activity series as canthaxanthin > β -carotene at 62.5-1000 μ g/mL and β -carotene > canthaxanthin at 1000-4000 μ g/mL. Astaxanthin exhibited partial neuroprotective activity against H_2O_2 and the strongest neuroprotective activity against amyloid beta-peptide(25-35) [$A\beta$ (25-35)]-induced undifferentiated PC12 cell deaths at 0.5-5.0 μ M. Canthaxanthin showed partial neuroprotective activity in $A\beta$ (25-35)-induced undifferentiated PC12 cell deaths at 1.0-5.0 μ M. Astaxanthin protected undifferentiated PC12 cells from the damaging effects of H_2O_2 and $A\beta$ (25-35) by the following ways: (1) scavenging superoxide anion radicals, hydroxyl radicals, and H_2O_2 ; (2) securing cell viability; (3) suppressing the production of reactive oxygen species; and (4) eliminating calcium ion influx. Our results conclusively show that astaxanthin has the merit as a potential neuron protectant.

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KEYWORDS:

Astaxanthin; Canthaxanthin; Chemiluminescence antioxidant activity; Neuroprotective effect; β -carotene

Astaxanthin decreases blood flow time [increases blood flow] at 6mg per day in placebo-controlled human clinical trial.

[J Clin Biochem Nutr.](#) 2008 Sep;43(2):69-74. doi: 10.3164/jcfn.2008048.

Effects of astaxanthin on human blood rheology.

[Miyawaki H¹](#), [Takahashi J](#), [Tsukahara H](#), [Takehara I](#).

Author information

Abstract

Effects of astaxanthin (AX) derived from *H. pluvialis* on human blood rheology were investigated in 20 adult men with a single-blind method. The experimental group was 57.5 +/- 9.8 years of age and the placebo group was 50.8 +/- 13.1 years of age. A blood rheology test that measures whole blood transit time was conducted using heparinized blood of the volunteers by a MC-FAN apparatus (microchannel array flow analyzer). After administration of AX 6 mg/day for 10 days, the values of the experimental group were decreased from 52.8 +/- 4.9 s to 47.6 +/- 4.2 s ($p < 0.01$) and a comparison of the values between the experimental (47.6 +/- 4.2 s) and the placebo (54.2 +/- 6.7 s) groups showed a significant difference ($p < 0.05$). There were no adverse effects resulting from the administration of AX 6 mg/day for 10 days. Informed consent was obtained from each subject.

KEYWORDS:

astaxanthin; blood rheology; blood transit time; male volunteers; microchannel array flow analyzer

PMID:

18818755

[PubMed]

PMCID:

PMC2533721

[Free PMC Article](#)

Astaxanthin dose-dependently improves visual acuity and eye accommodation in human clinical trial.

Japanese Journal of Clinical Ophthalmology VOL.58;NO.6;PAGE.1051-1054(2004)

Changes in visual function following peroral astaxanthin

NAKAMURA AKIRA; ISOBE RYOKO; OTAKA YASUHIRO; ABEMATSU YASUKO; NAKATA DAISUKE; HONMA CHIKA ; SAKURAI SHIZUKA; SHIMADA YOSHIAKI; Horiguchi Masayuki

We evaluated the effect of astaxanthin on visual function in 49 eyes of 49 healthy volunteers. They were over 40 years of age. They were divided into 4 groups matched for age and gender. Each group was given peroral astaxanthin once a day. The dosage was 0mg, 2mg, 4mg, or 12mg for each group. After ingestion of astaxanthin for consecutive 28 days, the uncorrected far visual acuity significantly improved in groups receiving 4mg or 12mg. The accommodation time significantly shortened in groups receiving 4mg or 12mg. There was no change in refraction, flicker fusion frequency, or pupillary reflex.

Astaxanthin improves eye fatigue in double-blind, placebo-controlled randomized human clinical trial.

Journal of Clinical Therapeutics & Medicines VOL.22;NO.1;PAGE.41-54(2006)

The supplementation effect of Astaxanthin on Accommodation and Asthenopia

NAGAKI YASUNORI; MIHARA MIHARU; TSUKAHARA HIROKI; ONO SHIGEAKI

This double blind randomized placebo controlled study examined the supplementation effects of Haematococcus (H) pluvialis derived astaxanthin on subjects suffering from visual display terminal (VDT) induced visual fatigue. Subjects were divided into two groups: 6 mg astaxanthin treated and placebo groups. Furthermore, the safety of astaxanthin intake was simultaneously assessed. After the 4 week supplementation period, the groups' visual accommodation was evaluated as well as a subjective questionnaire designed to evaluate visual asthenopia (eye fatigue). Twenty five subjects of the astaxanthin treated group and 23 subjects of the placebo group were examined for eye fatigue. For safety evaluation, 31 treated subjects and 28 placebo subjects were analysed. We report the following observations: 1. In the astaxanthin treated group, the change of accommodation before and after supplementation significantly improved compared with the placebo group. 2. The astaxanthin supplemented group exhibited a significant rate of change in the accommodation compared with the placebo group. 3. The subjective questionnaire evaluating visual asthenopia revealed a marked reduction in "heavy head" claims. Other typical improvements of fatigue symptoms included "dimness of sight" and "stiff shoulders and back". 4. No significant differences were detected between the treatment and the placebo groups after 4 weeks of supplementation in the safety parameters analyzed, and adverse event. These results suggest that 6 mg of astaxanthin per day from a H. pluvialis algal extract can improve eye fatigue. Moreover, astaxanthin can be safely consumed at this level by healthy adults.

Astaxanthin increases retinal capillary blood flow in double-blind, placebo-controlled randomized human clinical trial.

Journal of Clinical Therapeutics & Medicines VOL.21;NO.5;PAGE.537-542(2005)

The Effect of Astaxanthin on Retinal Capillary Blood Flow in Normal Volunteers

NAGAKI YASUNORI; MIHARA MIHARU; TAKAHASHI JIRO; KITAMURA AKITOSHI; HORITA YOSHIHARU; SUGIURA YURI; TSUKAHARA HIROKI

Objective: We evaluated the effect of astaxanthin on retinal circulation in healthy volunteers. Design A double blind randomized placebo controlled study. Methods: Thirty-six volunteers were randomized into two groups: Astaxanthin group that consisted of 18 subjects who received oral astaxanthin, 6mg/day, for 4 weeks and a placebo group that consisted of 18 subjects who received an identical looking oral placebo for 4 weeks. Retinal capillary blood flow was measured by the Heidelberg Retina Flowmeter. Changes in blood pressure, blood cell counts, fasting plasma glucose level, fasting plasma astaxanthin level, retinal capillary blood flow, intraocular pressure, inquiry about eye strain were examined before and after supplementation in both groups. Results: The fasting plasma astaxanthin level in the astaxanthin group was significantly ($P<0.001$) higher than before supplementation. The fasting plasma astaxanthin level in the placebo group after placebo treatment remained unchanged. After 4 weeks supplementation, retinal capillary blood flow in the astaxanthin group was significantly ($P<0.01$) higher than before supplementation in both eyes, while retinal capillary blood flow in the placebo group after placebo treatment was unchanged. Intraocular pressures in both groups remained unchanged during the supplementation period. Conclusion: Our results suggest that astaxanthin supplementation may increase retinal capillary blood flow.

Astaxanthin improves eye strain and eye accommodation in double-blind, placebo-controlled human clinical study.

Journal of Clinical Therapeutics & Medicines VOL.21;NO.6;PAGE.637-650(2005)

Effect of Astaxanthin on Accommodation and Asthenopia-Efficacy-Identification Study in Healthy Volunteers-

SHIRATORI KENJI; OGAMI KAZUHIRO; NITTA TAKUYA; SHINMEI YASUHIRO; CHIN SHINKI; YOSHIDA KAZUHIKO; TSUKAHARA HIROKI; TAKEHARA ISAO; ONO SHIGEAKI

A double-blind study was conducted to confirm the efficacy of *H. pluvialis* Astaxanthin on accommodation and asthenopia and its safety. Two groups of subjects were compared, wherein one was given 0mg of Astaxanthin (as a control group) and the other was given 6mg of Astaxanthin (AX group). The subjects were healthy volunteers who complained of asthenopia. Twenty were enrolled in each group, and the testing food was administered during 4 weeks. Sub-objective accommodation power, positive accommodation time and negative accommodation time were measured before and after administration to objectively evaluate the degree of asthenopia. Additionally, subjective degree of asthenopia by volunteers was evaluated using VAS. The safety was assessed by changes in value of laboratory tests between pre- and post-administrations and by the doctor's questions. 1) Sub-objective accommodation power (rate of change) of the AX group was significantly higher than that of the control group. 2) The AX group showed significantly higher rate of positive and negative accommodation times (rate of change) compared to those of the control group. 3) In the AX group, subjective degree of asthenopia measured by VAS showed significant improvement in two parameters, i.e., "blar-eye feeling" and "tendency of irritation" than the control group. 4) No changes in laboratory tests of clinically controversial were noted and also no adverse events suggesting causal relationship with the testing food were found. In conclusion, administration of 6mg/day (in a daily dosage of 2 capsules; 3mg/capsule) of *H. pluvialis* Astaxanthin improved accommodation power and subjective symptoms of asthenopia. Also, Astaxanthin was confirmed to be completely safe.

Astaxanthin improves eye accommodative recovery and prevents eye fatigue in human clinical trial.

Journal of Clinical Therapeutics & Medicines VOL.21;NO.4;PAGE.431-436(2005)

Effects of Astaxanthin on Accommodative Recovery

TAKAHASHI NANAOKO (Kajitaganka) **KAJITA MASAYOSHI** (Kajitaganka)

Effects of astaxanthin on accommodative recovery derived from a rest after VDT (visual display terminal) working was studied. Ten healthy volunteers were entered into the study, and except one subject who developed allergic conjunctivitis during the study, 9 of whom were evaluated (9 dominant eyes) by values of objective diopter, HFC (High Frequency Component in Accommodative micro-fluctuation) and accommodative reaction. Consequently, increase of HFC after the rest was significantly restrained by astaxanthin uptake compared to that shortly after working. Therefore, Astaxanthin was suggested to have effects on accommodation during recovery process of accommodative fatigue to relieve fatigue rapidly.

Astaxanthin increases blood flow velocity in the vascular layer of the eye in a double-blind, placebo-controlled randomized human clinical trial.

[Graefes Arch Clin Exp Ophthalmol](#). 2012 Feb;250(2):239-45. doi: 10.1007/s00417-011-1843-1. Epub 2011 Nov 10.

Astaxanthin increases choroidal blood flow velocity.

[Saito M¹](#), [Yoshida K](#), [Saito W](#), [Fujiya A](#), [Ohgami K](#), [Kitaichi N](#), [Tsukahara H](#), [Ishida S](#), [Ohno S](#).
Author information

Abstract

PURPOSE:

Previous studies have reported that astaxanthin (AXT) has antioxidative and anti-inflammatory effects in addition to its ability to shorten blood transit times. As laser speckle flowgraphy (LSFG) can noninvasively visualize the hemodynamics of the choroidal circulation, we used the technique to evaluate whether continuous ingestion of 12 mg of AXT per day could increase quantitative blood flow velocity.

METHODS:

In this randomized, double-blind, placebo-controlled study, we examined 20 healthy volunteers who ingested 12 mg AXT or placebo capsules over a 4-week period. LSFG was measured in the right eyes of all subjects at pre-ingestion, and at 2 and 4 weeks after the treatment of AXT. LSFG values were used to calculate the square blur rate (SBR), which is a quantitative index of relative blood flow velocity.

RESULTS:

A significant increase of the macular SBR was seen 4 weeks after AXT ingestion when compared to the pre-ingestion values (Wilcoxon signed-rank test, $P = 0.018$). In contrast, no statistical difference in the macular SBR was detected in the placebo group (Friedman test, $P = 0.598$). No subjective or objective adverse events were found after the 12-mg AXT ingestion.

CONCLUSIONS:

Results suggest that administration of AXT over a 4-week period can elevate the choroidal blood flow velocity without any adverse effects.

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22072378

[PubMed - indexed for MEDLINE]

Astaxanthin improves visual acuity (the ability to see fine detail) and muscle fatigue in placebo-controlled human clinical trial.

Journal of Clinical Therapeutics & Medicines VOL.18;NO.9;PAGE.1085-1100(2002)

Sports Performance Benefits from Taking Natural Astaxanthin Characterized by Visual Acuity and Muscle Fatigue Improvement in Humans.

SAWAKI KEISUKE; YOSHIGI HIROSHI; AOKI KAZUHIRO; KOIKAWA NATSUE; AZUMANE AKITO; KANEKO KESATOKI; YAMAGUCHI MASAHIRO

The effects of astaxanthin on visual acuity and muscle fatigue were studied. Astaxanthin (3,3'-Dihydroxy-.BETA.,.BETA.-carotene-4,4'-dione) is a red pigment found in salmon and krill and has strong antioxidant properties. In the two supplementation studies, astaxanthin extracted from algae (*Haematococcus pluvialis*) was used. Four visual acuity parameters were examined in experiment A in 18 healthy adult male volunteers that were equally divided into two groups (treatment and control). The measured parameters were deep vision, critical flicker fusion, static and kinetic visual acuity before and after supplementation. A second investigation (experiment B) involved 16 adult male volunteers to establish the effect of astaxanthin supplementation on the build up of lactic acid before and after running 1200 metres. In both experiments, the treated groups ingested an astaxanthin capsule per day for 4 weeks (6mg astaxanthin per day) and the control groups received a placebo capsule. Results: In experiment A, the deep vision and the critical flicker fusion of the treated groups were significantly improved compared to the control group. No effects of treated group were observed on static and kinetic visual acuity. In experiment B, serum lactic acid concentration at 2 minutes after activity (1,200m running) of the treatment group was significantly lower than that of the control one. No other effects related to supplementation of astaxanthin on serum biological and hematological examinations were observed. Based on these preliminary findings, it suggested that supplementation of astaxanthin is effective for the improvement of visual acuity and muscle fatigue that may lead to sports performance benefits.

Astaxanthin at 6mg per day improves eye fatigue and eye accommodation in double-blind, placebo-controlled human clinical trial.

Journal of Clinical Therapeutics & Medicines VOL.21;NO.5;PAGE.543-556(2005)

Effects of Astaxanthin on Accommodation and Asthenopia-Dose Finding Study in Healthy Volunteers-

NITTA TAKUYA; OGAMI KAZUHIRO; SHIRATORI KENJI; SHINMEI YASUHIRO; CHIN SHINKI; YOSHIDA KAZUHIKO; TSUKAHARA HIROKI; ONO SHIGEAKI

A double-blind study was conducted in healthy volunteers to objectively evaluate the optimum dose and safety of astaxanthin (AX) on accommodation and asthenopia. The subjects were divided into 3 groups: 0mg (AX 0mg group), 6mg (AX 6mg group) and 12mg (AX 12mg group) of astaxanthin administered. Ten subjects, total thirty subjects were included in each group. Mean time consumed for close working (e.g., VDT working) was approximately 7 hours a day. The testing food was given to the subjects for 4 weeks. Then, the subjects were traced for 4 weeks and assessed by comparison of the observed values between pre- and post-dosing. As a result 1. Objective accommodation power of the AX 12mg group was significantly increased compared to that of pre-dosing. 2. Positive accommodation time was significantly shortened in the AX 6mg and the 12mg groups compared to those of pre-dosing, and negative accommodation time was significantly shortened in the AX 0mg and the 6mg groups compared to those of pre-dosing. 3. According to the assessment by VAS, many parameters in subjective symptoms were improved in the AX 6mg group. 4. No changes were noted in laboratory tests of controversial in clinical setting due to AX uptake. Also, there were no adverse events caused by the administration of the testing food. In conclusion, accommodation power and subjective symptoms relating asthenopia were improved by taking 6mg/day of astaxanthin, therefore more than 6mg/day was considered to be optimal dosage of astaxanthin.

Astaxanthin prevents eye strain in double-blind, placebo-controlled human crossover study.

Journal of the Eye VOL.23;NO.6;PAGE.829-834(2006)

Effects of Astaxanthin on Eyestrain Induced by Accommodative Dysfunction

IWASAKI TSUNETO; TAHARA AKIHIKO

We investigated effects of astaxanthin on eyestrain induced by accommodative dysfunction. The 10 healthy subjects received 6mg/day of astaxanthin (Ax group) or 0mg/day (placebo; P group) for 14 days, and were then assigned a near visual task for 20min. Accommodative function and subjective symptoms relating to eyestrain were measured before and after the task, and after the 10-minute rest following the task. The data were then compared between Ax and P groups by the double-blind cross-over method. After the task, accommodation contraction and relaxation times were extended in both the Ax and P groups. Comparison between the two groups showed that after the task, accommodation relaxation time was significantly extended in P group, in contrast to Ax. Accommodative contraction and relaxation times were significantly prolonged after the 10-minute rest in P group as compared to Ax. The symptoms eye fatigue, eye heaviness, blurred vision and eye dryness in P group were increased, but Ax group showed increased in eye fatigue and eye heaviness. On the basis of these results, we concluded that astaxanthin has the effects of reducing and preventing eyestrain induced by accommodative dysfunction.

Astaxanthin improves eye accommodation in randomized placebo-controlled human clinical trial.

Journal of Traditional Medicines VOL.19;NO.5;PAGE.170-173(2002)

Effects of astaxanthin on accommodation, critical flicker fusion, and pattern visual evoked potential in visual display terminal workers.

NAGAKI Y; HAYASAKA S ; YAMADA T ; HAYASAKA Y; SANADA M; UONOMI T

We evaluated the effects of astaxanthin, a red carotenoid, on accommodation, critical flicker fusion(CFF), and pattern visual evoked potential(PVEP) in visual display terminal(VDT) workers. As controls, 13 non-VDT workers received no supplementation (Group A). Twenty-six VDT workers were randomized into 2 groups: Group B consisted of 13 subjects who received oral astaxanthin, 5mg/day, for 4 weeks, and Group C consisted of 13 subjects who received an oral placebo, 5mg/day, for 4 weeks. No significant difference in age was noted among the 3 groups. A double-masked study was designed in Groups B and C. Accommodation amplitude in Group A was 3.7. \pm .1.5 diopters. Accommodation amplitudes (2.3. \pm .1.4 and 2.2. \pm .1.0 diopters) in Groups B and C before supplementation were significantly ($p < 0.05$) lower than in Group A. Accommodation amplitude (2.8. \pm .1.6 diopters) in Group B after astaxanthin treatment was significantly ($p < 0.01$) larger than before supplementation, while accommodation amplitude (2.3. \pm .1.1 diopters) in Group C after placebo supplementation was unchanged. The CFFs and amplitude and latency of P100 in PVEP in Group A were 45.0. \pm .4.2Hz, 6.5 \pm 1.8.MU.V, and 101.3. \pm .6.5msec, respectively. The CFFs in Groups B and C before supplementation were significantly ($p < 0.05$) lower than in Group A. The CFFs in Groups B and C did not change after supplementation. Amplitudes and latencies of P100 in PVEP in Groups B and C before supplementation were similar to those in Group A and did not change after supplementation. Findings of the present study indicated that accommodation amplitude improved after astaxanthin supplementation in VDT workers.

Astaxanthin reduces eye strain in 46% of subjects in 4 weeks at 5mg per day in double-blind human clinical trial.

Journal of Traditional Medicines 2002: 19 (5), 170 – 173.

Effects of Astaxanthin on accommodation, critical flicker fusion, and pattern visual evoked potential in visual display terminal workers.

Nagaki Y., Hayasaka S., Yamada T., Hayasaka Y., Sanada M., Uonomi T.

Working for long periods at visual display terminals reportedly induces various visual problems such as eye strain, blurring and diplopia (a disorder of vision in which two images of a single object are seen because of unequal action of the eye muscles – also called double vision). In a double blind study performed in Japan, after four weeks of supplementation with 5 mg of Astaxanthin per day (extracted from *Haematococcus Pluvialis* algae meal) the authors reported a 46% reduction of eye strain subjects and higher accommodation amplitude in visual display terminal subjects.

Although the mechanism of action is unclear, Astaxanthin's potent antioxidant properties may relieve chronic stress of visual display terminal use that may induce hypofunction of the ciliary body, resulting in decreased accommodation.

Natural Astaxanthin more effective than Synthetic in inhibiting skin cancer.

[J Agric Food Chem](#). 2013 Apr 24;61(16):3842-51. doi: 10.1021/jf304609j. Epub 2013 Apr 16.

Effective inhibition of skin cancer, tyrosinase, and antioxidative properties by astaxanthin and astaxanthin esters from the green alga *Haematococcus pluvialis*.

[Rao AR¹](#), [Sindhuja HN](#), [Dharmesh SM](#), [Sankar KU](#), [Sarada R](#), [Ravishankar GA](#).

Author information

Abstract

Astaxanthin mono- (AXME) and diesters (AXDE) were characterized and examined for anticancer potency with total carotenoids (TC) and astaxanthin (AX) against UV-7,12-dimethylbenz(a)anthracene (DMBA)-induced skin cancer model in rat. At 200 µg/kg bw, AXDE and AXME reduced UV-DMBA-induced tumor incidences up to 96 and 88%, respectively, when compared to AX (66%) and TC (85%). UV-DMBA has been known to generate high levels of free radicals and tyrosinase enzyme, leading to characteristic symptoms of skin pigmentation and tumor initiation. Intriguingly, ~7-fold increase in tyrosinase and 10-fold decrease in antioxidant levels were normalized by AXDE and AXME as opposed to only ~1.4-2.2-fold by AX and TC, respectively. This result together with the appearance of 72 and 58 ng/mL of retinol in the serum of respective AXE-treated (AXDE + AXME) and AX-treated animals suggested that better anticancer potency of AXEs could be due to increased bioavailability.

PMID:

23473626

[PubMed - indexed for MEDLINE]

Astaxanthin taken internally improves the beauty of the skin in human clinical trial.

[Acta Biochim Pol.](#) 2012;59(1):43-7. Epub 2012 Mar 17.

Cosmetic benefits of astaxanthin on humans subjects.

[Tominaga K¹](#), [Hongo N](#), [Karato M](#), [Yamashita E](#).

Author information

Abstract

Two human clinical studies were performed. One was an open-label non-controlled study involving 30 healthy female subjects for 8 weeks. Significant improvements were observed by combining 6 mg per day oral supplementation and 2 ml (78.9 µM solution) per day topical application of astaxanthin. Astaxanthin derived from the microalgae, *Haematococcus pluvialis* showed improvements in skin wrinkle (crow's feet at week-8), age spot size (cheek at week-8), elasticity (crow's feet at week-8), skin texture (cheek at week-4), moisture content of corneocyte layer (cheek in 10 dryskin subjects at week-8) and corneocyte condition (cheek at week-8). It may suggest that astaxanthin derived from *H. pluvialis* can improve skin condition in all layers such as corneocyte layer, epidermis, basal layer and dermis by combining oral supplementation and topical treatment. Another was a randomized double-blind placebo controlled study involving 36 healthy male subjects for 6 weeks. Crow's feet wrinkle and elasticity; and transepidermal water loss (TEWL) were improved after 6 mg of astaxanthin (the same as former study) daily supplementation. Moisture content and sebum oil level at the cheek zone showed strong tendencies for improvement. These results suggest that astaxanthin derived from *Haematococcus pluvialis* may improve the skin condition in not only in women but also in men.

PMID:

22428137

[PubMed - indexed for MEDLINE]

Free full text

Effects of palmitate and astaxanthin on cell viability and proinflammatory characteristics of mesenchymal stem cells

[Hamid Yaghooti](#)¹, [Narges Mohammadtaghvaei](#)², [Khadijeh Mahboobnia](#)³

PMID: 30639962 DOI: [10.1016/j.intimp.2018.12.063](https://doi.org/10.1016/j.intimp.2018.12.063)

Abstract

Mesenchymal stem cells (MSCs) have broad immunomodulatory activities. These cells are a stable source of cytokine production such as interleukin-6 (IL6), monocyte chemoattractant protein-1 (MCP-1/CCL2) and vascular endothelial growth factor (VEGF). Fatty acid elevation in chronic metabolic diseases alters the microenvironment of MSCs and thereby, might affect their survival and cytokine production. In the present study, we investigated the effects of palmitate, the most abundant saturated free fatty acid (FFA) in plasma, and astaxanthin, a potent antioxidant, on cell viability and apoptosis in human bone marrow-driven mesenchymal stem cells. We also elucidated how palmitate and astaxanthin influence the inflammation in MSCs. Human mesenchymal stem cells were collected from an aspirate of the femurs and tibias marrow compartment. The effect of palmitate on cell viability, caspase activity and pro-inflammatory cytokines expression and secretion were evaluated. In addition, activation of the MAP kinases and NF- κ B signaling pathways were investigated. The results showed that astaxanthin protected MSCs from palmitate-induced cell death. We found that palmitate significantly enhanced IL-6, VEGF and MCP-1 expression, and secretion in MSC cells. Increased cytokine expression was parallel to the enhanced phosphorylation of P38, ERK and IKK α -IKK β . In addition, pretreatment with JNK, ERK, P38, and NF- κ B inhibitors could correspondingly attenuate palmitate-induced expression of VEGF, IL-6, and MCP-1. Our results demonstrated that fatty acid exposure causes inflammatory responses in MSCs that can be alleviated favorably by astaxanthin treatment.

Astaxanthin has superior photo-aging preventive properties than other carotenoids.

[Exp Dermatol](#). 2009 Mar;18(3):222-31. doi: 10.1111/j.1600-0625.2008.00790.x. Epub 2008 Sep 18.

Astaxanthin, canthaxanthin and beta-carotene differently affect UVA-induced oxidative damage and expression of oxidative stress-responsive enzymes.

[Camera E¹](#), [Mastrofrancesco A](#), [Fabbri C](#), [Daubrawa F](#), [Picardo M](#), [Sies H](#), [Stahl W](#).

Author information

Abstract

Carotenoids are used for systemic photoprotection in humans. Regarding mechanisms underlying photoprotective effects of carotenoids, here we compared the modulation of UVA-related injury by carotenoids. Human dermal fibroblasts (HDF) were exposed to moderate doses of UVA, which stimulated apoptosis, increased levels of reactive oxygen species and thiobarbituric acid reactive substances, decreased antioxidant enzymes activities, promoted membrane perturbation, and induced the expression of heme oxygenase-1 (HO-1). The carotenoids astaxanthin (AX), canthaxanthin (CX) and beta-carotene (betaC) were delivered to HDF 24 h before exposure to UVA. Astaxanthin exhibited a pronounced photoprotective effect and counteracted all of the above-mentioned UVA-induced alterations to a significant extent. beta-Carotene only partially prevented the UVA-induced decline of catalase and superoxide dismutase activities, but it increased membrane damage and stimulated HO-1 expression. Moreover, betaC dose-dependently induced caspase-3 activity following UVA exposure. In contrast, CX had no effect on oxidative damage, except for HO-1 expression, which was augmented. Uptake of AX by fibroblasts was higher than that of the other two carotenoids. The photostability of the three compounds in fibroblasts was AX > CX >> betaC. The data indicate that the oxo-carotenoid AX has a superior preventive effect towards photo-oxidative changes in cell culture.

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18803658

[PubMed - indexed for MEDLINE]

Carotenoid Science Vol 10, p 91-5 (2006)

The Effects of a Dietary Supplement Containing Astaxanthin on Skin Condition

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The cosmetic effects on human skin by 4mg per day astaxanthin supplementation were demonstrated in a single blind placebo controlled study using forty-nine US healthy middle-aged women. There were significant improvements in fine lines/wrinkles and elasticity by dermatologist's assessment and in the moisture content by instrumental assessment at week 6 compared to base-line initial values.

Astaxanthin, widely and naturally distributed in marine organisms, including Crustacea such as shrimps and crabs and such fish as salmon and sea bream exhibits a strong anti-oxidative effect, and its action is reported to 1,000 times stronger than alpha-tocopherol and approximately 40 times stronger than beta-carotene. It has also been reported that astaxanthin doesn't have any pro-oxidative nature like beta-carotene and lycopene and its potent anti-oxidant property is exhibited at the cell membrane. Although used only as a coloring in the past (either as a food additive or a dye-up agent for cultured fish), astaxanthin has become one of the major materials eagerly anticipated by industries for dietary supplements and personal care products.

Furthermore its other various important benefits to date have suggested for human health such as anti-inflammation, LDL cholesterol oxidation suppression, immunomodulation, anti-stress, limiting diabetic nephropathy, improved semen quality, attenuating eye fatigue, sport performance and endurance, limiting exercised induced muscle damage and improving hypertension.

In terms of dermatological actions, suppression of hyper-pigmentation, inhibitions of melanin synthesis and photo-aging have been reported. We have also reported visual wrinkled reduction by topical astaxanthin. However, only one study for internal use about cosmetic benefit of a dietary supplement including astaxanthin and tocotrienol on human skin has been reported.

Here we report the effects of a dietary supplement containing astaxanthin on skin condition performed in the United States of America.

Astaxanthin may have protective effect against photo-aging, wrinkles and sagging.

[J Dermatol Sci](#). 2010 May;58(2):136-42. doi: 10.1016/j.jdermsci.2010.02.009. Epub 2010 Feb 18.

Astaxanthin attenuates the UVA-induced up-regulation of matrix-metalloproteinase-1 and skin fibroblast elastase in human dermal fibroblasts.

[Suganuma K¹](#), [Nakajima H](#), [Ohtsuki M](#), [Imokawa G](#).

Author information

Abstract

BACKGROUND:

Repetitive exposure of the skin to UVA radiation elicits sagging more frequently than wrinkling, which is mainly attributed to its biochemical mechanism to up-regulate the expression of matrix-metalloproteinase (MMP)-1 and skin fibroblast elastase (SFE)/neutral endopeptidase (NEP), respectively.

OBJECTIVE:

In this study, we examined the effects of a potent antioxidant, astaxanthin (AX), on the induction of MMP-1 and SFE by UVA treatment of cultured human dermal fibroblasts.

METHODS:

Those effects were assessed by real-time RT-PCR, Western blotting and enzymic activity assays.

RESULTS:

UVA radiation elicited a significant increase in the gene expression of MMP-1 as well as SFE/NEP (to a lesser extent) which was followed by distinct increases in their protein and enzymatic activity levels. The addition of AX at concentrations of 4-8 microM immediately after UVA exposure significantly attenuated the induction of MMP-1 and SFE/NEP expression elicited by UVA at the gene, protein and activity levels although both the UVA stimulation and the subsequent AX inhibition were greater for MMP-1 than for SFE/NEP. Analysis of the UVA-induced release of cytokines revealed that UVA significantly stimulated only the secretion of IL-6 among the cytokines tested and that AX significantly diminished only the IL-6 secretion.

CONCLUSION:

These findings indicate that, based on different effective concentrations of AX, a major mode of action leading to the inhibition elicited by AX depends on inhibition of UVA effects of the reactive oxygen species-directed signaling cascade, but not on interruption of the IL-6-mediated signaling cascade. We hypothesize that AX would have a significant benefit on protecting against UVA-induced skin photo-aging such as sagging and wrinkles.

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20219323

[PubMed - indexed for MEDLINE]

Astaxanthin improves immune capacity, increases survival and reduces susceptibility to environmental stress in shrimp.

[Fish Shellfish Immunol.](#) 2018 Sep;80:452-457. doi: 10.1016/j.fsi.2018.06.039. Epub 2018 Jun 20.

Dietary supplementation of *Haematococcus pluvialis* improved the immune capacity and low salinity tolerance ability of post-larval white shrimp, *Litopenaeus vannamei*.

[Xie S¹](#), [Fang W¹](#), [Wei D¹](#), [Liu Y¹](#), [Yin P¹](#), [Niu J¹](#), [Tian L²](#).

Author information

Abstract

A 25-days experiment was conducted to evaluate the effect of dietary *Haematococcus pluvialis* on growth, survival, immune response and stress tolerance ability of post-larval *Litopenaeus vannamei*. Post-larval white shrimp (mean initial weight 2.1 mg) were fed five isoenergetic and isonitrogenous diets containing grade levels of *Haematococcus pluvialis* (0, 1.7, 3.3, 6.7 and 13.3 g kg⁻¹ diet, respectively). Results indicated that 3.3 g *Haematococcus pluvialis* kg⁻¹ diet increased the survival rate of post-larval white shrimp. Specific growth rate (SGR) and weight gain (WG) showed no difference among each groups. After the acute salinity stress (salinity decreased rapidly from 28‰ to 5‰), survival of shrimp fed 6.7 g *Haematococcus pluvialis* kg⁻¹ diet significant higher than the control ($P < 0.05$), and the total antioxidant capacity (T-AOC) was increased with the increasing dietary *Haematococcus pluvialis* levels. The malonaldehyde (MDA) contents in whole body decreased with the increasing dietary *Haematococcus pluvialis* levels before and after the salinity stress. Before the salinity stress, relative mRNA levels of Caspase 3, Rho and Janus kinase (JAK) decreased in shrimp fed diets contain *Haematococcus pluvialis*. After the salinity stress, relative mRNA levels of anti-oxidative related genes and immune related genes decreased with the dietary *Haematococcus pluvialis* level increased to 3.3 g kg⁻¹. Based on the effect of *Haematococcus pluvialis* on survival, salinity stress tolerance ability and the immune response of post-larval *L. vannamei*, the optimal level of *Haematococcus pluvialis* was 3.3-6.7 g kg⁻¹ diet (100-200 mg astaxanthin kg⁻¹ diet).

KEYWORDS:

Haematococcus pluvialis; Immune capacity; NF-κB pathway; Post-larval; Salinity stress

PMID: 29933110

DOI: [10.1016/j.fsi.2018.06.039](https://doi.org/10.1016/j.fsi.2018.06.039)

Astaxanthin shows cell-protective effects in human stem cells.

[Avicenna J Med Biotechnol.](#) 2018 Apr-Jun;10(2):69-74.

The Evaluation of Astaxanthin Effects on Differentiation of Human Adipose Derived Stem Cells into Oligodendrocyte Precursor Cells.

[Ghasemi N](#)¹.

[Author information](#)

Abstract

BACKGROUND: Multiple Sclerosis (MS) has been explained as an autoimmune mediated disorder in central nerve system. Since conventional therapies for MS are not able to stop or reverse the destruction of nerve tissue, stem cell-based therapy has been proposed for the treatment of MS. Astaxanthin (AST) is a red fat-soluble xanthophyll with neuroprotection activity. The aim of this study was evaluation of pre-inducer function of AST on differentiation of human Adipose-Derived Stem Cells (hADSCs) into oligodendrocyte precursor cells.

METHODS: After stem cell isolation, culture and characterization by flow cytometry, hanging drop technique was done for embryoid body formation. In the following, hADSCs were differentiated into oligodendrocyte cells in the presence of AST at various concentrations (1, 5, and 10 *ng/ml*). Finally, immunocytochemistry and real-time PCR techniques were used for assessment of oligodendrocyte differentiation.

RESULTS: Flow cytometry results indicated that hADSCs were CD44, CD49-positive, but were negative for CD14, CD45 markers. In addition, immunocytochemistry results revealed that, in AST treated groups, the mean percentage of Olig 2 and A2B5 positive cells increased especially in 5 *ng/ml* AST treated group compared to control group ($p < 0.001$). Moreover, real-time PCR analysis confirmed the results of immunocytochemistry.

CONCLUSION: Since hADSCs have the potential to differentiate into multi lineage cells and due to important functions of AST in regulating various cellular processes, it seems that AST can be used as a promoter for oligodendrocyte differentiation of hADSCs for being used in cell transplantation in multiple sclerosis.

KEYWORDS: Adult stem cells; Astaxanthin; Multiple sclerosis; Oligodendroglia

PMID: 29849982 PMCID: [PMC5960062](#) [Free PMC Article](#)

Astaxanthin reduces spinal cord lesions, prevents cell death and inhibits lipid peroxidation in rats.

[Zhongguo Xiu Fu Chong Jian Wai Ke Za Zhi](#). 2018 May 1;32(5):548-553. doi: 10.7507/1002-1892.201712127.

[Effect of astaxanthin on the apoptosis after spinal cord injury in rats].

[Article in Chinese; Abstract available in Chinese from the publisher]

[Ren X¹](#), [Ding W²](#), [Yang X³](#).

Author information

Abstract

in [English](#), [Chinese](#)

OBJECTIVE:

To study the effects of astaxanthin on the apoptosis after spinal cord injury in rats.

METHODS:

One hundred and forty-four healthy adult Sprague Dawley rats were divided into experimental group, control group, and sham group according to the random number table ($n=48$). In the control group and the experimental group, the modified Allen's method was used to make the spinal cord injury model; in the sham group, only the lamina was cut without damaging the spinal cord. At immediate after operation, the rats in the experimental group were given intragastric administration of astaxanthin (75 mg/kg) twice a day; and the rats in the control group and the sham group were given equal amount of olive oil by gavage twice a day. BBB score was used to assess the motor function at 1 day and 1, 2, 3, and 4 weeks after operation. The malondialdehyde (MDA) content was determined by the thiobarbituric acid method at 24 hours after operation; and the activity of superoxide dismutase (SOD) was determined by the xanthine oxidase method. Apoptosis index (AI) was determined by TUNEL method at 6, 24, and 48 hours after operation. At 48 hours after operation, the water content of spinal cord was measured by dry-wet weight method, the lesion ratio of spinal cord was calculated, the ultrastructure of the spinal cord was observed by transmission electron microscopy, and ultrastructure scoring was performed using the Kaptanoglu score method.

RESULTS:

The BBB score in the control group and the experimental group was significantly lower than that in the sham group at each postoperative time point ($P<0.05$); and the BBB score in the experimental group were significantly higher than that in the control group at 1-4 weeks postoperatively ($P<0.05$). The MDA content in the control group and the experimental group was significantly higher than that in the sham group at 24 hours after operation, and in the experimental group was significantly lower than in the control group ($P<0.05$). The SOD activity in the control group and the experimental group was significantly lower than that in the sham group, and in the experimental group was significantly

higher than in the control group ($P<0.05$). At each time point postoperatively, the AI in the control group and the experimental group was significantly higher than that in the sham group, and in the experimental group was significantly lower than in the control group ($P<0.05$). At 48 hours after operation, the water content of spinal cord, the lesion ratio of spinal cord, and the ultrastructure score in the control group and the experimental group were significantly higher than those in the sham group, and in the experimental group were significantly lower than in the control group ($P<0.05$).

CONCLUSION:

Astaxanthin can inhibit the lipid peroxidation, reduce the apoptosis, reduce the spinal cord edema, reduce the spinal cord lesion, reduce the histopathological damage after spinal cord injury, and improve the motor function of rats with spinal cord injury, and protect the spinal cord tissue, showing an obvious neuroprotective effect.

KEYWORDS:

Astaxanthin; apoptosis; rat; spinal cord injury

PMID: 29806341

DOI: [10.7507/1002-1892.201712127](https://doi.org/10.7507/1002-1892.201712127)

[Indexed for MEDLINE]

Astaxanthin increases lifespan, decreases cell death and decreases oxidative stress in *Saccharomyces cerevisiae* (a yeast that is a model for cell death and aging).

[FEMS Yeast Res.](#) 2019 Jan 1;19(1). doi: 10.1093/femsyr/foy113.

Astaxanthin enhances the longevity of *Saccharomyces cerevisiae* by decreasing oxidative stress and apoptosis.

[Sj S¹](#), [Veerabhadrapa B¹](#), [Subramanian S¹](#), [Dyavaiah M¹](#).

Author information

Abstract

The budding yeast, *Saccharomyces cerevisiae*, is an efficient model for studying oxidative stress, programmed cell death and aging. The present study was carried out to investigate antioxidant, the anti-apoptotic and anti-aging activity of a natural compound, astaxanthin, in *S. cerevisiae* model. The survivability of yeast antioxidant-deficient strains (*sod1Δ*, *sod2Δ*, *cta1Δ*, *ctt1Δ* and *tsa1Δ*) increased by 20%-40% when cells were pre-treated with astaxanthin, compared to hydrogen peroxide alone, as demonstrated in spot and colony forming unit assays. Reduced reactive oxygen species (ROS) levels, increased glutathione, decreased lipid peroxidation and induced superoxide dismutase activity in astaxanthin-treated cells indicate that astaxanthin protected the cells from oxidative-stress-induced cell death. In addition, astaxanthin protected anti-apoptotic-deficient strains (*pep4Δ* and *fis1Δ*) against acetic acid and hydrogen peroxide-induced cell death that suggests anti-apoptotic property of astaxanthin, and it was further confirmed by acridine orange/ethidium bromide, annexin V and 4',6-diamidino-2-phenylindole staining. The yeast chronological lifespan assay results showed that astaxanthin extends the lifespan of antioxidant-deficient strains by scavenging ROS, and anti-apoptotic-deficient mutants by protecting from apoptotic cell death compared to their respective untreated cells and wild type. Our results suggest that astaxanthin enhances the longevity of yeast *S. cerevisiae* by reducing oxidative stress and apoptosis.

PMID: 30312390

DOI: [10.1093/femsyr/foy113](https://doi.org/10.1093/femsyr/foy113)

Astaxanthin protects against UV-induced inflammation.

[Exp Dermatol](#). 2014 Mar;23(3):178-83. doi: 10.1111/exd.12347.

Astaxanthin, a xanthophyll carotenoid, inhibits ultraviolet-induced apoptosis in keratinocytes.

[Yoshihisa Y¹](#), [Rehman MU](#), [Shimizu T](#).

Author information

Abstract

Intra-cellular reactive nitrogen/oxygen species and apoptosis play important roles in ultraviolet (UV)-induced inflammatory responses in the skin. Astaxanthin (AST), a xanthophyll carotenoid, exhibits diverse clinical benefits. The protective effects of AST against UV-induced apoptosis were investigated in the present study. Astaxanthin (5 μ m) caused a significant decrease in the protein content and the mRNA levels of inducible nitric oxide (iNOS) and cyclooxygenase (COX)-2, and decreased the release of prostaglandin E2 from HaCaT keratinocytes after UVB (20 mJ/cm²) or UVC (5 mJ/cm²) irradiation. No significant protective effects against UV-induced reactive oxygen species (ROS) were observed in AST-pretreated cells. Astaxanthin caused a significant inhibition of UV-irradiation-induced apoptosis, as evidence by a DNA fragmentation assay. Furthermore, we found that the treatment with AST caused a reduction in the UVB- or UVC-induced protein and mRNA expression of macrophage migration inhibitory factor (MIF), IL-1 β and TNF- α in HaCaT keratinocytes. These results suggest that AST effectively protects against UV-induced inflammation by decreasing iNOS and COX-2, and thereby inhibiting the apoptosis of keratinocytes.

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KEYWORDS:

apoptosis; astaxanthin; keratinocyte; reactive oxygen species; ultraviolet

PMID:

24521161

[PubMed - indexed for MEDLINE]

Astaxanthin superior to lutein and beta-carotene in protecting against UV-induced oxidative stress.

[J Dermatol Sci.](#) 1998 Mar;16(3):226-30.

Modulation of UVA light-induced oxidative stress by beta-carotene, lutein and astaxanthin in cultured fibroblasts.

[O'Connor I](#), [O'Brien N](#).

Department of Nutrition, University College, Cork, Ireland.

The ability of beta-carotene, lutein or astaxanthin to protect against UVA-induced oxidative stress in rat kidney fibroblasts (NRK) was assessed. Activities of the antioxidant enzymes catalase (CAT) and superoxide dismutase (SOD), and changes in thiobarbituric acid reactive substances (TBARS) were measured as indices of oxidative stress. Exposure to UVA light at a dose intensity of 5.6 mW/cm² for 4 h resulted in a significant decrease in CAT and SOD activities and a significant increase in TBARS. No cytotoxicity, as indicated by lactate dehydrogenase (LDH) release, was observed. beta-Carotene (1 microM), lutein (1 microM) and astaxanthin (10 nM) protect against UVA light-induced oxidative stress in vitro with astaxanthin exhibiting superior protective properties.

Publication Types:

PMID: 9651820 [PubMed - indexed for MEDLINE]

Astaxanthin improves sperm functioning in placebo-controlled human clinical trial leading to the conclusion that Astaxanthin may be used to decrease male infertility.

[Mar Drugs](#). 2015 Aug 25;13(9):5533-51. doi: 10.3390/md13095533.

Astaxanthin Improves Human Sperm Capacitation by Inducing Lyn Displacement and Activation.

[Andrisani A](#)¹, [Donà G](#)², [Tibaldi E](#)³, [Brunati AM](#)⁴, [Sabbadin C](#)⁵, [Armanini D](#)⁶, [Alvisi G](#)⁷, [Gizzo S](#)⁸, [Ambrosini G](#)⁹, [Ragazzi E](#)¹⁰, [Bordin L](#)¹¹.

Author information

Abstract

Astaxanthin (Asta), a photo-protective red pigment of the carotenoid family, is known for its multiple beneficial properties. In this study, the effects of Asta on isolated human sperm were evaluated. Capacitation involves a series of transformations to let sperm acquire the correct features for potential oocyte fertilization, including the generation of a controlled amount of reactive oxygen species (ROS), cholesterol depletion of the sperm outer membrane, and protein tyrosine phosphorylation (Tyr-P) process in the head region. Volunteers, with normal spermiogram values, were divided in two separate groups on the basis of their ability to generate the correct content of endogenous ROS. Both patient group (PG) and control group (CG) were analysed for Tyr-phosphorylation (Tyr-P) pattern and percentages of acrosome-reacted cells (ARC) and non-viable cells (NVC), in the presence or absence of Asta. In addition, the involvement of ROS on membrane reorganization and the presence of Lyn, a Src family kinase associated with lipid rafts, were investigated. Results show that Lyn is present in the membranes of human sperm, mainly confined in midpiece in resting conditions. Following capacitation, Lyn translocated to the head concomitantly with raft relocation, thus allowing the Tyr-P of head proteins. Asta succeeded to trigger Lyn translocation in PG sperm thus bypassing the impaired ROS-related mechanism for rafts and Lyn translocation. In this study, we showed an interdependence between ROS generation and lipid rafts and Lyn relocation leading the cells to undergo the successive acrosome reaction (AR). Asta, by ameliorating PG sperm functioning, may be utilised to decrease male idiopathic infertility.

KEYWORDS:

: astaxanthin; acrosome reaction; cholera toxin subunit B (CTB); human sperm capacitation; tyrosine kinase Lyn

PMID: 26308013 [PubMed - in process] PMID: PMC4584338

[Free PMC Article](#)

Male fertility increased and sperm quality and motility increased in double-blind, placebo-controlled randomized human clinical trial.

[Asian J Androl.](#) 2005 Sep;7(3):257-62.

Combined conventional/antioxidant "Astaxanthin" treatment for male infertility: a double blind, randomized trial.

[Comhaire FH](#), [El Garem Y](#), [Mahmoud A](#), [Eertmans F](#), [Schoonjans F](#).

Ghent University Hospital, Department of Medical and Urological Andrology, 9k12 IE, De Pintelaan, 185, B 9000, Gent, Belgium. frank.comhaire@ugent.be

AIM: To evaluate the treatment of male infertility with a strong natural antioxidant, in addition to conventional treatment. **METHODS:** Using a double blind, randomized trial design, 30 men with infertility of > or =2 months and female partners with no demonstrable cause of infertility received conventional treatment according to the guidelines of the World Health Organization (WHO), and either a strong antioxidant Astaxanthin 16 mg/day (AstaCarox, AstaReal AB, Gustavsberg, Sweden) or placebo for 3 months. The effects of treatment on semen parameters, reactive oxygen species (ROS), zona-free hamster oocyte test, serum hormones including testosterone, luteinizing hormone (LH), follicle stimulating hormone (FSH) and Inhibin B, and spontaneous or intrauterine insemination (IUI)-induced pregnancies were evaluated. **RESULTS:** ROS and Inhibin B decreased significantly and sperm linear velocity increased in the Astaxanthin group (n = 11), but not in the placebo group (n = 19). The results of the zona-free hamster oocyte test tended to improve in the Astaxanthin group in contrast with the placebo group, though not reaching statistical significance. The total and per cycle pregnancy rates among the placebo cases (10.5 % and 3.6 %) were lower compared with 54.5 % and 23.1 % respectively in the Astaxanthin group (P = 0.028; P = 0.036). **CONCLUSION:** Although the present study suggests a positive effect of Astaxanthin on sperm parameters and fertility, the results need to be confirmed in a larger trial before recommending Astaxanthin for the complementary treatment of infertile men.

Publication Types:

[Clinical Trial](#)

[Randomized Controlled Trial](#)

[Research Support, Non-U.S. Gov't](#)

PMID: 16110353 [PubMed - indexed for MEDLINE]

Astaxanthin improves conception rate and sperm quality in Infertile Men in placebo-controlled human clinical trial.

XIII International Carotenoid Symposium Hawaii January 2002. Patent Cooperation Treaty Application
WO99 / 29313. AstaCarotene AB, Sweden.

Natural Astaxanthin Improves Semen Quality in Infertile Men

GAREM, Y.E., A. LIGNELL u. F. COMHAIRE

Summary: Natural Astaxanthin from Haematococcus Algae has been shown in a double blind, placebo controlled clinical to improve fertility in infertile men. Natural Astaxanthin had previously been shown to improve fertility in male animals such as boars and stallions. This study was conducted on men who were diagnosed as infertile due to abnormal sperm quality. The experimental group received 16 mg of Natural Astaxanthin per day for three months. The results were an improvement in conception rate in the experimental group by 478% over the placebo group. The scientist concluded that supplementation with Natural Astaxanthin improved the quality of the spermatozoa, which is suggested to be the plausible explanation for the increased frequency of conception.

Astaxanthin improves human sperm capacitation.

[Mar Drugs](#). 2013 Jun 3;11(6):1909-19. doi: 10.3390/md11061909.

Effect of astaxanthin on human sperm capacitation.

[Donà G¹](#), [Kožuh I](#), [Brunati AM](#), [Andrisani A](#), [Ambrosini G](#), [Bonanni G](#), [Ragazzi E](#), [Armanini D](#), [Clari G](#), [Bordin L](#).

Author information

Abstract

In order to be able to fertilize oocytes, human sperm must undergo a series of morphological and structural alterations, known as capacitation. It has been shown that the production of endogenous sperm reactive oxygen species (ROS) plays a key role in causing cells to undergo a massive acrosome reaction (AR). Astaxanthin (Asta), a photo-protective red pigment belonging to the carotenoid family, is recognized as having anti-oxidant, anti-cancer, anti-diabetic and anti-inflammatory properties and is present in many dietary supplements. This study evaluates the effect of Asta in a capacitating buffer which induces low ROS production and low percentages of acrosome-reacted cells (ARC). Sperm cells were incubated in the presence or absence of increasing concentrations of Asta or diamide (Diam) and analyzed for their ROS production, Tyr-phosphorylation (Tyr-P) pattern and percentages of ARC and non-viable cells (NVC). Results show that Asta ameliorated both sperm head Tyr-P and ARC values without affecting the ROS generation curve, whereas Diam succeeded in enhancing the Tyr-P level but only of the flagellum without increasing ARC values. It is suggested that Asta can be inserted in the membrane and therefore create capacitation-like membrane alteration which allow Tyr-P of the head. Once this has occurred, AR can take place and involves a higher numbers of cells.

PMID:

23736766

[PubMed - indexed for MEDLINE]

PMCID:

PMC3721213

Free PMC Article

Astaxanthin improves sperm quality and function.

[Reprod Biomed Online](#). 2003 Oct-Nov;7(4):385-91.

The role of food supplements in the treatment of the infertile man.

Comhaire FH, Mahmoud A.

Centre for Medical and Urological Andrology, Ghent University Hospital, De Pintelaan, 185, B 9000 Gent, Belgium. frank.comhaire@rug.ac.be

Recently, concerns have been raised about the presumptive increased risk of serious undesirable side effects in children born after IVF and intracytoplasmic sperm injection (ICSI). These treatments must, therefore, be reserved as the ultimate option after evidence-based and cause-directed treatment of the male patient with deficient semen has been exhausted. The present authors found that sperm quality and function improved with the intake of complementary food supplementation using a combination of zinc and folic acid, or the antioxidant astaxanthin (AstacaroX), or an energy-providing combination containing (acetyl)-carnitine (Proxeed). Also, double blind trials showed that the latter two substances increase spontaneous or intrauterine insemination- (IUI-) assisted conception rates. Extracts of *Pinus maritima* bark (Pycnogenol), which inhibits the cyclo-oxygenase enzyme, reducing prostaglandin production and inflammatory reaction, and extracts of the Peruvian plant *Lepidium meyenii* were shown to improve sperm morphology and concentration, respectively, in uncontrolled trials. Linseed (flaxseed) oil contains alpha-linolenic acid and lignans. The former corrects the deficient intake of omega-3 essential fatty acids, which is correlated with impaired sperm motility among subfertile men. Lignans are precursors of enterolacton, which inhibits aromatase and reduces the ratio of 16-OH over 2-OH oestrogen metabolites. The resulting reduction in oestrogen load may favourably influence Sertoli cell function.

PMID: 14656398 [PubMed - indexed for MEDLINE]

Astaxanthin alleviates brain aging in rats by reducing oxidative stress levels.

[Food Funct.](#) 2014 Jan;5(1):158-66. doi: 10.1039/c3fo60400d.

Astaxanthin alleviates brain aging in rats by attenuating oxidative stress and increasing BDNF levels.

[Wu W¹](#), [Wang X](#), [Xiang Q](#), [Meng X](#), [Peng Y](#), [Du N](#), [Liu Z](#), [Sun Q](#), [Wang C](#), [Liu X](#).

Author information

Abstract

Astaxanthin (AST) is a carotenoid pigment which possesses potent antioxidative, anti-inflammatory, and neuroprotective properties. The aim of this study was to investigate whether administration of AST had protective effects on D-galactose-induced brain aging in rats, and further examined its protective mechanisms. The results showed that AST treatment significantly restored the activities of glutathione peroxidase (GSH-PX) and superoxide dismutase (SOD), and increased glutathione (GSH) contents and total antioxidant capacity (T-AOC), but decreased malondialdehyde (MDA), protein carbonylation and 8-hydroxy-2'-deoxyguanosine (8-OHdG) levels in the brains of aging rats. Furthermore, AST increased the ratio of Bcl-2/Bax, but decreased the expression of Cyclooxygenase-2 (COX-2) in the brains of aging rats. Additionally, AST ameliorated histopathological changes in the hippocampus and restored brain derived neurotrophic factor (BDNF) levels in both the brains and hippocampus of aging rats. These results suggested that AST could alleviate brain aging, which may be due to attenuating oxidative stress, ameliorating hippocampus damage, and upregulating BDNF expression.

PMID:

24326685

[PubMed - indexed for MEDLINE]

ASTAXANTHIN EFFECTIVE AGAINST HEAT STRESS IN RATS.

Cell Stress Chaperones. 2020 May;25(3):549-558.

doi: 10.1007/s12192-019-01061-4. Epub 2020 Jan 22.

Astaxanthin supplementation impacts the cellular HSP expression profile during passive heating

[Chen Fleischmann](#)^{1,2,3}, [Netta Bar-Ilan](#)⁴, [Michal Horowitz](#)⁴, [Yaron Bruchim](#)^{4,5}, [Patricia Deuster](#)⁶, [Yuval Heled](#)^{7,8}

- PMID: [31970694](#)
- PMCID: [PMC7192986](#)
- DOI: [10.1007/s12192-019-01061-4](#)

[Free PMC article](#)

Abstract

Astaxanthin is a powerful carotenoid antioxidant prevalent in marine organisms and approved as a food supplement. Recent studies have demonstrated Astaxanthin's beneficial attributes in various health states. Following initial reports of potential heat protective properties in Astaxanthin supplemented rats, we present here results of a novel study examining the effect of Astaxanthin supplementation on the heat shock response in rats in relation to core temperature (T_c) and the ensuing physiological strain. Two hours of heat stress at 41 °C during which rats developed their thermoregulatory hyperthermic plateau resulted in progressive increases in HSP72 and HSP27 in the Astaxanthin (Oleoresin)-treated group but not in the control (Olive oil) group. Enhanced elevation in HSPs suggests that Astaxanthin supplementation may augment the cellular stress protective response to heat stress.

Biogerontology. 2021 Feb;22(1):81-100.

doi: 10.1007/s10522-020-09904-9. Epub 2020 Oct 27.

Astaxanthin protects oxidative stress mediated DNA damage and enhances longevity in *Saccharomyces cerevisiae*

[S J Sudharshan](#)¹, [Madhu Dyavaiah](#)²

- PMID: **33108581**
- DOI: [10.1007/s10522-020-09904-9](https://doi.org/10.1007/s10522-020-09904-9)

Abstract

Reactive oxygen species (ROS) have long been found to play an important role in oxidative mediated DNA damage. Fortunately, cells possess an antioxidant system that can neutralize ROS. However, oxidative stress occurs when antioxidants are overwhelmed by ROS or impaired antioxidant pathways. This study was carried out to find the protective effect of astaxanthin on the yeast DNA repair-deficient mutant cells under hydrogen peroxide stress. The results showed that astaxanthin enhances the percent cell growth of *rad1Δ*, *rad51Δ*, *apn1Δ*, *apn2Δ* and *ogg1Δ* cells. Further, the spot test and colony-forming unit count results confirmed that astaxanthin protects DNA repair mutant cells from oxidative stress. The DNA binding property of astaxanthin studied by *in silico* and *in vitro* methods indicated that astaxanthin binds to the DNA in the major and minor groove, and that might protect DNA against oxidative stress induced by Fenton's reagent. The intracellular ROS, 8-OHdG level and the DNA fragmentation as measured by comet tail was reduced by astaxanthin under oxidative stress. Similarly, reduced nuclear fragmentation and chromatin condensation results suggest that astaxanthin might reduce apoptosis. Finally, we show that astaxanthin decreases the accumulation of mutation rate and enhances the longevity of DNA repair-deficient mutants' cells during a chronological lifespan.

ASTAXANTHIN AND FUCOXANTHIN BOTH SHOW POTENTIAL TO PREVENT AND/OR TREAT AGE-RELATED PATHOLOGIES, STRESS, DNA DAMAGE AND PROTEIN DEAGGREGATION IN-VITRO.

Mar Drugs. 2019 Mar 23;17(3):189.
doi: 10.3390/md17030189.

Rat Glioma Cell-Based Functional Characterization of Anti-Stress and Protein Deaggregation Activities in the Marine Carotenoids, Astaxanthin and Fucoxanthin

[Sajal Afzal](#)^{1,2}, [Sukant Garg](#)³, [Yoshiyuki Ishida](#)⁴, [Keiji Terao](#)⁵, [Sunil C Kaul](#)⁶, [Renu Wadhwa](#)^{7,8}

- PMID: [30909572](#)
- PMCID: [PMC6470788](#)
- DOI: [10.3390/md17030189](#)

Free PMC article

Abstract

Stress, protein aggregation, and loss of functional properties of cells have been shown to contribute to several deleterious pathologies including cancer and neurodegeneration. The incidence of these pathologies has also been shown to increase with age and are often presented as evidence to the cumulative effect of stress and protein aggregation. Prevention or delay of onset of these diseases may prove to be unprecedentedly beneficial. In this study, we explored the anti-stress and differentiation-inducing potential of two marine bioactive carotenoids (astaxanthin and fucoxanthin) using rat glioma cells as a model. We found that the low (nontoxic) doses of both protected cells against UV-induced DNA damage, heavy metal, and heat-induced protein misfolding and aggregation of proteins. Their long-term treatment in glioma cells caused the induction of physiological differentiation into astrocytes. These phenotypes were supported by upregulation of proteins that regulate cell proliferation, DNA damage repair mechanism, and glial differentiation, suggesting their potential for prevention and treatment of stress, protein aggregation, and age-related pathologies.

ASTAXANTHIN PROTECTS MITOCHONDRIA EXPOSED TO HYDROGEN PEROXIDE IN HUMAN CELL STUDY.

Neurochem Int. 2021 Jun;146:105024.

doi: 10.1016/j.neuint.2021.105024. Epub 2021 Mar 26.

The signaling pathway PI3K/Akt/Nrf2/HO-1 plays a role in the mitochondrial protection promoted by astaxanthin in the SH-SY5Y cells exposed to hydrogen peroxide

[Flávia Bittencourt Brasil](#)¹, [Rênata Cristina Bertolini Gobbo](#)², [Fhelipe Jolner Souza de Almeida](#)³, [Matheus Dargesso Luckachaki](#)⁴, [Evandro Luiz Dall'Oglio](#)⁴, [Marcos Roberto de Oliveira](#)⁵

- PMID: 33775716 DOI: [10.1016/j.neuint.2021.105024](https://doi.org/10.1016/j.neuint.2021.105024)

Abstract

The mitochondria are the major source of reactive species in the mammalian cells. Hydrogen peroxide (H₂O₂) is a potent inducer of redox impairment by a mechanism, at least in part, dependent on its ability to impair mitochondrial function. H₂O₂ plays an important role in several pathological conditions, including neurodegeneration and cardiovascular diseases. Astaxanthin (AST) is a xanthophyll that may be found in microalgae, crustaceans, and salmon and exhibits antioxidant and anti-inflammatory effects in different cell types. Even though there is evidence pointing to a role for AST as mitochondrial protectant agent, it was not clearly demonstrated how this xanthophyll attenuates mitochondrial stress. Therefore, we investigated here whether and how AST would be able to prevent the H₂O₂-induced mitochondrial dysfunction in the human neuroblastoma SH-SY5Y cells. We found that AST (20 μM) prevented the H₂O₂-induced loss of mitochondrial membrane potential (MMP) and decrease in the activity of the Complexes I and V. AST pretreatment blocked the mitochondria-related pro-apoptotic effects elicited by H₂O₂. AST upregulated the enzyme heme oxygenase-1 (HO-1) and the transcription factor nuclear factor erythroid 2-related factor 2 (Nrf2) by a mechanism dependent on the phosphoinositide 3-kinase/Akt (PI3K/Akt) signaling pathway. Inhibition of the PI3K/Akt or of the HO-1 enzyme abolished the AST-induced mitochondrial protection in cells challenged with H₂O₂. Silencing of Nrf2 caused similar effects. Thus, we suggest that AST promotes mitochondrial protection by a mechanism dependent on the PI3K/Akt/Nrf2/HO-1 signaling pathway in SH-SY5Y cells exposed to H₂O₂.

ASTAXANTHIN SHOWS POTENTIAL TO ENHANCE THE VIABILITY OF STEM CELLS DURING TRANSPLANTATION UNDER HARSH CONDITIONS.

Chem Biol Interact. 2021 Jan 5;333:109324.

doi: 10.1016/j.cbi.2020.109324. Epub 2020 Nov 17.

Astaxanthin protects mesenchymal stem cells from oxidative stress by direct scavenging of free radicals and modulation of cell signaling

[Solmaz Mohammadi](#)¹, [Abolfazl Barzegari](#)², [Alireza Dehnad](#)³, [Jaleh Barar](#)⁴, [Yadollah Omid](#)⁵

- PMID: 33212048 DOI: [10.1016/j.cbi.2020.109324](https://doi.org/10.1016/j.cbi.2020.109324)

Abstract

Recent evidence has shown that mesenchymal stem cells (MSCs) play vital roles in cell therapy of ischemia/hypoxia damaged tissues. However, after the transplantation, they might undergo apoptosis due to oxidative stress. Thus, some strategies have been developed to support stem cells in harsh conditions, including pre-treatment of the cells with antioxidants. Of various antioxidants, in this study, astaxanthin (ATX) was used to protect adipose-derived MSCs against oxidative stress. The MSCs were exposed to different doses of hydrogen peroxide, and then the expression of key genes involved in the redox signaling pathway was studied, including nuclear factor erythroid 2-related factor 2 (Nrf2), heme oxygenase-1 (HO-1), and NADPH quinone oxidoreductase 1 (NQO1). The balance of intracellular reactive oxygen species was detected with the H₂DCFDA molecular probe. Additionally, for the detection of apoptosis and protective effect of ATX, the DAPI/Phalloidin and annexin V cell staining were performed. The results of cellular studies revealed that ATX reduced the H₂O₂-induced cell apoptosis and oxidative stress. Furthermore, after the induction of oxidative stress, the cells' native antioxidants (HO-1 and NQO1) were overexpressed but they were modulated with ATX treatments ($p < 0.023$). Based on our findings, ATX could increase the expression of Nrf2 as a key transcription factor of antioxidant enzymes ($p < 0.05$). These findings support the notion that ATX can act as an effective antioxidant in the pre-treatment of MSCs before cell therapy. Thus, to enhance the viability of stem cells during the transplantation in harsh conditions, the concurrent use of ATX in cell therapy modalities is proposed.

Astaxanthin shows a neuroprotective effect in rat cells and aids against oxidative stress, glutamate stress and DNA damage.

[Mol Vis.](#) 2014 Dec 31;20:1796-805. eCollection 2014.

Neuroprotective effect of astaxanthin against rat retinal ganglion cell death under various stresses that induce apoptosis and necrosis.

[Yamaqishi R¹](#), [Aihara M²](#).

Author information

Abstract

PURPOSE:

Astaxanthin is a type of carotenoid known to have strong antioxidant effects. The purpose of this study was to investigate whether astaxanthin confers a neuroprotective effect against glutamate stress, oxidative stress, and hypoxia-induced apoptotic or necrotic cell death in primary cultures of rat retinal ganglion cells (RGCs).

METHODS:

Purified rat RGCs were exposed to three kinds of stressors induced by 25 μ M glutamate for 72 h, B27 medium without an antioxidant for 4 h, and a reduced oxygen level of 5% for 12 h. Each assay was repeated 12 times, with or without 1 nM, 10 nM, and 100 nM astaxanthin. The number of live RGCs was then counted using a cell viability assay. RGC viability in each condition was evaluated and compared with controls. In addition, we measured apoptosis and DNA damage.

RESULTS:

We found that under glutamate stress, RGC viability was reduced to 58%. Cultures with 1 nM, 10 nM, and 100 nM astaxanthin showed an increase in RGC viability of 63%, 74%, and 84%, respectively. Under oxidative stress, RGC viability was reduced to 40%, and astaxanthin administration resulted in increased viability of 43%, 50%, and 67%, respectively. Under hypoxia, RGC viability was reduced to 66%, and astaxanthin administration resulted in a significant increase in viability to 67%, 77%, and 93%, respectively. These results indicate that 100 nM astaxanthin leads to a statistically significant increase in RGC viability under the three kinds of stressors tested, compared to controls (Dunnett's test, $p < 0.05$). The apoptotic activity of RGCs under glutamate stress increased to 32%, but was reduced to 15% with 100 nM astaxanthin administration. Glutamate stress led to a 58% increase in DNA damage, which was reduced to 43% when cultured with 100 nM astaxanthin. Thus, 100 nM astaxanthin showed a statistically significant reduction in apoptosis and DNA damage in RGCs (Wilcoxon rank-sum test, $p < 0.05$).

CONCLUSIONS:

Our results suggest that astaxanthin has a neuroprotective effect against RGC death induced by glutamate stress, oxidative stress, and hypoxia, which induce apoptotic and necrotic cell death.

PMID: 25593507 [PubMed - in process] PMCID: PMC4287717

[Free PMC Article](#)

Astaxanthin protects mitochondrial redox state and functional integrity against oxidative stress.

[J Nutr Biochem](#). 2010 May;21(5):381-9. doi: 10.1016/j.jnutbio.2009.01.011. Epub 2009 May 7.

Astaxanthin protects mitochondrial redox state and functional integrity against oxidative stress.

[Wolf AM](#)¹, [Asoh S](#), [Hiranuma H](#), [Ohsawa I](#), [Iio K](#), [Satou A](#), [Ishikura M](#), [Ohta S](#).

Author information

Abstract

Mitochondria combine the production of energy with an efficient chain of reduction-oxidation (redox) reactions but also with the unavoidable production of reactive oxygen species. Oxidative stress leading to mitochondrial dysfunction is a critical factor in many diseases, such as cancer and neurodegenerative and lifestyle-related diseases. Effective antioxidants thus offer great therapeutic and preventive promise. Investigating the efficacy of antioxidants, we found that a carotenoid, astaxanthin (AX), decreased physiologically occurring oxidative stress and protected cultured cells against strong oxidative stress induced with a respiratory inhibitor. Moreover, AX improved maintenance of a high mitochondrial membrane potential and stimulated respiration. Investigating how AX stimulates and interacts with mitochondria, a redox-sensitive fluorescent protein (roGFP1) was stably expressed in the cytosol and mitochondrial matrix to measure the redox state in the respective compartments. AX at nanomolar concentrations was effective in maintaining mitochondria in a reduced state. Additionally, AX improved the ability of mitochondria to remain in a reduced state under oxidative challenge. Taken together, these results suggest that AX is effective in improving mitochondrial function through retaining mitochondria in the reduced state.

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PMID:

19423317

[PubMed - indexed for MEDLINE]

Astaxanthin enhances a DNA repair enzyme and is a novel candidate for cancer prevention.

[Biochimie](#). 2013 Aug;95(8):1629-39. doi: 10.1016/j.biochi.2013.05.004. Epub 2013 May 21.

Chemopreventive effects of diverse dietary phytochemicals against DMBA-induced hamster buccal pouch carcinogenesis via the induction of Nrf2-mediated cytoprotective antioxidant, detoxification, and DNA repair enzymes.

[Kavitha K¹](#), [Thiyagarajan P](#), [Rathna Nandhini J](#), [Mishra R](#), [Nagini S](#).

Author information

Abstract

Identifying agents that activate nuclear factor erythroid-2 related factor-2 (Nrf2), a key regulator of various cytoprotective antioxidant, and detoxifying enzymes has evolved as a promising strategy for cancer chemoprevention. In the present study, we investigated the effect of dietary supplementation of structurally diverse phytochemicals- astaxanthin, blueberry, chlorophyllin, ellagic acid, and theaphenon-E on Nrf2 signaling, and xenobiotic-metabolizing and antioxidant enzymes in the 7,12-dimethylbenz[a]anthracene (DMBA)-induced hamster buccal pouch (HBP) carcinogenesis model. We observed that these phytochemicals induce nuclear accumulation of Nrf2 while downregulating its negative regulator, Keap-1. This was associated with reduced expression of CYP1A1 and CYP1B1, the cytochrome P450 isoforms involved in the activation of DMBA, and the oxidative stress marker 8-hydroxy-2'-deoxyguanosine coupled with upregulation of the phase II detoxification enzymes glutathione S-transferases and NAD(P)H:quinone oxidoreductase 1 and the antioxidant enzymes superoxide dismutase, catalase, and glutathione peroxidase. In addition, these dietary phytochemicals also enhanced the DNA repair enzymes 8-oxoguanine glycosylase 1 (OGG1), xeroderma pigmentosum D (XPD), xeroderma pigmentosum G (XPG), and x-ray repair cross complementing group 1 (XRCC1). Our data provide substantial evidence that the dietary phytochemicals inhibit the development of HBP carcinomas through the activation of Nrf2/Keap-1 signaling and by upregulating cytoprotective enzymes. The extent of the chemopreventive effects of the phytochemicals was in the order: chlorophyllin > blueberry > ellagic acid > astaxanthin > theaphenon-E. Thus these dietary phytochemicals that function as potent activators of Nrf2 and its orchestrated response are novel candidates for cancer chemoprevention.

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PMID:

23707664

[PubMed - indexed for MEDLINE]

Astaxanthin improves oxidative stress markers and an indicator of oxidative DNA damage in mouse cells and may be developed as an antioxidant drug to treat diabetic retinopathy.

[Mar Drugs](#). 2013 Mar 21;11(3):960-74. doi: 10.3390/md11030960.

Astaxanthin attenuates the apoptosis of retinal ganglion cells in db/db mice by inhibition of oxidative stress.

[Dong LY¹](#), [Jin J](#), [Lu G](#), [Kang XL](#).

Author information

Abstract

Diabetic retinopathy is a common diabetic eye disease caused by changes in retinal ganglion cells (RGCs). It is an ocular manifestation of systemic disease, which affects up to 80% of all patients who have had diabetes for 10 years or more. The genetically diabetic db/db mouse, as a model of type-2 diabetes, shows diabetic retinopathy induced by apoptosis of RGCs. Astaxanthin is a carotenoid with powerful antioxidant properties that exists naturally in various plants, algae and seafood. Here, astaxanthin was shown to reduce the apoptosis of RGCs and improve the levels of oxidative stress markers, including superoxide anion, malondialdehyde (MDA, a marker of lipid peroxidation), 8-hydroxy-2-deoxyguanosine (8-OHdG, indicator of oxidative DNA damage) and MnSOD (manganese superoxide dismutase) activity in the retinal tissue of db/db mouse. In addition, astaxanthin attenuated hydrogen peroxide(H₂O₂)-induced apoptosis in the transformed rat retinal ganglion cell line RGC-5. Therefore, astaxanthin may be developed as an antioxidant drug to treat diabetic retinopathy.

PMID:

23519150

[PubMed - indexed for MEDLINE]

PMCID:

PMC3705382

Free PMC Article

Astaxanthin modulates age-associated mitochondrial dysfunction in dogs which is attributed to alleviating oxidative damage to cellular DNA and protein.

[J Anim Sci.](#) 2013 Jan;91(1):268-75. doi: 10.2527/jas.2012-5341. Epub 2012 Oct 16.

Astaxanthin modulates age-associated mitochondrial dysfunction in healthy dogs.

[Park JS¹](#), [Mathison BD](#), [Hayek MG](#), [Zhang J](#), [Reinhart GA](#), [Chew BP](#).

Author information

Abstract

Young (2.97±0.01 yr; 8.16±0.15 kg BW) and geriatric (10.71±0.01 yr; 9.46±0.18 kg BW) healthy female Beagle dogs (n=14/age group) were fed 0 or 20 mg astaxanthin daily for 16 wk to examine modulation of mitochondrial function. Fasted blood was sampled on wk 0, 8, and 16. Mitochondria membrane permeability, ATP production, cytochrome c oxidase/reductase, and number were assessed in leukocytes whereas astaxanthin uptake, glutathione, superoxide dismutase, nitric oxide, 8-hydroxy-2'-deoxyguanosine, 8-isoprostane, and protein carbonyl were measured in plasma. Aging increased (P<0.05) complex III cytochrome c oxidoreductase but decreased (P<0.05) 8-hydroxy-2'-deoxyguanosine and protein carbonyl. Mitochondrial function improved in both young and geriatric dogs by increasing (P<0.05) ATP production, mitochondria mass, and cytochrome c oxidoreductase activity, especially in geriatric dogs compared with young dogs. Astaxanthin feeding also increased (P<0.05) the reduced glutathione to oxidized glutathione ratio in young dogs and decreased (P<0.05) nitric oxide in both young and geriatric dogs. Dietary astaxanthin improved mitochondrial function in blood leukocytes, most likely by alleviating oxidative damage to cellular DNA and protein.

PMID:

23100599

[PubMed - indexed for MEDLINE]

Free full text

Astaxanthin reduces DNA damage in rat liver cells.

[Toxicol Ind Health](#). 2014 Mar;30(2):101-12. doi: 10.1177/0748233712452607. Epub 2012 Jul 9.

Hepatoprotective potential of astaxanthin against 2,3,7,8-tetrachlorodibenzo-p-dioxin in cultured rat hepatocytes.

[Turkez H¹](#), [Geyikoglu F](#), [Yousef MI](#), [Togar B](#), [Gürbüz H](#), [Celik K](#), [Akbaba GB](#), [Polat Z](#).

Author information

Abstract

The purpose of this study was to evaluate the effect of carotenoid astaxanthin (ASTA) on cultured primary rat hepatocytes treated with 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) on the cell viability (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide, MTT), lactate dehydrogenase (LDH) activity, 8-oxo-2-deoxyguanosine (8-OH-dG), total antioxidant capacity (TAC), and total oxidative stress (TOS) levels, and liver micronucleus rates. ASTA (2.5, 5, and 10 μ M) was added to cultures alone or simultaneously with TCDD (5 and 10 μ M) for 48 h. The results of MTT and LDH assays showed that both doses of TCDD caused significant decrease in cell viability. Also, TCDD significantly increased TOS and decreased TAC level in rat hepatocytes. On the basis of increasing doses, the dioxin caused significant increase in micronucleated hepatocytes) and 8-OH-dG level as compared to control culture. The presence of ASTA with TCDD minimized its effects on primary hepatocytes cultures and DNA damages.

KEYWORDS:

TCDD; astaxanthin; cell viability; cultured rat hepatocytes; genotoxicity; oxidative status

PMID:

22778115

[PubMed - indexed for MEDLINE]

Astaxanthin may protect against oxidative impairment and DNA damage.

[Wei Sheng Yan Jiu](#). 2011 Sep;40(5):551-4.

[Protective effects of astaxanthin against oxidative damage induced by 60Co gamma-ray irradiation].

[Article in Chinese]

[Zhao W¹](#), [Jing X](#), [Chen C](#), [Cui J](#), [Yang M](#), [Zhang Z](#).

Author information

Abstract

OBJECTIVE:

To investigate the protection effect of haematococcus pluvialis (containing astaxanthin) against the impairment of anti-oxidative system and DNA damage in mice induced by 60Co gamma-rays.

METHODS:

Fifty mice were randomly divided into five groups, i.e. three haematococcus pluvialis groups (41.7, 83.3 and 166.7 mg/kg in vegetable oil, respectively), control group and model group (vegetable oil only). All mice except control group were irradiated by 8 Gy 60Co gamma-rays 30 days later, and executed in the 4th day after irradiation. Liver cells were collected for the analysis of the integrity of DNA by comet assay, as well as MDA contents, SOD and GSH-Px activities in liver by commercial kits. Peripheral granulocyte and bone marrow nucleated cells were counted by hematocyte counter.

RESULTS:

MDA contents of model group were higher than those of control group ($P < 0.01$), and SOD, GSH-Px activities of model group were lower than those of control group ($P < 0.01$). Compared with the model group, MDA contents were decreased ($P < 0.01$), and SOD and GSH-Px activities were increased ($P < 0.01$) in all haematococcus pluvialis groups, especially in the high haematococcus pluvialis group, and the more haematococcus pluvialis in the diet of mice, the lower rate of comet tail and OTM value were shown ($P < 0.01$). Furthermore, the counts of peripheral granulocyte and bone marrow nucleated cells of model group were lower than those of the control group, while the counts of peripheral granulocyte and bone marrow nucleated cells of medium and high haematococcus pluvialis groups were increased significantly when compared with the model group ($P < 0.01$).

CONCLUSION:

Astaxanthin might have some protective effect against oxidative impairment and DNA damage induced by 60Co gamma-rays in mice.

PMID:

22043699

[PubMed - indexed for MEDLINE]

Astaxanthin heightens the immune response and reduces DNA damage and inflammation in dogs.

[Vet Immunol Immunopathol.](#) 2011 Apr 15;140(3-4):199-206. doi: 10.1016/j.vetimm.2010.12.004. Epub 2010 Dec 14.

Dietary astaxanthin enhances immune response in dogs.

[Chew BP¹](#), [Mathison BD](#), [Hayek MG](#), [Massimino S](#), [Reinhart GA](#), [Park JS](#).

Author information

Abstract

No information is available on the possible role of astaxanthin on immune response in domestic canine. Female Beagle dogs (9-10 mo old; 8.2 ± 0.2 kg body weight) were fed 0, 10, 20 or 40 mg astaxanthin daily and blood sampled on wk 0, 6, 12, and 16 for assessing the following: lymphoproliferation, leukocyte subpopulations, natural killer (NK) cell cytotoxicity, and concentrations of blood astaxanthin, IgG, IgM and acute phase proteins. Delayed-type hypersensitivity (DTH) response was assessed on wk 0, 12 and 16. Plasma astaxanthin increased dose-dependently and reached maximum concentrations on wk 6. Dietary astaxanthin enhanced DTH response to vaccine, concanavalin A-induced lymphocyte proliferation (with the 20mg dose at wk 12) and NK cell cytotoxic activity. In addition, dietary astaxanthin increased concentrations of IgG and IgM, and B cell population. Plasma concentrations of C reactive protein were lower in astaxanthin-fed dogs. Therefore, dietary astaxanthin heightened cell-mediated and humoral immune response and reduced DNA damage and inflammation in dogs.

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PMID:

21208664

[PubMed - indexed for MEDLINE]

Astaxanthin improves oxidative stress and DNA damage in rats.

[Mutat Res.](#) 2010 Feb;696(1):69-80. doi: 10.1016/j.mrgentox.2009.12.014. Epub 2009 Dec 28.

Astaxanthin intervention ameliorates cyclophosphamide-induced oxidative stress, DNA damage and early hepatocarcinogenesis in rat: role of Nrf2, p53, p38 and phase-II enzymes.

[Tripathi DN¹](#), [Jena GB](#).

Author information

Abstract

Cyclophosphamide, an alkylating agent, disturbs the oxidant and antioxidant balance that is associated with several unwanted toxic effects and induction of secondary cancers. Astaxanthin is a powerful antioxidant and possess several beneficial effects against various human diseases and physiological disorders. The present study was aimed to investigate the effects of astaxanthin against cyclophosphamide-induced oxidative stress, DNA damage, cell death and induction of GST-P foci in rat liver. Further attempt has been made to study the influence of astaxanthin on antioxidant response element (ARE) and the transcription factor Nrf2 (nuclear factor E(2)-related factor 2) in the induction of phase-II enzymes NAD(P)H: quinine oxidoreductase-1 (NQO-1) and Hemoxygenase-1 (HO-1). Both pre- and post-treatment with astaxanthin (25mg/kg) decreased cyclophosphamide-induced oxidative stress and DNA damage in the liver as evident from the restoration in malondialdehyde and glutathione level as well as modified comet assay parameters. Significant decrease in the number as well as area of GST-P foci in rat hepatocytes was observed with astaxanthin post-treatment. Treatment with astaxanthin significantly decreased the expression of p53 and p38 as compared to cyclophosphamide treated group. It was further observed that the level of Nrf2 and phase-II enzymes, i.e. NQO-1 and HO-1 were increased with astaxanthin treatment. The present study confirms that astaxanthin is a potent antioxidant and attenuates oxidative stress, DNA damage, cell death as well as induction of early hepatocarcinogenesis in rat induced by cyclophosphamide. Our results provide the evidence that one of the mechanism of chemoprotection offered by astaxanthin is mediated through Nrf2-ARE pathway.

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PMID:

20038455

[PubMed - indexed for MEDLINE]

Astaxanthin improves oxidative stress and DNA damage in mice.

[Chem Biol Interact.](#) 2009 Aug 14;180(3):398-406. doi: 10.1016/j.cbi.2009.03.017. Epub 2009 Apr 2.

Intervention of astaxanthin against cyclophosphamide-induced oxidative stress and DNA damage: a study in mice.

[Tripathi DN¹](#), [Jena GB.](#)

Author information

Abstract

Astaxanthin, a natural and nutritional red carotenoid pigment, is used as a dietary supplement. The intention of the present study was to investigate the beneficial effects of dietary pigment astaxanthin, against cyclophosphamide-induced oxidative stress and DNA damage. The end points of evaluation of the study included: (a) malondialdehyde, glutathione and superoxide dismutase concentration in liver to detect oxidative stress; (b) normal and modified alkaline comet assays (the latter includes lesion-specific enzymes formamidopyrimidine-DNA glycosylase and endonuclease-III) to detect normal and oxidative stress-induced DNA damage by cyclophosphamide in the mouse bone marrow and the peripheral blood lymphocytes. In addition, micronucleus assay and chromosomal aberration test capable of detecting the DNA damage were also carried out in peripheral blood and bone marrow of mice. Cyclophosphamide (100 mg/kg intra-peritoneal) treatment led to significant increase in liver malondialdehyde and decreased the antioxidant enzymes glutathione and superoxide dismutase. Further, cyclophosphamide also significantly increased the DNA damage as observed from normal and modified comet assays as well as micronucleus and chromosomal aberration assay. Pre-treatment with astaxanthin (12.5, 25 and 50 mg/kg/day for 5 days per oral) resulted in the restoration of oxidative stress markers such as malondialdehyde, glutathione and superoxide dismutase in liver. The amelioration of oxidative stress with astaxanthin pre-treatment correlated well with the decreased DNA damage as evident from normal and modified alkaline comet assays of bone marrow cells and peripheral blood lymphocytes. Further astaxanthin pre-treatment also reduced the frequency of chromosomal breakage and micronucleus formation in the mouse bone marrow cells and peripheral blood reticulocytes. It is thus concluded that pre-treatment with astaxanthin attenuates cyclophosphamide-induced oxidative stress and subsequent DNA damage in mice and it can be used as a chemoprotective agent against the toxicity of anticancer drug cyclophosphamide.

PMID:

19539803

[PubMed - indexed for MEDLINE]

Astaxanthin protects retinal cells against oxidative stress and reduces an indicator of DNA damage in mice.

[J Pharm Pharmacol](#). 2008 Oct;60(10):1365-74. doi: 10.1211/jpp/60.10.0013.

Astaxanthin, a dietary carotenoid, protects retinal cells against oxidative stress in-vitro and in mice in-vivo.

[Nakajima Y¹](#), [Inokuchi Y](#), [Shimazawa M](#), [Otsubo K](#), [Ishibashi T](#), [Hara H](#).

Author information

Abstract

We have investigated whether astaxanthin exerted neuroprotective effects in retinal ganglion cells in-vitro and in-vivo. In-vitro, retinal damage was induced by 24-h hydrogen peroxide (H₂O₂) exposure or serum deprivation, and cell viability was measured using a WST assay. In cultured retinal ganglion cells (RGC-5, a rat ganglion cell-line transformed using E1A virus), astaxanthin inhibited the neurotoxicity induced by H₂O₂ or serum deprivation, and reduced the intracellular oxidation induced by various reactive oxygen species (ROS). Furthermore, astaxanthin decreased the radical generation induced by serum deprivation in RGC-5. In mice in-vivo, astaxanthin (100 mg kg⁻¹), p.o., four times) reduced the retinal damage (a decrease in retinal ganglion cells and in thickness of inner plexiform layer) induced by intravitreal N-methyl-D-aspartate (NMDA) injection. Furthermore, astaxanthin reduced the expressions of 4-hydroxy-2-nonenal (4-HNE)-modified protein (indicator of lipid peroxidation) and 8-hydroxy-deoxyguanosine (8-OHdG; indicator of oxidative DNA damage). These findings indicated that astaxanthin had neuroprotective effects against retinal damage in-vitro and in-vivo, and that its protective effects may have been partly mediated via its antioxidant effects.

PMID:

18812030

[PubMed - indexed for MEDLINE]

Astaxanthin inhibits cytotoxic and genotoxic effects and restores DNA damage in mouse cells.

[Toxicology](#). 2008 Jun 27;248(2-3):96-103. doi: 10.1016/j.tox.2008.03.015. Epub 2008 Mar 27.

Astaxanthin inhibits cytotoxic and genotoxic effects of cyclophosphamide in mice germ cells.

[Tripathi DN¹](#), [Jena GB](#).

Author information

Abstract

Cyclophosphamide (CP), an alkylating agent used in the treatment of several cancers as well as an immunosuppressant in rheumatoid arthritis. It is used against several cancers due to its broad spectrum efficacy, but at the same time possesses unwanted risks for occupational exposure as well as therapy related toxicities to patients. The present study was aimed to investigate the protective effect of astaxanthin (AST) a red carotenoid pigment on CP induced germ cell toxicity in male mice. CP was administered intraperitoneally (i.p.) at the dose of 50, 100 and 200mg/kg body weight to mice (20-25 g) once in a week for a period of five weeks. AST was given at the dose of 25mg/kg per oral (p.o.) for five consecutive days in a week for five weeks. The animals were sacrificed one week after the last injection of CP. The protective effect of AST against CP induced male germ cell toxicity was evaluated using body weight, testes and epididymis weight, sperm count, sperm head morphology, sperm comet assay, histology of testes and TUNEL assay. AST treatment significantly improved the testes weight, sperm count and sperm head morphology as compared to only CP treated animals. The result of comet assay showed that AST treatment significantly restored the sperm DNA damage induced by CP. Further, AST treatment showed protection against CP induced testicular toxicity as evident from testes histology and TUNEL assay. The present results indicate the chemoprotective potential of AST against CP induced germ cell toxicity in mice.

PMID:

18485558

[PubMed - indexed for MEDLINE]

Astaxanthin applied topically shows anti-aging potential for skin.

J Cosmet Dermatol. 2018 May 10. doi: 10.1111/jocd.12665. [Epub ahead of print]

Antioxidant properties evaluation of topical astaxanthin formulations as anti-aging products.

Eren B¹, Tuncay Tanrıverdi S¹, Aydın Köse F², Özer Ö¹.

Author information

Abstract

BACKGROUND: The reactive oxygen species lead to skin aging via oxidative damage that are induced by UV radiation. Therefore, topical formulations which have antioxidant effect could reduce aging level. Astaxanthin is an antioxidant substance.

AIMS: The aim of this study was to investigate antioxidant activity and cytotoxicity potential of the astaxanthin-loaded gel formulations.

METHODS: Astaxanthin-loaded oleoresin and algae extract were used as natural active materials. The lipogel and hydrogel of these natural materials were prepared as anti-aging formulations. The formulations were characterized via parameters such as, pH, rheological analysis, mechanical properties, and stability. And also in vitro release experiments of the formulations were carried out. The antioxidant activity and cytotoxicity test were performed.

RESULTS: The results of characterization studies confirmed the formulations suitable for topical application. After 24 hours, 99 µg, 88.3 µg, 403 µg, and 234.8 µg of astaxanthin released through oleoresin lipogel, oleoresin hydrogel, algae extract lipogel, and algae extract hydrogel, respectively. It was found by the cytotoxicity tests that astaxanthin is more proliferative in lipogel formulations compared to hydrogel formulations. And finally, the highest antioxidant activity was found in the algae extract hydrogel and algae extract lipogel formulation, respectively ($P < .05$).

CONCLUSIONS: Topical formulations of astaxanthin-loaded oleoresin and algae extract were prepared successfully. At the same time, according to antioxidant activity and release studies, algae extract loaded could be suggested as topical anti-aging formulations.

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KEYWORDS: algae extract; anti-aging; antioxidant; astaxanthin; cell culture; gel systems

PMID: 29745467 DOI: [10.1111/jocd.12665](https://doi.org/10.1111/jocd.12665)

Astaxanthin exerts significant anti-aging effects, prevents liver weight loss and improves locomotive muscular function in mouse model of jet lag.

[Endocr J.](#) 2018 May 28;65(5):569-578. doi: 10.1507/endocrj.EJ17-0500. Epub 2018 Mar 10.

Protective effects of astaxanthin on a combination of D-galactose and jet lag-induced aging model in mice.

[Ni Y¹](#), [Wu T¹](#), [Yang L¹](#), [Xu Y¹](#), [Ota T²](#), [Fu Z¹](#).

Author information

Abstract

Oxidative stress caused free radical and mitochondrial damage plays a critical role in the progression of aging and age-related damage at the cellular and tissue levels. Antioxidant supplementation has received growing attention and the effects of antioxidant on aging are increasingly assessed in both animal and human studies. However, additional and more promising treatments that contribute to the expansion of anti-aging therapies are needed. Astaxanthin, a super antioxidant carotenoid and free radical scavenger, inhibits lipid peroxidation more potently than vitamin E. In the present study, we investigated the preventative effects of astaxanthin on aging using an accelerated aging model: mice chronically treated with a combination of D-galactose and jet lag. After 6 weeks of treatment, astaxanthin administration tended to protect the liver weight loss in aged mice. It is probably by upregulating the mRNA expression of galactose-1-phosphate uridylyltransferase, which contribute to the enhancement of D-galactose metabolism. Astaxanthin supplementation also improved muscle endurance of aged mice in a swimming test. These results were associated with reduced oxidative stress in serum and increased anti-oxidative enzymes activities and mRNA expression in vivo. Moreover, astaxanthin reversed the dysregulation of aging-related gene expression caused by the combination of D-galactose and jet lag in the liver and kidney of mice. In conclusion, astaxanthin prevents liver weight loss, ameliorates locomotive muscular function, exerts significant anti-aging effects by reducing oxidative stress and improving the expression of age-related genes in D-galactose and jet lag-induced aging model.

KEYWORDS:

Aging; Antioxidant; Astaxanthin; D-galactose; Jet lag

PMID: 29526991

DOI: [10.1507/endocrj.EJ17-0500](https://doi.org/10.1507/endocrj.EJ17-0500)

[Indexed for MEDLINE]

Free full text

Astaxanthin increases survival and provides antioxidant protection in citrus red mites.

Environ Entomol. 2017 Oct 1;46(5):1143-1150. doi: 10.1093/ee/nvx121.

Antioxidant Protection by Astaxanthin in the Citrus Red Mite (Acari: Tetranychidae).

[Atarashi M](#)¹, [Manabe Y](#)², [Kishimoto H](#)³, [Sugawara T](#)², [Osakabe M](#)¹.

Author information

Abstract

Solar ultraviolet-B (UVB) radiation and radiant heat have lethal effects on plant-dwelling mites, including spider mites, and their natural enemies, such as phytoseiid mites, leading them to reside on lower leaf surfaces. Panonychus spider mites are outcompeted by Tetranychus spider mites and thus exploit upper leaf surfaces, where they are exposed to both UVB radiation and radiant heat. Panonychus spider mites are thought to produce astaxanthin constitutionally. In this study, we compared carotenoid components, antioxidant capacity, lipid peroxidation, survival, and egg production in wild-type (WTS) and albino-type strains (ATS) of Panonychus citri (McGregor). Four carotenoids (neoxanthin, violaxanthin, lutein, and carotene) and their isomers and esters were identified in both strains, but astaxanthin and its esters were present only in WTS. The singlet oxygen scavenging capacity of lipid-soluble ingredients was greater in WTS than in ATS, whereas the oxygen radical absorbance capacities of hydrophilic ingredients were equivalent between them. Lipid peroxide accumulation was clearly higher in ATS than in WTS under both UVB irradiation (25 °C) and high temperature (35 °C) conditions. The findings are consistent with an antioxidant protective function of astaxanthin in this mite. Survival periods at 38 °C were longer in WTS than in ATS, although no difference was shown at 35 °C or under UVB irradiation. Therefore, astaxanthin accumulation was shown to be a major mechanism for survival under radiant heat, although other mechanisms, such as photoreactivation, might play a major role in survival under UVB radiation.

KEYWORDS:

Carotenoid; Lipid peroxidation; Oxygen Radical Absorbance Capacity; Singlet Oxygen Scavenging Capacity; Tetranychidae

PMID: 28981670

DOI: [10.1093/ee/nvx121](https://doi.org/10.1093/ee/nvx121)

[Indexed for MEDLINE]

Astaxanthin prevents central nervous system cell death after traumatic injury.

[BMC Neurosci.](#) 2017 May 10;18(1):42. doi: 10.1186/s12868-017-0358-z.

Astaxanthin protects astrocytes against trauma-induced apoptosis through inhibition of NKCC1 expression via the NF- κ B signaling pathway.

[Zhang M](#)^{1,2}, [Cui Z](#)^{2,3}, [Cui H](#)¹, [Wang Y](#)⁴, [Zhong C](#)⁵.

Author information

Abstract

BACKGROUND: Astaxanthin (ATX) is a carotenoid pigment with pleiotropic pharmacological properties that is seen as a possible drug for treating cerebral ischemic injury and subarachnoid hemorrhage. Na⁺-K⁺-2Cl⁻ co-transporter-1 (NKCC1), an intrinsic membrane protein expressed by many cell types, is activated by various insults, leading to the formation of cell swelling and brain edema. We previously established that ATX attenuated brain edema and improved neurological outcomes by modulating NKCC1 expression after traumatic brain injury in mice. This paper explored the molecular mechanism of ATX-mediated inhibition of NKCC1 utilizing an in vitro astrocyte stretch injury model.

RESULTS: Stretch injury in cultured astrocytes lowered cell viability time-dependently, which was substantially reducing by pretreating with ATX (50 μ mol/L). Stretch injury increased Bax level and cleaved caspase-3 activity, and decreased Bcl-2 level and pro-caspase 3 activity, resulting in the apoptosis of astrocytes. Additionally, stretch injury substantially raised the gene and protein expressions of interleukin (IL)-1 β , IL-6, and tumor necrosis factor (TNF)- α and prompted the expression and nuclear translocation of NF- κ B. Pretreatment with ATX remarkably prevented the trauma-induced initiation of NF- κ B, expressions of pro-inflammatory cytokines, and cell apoptosis. Moreover, stretch injury markedly elevated the gene and protein expression of NKCC1, which was partly blocked by co-treatment with ATX (50 μ mol/L) or an NF- κ B inhibitor (PDTC, 10 μ mol/L). Cleaved caspase-3 activity was partially reduced by PDTC (10 μ mol/L) or an NKCC1 inhibitor (bumetanide, 50 μ mol/L).

CONCLUSIONS: ATX attenuates apoptosis after stretch injury in cultured astrocytes by inhibiting NKCC1 expression, and it acts by reducing the expression of NF- κ B-mediated pro-inflammatory factors.

KEYWORDS: Apoptosis; Astaxanthin; Astrocyte; NF- κ B; Na⁺-K⁺-2Cl⁻ co-transporter-1; Traumatic brain injury

PMID: 28490320 PMCID: [PMC5425995](#) DOI: [10.1186/s12868-017-0358-z](#)

[Indexed for MEDLINE]

[Free PMC Article](#)

Astaxanthin prevents cell death in cells exposed to glutamate.

[Eur J Pharmacol](#). 2017 Jul 5;806:43-51. doi: 10.1016/j.ejphar.2017.04.008. Epub 2017 Apr 8.

Astaxanthin attenuates glutamate-induced apoptosis via inhibition of calcium influx and endoplasmic reticulum stress.

[Lin X¹](#), [Zhao Y²](#), [Li S¹](#).

[Author information](#)

Abstract

Astaxanthin (AST) is a carotenoid that has been shown to have neuroprotective effects. In this study, it was found that AST significantly inhibited glutamate-induced loss of cell viability and apoptosis. AST pretreatment attenuated glutamate-induced activation of caspase-3, reduction of anti-apoptotic protein Bcl-2, and increase of pro-apoptotic protein Bak. In addition, AST pretreatment suppressed the production of intracellular reactive oxygen species. AST treatment also prevented glutamate-induced increase of the level of activated p38 mitogen-activated protein kinase (MAPK), which has been shown to promote apoptotic events. Furthermore, AST treatment greatly reduced the elevation of intracellular calcium level induced by glutamate and inhibited the activity of calpain, a calcium-dependent protease that plays an important role in mediating apoptosis stimulated by calcium overload in cytoplasm. Both oxidative stress and calcium overload can lead to endoplasmic reticulum (ER) stress. C/EBP-homologous protein (CHOP) is a bZIP transcription factor that can be activated by ER stress and promotes apoptosis. Here we found that AST attenuated glutamate-induced elevation of CHOP and ER chaperone glucose-regulated protein (GRP78). Overall, these results suggested that AST might protect cells against glutamate-induced apoptosis through maintaining redox balance and inhibiting glutamate-induced calcium influx and ER stress.

KEYWORDS:

Apoptosis; Astaxanthin; Astaxanthin (PubChem CID: 5281224); Calcium influx; Endoplasmic reticulum stress; Glutamate; Oxidative stress

PMID: 28400209

DOI: [10.1016/j.ejphar.2017.04.008](https://doi.org/10.1016/j.ejphar.2017.04.008)

[Indexed for MEDLINE]

Astaxanthin protects stem cells from irradiation by inhibiting oxidative stress and cell death.

[Stem Cell Res Ther.](#) 2017 Jan 23;8(1):7. doi: 10.1186/s13287-016-0464-3.

Astaxanthin attenuates total body irradiation-induced hematopoietic system injury in mice via inhibition of oxidative stress and apoptosis.

[Xue XL¹](#), [Han XD¹](#), [Li Y¹](#), [Chu XF¹](#), [Miao WM²](#), [Zhang JL³](#), [Fan SJ⁴](#).

Author information

Abstract

BACKGROUND: The hematopoietic system is especially sensitive to total body irradiation (TBI), and myelosuppression is one of the major effects of TBI. Astaxanthin (ATX) is a powerful natural anti-oxidant with low toxicity. In this study, the effect of ATX on hematopoietic system injury after TBI was investigated.

METHODS: Flow cytometry was used to detect the proportion of hematopoietic progenitor cells (HPCs) and hematopoietic stem cells (HSCs), the level of intracellular reactive oxygen species (ROS), expression of cytochrome C, cell apoptosis, and NRF2-related proteins. Immunofluorescence staining was used to detect Nrf2 translocation. Western blot analysis was used to evaluate the expression of apoptotic-related proteins. Enzymatic activities assay kits were used to analyze SOD2, CAT, and GPX1 activities.

RESULTS: Compared with the TBI group, ATX can improve radiation-induced skewed differentiation of peripheral blood cells and accelerate hematopoietic self-renewal and regeneration. The radio-protective effect of ATX is probably attributable to the scavenging of ROS and the reduction of cell apoptosis. These changes were associated with increased activation of Nrf2 and downstream anti-oxidative proteins, and regulation of apoptotic-related proteins.

CONCLUSIONS: This study suggests that ATX could be used as a potent therapeutic agent to protect the hematopoietic system against TBI-induced bone marrow suppression.

KEYWORDS: Astaxanthin; Cell apoptosis; Hematopoietic stem cells; Ionizing radiation; Reactive oxygen species

PMID: 28115023

PMCID: [PMC5260077](#)

DOI: [10.1186/s13287-016-0464-3](#)

[Indexed for MEDLINE]

[Free PMC Article](#)

Astaxanthin improves status of cells that imbed in cartilage and is suggested as a possible treatment for Osteoarthritis.

[Int Immunopharmacol.](#) 2014 Mar;19(1):174-7. doi: 10.1016/j.intimp.2013.12.007. Epub 2014 Jan 27.

Astaxanthin reduces matrix metalloproteinase expression in human chondrocytes.

[Chen WP¹](#), [Xiong Y¹](#), [Shi YX¹](#), [Hu PF¹](#), [Bao JP¹](#), [Wu LD²](#).

Author information

Abstract

Astaxanthin is a red carotenoid pigment which exerts multiple biological activities. However, little is known about the effects of astaxanthin on matrix metalloproteinases (MMPs) in OA. The present study investigated the effects of astaxanthin on MMPs in human chondrocytes. Human chondrocytes were pretreated with astaxanthin at 1, 10 or 50 μ M, then, cells were stimulated with IL-1 β (10ng/ml) for 24h. MMP-1, MMP-3 and MMP-13 were observed. We found that astaxanthin reduced the expression of MMP-1, MMP-3 and MMP-13 as well as the phosphorylation of two mitogen-activated protein kinases (MAPK) (p38 and ERK1/2) in IL-1 β -stimulated chondrocytes. Astaxanthin also blocked the I κ B- α degradation. These results suggest that astaxanthin may be beneficial in the treatment of OA.

KEYWORDS:

Astaxanthin; Matrix metalloproteinase; Osteoarthritis

PMID: 24480614

DOI: [10.1016/j.intimp.2013.12.007](#)

[Indexed for MEDLINE]

Astaxanthin protects against DNA damage in human neuroblastoma cells.

[J Photochem Photobiol B](#). 2007 Jul 27;88(1):1-10. Epub 2007 May 1.

Lutein, zeaxanthin and astaxanthin protect against DNA damage in SK-N-SH human neuroblastoma cells induced by reactive nitrogen species.

[Santocono M](#)¹, [Zurria M](#), [Berrettini M](#), [Fedeli D](#), [Falcioni G](#).

Author information

Abstract

The purpose of this study was to evaluate the ability of the predominant carotenoids (lutein and zeaxanthin) of the macular pigment of the human retina, to protect SK-N-SH human neuroblastoma cells against DNA damage induced by different RNOS donors. Although astaxanthin has never been isolated from the human eye, it was included in this study because its structure is very close to that of lutein and zeaxanthin and because it affords protection from UV-light. DNA damage was induced by GSNO-MEE, a nitric oxide donor, by Na(2)N(2)O(3), a nitroxyl anion donor and by SIN-1, a peroxynitrite-generating agent. DNA damage was assessed using the comet assay, a rapid and sensitive single cell gel electrophoresis technique able to detect primary DNA damage in individual cells. The tail moment parameter was used as an index of DNA damage. The values of tail moment increased in all the samples incubated with the RNOS donors, indicating DNA impairment. Data obtained show that the ability of zeaxanthin, lutein, and astaxanthin to reduce the DNA damage depends on the type of RNOS donor and the carotenoid concentration used. All the carotenoids studied were capable of protecting against DNA damage in neuroblastoma cells when the cells were exposed to GSNO-MEE. However, a different behaviour was present when the other two RNOS donors were used. The presence of a carotenoid alone (without an RNOS donor) did not cause DNA damage. Spectrophotometric studies showed that the order with which tested carotenoids reacted with RNOS was not always in agreement with the DNA protection results. The data from this study provides additional information on the activities of the macular pigment carotenoids of the human retina.

PMID:

17548202

[PubMed - indexed for MEDLINE]

Astaxanthin reduces DNA damage in UVA-irradiated cells.

[J Photochem Photobiol B](#). 2006 Dec 1;85(3):205-15. Epub 2006 Sep 8.

Influence of astaxanthin, zeaxanthin and lutein on DNA damage and repair in UVA-irradiated cells.

[Santocono M](#)¹, [Zurria M](#), [Berrettini M](#), [Fedeli D](#), [Falcioni G](#).

Author information

Abstract

In order to gain more knowledge about the antioxidant role of the predominant carotenoids (lutein and zeaxanthin) of the human retina, this study investigated their antioxidant activity and capacity. Astaxanthin was also studied, because its structure is very close to that of lutein and zeaxanthin. The antioxidant activity of these molecules was evaluated using chemiluminescence techniques, with lucigenin and luminol as chemiluminogenic probes for the superoxide radical and hydrogen peroxide, respectively. It was found that all three carotenoids have similar superoxide-scavenging activity. The effect on the reduction of H₂O₂-luminol chemiluminescence was present in the following order, zeaxanthin>astaxanthin>lutein. Possible antioxidant capacity of these three compounds was sought using a biological system consisting of SK.N.SH human neuroblastoma and rat trachea epithelial cells subjected to oxidative stress from exposure to UVA radiation. In particular, we determined whether these compounds were capable of minimizing DNA damage and influencing the kinetics of DNA repair. DNA damage was assessed using the Comet assay, a rapid and sensitive single-cell gel electrophoresis technique used to detect primary DNA damage in individual cells. Neuroblastoma cells appeared more resistant to oxidative irradiation insult. The presence of carotenoids reduced DNA damage when rat epithelial cells were exposed to UVA radiation for 2min. A different result was obtained in experiments performed on neuroblastoma cells; in this case, the presence of carotenoid during UVA exposition increased the damage. The addition of carotenoids to epithelial cells after 2min of UVA exposition did not seem to improve the kinetics of DNA repair; on the contrary, zeaxanthin (after 60' incubation) and lutein (after 180' incubation) showed a genotoxic effect. The addition of carotenoids to neuroblastoma cells after 30' UVA exposition positively influences the kinetics of DNA repair in the first 15min of incubation. At longer exposition times, while the behaviour measured was not constant, a genotoxic effect was not observed. The data from this study provide additional information on the antioxidant and pro-oxidant activities of the predominant macular pigment carotenoids of the human retina.

PMID:

16962787

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Astaxanthin prevents cell death in cells exposed to glutamate.

[Eur J Pharmacol](#). 2017 Jul 5;806:43-51. doi: 10.1016/j.ejphar.2017.04.008. Epub 2017 Apr 8.

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Abstract

Astaxanthin (AST) is a carotenoid that has been shown to have neuroprotective effects. In this study, it was found that AST significantly inhibited glutamate-induced loss of cell viability and apoptosis. AST pretreatment attenuated glutamate-induced activation of caspase-3, reduction of anti-apoptotic protein Bcl-2, and increase of pro-apoptotic protein Bak. In addition, AST pretreatment suppressed the production of intracellular reactive oxygen species. AST treatment also prevented glutamate-induced increase of the level of activated p38 mitogen-activated protein kinase (MAPK), which has been shown to promote apoptotic events. Furthermore, AST treatment greatly reduced the elevation of intracellular calcium level induced by glutamate and inhibited the activity of calpain, a calcium-dependent protease that plays an important role in mediating apoptosis stimulated by calcium overload in cytoplasm. Both oxidative stress and calcium overload can lead to endoplasmic reticulum (ER) stress. C/EBP-homologous protein (CHOP) is a bZIP transcription factor that can be activated by ER stress and promotes apoptosis. Here we found that AST attenuated glutamate-induced elevation of CHOP and ER chaperone glucose-regulated protein (GRP78). Overall, these results suggested that AST might protect cells against glutamate-induced apoptosis through maintaining redox balance and inhibiting glutamate-induced calcium influx and ER stress.

KEYWORDS:

Apoptosis; Astaxanthin; Astaxanthin (PubChem CID: 5281224); Calcium influx; Endoplasmic reticulum stress; Glutamate; Oxidative stress

PMID: 28400209

DOI: [10.1016/j.ejphar.2017.04.008](https://doi.org/10.1016/j.ejphar.2017.04.008)

[Indexed for MEDLINE]

Astaxanthin positively affects human prostate cells.

[AAPS J.](#) 2017 Mar;19(2):421-430. doi: 10.1208/s12248-016-0016-x. Epub 2016 Dec 2.

Epigenetic CpG Methylation of the Promoter and Reactivation of the Expression of GSTP1 by Astaxanthin in Human Prostate LNCaP Cells.

[Yang Y](#)^{1,2,3}, [Fuentes F](#)^{1,2}, [Shu L](#)^{1,2}, [Wang C](#)^{1,2}, [Pung D](#)^{1,2,3}, [Li W](#)^{1,2}, [Zhang C](#)^{1,2,3}, [Guo Y](#)^{1,2,3}, [Kong AN](#)^{4,5,6}.

Author information

Abstract

Astaxanthin (AST), a red dietary carotenoid, has synergistic antioxidant effects with polyunsaturated fatty acids at low concentrations via Nuclear factor (erythroid-derived 2)-like 2 (NFE2L2 or Nrf2)/antioxidant response element (ARE) signaling. In addition, chromatin remodeling and DNA methylation-based gene silencing represent a common mechanism in prostate carcinogenesis and tumor progression from normal cells to pre-initiated cells and ultimately to invasive carcinoma. Therefore, the control of epigenetic modification and the transcriptional/translational control of the activation of Nrf2 and Nrf2-target genes, including glutathione S-transferases (GSTs), appear to be an important mechanism that protects cells against injuries from oxidative stress and cancer development. In this study, we aim to investigate the role of AST in reactivating the expression of Nrf2 and GSTP1 through epigenetic modification in human prostate LNCaP cells. Treatment with AST in human LNCaP cells reduced the methylation of 21 CpG sites of the GSTP1 CpG island but did not affect the three CpG sites of the Nrf2 promoter region. AST induced the mRNA expression and protein expression of both Nrf2 and GSTP1. It also increased the mRNA expression of NQO1 in sh-mock LNCaP cells but not in sh-SETD7 LNCaP cells. Furthermore, AST reduced the protein expression of DNMT3b and significantly inhibited DNMT and HDAC activities in vitro. Taken together, these results suggest that AST decreased the methylation status of the GSTP1, and these epigenetic modifying effects may originate from the decreasing activities of epigenetic modification enzymes, contributing to the overall beneficial health effects of AST.

KEYWORDS:

DNA methylation; GSTP1; astaxanthin; epigenetics; prostate cancer

PMID: 27913949

DOI: [10.1208/s12248-016-0016-x](https://doi.org/10.1208/s12248-016-0016-x)

[Indexed for MEDLINE]

Astaxanthin's antioxidative properties lead to prevention of cytotoxicity from cobalt.

[BMC Pharmacol Toxicol.](#) 2017 Jul 24;18(1):58. doi: 10.1186/s40360-017-0166-1.

Astaxanthin mitigates cobalt cytotoxicity in the MG-63 cells by modulating the oxidative stress.

[Li D](#)¹, [Tong W](#)², [Liu D](#)², [Zou Y](#)², [Zhang C](#)², [Xu W](#)³.

Author information

Abstract

BACKGROUND: With the re-popularity of metal-on-metal (MoM) bearing in recent years, the cobalt toxicity has been a cause for concern in the total hip replacement surgery by both physicians and patients.

METHODS: MG-63 cell line was cultured in vitro and incubated with cobalt (II) chloride (CoCl₂) and/or with astaxanthin (ASX) for 24 h. MTT assay was conducted to evaluate the cell viability after cobalt exposure and ASX treatment. Fluorescence-activated cell sorting (FACS) analysis was performed to examine the reactive oxygen species (ROS) level. Quantitative real-time polymerase chain reaction (PCR) was adopted to determine the mRNA levels of related targets. And western blot analysis was used to examine the protein expressions. One-way ANOVA with posttest Newman-Keuls multiple comparisons was adopted to analysis all the obtained data.

RESULTS: In the current study, ASX exhibited significant protective effect against the Co(II)-induced cytotoxicity in MG-63 cell line. We also found that ASX protected the cells against Co-induced apoptosis by regulating the expression of Bcl-2 family proteins. Besides, heme oxygenase 1 (HO-1) could be activated by Co exposure; ASX treatment significantly inhibited HO-1 activation, suppressing the oxidative stress induced by Co exposure. Moreover, c-Jun N-terminal Kinase (JNK) phosphorylation was shown to participate in the signaling pathway of the protective effect of ASX. However, knockdown of JNK expression by siRNA transfection or JNK inhibitor SP600125 treatment did not affect the protective effect of ASX against cobalt cytotoxicity in MG-63 cells.

CONCLUSIONS: ASX mitigated cobalt cytotoxicity in the MG-63 cells by modulating the oxidative stress. And ASX could be a promising therapy against cobalt toxicity in the hip articulation surgery.

KEYWORDS: Astaxanthin; Cobalt cytotoxicity; MG-63 cells; Oxidative stress

PMID: 28738843

PMCID: [PMC5525213](#)

DOI: [10.1186/s40360-017-0166-1](#)

[Indexed for MEDLINE]

[Free PMC Article](#)

Oxid Med Cell Longev. 2019 Nov 11;2019:3849692.

doi: 10.1155/2019/3849692. eCollection 2019.

Astaxanthin: A Potential Mitochondrial-Targeted Antioxidant Treatment in Diseases and with Aging

[Mónika Sztretye](#)¹, [Beatrix Dienes](#)¹, [Mónika Gönczi](#)¹, [Tamás Cziriák](#)¹, [László Csernoch](#)¹, [László Dux](#)², [Péter Szentesi](#)¹, [Anikó Keller-Pintér](#)²

PMID: **31814873** PMCID: [PMC6878783](#) DOI: [10.1155/2019/3849692](#) **Free PMC article**

Abstract

Oxidative stress is characterized by an imbalance between prooxidant and antioxidant species, leading to macromolecular damage and disruption of redox signaling and cellular control. It is a hallmark of various diseases including metabolic syndrome, chronic fatigue syndrome, neurodegenerative, cardiovascular, inflammatory, and age-related diseases. Several mitochondrial defects have been considered to contribute to the development of oxidative stress and known as the major mediators of the aging process and subsequent age-associated diseases. Thus, mitochondrial-targeted antioxidants should prevent or slow down these processes and prolong longevity. This is the reason why antioxidant treatments are extensively studied and newer and newer compounds with such an effect appear. Astaxanthin, a xanthophyll carotenoid, is the most abundant carotenoid in marine organisms and is one of the most powerful natural compounds with remarkable antioxidant activity. Here, we summarize its antioxidant targets, effects, and benefits in diseases and with aging.

Emerging Areas of mostly *Pre-Clinical* **Astaxanthin Research**

While there must be multiple positive human clinical studies in order to determine the material probability of health benefits for nutritional supplements, the basis for such human investigative research is most often found in pre-clinical research in animals and in test tubes. While we certainly are not trying to infer that the following studies indicate that Astaxanthin may positively affect human beings in the areas reviewed such as cancer prevention, the fact that there are multiple positive studies in mammals is a strong indicator of Astaxanthin's potential to support human health in these areas. And in particular, the sheer volume of pre-clinical trials (mostly in rodents) related to cancer prevention & tumor reduction; diabetes; liver & kidney health; gastrointestinal health; and respiratory health; with a range of fifteen to over 80 studies in each of these five areas, is extremely promising. In particular, diabetes as an area of research on Astaxanthin is emerging into an area of credible potential in humans with two clinical trials and 44 pre-clinical trials already completed, all of which show positive effects. In fact, for several of the other areas of research below, there is already one, or in some cases, two, positive human clinical studies.

We hope to see extensive human research for each of these health benefits in the future; in the interim we report these studies so that our Readers may broaden their knowledge of the vast amount of medical research on Astaxanthin and its far-ranging potential in ever-expanding areas of health.

Cancer Prevention and Tumor Reduction

ASTAXANTHIN'S MECHANISM FOR CANCER PREVENTION SUGGESTED TO BE ITS INHIBITION OF OXIDATIVE STRESS.

Nutr Cancer 2021 Aug 2;1-12. doi: 10.1080/01635581.2021.1952449. Online ahead of print.

Antitumor Effects of Astaxanthin on Esophageal Squamous Cell Carcinoma by up-Regulation of PPAR γ

[Lingling Cui](#)¹, [Zhonglei Li](#)¹, [Fan Xu](#)^{1,2}, [Yalan Tian](#)³, [Tingting Chen](#)¹, [Jiixin Li](#)¹, [Yingying Guo](#)¹, [Quanjun Lyu](#)⁴

- PMID: 34334076 DOI: [10.1080/01635581.2021.1952449](https://doi.org/10.1080/01635581.2021.1952449)

Abstract

Esophageal squamous cell carcinoma is a malignant tumor that is difficult to find and has a poor prognosis. The aim of this study is to explore the chemoprevention effect of Astaxanthin (AST) and reveal the possible mechanism of AST on the development of esophageal cancer based on PPAR γ . We found that a stable and strong binding between PPAR γ molecules and AST molecules using Autodock 4.0 software. AST significantly inhibited the viability of EC109 cells in a dose and time dependent manners (all $P < 0.05$), and up-regulated the protein expression level of PPAR γ from the concentration of 6.25 μM ($P < 0.05$). Animal experiment showed that AST significantly decreased the incidences of NMBzA-induced esophageal carcinogenesis at 50 mg/kg AST in F344 rats ($P < 0.05$). AST inhibited the oxidative stress by improving the levels of superoxide dismutase (SOD), total antioxidant capacity (TAOC) and suppressing malondialdehyde (MDA) in serum, and increasing the protein of PPAR γ , Bax/Bcl-2, Caspase-3 in esophagus tissue, especially in the 50 mg/kg of AST intervention group (all $P < 0.05$). In conclusion, our data suggested that protective effect of AST on esophageal cancer by inhibiting oxidative stress, up-regulating PPAR γ , and activating the apoptotic pathway, which could provide a basis for clinical application of AST.

[Mar Drugs](#). 2015 Jul 14;13(7):4310-30. doi: 10.3390/md13074310.

Multiple Mechanisms of Anti-Cancer Effects Exerted by Astaxanthin.

[Zhang L](#)¹, [Wang H](#)².

[Author information](#)

Abstract

Astaxanthin (ATX) is a xanthophyll carotenoid which has been approved by the United States Food and Drug Administration (USFDA) as food colorant in animal and fish feed. It is widely found in algae and aquatic animals and has powerful anti-oxidative activity. Previous studies have revealed that ATX, with its anti-oxidative property, is beneficial as a therapeutic agent for various diseases without any side effects or toxicity. In addition, ATX also shows preclinical anti-tumor efficacy both in vivo and in vitro in various cancer models. Several researches have deciphered that ATX exerts its anti-proliferative, anti-apoptosis and anti-invasion influence via different molecules and pathways including signal transducer and activator of transcription 3 (STAT3), nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) and peroxisome proliferator-activated receptor gamma (PPARγ). Hence, ATX shows great promise as chemotherapeutic agents in cancer. Here, we review the rapidly advancing field of ATX in cancer therapy as well as some molecular targets of ATX.

KEYWORDS:

astaxanthin; cancer; molecular targets

PMID:

26184238

[PubMed - in process]

PMCID:

PMC4515619

[Free PMC Article](#)

[Antioxidants \(Basel\)](#). 2018 Oct 4;7(10). pii: E135. doi: 10.3390/antiox7100135.

Effects of Astaxanthin on the Proliferation and Migration of Breast Cancer Cells In Vitro.

[McCall B](#)¹, [McPartland CK](#)², [Moore R](#)³, [Frank-Kamenetskii A](#)⁴, [Booth BW](#)⁵.

[Author information](#)

Abstract

Astaxanthin (ASX) is a marine-based ketocarotenoid; an accessory pigment in plants in that it has many different potential functions. ASX is an antioxidant that is notably more potent than many other antioxidants. Antioxidants have anti-inflammatory and oxidative stress-reducing properties to potentially reduce the incidence of cancer or inhibit the expansion of tumor cells. In this study, we tested the hypothesis that ASX would inhibit proliferation and migration of breast cancer cells in vitro. We found that application of ASX significantly reduced proliferation rates and inhibited breast cancer cell migration compared to control normal breast epithelial cells. Based on these results, further investigation of the effects of ASX on not only breast cancer cells, but other forms of tumor cells, should be carried out.

KEYWORDS:

Xanthoph; antioxidant; astaxanthin; breast cancer; carotenoid; migration; proliferation

PMID: 30287735

PMCID: [PMC6210693](#)

DOI: [10.3390/antiox7100135](#)

[Free PMC Article](#)

Effects of carbendazim and astaxanthin co-treatment on the proliferation of MCF-7 breast cancer cells.

[Atalay PB](#)¹, [Kuku G](#)², [Tuna BG](#)³.

Author information

Abstract

There has been a controversy in the oncology field about the use of antioxidants along with chemotherapeutics in cancer treatment. This study aimed to investigate the effects of a potent antioxidant (astaxanthin) co-treatment with a promising anti-cancer drug (carbendazim), which is in phase I clinical trials, on MCF-7 breast cancer cell proliferation. MCF-7 cells were treated with carbendazim, astaxanthin, or their combinations and incubated for 24 h. After the incubation, each treatment group was evaluated for proliferation, cell cycle progression, and production of reactive oxygen species (ROS) using WST-1, flow cytometry, and CM-H2DCFDA, respectively. All tested carbendazim and astaxanthin combinations increased the anti-proliferative effect of Carb treatment alone and increased the G2/M phase cell cycle arrest compared to the DMSO-treated control. Astaxanthin, at all concentrations tested, reduced the elevated intracellular ROS levels induced by the carbendazim treatment. Our data suggest that astaxanthin and carbendazim co-treatment enhances the anti-proliferative effect of carbendazim as a single agent, while alleviating the carbendazim treatment-associated ROS production in MCF-7 cells. These findings may contribute to the current debate on the use of antioxidants along with anti-cancer drugs in cancer chemotherapy.

KEYWORDS:

Astaxanthin; Breast cancer; Carbendazim; MCF-7

PMID: 30547284

DOI: [10.1007/s11626-018-0312-0](https://doi.org/10.1007/s11626-018-0312-0)

Astaxanthin enhances erlotinib-induced cytotoxicity by p38 MAPK mediated xeroderma pigmentosum complementation group C (XPC) down-regulation in human lung cancer cells.

[Chen JC](#)¹, [Wu CH](#)², [Peng YS](#)², [Zheng HY](#)², [Lin YC](#)², [Ma PF](#)², [Yen TC](#)², [Chen TY](#)², [Lin YW](#)².

[Author information](#)

Abstract

Astaxanthin has been demonstrated to exhibit a wide range of beneficial effects that include anti-cancer and anti-inflammatory properties. Xeroderma pigmentosum complementation group C (XPC) protein is an important DNA damage recognition factor in nucleotide excision repair and is involved in regulating non-small cell lung cancer (NSCLC) cell proliferation and viability. Erlotinib (Tarceva[®]) is a selective epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor that has demonstrated clinical activity in NSCLC cells. However, whether astaxanthin and erlotinib could induce synergistic cytotoxicity in NSCLC cells through modulating XPC expression is unknown. In this study, we found that p38 MAPK activation by astaxanthin decreased XPC expression in two human lung adenocarcinoma A549 and H1975 cells. Inactivation of p38 MAPK by pharmacological inhibitor SB203580 or the specific small interfering RNA (siRNA) rescued the astaxanthin-reduced XPC mRNA and protein levels. Enforced expression of XPC cDNA or inhibiting the p38 MAPK activity reduced the cytotoxicity and cell growth inhibition of astaxanthin. In contrast, knockdown of XPC using siRNA enhanced the cytotoxic effects of astaxanthin. Moreover, astaxanthin synergistically enhanced cytotoxicity and cell growth inhibition of erlotinib in NSCLC cells, which were associated with the down-regulation of XPC expression and activation of p38 MAPK. Our findings suggested that the astaxanthin induced p38 MAPK mediated XPC down-regulation enhanced the erlotinib-induced cytotoxicity in A549 and H1975 cells.

PMID: 30555679

PMCID: [PMC6247823](#)

DOI: [10.1039/c7tx00292k](#)

[Free PMC Article](#)

Preventive effects of astaxanthin on diethylnitrosamine-induced liver tumorigenesis in C57/BL/KsJ-db/db obese mice.

[Ohno T¹](#), [Shimizu M¹](#), [Shirakami Y¹](#), [Miyazaki T¹](#), [Ideta T¹](#), [Kochi T¹](#), [Kubota M¹](#), [Sakai H¹](#), [Tanaka T²](#), [Moriwaki H¹](#).

[Author information](#)

Abstract

AIM:

Obesity and its related metabolic abnormalities, including oxidative stress and adipokine imbalance, are involved in liver carcinogenesis. The aim of the present study was to examine the effects of astaxanthin, a powerful biological antioxidant, on the development of diethylnitrosamine (DEN)-induced liver tumorigenesis in C57BL/KsJ-db/db (db/db) obese mice.

METHODS:

Male db/db mice were given a single i.p. injection of DEN (25 mg/kg bodyweight) at 2 weeks of age, and, subsequently, from 4 weeks of age, they were fed a diet containing 200 p.p.m. astaxanthin throughout the experiment.

RESULTS:

Twenty weeks of astaxanthin administration significantly inhibited the development of hepatocellular neoplasms (liver cell adenoma and hepatocellular carcinoma) and the hepatic expression of cyclin D1 mRNA compared with the basal diet group in DEN-treated db/db mice. Astaxanthin administration in DEN-treated experimental mice markedly reduced the derivatives of reactive oxygen metabolites/biological antioxidant potential ratio, which is a serum marker of oxidative stress, while increasing the mRNA expression of the antioxidant enzymes superoxide dismutase 2 and glutathione peroxidase 1 in the liver and white adipose tissue. The serum levels of adiponectin increased after astaxanthin administration in these mice.

CONCLUSION:

Dietary astaxanthin prevented the development of liver tumorigenesis in obese mice by improving oxidative stress and ameliorating serum adiponectin level. Therefore, astaxanthin may be useful in the chemoprevention of liver tumorigenesis in obese individuals.

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KEYWORDS:

adiponectin; astaxanthin; liver tumorigenesis; obesity; oxidative stress

PMID:

26147624

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Astaxanthin inhibits JAK/STAT-3 signaling to abrogate cell proliferation, invasion and angiogenesis in a hamster model of oral cancer.

[Kowshik J](#)¹, [Baba AB](#)¹, [Giri H](#)², [Deepak Reddy G](#)³, [Dixit M](#)², [Nagini S](#)¹.

Author information

Abstract

Identifying agents that inhibit STAT-3, a cytosolic transcription factor involved in the activation of various genes implicated in tumour progression is a promising strategy for cancer chemoprevention. In the present study, we investigated the effect of dietary astaxanthin on JAK-2/STAT-3 signaling in the 7,12-dimethylbenz[a]anthracene (DMBA)-induced hamster buccal pouch (HBP) carcinogenesis model by examining the mRNA and protein expression of JAK/STAT-3 and its target genes. Quantitative RT-PCR, immunoblotting and immunohistochemical analyses revealed that astaxanthin supplementation inhibits key events in JAK/STAT signaling especially STAT-3 phosphorylation and subsequent nuclear translocation of STAT-3. Furthermore, astaxanthin downregulated the expression of STAT-3 target genes involved in cell proliferation, invasion and angiogenesis, and reduced microvascular density, thereby preventing tumour progression. Molecular docking analysis confirmed inhibitory effects of astaxanthin on STAT signaling and angiogenesis. Cell culture experiments with the endothelial cell line ECV304 substantiated the role of astaxanthin in suppressing angiogenesis. Taken together, our data provide substantial evidence that dietary astaxanthin prevents the development and progression of HBP carcinomas through the inhibition of JAK-2/STAT-3 signaling and its downstream events. Thus, astaxanthin that functions as a potent inhibitor of tumour development and progression by targeting JAK/STAT signaling may be an ideal candidate for cancer chemoprevention.

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[Free PMC Article](#)

[In Vivo](#). 2016 11-12;30(6):795-800.

Effects of Dietary Xanthophylls, Canthaxanthin and Astaxanthin on N-Methyl-N-nitrosourea-induced Rat Mammary Carcinogenesis.

[Yuri T¹](#), [Yoshizawa K²](#), [Emoto Y²](#), [Kinoshita Y²](#), [Yuki M²](#), [Tsubura A²](#).

Author information

Abstract

BACKGROUND: Natural xanthophylls, canthaxanthin and astaxanthin are known to exhibit anticancer activity. However, the dietary effects of canthaxanthin and astaxanthin on N-methyl-N-nitrosourea (MNU)-induced mammary cancer remain controversial, and their mechanisms of action have not been clearly identified.

MATERIALS AND METHODS: Three-week-old female Sprague-Dawley rats were fed a xanthophyll-free (basal diet) diet or experimental diets containing canthaxanthin or astaxanthin (0.04% and 0.4%) for 5 weeks (until 8 weeks of age), after which all rats were provided the basal diet (n=15 each). Rats were administered MNU at 6 weeks of age, and the incidence of mammary tumors at 20 weeks of age was compared. The expression of adiponectin in mammary adipose tissues taken at 7 weeks of age was also compared.

RESULTS: Compared to the basal diet group, the 0.4% (but not the 0.04%) astaxanthin diet significantly reduced the incidence of palpable mammary carcinoma (92% vs. 42%; $p < 0.05$), while the low and high canthaxanthin diets produced no significant inhibition. Adiponectin immunoblotting showed significantly higher expression in the 0.4% astaxanthin diet group, while the other groups were similar to the basal diet group.

CONCLUSION: High concentrations of astaxanthin suppress MNU-induced mammary carcinoma. Changes in adiponectin may be involved in the mechanism of action.

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KEYWORDS: Xanthophyll; adiponectin; astaxanthin; canthaxanthin; mammary cancer

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[Indexed for MEDLINE]

Astaxanthin enhances pemetrexed-induced cytotoxicity by downregulation of thymidylate synthase expression in human lung cancer cells.

[Liao KS](#)¹, [Wei CL](#)², [Chen JC](#)³, [Zheng HY](#)², [Chen WC](#)², [Wu CH](#)², [Wang TJ](#)², [Peng YS](#)², [Chang PY](#)², [Lin YW](#)⁴.

Author information

Abstract

Pemetrexed, a multitargeted antifolate agent, has demonstrated clinical activity in non-small cell lung cancer (NSCLC) cells. Increased expression of thymidylate synthase (TS) is thought to be associated with resistance to pemetrexed. Astaxanthin exhibits a wide range of beneficial effects including anti-cancer and anti-inflammatory properties. In this study, we showed that down-regulating of TS expression in two NSCLC cell lines, human lung adenocarcinoma H1650 and squamous cell carcinoma H1703 cells, with astaxanthin were associated with decreased MKK1/2-ERK1/2 activity. Enforced expression of constitutively active MKK1 (MKK1-CA) vector significantly rescued the decreased TS mRNA and protein levels in astaxanthin-treated NSCLC cells. Combined treatment with a MKK1/2 inhibitor (U0126 or PD98059) further decreased the TS expression in astaxanthin-exposed NSCLC cells. Knockdown of TS using small interfering RNA (siRNA) or inhibiting ERK1/2 activity enhanced the cytotoxicity and cell growth inhibition of astaxanthin. Combination of pemetrexed and astaxanthin resulted in synergistic enhancing cytotoxicity and cell growth inhibition in NSCLC cells, accompanied with reduced activation of phospho-MKK1/2, phospho-ERK1/2, and TS expression. Overexpression of MKK1/2-CA reversed the astaxanthin and pemetrexed-induced synergistic cytotoxicity. Our findings suggested that the down-regulation of MKK1/2-ERK1/2-mediated TS expression by astaxanthin is an important regulator of enhancing the pemetrexed-induced cytotoxicity in NSCLC cells.

KEYWORDS:

Astaxanthin; ERK1/2; Non-small cell lung cancer; Pemetrexed; Thymidylate synthase

PMID: 27693704

DOI: [10.1016/j.yrtph.2016.09.031](https://doi.org/10.1016/j.yrtph.2016.09.031)

[Indexed for MEDLINE]

[Astaxanthin inhibits proliferation and promotes apoptosis of A549 lung cancer cells via blocking JAK1/STAT3 pathway].

[Article in Chinese]

[Wu C](#)¹, [Zhang J](#)¹, [Liu T](#)², [Jiao G](#)¹, [Li C](#)¹, [Hu B](#)¹.

Author information

Abstract

Objective To investigate the anti-tumor effects of astaxanthin on A549 lung cancer cells and the related mechanisms. **Methods** A549 cells were cultured with various concentrations of astaxanthin (20, 40, 60, 80, 100 μmol/L), and DMSO at the same concentrations served as vehicle controls. The viability of A549 cells was detected by CCK-8 assay; cell cycle and apoptosis were observed by flow cytometry; and the expressions of B-cell lymphoma-2 (Bcl-2), Bcl-2 associated X protein (Bax), signal transducers and activators of transcription 3 (STAT3), and Janus kinase 1 (JAK1) were evaluated by Western blotting. **Results** CCK-8 assay showed that astaxanthin decreased the proliferation of A549 cells in a dose-dependent manner. Flow cytometry showed that astaxanthin increased the number of cells in the G0/G1 phase and induced apoptosis in A549 cells. Western blotting showed that astaxanthin up-regulated the expression of Bax and down-regulated the expressions of Bcl-2, STAT3 and JAK1.

Conclusion Astaxanthin functions as a potent inhibitor of A549 lung cancer cell growth by targeting JAK1/STAT3 signaling pathway.

PMID: 27371847

[Indexed for MEDLINE]

Astaxanthin Inhibits Proliferation and Induces Apoptosis and Cell Cycle Arrest of Mice H22 Hepatoma Cells.

[Shao Y](#)¹, [Ni Y](#)², [Yang J](#)³, [Lin X](#)⁴, [Li J](#)⁵, [Zhang L](#)⁶.

Author information

Abstract

BACKGROUND It is widely recognized that astaxanthin (ASX), a member of the carotenoid family, has strong biological activities including antioxidant, anti-inflammation, and immune-modulation activities. Previous studies have confirmed that ASX can effectively inhibit hepatoma cells in vitro.

MATERIAL AND METHODS MTT was used to assay proliferation of mice H22 cells, and flow cytometry was used to determine apoptosis and cell cycle arrest of H22 cells in vitro and in vivo.

Moreover, anti-tumor activity of ASX was observed in mice. **RESULTS** ASX inhibited the proliferation of H22 cells, promoted cell necrosis, and induced cell cycle arrest in G2 phase in vitro and in vivo.

CONCLUSIONS This study indicated that ASX can inhibit proliferation and induce apoptosis and cell cycle arrest in mice H22 hepatoma cells in vitro and in vivo.

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[Indexed for MEDLINE]

[Free PMC Article](#)

Stereoisomers of Astaxanthin Inhibit Human Colon Cancer Cell Growth by Inducing G2/M Cell Cycle Arrest and Apoptosis.

[Liu X](#)^{1,2}, [Song M](#)², [Gao Z](#)², [Cai X](#)², [Dixon W](#)², [Chen X](#)¹, [Cao Y](#)¹, [Xiao H](#)².

Author information

Abstract

Astaxanthin (AST) is a xanthophyll carotenoid with potential protective effects against carcinogenesis. Different stereoisomers of AST (ASTs) exist in a variety of food sources. Due to limited information on the bioactivities of ASTs, the present study investigated the inhibitory effects of ASTs on HCT116 and HT29 human colon cancer cells. ASTs investigated herein included 3S,3'S (S) from *Haematococcus pluvialis*, 3R,3'R (R) from *Phaffia rhodozyma*, and a statistical mixture (S: meso: R = 1:2:1) (M) from synthetic AST. Cell viability assay showed that ASTs all inhibited colon cancer cell growth in a time-dependent (24-72 h) and dose-dependent (4-16 μM) manner, and there was no significant difference among the IC_{50} values of ASTs ($p > 0.05$). Flow cytometry analysis indicated that ASTs induced G2/M cell cycle arrest and cellular apoptosis in cancer cells. The cell cycle arrest caused by ASTs was associated with increases in the expression levels of p21^{Cip1/Waf1}, p27, and p53, as well as decreases in the levels of CDK4 and CDK6. Meanwhile, the apoptosis induced by ASTs was confirmed by activation of caspase-3 and PARP in the cancer cells. The results indicated that hydroxyl (OH) at C3 and C3' of terminal ring structure might not be the major factor that affects the anticancer activity of AST. This study revealed important information on the inhibitory effects of ASTs on human colon cancer cells, which provided a basis for using ASTs as chemopreventive agents for colon cancer.

KEYWORDS:

apoptosis; astaxanthin; cell cycle; colon cancer

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Astaxanthin inhibits NF- κ B and Wnt/ β -catenin signaling pathways via inactivation of Erk/MAPK and PI3K/Akt to induce intrinsic apoptosis in a hamster model of oral cancer.

[Kavitha K¹](#), [Kowshik J](#), [Kishore TK](#), [Baba AB](#), [Nagini S](#).

Author information

Abstract

BACKGROUND:

The oncogenic transcription factors NF- κ B and β -catenin, constitutively activated by upstream serine/threonine kinases control several cellular processes implicated in malignant transformation including apoptosis evasion. The aim of this study was to investigate the chemopreventive effects of astaxanthin, an antioxidant carotenoid, in the hamster buccal pouch (HBP) carcinogenesis model based on its ability to modulate NF- κ B and Wnt signaling pathways and induce apoptosis.

METHODS:

We determined the effect of dietary supplementation of astaxanthin on the oncogenic signaling pathways - NF- κ B and Wnt/ β -catenin, their upstream activator kinases - Erk/MAPK and PI-3K/Akt, and the downstream event - apoptosis evasion by real-time quantitative RT-PCR, western blot, and immunohistochemical analyses.

RESULTS:

We found that astaxanthin inhibits NF- κ B and Wnt signaling by downregulating the key regulatory enzymes IKK β and GSK-3 β . Analysis of gene expression and docking interactions revealed that inhibition of these pathways may be mediated via inactivation of the upstream signaling kinases Erk/Akt by astaxanthin. Astaxanthin also induced caspase-mediated mitochondrial apoptosis by downregulating the expression of antiapoptotic Bcl-2, p-Bad, and survivin and upregulating proapoptotic Bax and Bad, accompanied by efflux of Smac/Diablo and cytochrome-c into the cytosol, and induced cleavage of poly (ADP-ribose) polymerase (PARP).

CONCLUSIONS:

The results provide compelling evidence that astaxanthin exerts chemopreventive effects by concurrently inhibiting phosphorylation of transcription factors and signaling kinases and inducing intrinsic apoptosis.

GENERAL SIGNIFICANCE:

Astaxanthin targets key molecules in oncogenic signaling pathways and induces apoptosis and is a promising candidate agent for cancer prevention and therapy.

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KEYWORDS:

Astaxanthin; Extracellular signal-regulated kinase/Mitogen activated protein kinase; Intrinsic apoptosis; Nuclear factor kappa B; Phosphatidylinositol-3-kinase/Akt; Wnt/ β -catenin

PMID: 23726989

[PubMed - indexed for MEDLINE]

[J Agric Food Chem](#). 2013 Apr 24;61(16):3842-51. doi: 10.1021/jf304609j. Epub 2013 Apr 16.

Effective inhibition of skin cancer, tyrosinase, and antioxidative properties by astaxanthin and astaxanthin esters from the green alga *Haematococcus pluvialis*.

[Rao AR](#)¹, [Sindhuja HN](#), [Dharmesh SM](#), [Sankar KU](#), [Sarada R](#), [Ravishankar GA](#).

Author information

Abstract

Astaxanthin mono- (AXME) and diesters (AXDE) were characterized and examined for anticancer potency with total carotenoids (TC) and astaxanthin (AX) against UV-7,12-dimethylbenz(a)anthracene (DMBA)-induced skin cancer model in rat. At 200 µg/kg bw, AXDE and AXME reduced UV-DMBA-induced tumor incidences up to 96 and 88%, respectively, when compared to AX (66%) and TC (85%). UV-DMBA has been known to generate high levels of free radicals and tyrosinase enzyme, leading to characteristic symptoms of skin pigmentation and tumor initiation. Intriguingly, ~7-fold increase in tyrosinase and 10-fold decrease in antioxidant levels were normalized by AXDE and AXME as opposed to only ~1.4-2.2-fold by AX and TC, respectively. This result together with the appearance of 72 and 58 ng/mL of retinol in the serum of respective AXE-treated (AXDE + AXME) and AX-treated animals suggested that better anticancer potency of AXEs could be due to increased bioavailability.

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23473626

[PubMed - indexed for MEDLINE]

Effects of astaxanthin supplementation on chemically induced tumorigenesis in Wistar rats.

[Gal AF¹](#), [Andrei S](#), [Cernea C](#), [Taulescu M](#), [Catoi C](#).

Author information

Abstract

BACKGROUND:

Astaxanthin (ASTA) is a fat-soluble xanthophyll with powerful antioxidant functions. It is extracted from e.g. salmon, an important food source for certain human populations known to have a reduced risk of tumor development. It is possible that ASTA plays a role in cancerchemoprevention in such populations. The purpose of this study was to investigate the effects of dietary ASTA on chemically induced mammary tumorigenesis using N-methyl-N-nitroso-urea (MNU) in immature Wistar rats.

METHODS:

Thirty-six 37 days old juvenile female Wistar rats were at random allocated to 4 groups of which Groups 1 and 2 received a single dose of 55 mg MNU/kg body weight. The effects of ASTA was evaluated by giving rats of Groups 2 and 4 a dose of 50 mg ASTA/kg/day for the entire duration of the study. Group 3 rats received feed added alimentary oil. Necropsy and histopathological examinations were carried out on each rat 14 months after the administration of MNU. Haematological values and antioxidative status were determined. Oxidative stress was evaluated by monitoring superoxide dismutase (SOD) and glutathione peroxidase (GPx) activities in hepatic tissue. Lipid peroxidation and carbonylation of proteins was determined in protein extracts from the liver.

RESULTS:

Tumor development occurred only in rats of Groups 1 and 2, i.e. MNU exposed animals. Frequency of tumor development in general and average number of tumors per animal were insignificant between these two groups. Mammary gland tumors developed in equal frequencies in Group 1 and 2 rats, respectively. Although only rather few tumors were found in the mammary glands, a substantial number of other tumors were found in Group 1 and 2 rats, but at equal rates. Biochemical analyses showed significant higher levels of GPx, malondialdehyde and dinitrophenylhydrazine in Group 1 rats that for rats in all other groups thus indicating protective effects of ASTA on MNU induced hepatic oxidative stress.

CONCLUSIONS:

Supplementation with ASTA did not reduce tumorigenesis induced by MNU in Wistar rats. However, supplementation with ASTA seemed to have anti-inflammatory effects.

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22935319

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PMC3511877

[Free PMC Article](#)

Inhibitory effects of astaxanthin on azoxymethane-induced colonic preneoplastic lesions in C57/BL/KsJ-db/db mice.

[Kochi T](#)¹, [Shimizu M](#)², [Sumi T](#)³, [Kubota M](#)⁴, [Shirakami Y](#)⁵, [Tanaka T](#)⁶, [Moriwaki H](#)⁷.

Author information

Abstract

BACKGROUND:

Obesity and related metabolic abnormalities, including excess oxidative stress and chronic inflammation, are associated with colorectal carcinogenesis. Astaxanthin, a xanthophyll carotenoid found in aquatic animals, is known to possess antioxidant, anti-inflammatory, and antineoplastic properties. The present study examined the effects of astaxanthin on the development of azoxymethane (AOM)-induced colonic premalignant lesions in C57BL/KsJ-db/db (db/db) obese mice.

METHOD:

Male db/db mice were administered 4 weekly subcutaneous injections of AOM (15 mg/kg body weight) from 5 weeks of age and subsequently, from 1 week after the last injection of AOM, were fed a diet containing 200 ppm astaxanthin throughout the experiment (8 weeks).

RESULT:

The development of colonic premalignant lesions, i.e., aberrant crypt foci and β -catenin accumulated crypts, was significantly inhibited in mice treated with astaxanthin than in mice fed the basal diet. Astaxanthin administration markedly reduced urinary levels of 8-OHdG and serum levels of d-ROMs, which are oxidative stress markers, while increasing the expression of mRNA for the antioxidant enzymes GPx1, SOD1, and CAT in the colonic mucosa of AOM-treated db/db mice. The expression levels of IL-1 β , IL-6, F4/80, CCL2, and CXCL2 mRNA in the colonic mucosa of AOM-treated mice were significantly decreased by astaxanthin. Dietary feeding with astaxanthin also resulted in a reduction in the numbers of NF- κ B- and PCNA-positive cells that were increased by AOM exposure, in the colonic epithelium.

CONCLUSION:

These findings suggest that astaxanthin inhibits the development of colonic premalignant lesions in an obesity-related colorectal carcinogenesis model by reducing oxidative stress, attenuating chronic inflammation, and inhibiting NF- κ B activation and cell proliferation in the colonic mucosa. Astaxanthin, therefore, may be a potential candidate as a chemoprevention agent against colorectal carcinogenesis in obese individuals.

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25515685

[PubMed - indexed for MEDLINE]

PMCID:

PMC4273491

[Free PMC Article](#)

[Toxicol Mech Methods](#). 2012 Nov;22(9):679-86. doi: 10.3109/15376516.2012.717119.

Changes in cell ultrastructure and inhibition of JAK1/STAT3 signaling pathway in CBRH-7919 cells withastaxanthin.

[Song X¹](#), [Wang M](#), [Zhang L](#), [Zhang J](#), [Wang X](#), [Liu W](#), [Gu X](#), [Lv C](#).

Author information

Abstract

Astaxanthin (AST), a xanthophylls carotenoid, possesses significant anticancer effects. However, to date, the molecular mechanism of anticancer remains unclear. In the present research, we studied the anticancer mechanism of AST, including the changes in cell ultrastructure, such as the mitochondrion, rough endoplasmic reticulum (RER), Golgi complex, and cytoskeleton, the inhibition of Janus kinase 1(JAK1)/transduction and the activators of the transcription-3 (STAT3) signaling pathway using rat hepatocellular carcinoma CBRH-7919 cells. Cell apoptosis was evaluated and the expressions of JAK1, STAT3, non-metastasis23-1 (nm23-1), and apoptotic gene like B-cell lymphoma/leukemia-2 (bcl-2), B-cell lymphoma-extra large (bcl-xl), proto-oncogene proteins c myc (c-myc) and bcl-2- associated X (bax) were also examined. The results showed that AST could inducecancer cell apoptosis. Under transmission electron microscope, the ultrastructure of treated cells were not clearly distinguishable, the membranes of the mitochondrion, RER, Golgi complex were broken or loosened, and the endoplasmic reticulum (ER) was degranulated. Cytoskeleton depolymerization of the microtubule system led to the collapse of extended vimentin intermediate filament bundles into short agglomerations with disordered distributions. AST inhibited the expression of STAT3, its upstream activator JAK1, and the STAT3 target antiapoptotic genes bcl-2, bcl-xl, and c-myc. Conversely, AST enhanced the expressions of nm23-1 and bax. Overall, our findings demonstrate that AST could induce the apoptosis of CBRH-7919 cells, which are involved in cell ultrastructure and the JAK1/STAT3 signaling pathway.

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22889354

[PubMed - indexed for MEDLINE]

Astaxanthin Inhibits Proliferation and Induces Apoptosis of Human Hepatocellular Carcinoma Cells via Inhibition of Nf-Kb P65 and Wnt/B-Catenin in Vitro.

[Li J](#)¹, [Dai W](#)², [Xia Y](#)³, [Chen K](#)⁴, [Li S](#)⁵, [Liu T](#)⁶, [Zhang R](#)^{7,8}, [Wang J](#)^{9,10}, [Lu W](#)^{11,12}, [Zhou Y](#)^{13,14}, [Yin Q](#)^{15,16}, [Abudumijiti H](#)¹⁷, [Chen R](#)¹⁸, [Zheng Y](#)¹⁹, [Wang F](#)²⁰, [Lu J](#)¹, [Zhou Y](#)²¹, [Guo C](#)²².

Author information

Abstract

Hepatocellular carcinoma (HCC) is a malignant tumor that can cause systemic invasion; however, the exact etiology and molecular mechanism are unknown. Astaxanthin (ASX), a powerful antioxidant, has efficient anti-oxidant, anti-inflammatory, and other activities, and has great research prospects in cancer therapy. We selected the human hepatoma cell lines, LM3 and SMMC-7721, to study the anti-tumor effect and related mechanisms of ASX. The cell lines were treated with different concentrations of ASX, and its solvent DMSO as a control, for different time periods and the results were determined using CCK8, qRT-PCR, WB, apoptotic staining, and flow cytometry. ASX induced significant apoptosis of HCC cells, and its effect may have been caused by NF- κ B p65 and Wnt/ β -catenin down-regulation via negative activation of PI3K/Akt and ERK. Antitumor research on ASX has provided us with a potential therapy for patients with hepatomas.

KEYWORDS:

apoptosis; astaxanthin; hepatocellular carcinoma

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26404320

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PMC4626679

[Free PMC Article](#)

ASTAXANTHIN SHOWS EFFECT AGAINST ESOPHAGEAL CANCER IN ANIMAL MODEL BY DECREASING INFLAMMATION AND OXIDATION.

Onco Targets Ther. 2019 Jul 1;12:5087-5096.
doi: 10.2147/OTT.S197044. eCollection 2019.

Dietary natural astaxanthin at an early stage inhibits *N*-nitrosomethylbenzylamine-induced esophageal cancer oxidative stress and inflammation via downregulation of NFκB and COX2 in F344 rats

[Lingling Cui](#)¹, [Fan Xu](#)¹, [Minkai Wang](#)², [Li Li](#)¹, [Tianyi Qiao](#)¹, [Han Cui](#)¹, [Zhonglei Li](#)¹, [Changqing Sun](#)³

PMID: 31308688 PMCID: [PMC6612988](#) DOI: [10.2147/OTT.S197044](#) [Free PMC article](#)

Abstract

Purpose: Esophageal cancer is a common malignant tumor that develops rapidly and has a poor prognosis clinically. Astaxanthin (AST) is a carotenoid pigment with strong antioxidant, anti-inflammation, and antitumor activities. However, little is known about the effects of astaxanthin in esophageal cancer. The present study aimed to investigate the protective effects and related mechanisms of natural astaxanthin against *N*-nitrosomethylbenzylamine (NMBA)-induced esophageal cancer in rats. **Methods:** F344 rats were induced subcutaneously with NMBA dissolved in dimethyl sulfoxide (0.35 mg/kg body weight three times per week for 5 weeks). Rats were fed normal diets with or without 25 mg/kg/day AST at different stages. At different time points, levels of oxidative stress factors in serum and esophagus tissue were analyzed. Western blotting was performed to observe the expression of NFκB and COX2 in esophagus tissue. **Results:** AST clearly reduced the incidence of visible tumors in esophageal cancer during the early-stage intervention group. Furthermore, when compared with the simple exposed group, AST significantly increased levels of GPx and SOD activity, decreased the activity level of malondialdehyde (all $P < 0.05$). Early-stage and whole-stage intervention groups effectively attenuated expression levels of NFκB and COX2 proteins compared with the simple exposed group (all $P < 0.05$). **Conclusion:** Natural AST significantly suppressed the occurrence of esophageal cancer by increasing antioxidant capacity and anti-inflammation capacity by inhibiting expression levels of NFκB and COX2 proteins.

ASTAXANTHIN INDUCES BENEFICIAL CHANGES IN CELLS OF TUMOR-BEARING MICE INDICATING POTENTIAL FOR TREATMENT OF TUMORS IN MAMMALS.

Antioxidants (Basel). 2020 Apr 23;9(4):350.
doi: 10.3390/antiox9040350.

Astaxanthin Treatment Induces Maturation and Functional Change of Myeloid-Derived Suppressor Cells in Tumor-Bearing Mice

[Seong Mun Jeong](#)¹, [Yeon-Jeong Kim](#)¹

PMID: [32340271](#) PMCID: [PMC7222357](#) DOI: [10.3390/antiox9040350](#) [Free PMC article](#)

Abstract

Myeloid-derived suppressor cells (MDSCs) are immature myeloid cells which accumulate in stress conditions such as infection and tumor. Astaxanthin (ATX) is a well-known antioxidant agent and has a little toxicity. It has been reported that ATX treatment induces antitumor effects via regulation of cell signaling pathways, including nuclear factor erythroid-derived 2-related factor 2 (Nrf2) signaling. In the present study, we hypothesized that treatment with ATX might induce maturation of MDSCs and modulate their immunosuppressive activity. Both in vivo and in vitro treatment with ATX resulted in up-regulation of surface markers such as CD80, MHC class II, and CD11c on both polymorphonuclear (PMN)-MDSCs and mononuclear (Mo)-MDSCs. Expression levels of functional mediators involved in immune suppression were significantly reduced, whereas mRNA levels of Nrf2 target genes were increased in ATX-treated MDSCs. In addition, ATX was found to have antioxidant activity reducing reactive oxygen species level in MDSCs. Finally, ATX-treated MDSCs were immunogenic enough to induce cytotoxic T lymphocyte response and contributed to the inhibition of tumor growth. This demonstrates the role of ATX as a regulator of the immunosuppressive tumor environment through induction of differentiation and functional conversion of MDSCs.

Astaxanthin Inhibits Proliferation of Human Gastric Cancer Cell Lines by Interrupting Cell Cycle Progression.

[Kim JH¹](#), [Park JJ¹](#), [Lee BJ¹](#), [Joo MK¹](#), [Chun HJ²](#), [Lee SW³](#), [Bak YT¹](#).

Author information

Abstract

BACKGROUND/AIMS:

Astaxanthin is a carotenoid pigment that has antioxidant, antitumoral, and anti-inflammatory properties. In this in vitro study, we investigated the mechanism of anticancer effects of astaxanthin in gastric carcinoma cell lines.

METHODS:

The human gastric adenocarcinoma cell lines AGS, KATO-III, MKN-45, and SNU-1 were treated with various concentrations of astaxanthin. A cell viability test, cell cycle analysis, and immunoblotting were performed.

RESULTS:

The viability of each cancer cell line was suppressed by astaxanthin in a dose-dependent manner with significantly decreased proliferation in KATO-III and SNU-1 cells. Astaxanthin increased the number of cells in the G0/G1 phase but reduced the proportion of S phase KATO-III and SNU-1 cells. Phosphorylated extracellular signal-regulated kinase (ERK) was decreased in an inverse dose-dependent correlation with astaxanthin concentration, and the expression of p27^{kip-1} increased in the KATO-III and SNU-1 cell lines in an astaxanthin dose-dependent manner.

CONCLUSIONS:

Astaxanthin inhibits proliferation by interrupting cell cycle progression in KATO-III and SNU-1 gastric cancer cells. This may be caused by the inhibition of the phosphorylation of ERK and the enhanced expression of p27^{kip-1}.

KEYWORDS:

Astaxanthin; Extracellular signal-regulated kinase; Human gastric adenocarcinoma; Proliferation; p27^{kip-1}

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26470770

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Free full text

[Cancer Lett.](#) 2009 May 5. [Epub ahead of print]

Growth-inhibitory effects of the astaxanthin-rich alga *Haematococcus pluvialis* in human colon cancer cells.

[Palozza P](#), [Torelli C](#), [Boninsegna A](#), [Simone R](#), [Catalano A](#), [Mele MC](#), [Picci N](#).

Institute of General Pathology, Catholic University School of Medicine, L. Go F. Vito, 1 00168 Rome, Italy.

The growth-inhibitory effects of the astaxanthin-rich *Haematococcus pluvialis* were studied in HCT-116 colon cancer cells. *H. pluvialis* extract (5-25µg/ml) inhibited cell growth in a dose- and time-dependent manner, by arresting cell cycle progression and by promoting apoptosis. At 25µg/ml of *H. pluvialis* extract, an increase of p53, p21(WAF-1/CIP-1) and p27 expression (220%, 160%, 250%, respectively) was observed, concomitantly with a decrease of cyclin D1 expression (58%) and AKT phosphorylation (21%). Moreover, the extract, at the same concentration, strongly up-regulated apoptosis by modifying the ratio of Bax/Bcl-2 and Bcl-XL, and increased the phosphorylation of p38, JNK, and ERK1/2 by 160%, 242%, 280%, respectively. Growth-inhibitory effects by *H. pluvialis* were also observed in HT-29, LS-174, WiDr, SW-480 cells. This study suggests that *H. pluvialis* may protect from colon cancer.

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[Toxicology](#). 2008 Jun 27;248(2-3):96-103. Epub 2008 Mar 27.

Astaxanthin inhibits cytotoxic and genotoxic effects of cyclophosphamide in mice germ cells.

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Cyclophosphamide (CP), an alkylating agent used in the treatment of several cancers as well as an immunosuppressant in rheumatoid arthritis. It is used against several cancers due to its broad spectrum efficacy, but at the same time possesses unwanted risks for occupational exposure as well as therapy related toxicities to patients. The present study was aimed to investigate the protective effect of astaxanthin (AST) a red carotenoid pigment on CP induced germ cell toxicity in male mice. CP was administered intraperitoneally (i.p.) at the dose of 50, 100 and 200mg/kg body weight to mice (20-25 g) once in a week for a period of five weeks. AST was given at the dose of 25mg/kg per oral (p.o.) for five consecutive days in a week for five weeks. The animals were sacrificed one week after the last injection of CP. The protective effect of AST against CP induced male germ cell toxicity was evaluated using body weight, testes and epididymis weight, sperm count, sperm head morphology, sperm comet assay, histology of testes and TUNEL assay. AST treatment significantly improved the testes weight, sperm count and sperm head morphology as compared to only CP treated animals. The result of comet assay showed that AST treatment significantly restored the sperm DNA damage induced by CP. Further, AST treatment showed protection against CP induced testicular toxicity as evident from testes histology and TUNEL assay. The present results indicate the chemoprotective potential of AST against CP induced germ cell toxicity in mice.

Publication Types:

PMID: 18485558 [PubMed - indexed for MEDLINE]

[Mol Nutr Food Res.](#) 2006 Nov;50(11):991-5.

Visualization of astaxanthin localization in HT29 human colon adenocarcinoma cells by combined confocal resonance Raman and fluorescence microspectroscopy.

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Astaxanthin, a carotenoid found in plants and seafood, exhibits antiproliferative, antioxidant and anticarcinogenic properties. We show that astaxanthin delivered with tetrahydrofuran is effectively taken up by cultured colon adenocarcinoma cells and is localized mostly in the cytoplasm as detected by confocal resonance Raman and broad-band fluorescence microspectroscopy image analysis. Cells incubated with beta-carotene at the same concentration as astaxanthin (10 microM) showed about a 50-fold lower cellular amount of beta-carotene, as detected by HPLC. No detectable Raman signal of beta-carotene was found in cells, but a weak broad-band fluorescence signal of beta-carotene was observed. beta-Carotene, like astaxanthin, was localized mostly in the cytoplasm. The heterogeneity of astaxanthin and beta-carotene cellular distribution in cells of intestinal origin suggests that the possible defense against reactive molecules by carotenoids in these cells may also be heterogeneous.

Publication Types:

- [Research Support, Non-U.S. Gov't](#)

PMID: 17039456 [PubMed - indexed for MEDLINE]

[Bioorg Med Chem.](#) 2006 Aug 15;14(16):5451-8. Epub 2006 May 23.

Molecular modeling of non-covalent binding of homochiral (3S,3'S)-astaxanthin to matrix metalloproteinase-13 (MMP-13).

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Inhibitors for matrix metalloproteinases (MMPs) are under investigation for the treatment of various important chronic illnesses, including cancer, arthritis, and cardiovascular disease (CVD). In particular, MMP-13 is currently being probed as a potential key target in CVD and malignant disease due to its documented effects on extracellular matrix (ECM) remodeling, important in the pathophysiology of these diseases. Within the family of related mammalian MMP enzymes, MMP-13 possesses a large hydrophobic binding pocket relative to that of other MMPs. Homochiral astaxanthin (3S,3'S-AST; 3S,3'S-dihydroxy-beta,beta-carotene-4,4'-dione), an important antioxidant and anti-inflammatory xanthophyll carotenoid, is an active metabolite of several novel soft drugs in clinical development; it is also extensively used and tested as a human nutraceutical. In the current study, the prediction of the geometry and energetics of its binding to human MMP-13 was conducted with molecular modeling. The method used was found to predict the energy of binding of known ligands of MMP-13 with great precision. Blind docking using the whole protein target was then used in order to identify the possible binding site(s) of AST. AST was predicted to bind at several sites in close proximity to the active center. Subsequent analyses focused on the binding site at the atomic (i.e., amino acid sequence) level suggested that AST can bind to MMP-13 with high affinity and favorable energetics. Therefore, the modeling study predicts potential direct enzyme-inhibitory activity of AST against MMP-13, a behavior that may be exploited in mammalian systems in which pathological upregulation of MMP activity is paramount.

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Antiproliferation and induction of cell death of *Phaffia rhodozyma* (*Xanthophyllomyces dendrorhous*) extract fermented by brewer malt waste on breast cancer cells.

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Astaxanthin has been shown to have antiproliferative activity on breast cancer and skin cancer cells. However, the high cost of production, isolation and purification of purified astaxanthin from natural sources or chemically synthetic methods limit its usage on cancer therapy. We show that astaxanthin could be produced by fermentating the *Phaffia rhodozyma* (*Xanthophyllomyces dendrorhous*) yeast cells with brewer malt waste using a 20 L B. Braun fermentor. The percentage composition of astaxanthin from the *P. rhodozyma* was >70% of total pigment as estimated by the high performance liquid chromatographic analysis. Furthermore, the antiproliferative activity of this *P. rhodozyma* cell extract (PRE) was demonstrated on breast cancer cell lines including the MCF-7 (estrogen receptor positive) and MDA-MB231 (estrogen receptor negative) by using the [3-(4,5-dimethylthiazol-2-yl)-5-(3-arboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium] (MTS) assay. No apoptotic cell death, but growth inhibitory effect was induced after 48 h of PRE incubation as suggested by morphological investigation. Anchorage-dependent clonogenicity assay showed that PRE could reduce the colony formation potential of both breast cancer cell lines. Cell death was observed from both breast cancer cell lines after incubation with PRE for 6 days. Taken together, our results showed that by using an economic method of brewer malt waste fermentation, we obtained *P. rhodozyma* with a high yield of astaxanthin and the corresponding PRE could have short-term growth inhibition and long-term cell death activity on breast cancer cells.

Publication Types:

PMID: 16211266 [PubMed - indexed for MEDLINE]

[Biochim Biophys Acta](#). 2005 May 30;1740(2):170-8. Epub 2005 Jan 25.

Cancer prevention by retinoids and carotenoids: independent action on a common target.

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Virtually all human tumors are deficient in gap junctional communication (GJC) and the restoration of GJC by forced expression of connexins reduces indices of neoplasia. The expression of connexin 43 (Cx43) is upregulated by cancer-preventive retinoids and carotenoids which correlates with the suppression of carcinogen-induced transformation in 10T1/2 cells. However, the molecular mechanism for upregulated expression is poorly understood. The retinoic acid receptor antagonist, Ro 41-5253, suppressed retinoid-induced Cx43 protein expression in 10T1/2 cells and the induction of a Cx43 luciferase reporter construct in F9 cells, but did not suppress protein expression or reporter activity induced by the non-pro-vitamin A carotenoid astaxanthin. In contrast, Cx43 induction by astaxanthin, but not by a RAR-specific retinoid, was inhibited by GW9662, a PPAR-gamma antagonist. Neither compound required protein synthesis for the induction of Cx43 mRNA, nor was the 5.0 h half-life of Cx43 mRNA altered, indicating direct transcriptional activation. The responsive region was found within -158 bp and +209 bp of the transcription start site. Site directed mutagenesis of a GC-box in this region increased basal levels of transcription and loss of retinoid responsiveness. Simultaneous treatment with a retinoid and beta-carotene or astaxanthin resulted in supra-additive Cx43 expression, again indicating separate mechanisms of gene regulation.

Publication Types:

PMID: 15949684 [PubMed - indexed for MEDLINE]

[Carcinogenesis](#). 2005 Sep;26(9):1634-41. Epub 2005 May 11.

Inhibition of chemically-induced neoplastic transformation by a novel tetrasodium diphosphate astaxanthin derivative.

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Carotenoids have been implicated in numerous epidemiological studies as being protective against cancer at many sites, and their chemopreventive properties have been confirmed in laboratory studies. Astaxanthin (AST), primarily a carotenoid of marine origin, responsible for the pink coloration of salmon, shrimp and lobster, has received relatively little attention. As with other carotenoids, its highly lipophilic properties complicate delivery to model systems. To overcome this issue we have synthesized a novel tetrasodium diphosphate astaxanthin (pAST) derivative with aqueous dispersibility of 25.21 mg/ml. pAST was delivered to C3H/10T1/2 cells in an aqueous/ethanol solution and compared with non-esterified AST dissolved in tetrahydrofuran. We show pAST to (i) upregulate connexin 43 (Cx43) protein expression; (ii) increase the formation of Cx43 immunoreactive plaques; (iii) upregulate gap junctional intercellular communication (GJIC); and (iv) cause 100% inhibition of methylcholanthrene-induced neoplastic transformation at 10^{-6} M. In all these assays, pAST was superior to non-esterified AST itself; in fact, pAST exceeded the potency of all other previously tested carotenoids in this model system. Cleavage of pAST to non-esterified (free) AST and uptake into cells was also verified by HPLC; however, levels of free AST were approximately 100-fold lower than in cells treated with AST itself, suggesting that pAST possesses intrinsic activity. The dual properties of water dispersibility (enabling parenteral administration in vivo) and increased potency should prove extremely useful in the future development of cancer chemopreventive agents.

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[Cancer Lett.](#) 2004 Jul 28;211(1):25-37.

Upregulation of connexin 43 protein expression and increased gap junctional communication by water soluble disodium disuccinate astaxanthin derivatives.

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Carotenoids are plant pigments whose consumption is associated with lower cancer rates in humans. Studies in experimental animal and cell systems have confirmed the cancer chemopreventive activity of these compounds. However, their extremely hydrophobic nature makes these compounds biologically unavailable unless delivered in organic solution to model systems. We have synthesized novel disodium salt disuccinate astaxanthin derivatives that possess high aqueous dispersibility. When delivered to mouse embryonic fibroblast C3H/10T1/2 cell cultures, either in aqueous or aqueous/ethanol solutions, these derivatives are biologically active. Biological activity was demonstrated by (1) upregulated expression of connexin 43 (Cx43) protein; (2) increased formation of Cx43 immunoreactive plaques in regions of the plasma membrane consistent with localization of gap junctions; (3) significantly upregulated gap junctional intercellular communication (GJIC) as demonstrated by Lucifer Yellow dye transfer after microinjection ($P < 0.03$; Fisher's Exact test). Enhanced expression of Cx43 and increased GJIC have been previously demonstrated to result in inhibition of in vitro neoplastic transformation of 10T1/2 cells as well as growth reduction of human tumors in xenografts. These novel derivatives possess increased utility as water soluble and water dispersible agents, allowing for aqueous delivery both in vitro and in vivo, properties that could enhance their potential clinical utility as potent cancer chemopreventive agents. Copyright 2004 Elsevier Ireland Ltd.

PMID: 15194214 [PubMed - indexed for MEDLINE]

Contribution of the antioxidative property of astaxanthin to its protective effect on the promotion of cancer metastasis in mice treated with restraint stress.

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We investigated the effects of astaxanthin on the antitumor effector activity of natural killer (NK) cells suppressed by stress in mice in order to define the immunological significance of astaxanthin (ASX) when combined with restraint stress treatment. When the mice were treated with restraint stress alone, the total number of spleen cells, and the level NK cell activity per spleen were reduced to a nadir on day 3. The stress also caused a significant increase in the lipid peroxidation of liver tissue. ASX (100 mg/kg/day, p.o., 4 days) improved the immunological dysfunction induced by restraint stress. On the other hand, metastatic nodules were observed in the livers of syngenic DBA/2 mice on day 12 after inoculation of P815 mastocytoma cells. Hepatic metastasis was promoted further by restraint stress when applied on day 3 before the inoculation of P815. Daily oral administration of ASX (1 mg/kg/day, p.o., 14 days) markedly attenuated the promotion of hepatic metastasis induced by restraint stress. These results suggested that astaxanthin improves antitumor immune responses by inhibiting of lipid peroxidation induced by stress.

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Antitumor activity of astaxanthin and its mode of action.

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Astaxanthin, a carotenoid without vitamin A activity, may exert antitumor activity through the enhancement of immune responses. Here, we determined the effects of dietary astaxanthin on tumor growth and tumor immunity against transplantable methylcholanthrene-induced fibrosarcoma (Meth-A tumor) cells. These tumor cells express a tumor antigen that induces T cell-mediated immune responses in syngenic mice. BALB/c mice were fed astaxanthin (0.02%, 40 micrograms/kg body wt/day in a beadlet form) mixed in a chemically defined diet starting zero, one, and three weeks before subcutaneous inoculation with tumor cells (3×10^5) cells, 2 times the minimal tumorigenic dose). Three weeks after inoculation, tumor size and weight were determined. We also determined cytotoxic T lymphocyte (CTL) activity and interferon-gamma (IFN-gamma) production by tumor-draining lymph node (TDLN) and spleen cells by restimulating cells with Meth-A tumor cells in culture. The astaxanthin-fed mice had significantly lower tumor size and weight than controls when supplementation was started one and three weeks before tumor inoculation. This antitumor activity was paralleled with higher CTL activity and IFN-gamma production by TDLN and spleen cells in the astaxanthin-fed mice. CTL activity by TDLN cells was highest in mice fed astaxanthin for three weeks before inoculation. When the astaxanthin-supplemented diet was started at the same time as tumor inoculation, none of these parameters were altered by dietary astaxanthin, except IFN-gamma production by spleen cells. Total serum astaxanthin concentrations were approximately 1.2 $\mu\text{mol/l}$ when mice were fed astaxanthin (0.02%) for four weeks and appeared to increase in correlation with the length of astaxanthin supplementation. Our results indicate that dietary astaxanthin suppressed Meth-A tumor cell growth and stimulated immunity against Meth-A tumor antigen.

Publication Types:

PMID: 10798217 [PubMed - indexed for MEDLINE]

[Cancer Lett.](#) 2000 Apr 3;151(1):111-5.

Inhibitory effects of carotenoids on the invasion of rat ascites hepatoma cells in culture.

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The effects of carotenoids--alpha-carotene, beta-carotene, lycopene, beta-cryptoxanthin, zeaxanthin, lutein, canthaxanthin, astaxanthin--on the invasion of rat ascites hepatoma AH109A cells were investigated by co-culturing the hepatoma cells with rat mesentery-derived mesothelial cells (M-cells). All the carotenoids examined inhibited AH109A invasion in a dose-dependent manner up to 5 microM. Cancer cells previously cultured with hypoxanthine (HX) and xanthine oxidase (XO) showed a highly invasive activity. Carotenoids, 5 microM of beta-carotene and astaxanthin, suppressed this reactive oxygen species-potentiated invasive capacity by simultaneously treating AH109A cells with the carotenoids, HX and XO. These results suggest that the antioxidative property of these carotenoids may be involved in their anti-invasive action.

Publication Types:

PMID: 10766430 [PubMed - indexed for MEDLINE]

Dietary beta-carotene and astaxanthin but not canthaxanthin stimulate splenocyte function in mice.

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The in vivo modulatory effect of beta-carotene, astaxanthin and canthaxanthin on lymphocyte function was investigated. Female BALB/c mice (8 wk old) were fed a basal diet containing 0, 0.1% or 0.4% beta-carotene, astaxanthin or canthaxanthin for 0, 2 or 4 wk (n = 8/diet/period). Splenic lymphocytes were isolated and mitogen-stimulated proliferation, IL-2 production and lymphocyte cytotoxicity were assessed. Body weight and feed intake were not different among dietary treatments. Plasma carotenoids were undetectable in unsupplemented mice but concentrations of the respective carotenoids were elevated in mice fed 0.1 or 0.4% beta-carotene (0.22 and 0.39 $\mu\text{mol/L}$), astaxanthin (16.4 and 50.2 $\mu\text{mol/L}$) and canthaxanthin (5.00 and 7.02 $\mu\text{mol/L}$) respectively. Mice fed both dietary levels of beta-carotene and astaxanthin had enhanced phytohemagglutinin-induced lymphoblastogenesis compared to unsupplemented mice ($P < 0.03$). No treatment difference was detected with concanavalin A- or lipopolysaccharide-induced lympho-proliferation nor with IL-2 production ($P < 0.05$). Astaxanthin (0.1%) also enhanced lymphocyte cytotoxic activity ($P < 0.08$). In contrast, canthaxanthin did not significantly influence any of the lymphocyte functions measured. Results indicate that beta-carotene and astaxanthin but not canthaxanthin exert enhanced splenic lymphocyte function in mice.

Publication Types:

PMID: 10697539 [PubMed - indexed for MEDLINE]

[Anticancer Res.](#) 1999 May-Jun;19(3A):1849-53.

A comparison of the anticancer activities of dietary beta-carotene, canthaxanthin and astaxanthin in mice in vivo.

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The anticancer activities of beta-carotene, astaxanthin and canthaxanthin against the growth of mammary tumors were studied in female eight-wk-old BALB/c mice. The mice were fed a synthetic diet containing 0, 0.1 or 0.4% beta-carotene, astaxanthin or canthaxanthin. After 3 weeks, all mice were inoculated with 1×10^6 WAZ-2T tumor cells into the mammary fat pad. All animals were killed on 45 d after inoculation with the tumor cells. No carotenoids were detectable in the plasma or tumor tissues of unsupplemented mice. Concentrations of plasma astaxanthin (20 to 28 $\mu\text{mol/L}$) were greater ($P < 0.05$) than that of beta-carotene (0.1 to 0.2 $\mu\text{mol/L}$) and canthaxanthin (3 to 6 nmol/L). However, in tumor tissues, the concentration of canthaxanthin (4.9 to 6.0 nmol/g) was higher than that of beta-carotene (0.2 to 0.5 nmol/g) and astaxanthin (1.2 to 2.7 nmol/g). In general, all three carotenoids decreased mammary tumor volume. Mammary tumor growth inhibition by astaxanthin was dose-dependent and was higher than that of canthaxanthin and beta-carotene. Mice fed 0.4% beta-carotene or canthaxanthin did not show further increases in tumor growth inhibition compared to those fed 0.1% of each carotenoid. Lipid peroxidation activity in tumors was lower ($P < 0.05$) in mice fed 0.4% astaxanthin, but not in those fed beta-carotene and canthaxanthin. Therefore, beta-carotene, canthaxanthin and especially astaxanthin inhibit the growth of mammary tumors in mice; their anti-tumor activity is also influenced by the supplemental dose.

Publication Types:

PMID: 10470126 [PubMed - indexed for MEDLINE]

Effect of dietary supplementation with carotenoids on xenobiotic metabolizing enzymes in the liver, lung, kidney and small intestine of the rat.

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The effect of 16 d intake of 300 mg carotenoids/kg diet (beta-carotene (beta C), bixin (BX), lycopene (LY), lutein (LU), canthaxanthin (CX) or astaxanthin (AX) on xenobiotic metabolizing enzymes in the liver, lung, kidney and small intestine of male Wistar rats was assessed. A control group received the basal diet (AIN-76) without carotenoids and a positive control group for enzyme induction received 3-methylcholanthrene (3-MC) at 666 mg/kg diet. Cytochrome P450 activity was assessed using the substrates ethoxyresorufin for P450 1A1, methoxyresorufin for P450 1A2, pentoxyresorufin for P450 2B1/2 and benzyloxyresorufin for P450 types 1A1/2, 2B1/2 and 3A. Glutathione-S-transferase (EC 2.5.1.18) and reduced glutathione status were assessed. Carotenoid uptake by the tissues was also determined. 3-MC and the carotenoids BX, CX and AX led to significant increases compared with control in liver, lung and kidney ethoxyresorufin-O-deethylation. Methoxyresorufin-O-demethylation activity was significantly increased in liver and lung by BX, CX and AX but only CX and AX significantly increased activity in kidney. Pentoxyresorufin-O-depentylation and benzyloxyresorufin-O-dearylation increased in liver of 3-MC-, BX-, CX- and AX-treated rats, but to a much lesser degree than for the other two substrates. Benzyloxyresorufin-O-dearylation in lung was significantly decreased by all carotenoids. Activities of any of the measured enzymes in the small intestine were undetectable in all treatment groups except the 3-MC group. Glutathione status was unaffected by any of the treatments. This is the first study identifying the carotenoids BX, CX and AX as inducers of rat lung and kidney xenobiotic metabolizing enzymes.

Publication Types:

PMID: 10434850 [PubMed - indexed for MEDLINE]

[Carcinogenesis](#). 1998 Mar;19(3):403-11.

Dietary carotenoids inhibit aflatoxin B1-induced liver preneoplastic foci and DNA damage in the rat: role of the modulation of aflatoxin B1 metabolism.

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To study the effects of carotenoids on the initiation of liver carcinogenesis by aflatoxin B1 (AFB1), male weanling rats were fed beta-carotene, beta-apo-8'-carotenal, canthaxanthin, astaxanthin or lycopene (300 mg/kg diet), or an excess of vitamin A (21000 RE/kg diet), or were injected i.p. with 3-methylcholanthrene (3-MC) (6 x 20 mg/kg body wt) before and during i.p. treatment with AFB1 (2 x 1 mg/kg body wt). The rats were later submitted to 2-acetylaminofluorene treatment and partial hepatectomy, and placental glutathione S-transferase-positive liver foci were detected and quantified. The *in vivo* effects of carotenoids or of 3-MC on AFB1-induced liver DNA damage were evaluated using different endpoints: liver DNA single-strand breaks (SSB) induced by AFB1, and *in vivo* binding of [3H]AFB1 to liver DNA and plasma albumin. Finally, the modulation of AFB1 metabolism by carotenoids or by 3-MC was investigated *in vitro* by incubating [14C]AFB1 with liver microsomes from rats that had been fed with carotenoids or treated by 3-MC, and the metabolites formed by HPLC were analyzed. In contrast to lycopene or to an excess of vitamin A, both of which had no effect, beta-carotene, beta-apo-8'-carotenal, astaxanthin and canthaxanthin, as well as 3-MC, were very efficient in reducing the number and the size of liver preneoplastic foci. In a similar way as 3-MC, the P4501A-inducer carotenoids, beta-apo-8'-carotenal, astaxanthin and canthaxanthin, decreased *in vivo* AFB1-induced DNA SSB and the binding of AFB1 to liver DNA and plasma albumin, and increased *in vitro* AFB1 metabolism to aflatoxin M1, a less genotoxic metabolite. It is concluded that these carotenoids exert their protective effect through the deviation of AFB1 metabolism towards detoxication pathways. In contrast, beta-carotene did not protect hepatic DNA from AFB1-induced alterations, and caused only minor changes of AFB1 metabolism: seemingly, its protective effect against the initiation of liver preneoplastic foci by AFB1 is mediated by other mechanisms.

Publication Types:

PMID: 9525273 [PubMed - indexed for MEDLINE]

[Cancer Lett.](#) 1997 Mar 19;114(1-2):221-3.

Modulation of aflatoxin B1 carcinogenicity, genotoxicity and metabolism in rat liver by dietary carotenoids: evidence for a protective effect of CYP1A inducers.

[Gradelet S](#), [Astorg P](#), [Le Bon AM](#), [Bergès R](#), [Suschetet M](#).

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The effects of several carotenoids of vitamin A and of 3-methylcholanthrene have been tested on the initiation of hepatocarcinogenesis by aflatoxin B1, using the sequential protocol of Solt and Farber. AFB1-induced DNA single-strand breaks and AFB1-metabolism were also assessed. The P4501A inducer carotenoids (canthaxanthin, astaxanthin, beta-apo-8'-carotenal) and 3-methylcholanthrene reduce the carcinogenicity of AFB1, divert AFB1-metabolism into the less genotoxic aflatoxin M1 and reduce AFB1-induced DNA single-strand breaks: we conclude that these carotenoids exert their protective effect through the deviation of AFB1 metabolism towards detoxification pathways. beta-Carotene decreased AFB1 carcinogenicity but did not alter its metabolism, probably acting by other mechanisms.

Publication Types:

PMID: 9103297 [PubMed - indexed for MEDLINE]

Chemoprevention by naturally occurring and synthetic agents in oral, liver, and large bowel carcinogenesis.

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A number of naturally occurring compounds and several related synthetic agents were confirmed to exert chemopreventive properties against carcinogenesis in the digestive organs. Phenolic compounds, widely distributed as plant constituents, possess chemopreventive activities in tongue, liver, and large bowel of rodents. Of them, a simple phenolic protocatechuic acid seems to be a promising compound. Organosulfur compounds contained in the cruciferous vegetables and known to activate detoxifying enzymes are regarded as a candidate group for cancer preventive agents. We proved a strong protective effect of S-methylmethanethiosulfonate, a constituent in these vegetables, on azoxymethane (AOM)-induced large bowel carcinogenesis. Some oxygenated carotenoids (xanthophylls) are reported to have antitumor effects. Naturally occurring xanthophylls astaxanthin and canthaxanthin have considerable preventive activities on 4-nitroquinoline-1-oxide (4-NQO)-induced tongue carcinogenesis and AOM-induced large bowel carcinogenesis. A novel synthesized retinoidal butenolide, KYN-54, which suppresses large bowel as well as tongue carcinogenesis could be a useful agent for prevention of digestive organ cancers. Some trace elements are known to have anticarcinogenic effects. Magnesium hydroxide, a protective agent in colorectal carcinogenesis, inhibits c-myc expression and ornithine decarboxylase activity in the mucosal epithelium of the intestine. Our results show that many agents with preventive effects in tongue, liver, and large bowel control carcinogen-induced hyperproliferation of cells in these organs. Carcinogens used to induce large bowel cancers also induce apoptosis in the target sites. Telomerase activity is increased in the tissues of preneoplastic as well as neoplastic lesions in experimental models such as dimethylbenz[a]anthracene-induced oral carcinogenesis in hamsters. These could be useful biomarkers in studies for cancer chemoprevention.

Publication Types:

PMID: 9591191 [PubMed - indexed for MEDLINE]

[Carcinogenesis](#). 1995 Dec;16(12):2957-63.

Suppression of azoxymethane-induced rat colon carcinogenesis by dietary administration of naturally occurring xanthophylls astaxanthin and canthaxanthin during the postinitiation phase.

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The modulating effects of dietary feeding of two xanthophylls, astaxanthin (AX) and canthaxanthin (CX) during the postinitiation phase on colon carcinogenesis initiated with azoxymethane (AOM) were investigated in male F344 rats. Animals were initiated with AOM by weekly s.c. injections of 15 mg/kg body wt for 3 weeks and then they were fed the diets containing AX or CX at concentrations of 100 and 500 p.p.m. for 34 weeks. The others contained the groups of rats treated with AX or CX alone and untreated. At the end of the study (week 37), the incidence and multiplicity of neoplasms (adenoma and adenocarcinoma) in the large intestine of rats initiated with AOM and followed by AX or CX containing diet at a high dose (500 p.p.m.) were significantly smaller than those of rats given AOM alone ($P < 0.001$). In addition, AX or CX feeding significantly inhibited the development of aberrant crypt foci induced by AOM. Dietary exposure to AX or CX also decreased cell proliferation activity as revealed by measuring 5'-bromodeoxyuridine-labeling index as crypt cells, colonic mucosal ornithine decarboxylase activity and blood polyamine levels. These results indicate that AX and CX are possible chemopreventers for carcinogenesis of colon in addition to urinary bladder and oral cavity and such effects may be partly due to suppression of cell proliferation.

Publication Types:

PMID: 8603470 [PubMed - indexed for MEDLINE]

[Cancer Res.](#) 1995 Sep 15;55(18):4059-64.

Chemoprevention of rat oral carcinogenesis by naturally occurring xanthophylls, astaxanthin and canthaxanthin.

[Tanaka T](#), [Makita H](#), [Ohnishi M](#), [Mori H](#), [Satoh K](#), [Hara A](#).

First Department of Pathology, Gifu University School of Medicine, Japan.

The chemopreventive effects of two xanthophylls, astaxanthin (AX) and canthaxanthin (CX) on oral carcinogenesis induced by 4-nitroquinoline 1-oxide (4-NQO) was investigated in male F344 rats. Rats were given 20 ppm of 4-NQO in their drinking water for 8 weeks to induce oral neoplasms or preneoplasms. Animals were fed diets containing 100 ppm AX or CX during the initiation or postinitiation phase of 4-NQO-induced oral carcinogenesis. The others contained the groups of rats treated with AX or CX alone and untreated. At the end of the study (week 32), the incidences of preneoplastic lesions and neoplasms in the oral cavity of rats treated with 4-NQO and AX or CX were significantly smaller than those of rats given 4-NQO alone ($P < 0.001$). In particular, no oral neoplasms developed in rats fed AX and CX during the 4-NQO exposure and in those given CX after the 4-NQO administration. Similarly, the incidences of oral preneoplastic lesions (hyperplasia and dysplasia) in rats treated with 4-NQO and AX or CX were significantly smaller than that of the 4-NQO-alone group ($P < 0.05$). In addition to such tumor inhibitory potential, dietary exposure of AX or CX decreased cell proliferation activity in the nonlesional squamous epithelium exposed to 4-NQO as revealed by measuring the silver-stained nucleolar organizer regions protein number/nucleus and 5'-bromodeoxyuridine-labeling index. Also, dietary AX and CX could reduce polyamine levels of oral mucosal tissues exposed to 4-NQO. These results indicate that AX and CX are possible chemopreventers for oral carcinogenesis, and such effects may be partly due to suppression of cell proliferation.

Publication Types:

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ASTAXANTHIN INHIBITS HALLMARKS OF CANCER IN ORAL CANCER CELLS AND SHOWS PROMISE AS AN ANTI-CANCER AGENT .

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doi: 10.1002/iub.2104. Epub 2019 Jun 28.

Astaxanthin inhibits hallmarks of cancer by targeting the PI3K/NF- κ B/STAT3 signalling axis in oral squamous cell carcinoma models

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- PMID: [31251469](#)
- DOI: [10.1002/iub.2104](#)

Free article

Abstract

Aberrant activation of the PI3K/Akt signalling pathway, a major driving force of diverse cellular processes has been implicated in tumour development and progression. Here, we report that astaxanthin (AXT), a potent antioxidant ketocarotenoid prevents cancer hallmarks by inhibiting PI3K/Akt and the associated downstream NF- κ B and STAT-3 signalling pathways in SCC131 and SCC4 oral cancer cells as well as in the hamster buccal pouch carcinogenesis model. Using small molecule inhibitors of NF- κ B, STAT-3 and PI3K and by overexpression of PI3K, we provide evidence to show that AXT inhibits NF- κ B and STAT-3 signalling and cancer hallmarks by restraining the kinase activity of PI3K/Akt. Additionally, AXT downregulated the noncoding RNAs (ncRNAs), miR-21 and HOTAIR that influence PI3K/Akt signalling emphasising its modulatory effects on epigenetic regulation. Ethyl cellulose-based AXT nanoparticles showed greater chemotherapeutic efficacy in the hamster oral carcinogenesis model compared to native AXT. We suggest that AXT prevents cell proliferation, apoptosis evasion, invasion and angiogenesis by intercepting the crosstalk between the PI3K/Akt, NF- κ B and STAT-3 signalling circuits both in vitro and in vivo. Astaxanthin that abrogates the PI3K/Akt signalling axis, a central hub that orchestrates acquisition of cancer hallmarks is a promising candidate for anticancer drug development.

ASTAXANTHIN SHOWS EFFICACY AGAINST BREAST CANCER CELLS AND MAY BE SUITABLE AS AN ALTERNATIVE FOR IMPROVING THE EFFICACY OF OTHER BREAST CANCER THERAPIES.

Mar Drugs. 2020 May 19;18(5):266.
doi: 10.3390/md18050266.

Astaxanthin Modulates Apoptotic Molecules to Induce Death of SKBR3 Breast Cancer Cells

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- PMID: [32438569](#)
- PMCID: [PMC7281348](#)
- DOI: [10.3390/md18050266](#)

Free PMC article

Abstract

Astaxanthin (AST) is related to apoptosis but the details of the mechanism of how AST makes apoptosis is not clear. The present study investigated apoptotic effects of AST to SKBR3, a breast cancer cell line in detail. Cell viability assay showed cellular proliferation and morphological changes of the cells were observed under AST treatment. FACS analysis indicated that AST blocked cell cycle progression at G0/G1, suppressed proliferation dose-dependently, and induced apoptosis of the cells. The apoptosis of the cells by AST was further demonstrated through the decreased expression level of mutp53 and cleaved a PARP-1 fragment, respectively. In addition, AST induced the intrinsic apoptosis of the cells by activation of Bax/Bcl2, cleaved caspase-3, and cleaved caspase-9 as well as the phosphorylation of ERK1/2, JNK, and p38. Furthermore, AST decreased production of intracellular reactive oxygen species as well as modulated expressions of superoxide dismutases and Pontin, an anti-apoptotic factor. Co-immunoprecipitation assay revealed AST reduced interaction between Pontin and mutant p53. Taken together, these studies proved that AST regulates the expression of apoptotic molecules to induce intrinsic apoptosis of the cells, suggesting AST therapy might provide an alternative for improving the efficacies of other anti-cancer therapies for breast cancer.

ASTAXANTHIN COMBINED WITH ANOTHER NATURAL ACTIVE INGREDIENT IMPROVED THE ANTI-CANCER ACTIVITY OF CANCER DRUG DOXORUBICIN.

BMC Pharmacol Toxicol. 2021 Jan 28;22(1):8.

doi: 10.1186/s40360-021-00473-2.

Epigenetic immunomodulatory effect of eugenol and astaxanthin on doxorubicin cytotoxicity in hormonal positive breast Cancer cells

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- PMID: **33509300**
- PMCID: [PMC7842008](#)
- DOI: [10.1186/s40360-021-00473-2](#)

Free PMC article

Abstract

Background: Hormonal receptor positive (HR+) breast cancer is the most commonly diagnosed molecular subtype of breast cancer; which showed good response to doxorubicin (DOX)-based chemotherapy. Eugenol (EUG) and astaxanthin (AST) are natural compounds with proved epigenetic and immunomodulatory effects in several cancer cell lines. This study has been initiated to investigate the molecular mechanism (s) whereby EUG and AST could enhance DOX cytotoxicity in MCF7 cells.

Methods: Cytotoxic activity of DOX alone and combined with either 1 mM EUG or 40 μ M AST was performed using sulphorhodamine-B assay in MCF7 cells. Global histones acetylation and some immunological markers were investigated using ELISA, western blotting and quantitative RT-PCR techniques. Functional assay of multidrug resistance was performed using rhodamine 123 and Hoechst 3342 dyes. Flow cytometry with annexin V and propidium iodide were used to assess the change in cell cycle and apoptosis along with the expression of some differentiation, apoptosis and autophagy proteins.

Results: DOX alone resulted in concentration-dependent cytotoxicity with IC_{50} of 0.5 μ M. Both EUG and AST significantly increased DOX cytotoxicity which is manifested as a significant decrease in DOX IC_{50} from 0.5 μ M to 0.088 μ M with EUG and to 0.06 μ M with AST. Combinations of DOX with 1 mM EUG or 40 μ M AST significantly increased the level of histones acetylation and histone acetyl transferase expression, while reduced the expression of aromatase and epidermal growth factor receptor (EGFR) when compared with 0.25 μ M DOX alone. Also both combinations showed higher uptake of rhodamine but lower of Hoechst stains, along with increased the percentage of caspase 3, and decreased the expression of CK7 and LC3BI/II ratio. EUG combination induced IF γ but reduced TNF α causing shifting of cells from G2/M to S and G0/ G1 phases. Combination of DOX with EUG induced apoptosis through the higher BAX/ BCL2 ratio, while with AST was through the increase in caspase 8 expressions.

Conclusion: EUG and AST potentiated the anticancer activity of DOX through epigenetic histones acetylation along with the immunomodulation of different apoptotic approaches in MCF7 cells.

ASTAXANTHIN PREVENTS THE GROWTH OF HUMAN PROSTATE CANCER CELLS AND CAN BE CONSIDERED AS A POTENTIAL TREATMENT FOR PROSTATE CANCER.

J Food Biochem. 2021 Mar 10;e13702.
doi: 10.1111/jfbc.13702. Online ahead of print.

Anti-androgenic effect of astaxanthin in LNCaP cells is mediated through the aryl hydrocarbon-androgen receptors cross talk

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PMID: 33694182 DOI: [10.1111/jfbc.13702](https://doi.org/10.1111/jfbc.13702)

Abstract

The aim of this study was to investigate the anti-androgenic effects of astaxanthin (AST) on human prostatic cancer cell growth, and its impact on androgen receptor (AR) signaling using prostate cancer (PCa) cell line LNCaP. LNCaP cells were treated with AST alone and in combination with CH223191 and flutamide (Flu) in the presence and absence of testosterone. MTT assay, cellular prostate-specific antigen (PSA) and dihydrotestosterone (DHT) production, mRNA levels of CYP1A1, PSA, Kallikrein-Related Peptidase 2 (KLK2), Transmembrane Serine Protease 2 (TMPRSS2), and AR genes were measured as endpoints. The expression of CYP1A1, PSA, KLK2, TMPRSS2, and AR mRNA levels was decreased which results in reducing the production of PSA and DHT in the presence of testosterone. Our data clearly demonstrate that AST has a potential ability to suppress the human prostate LNCaP cells growth at high concentrations. AST was able to repress the testosterone-induced transcription of AR-target genes. PRACTICAL APPLICATIONS: Astaxanthin is a natural compound with the most potent antioxidant activity among other antioxidants. In the current study, ASX suppressed the LNCaP cells at high concentrations. Furthermore, AST inhibited testosterone-induced transcriptional activation of androgen-related genes. AST induced the expression of CYP1A1, which is able to metabolize the steroid hormones. It seems that AST can act as AhR exogenous ligand by induction of CYP1A1, which results in testosterone metabolism and consequent suppression of AR genes. So that, AST could prevent the growth of testosterone-dependent PCa cells, downregulate downstream genes in testosterone pathways, and enhance the metabolism of testosterone via AhR pathway. Collectively, AST could be considered as a potential candidate for the treatment of PCa.

ASTAXANTHIN SHOWS POTENTIAL TO ASSIST WITH CHEMOTHERAPY SIDE EFFECTS IN MOUSE LIVER STUDY.

Food Funct. 2020 May 1;11(5):4659-4671.

doi: 10.1039/c9fo02429h. Epub 2020 May 14.

Astaxanthin from *Haematococcus pluvialis* ameliorates the chemotherapeutic drug (doxorubicin) induced liver injury through the Keap1/Nrf2/HO-1 pathway in mice

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PMID: 32405635 DOI: [10.1039/c9fo02429h](https://doi.org/10.1039/c9fo02429h)

Abstract

The aim of this study is to probe a new function of astaxanthin (AST) from *Haematococcus pluvialis* on chemotherapeutic drug induced liver injury in mice. Doxorubicin-induced liver injury was treated with different doses of AST, and the body weight, food intake, urinalysis, liver function, and oxidative stress indexes were examined. The hepatocyte apoptosis level, pathological sections of liver tissue and the expression of antioxidant related genes were also determined. This study found that DOX could induce serious liver injury through cytotoxicity. AST treatment could decrease the level of liver function indexes (ALT, GOT, ALP and TBil), reduce the concentration of MDA and ROS, and increase the activities of SOD, CAT and GPX in the liver. AST could also repair the damaged hepatocyte in mice with liver injury and reduce the degree of the cellular apoptosis. In addition, AST could interfere with the expression of some related genes in the Keap1/Nrf2 signaling pathway by downregulating the expression of Keap1 and activating the transcription factor Nrf2 via enhancing the level of ERK, which upregulates downstream peroxiredoxins. The present research found and illustrated a new food function of AST, indicating that AST could be used in the therapy of chemotherapy induced side effects.

ASTAXANTHIN REDUCES CELL DEATH CAUSED BY CHEMOTHERAPY DRUG BUSULFAN IN HUMAN STEM CELLS.

Reprod Sci. 2021 Jun 15.

doi: 10.1007/s43032-021-00651-x. Online ahead of print.

Astaxanthin Relieves Busulfan-Induced Oxidative Apoptosis in Cultured Human Spermatogonial Stem Cells by Activating the Nrf-2/HO-1 pathway

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- PMID: 34129218 DOI: [10.1007/s43032-021-00651-x](https://doi.org/10.1007/s43032-021-00651-x)

Abstract

Many child cancer patients endure anticancer therapy containing alkylating agents before sexual maturity. Busulfan (BU), as an alkylating agent, is a chemotherapy drug, causing DNA damage and cytotoxicity in germ cells. In the present study, we aimed to investigate the protective effect of astaxanthin (AST), as a potent antioxidant and powerful reactive oxygen species (ROS) scavenger, on BU-induced toxicity in human spermatogonial stem cells. For this purpose, testes were obtained from four brain-dead donors. After tissue enzymatic digestions, testicular cells were cultured for 3 weeks for spermatogonial stem cell (SSC) isolation and purification. K562 cell line was cultured to survey the effect of AST on cancer treatment. The cultured SSCs and K562 cell line were finally treated with AST (10 μ M), BU (0.1nM), and AST+BU. The expression of NRF-2, HO-1, SOD2, SOD3, TP53, and apoptotic genes, including CASP9, CASP3, BCL2, and BAX, were assayed using real-time PCR. Moreover, ROS level in different groups and malondialdehyde level and total antioxidant capacity in cell contraction of SSCs were measured using ELISA. Data showed that AST significantly upregulated the expression of NRF-2 gene (P<0.001) and protein (P<0.005) and also significantly decreased the production of BU-induced ROS (P<0.001). AST activated the NRF-2/HO-1 pathway that could remarkably restrain BU-induced apoptosis in SSCs. Interestingly, AST upregulated the expression level of apoptosis genes in the K562 cell line. The results of this study indicated that AST reduces the side effects of BU on SSCs without interference with its chemotherapy effect on cancerous cells through modulation of the NRF-2/HO-1 and mitochondria-mediated apoptosis pathways.

ASTAXANTHIN INCREASES THE ACTIVATION OF PROTEINS THAT SUPPRESS THE SPREAD OF CANCER CELLS IN HUMAN CELL STUDY.

Ann Ital Chir. 2021 May 3;10:S0003469X21035648.

Online ahead of print.

Effects of astaxanthin on metastasis suppressors in ductal carcinoma. A preliminary study

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- PMID: **34096509**

Background: Breast cancer (BC) is a major public health problem diagnosed in more than 2 million women worldwide in 2018, causing more than 600,000 deaths. 90% of deaths due to breast cancer are caused by metastasis. Metastasis is a complex process that is divided into several steps, including separation of tumor cells from the primary tumor, invasion, cell migration, intravasation, vasculature survival, extravasation, and colonization of the secondary site. Astaxanthin (AXT) is a marine-based ketocarotenoid that has many different potential functions such as anti-oxidant, anti-inflammatory and oxidative stress-reducing properties to potentially reduce the incidence of cancer or inhibit the expansion of tumor cells. This study aims to investigate the effects of astaxanthin as a new metastasis inhibitor on T47D human invasive ductal carcinoma breast cancer cell.

Material methods: To investigate the effects of the astaxanthin as a new metastasis inhibitor on T47D cell, expression levels of anti-maspin, anti-Kai1, anti-BRMS1, and anti-MKK4 were examined by western blot. Also, we evaluated differences of these suppressors expression levels in tissue sections of 10 patients diagnosed with in situ and invasive ductal carcinoma by immunohistochemistry method.

Result: 250 μ M astaxanthin increased the activation of all metastasis suppressing proteins. Also, these metastasis suppressors showed higher expression in invasive ductal carcinoma tissues than in situ ductal carcinoma patients.

Conclusion: We think that astaxanthin is a promising therapeutic agent for invasive ductal carcinoma patients. The effects of astaxanthin on metastasis in breast cancer should be investigated further based on these results.

ASTAXANTHIN REDUCES OXIDATIVE STRESS AND CELL DEATH IN MOUSE MODEL OF POLYCYSTIC OVARY SYNDROME.

Reprod Sci. 2021 Apr 19.

doi: [10.1007/s43032-021-00577-4](https://doi.org/10.1007/s43032-021-00577-4). Online ahead of print.

The Effect of Astaxanthin and Metformin on Oxidative Stress in Granulosa Cells of BALB C Mouse Model of Polycystic Ovary Syndrome

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- PMID: **33876387**
- DOI: [10.1007/s43032-021-00577-4](https://doi.org/10.1007/s43032-021-00577-4)

Abstract

Reactive oxygen species (ROS), involved in the pathogenesis of the polycystic ovary syndrome (PCOS), play a key role in the onset of apoptosis in follicles and granulosa cells (GCs). We aimed to investigate the antioxidant effects of AST and metformin separately and in combination on GCs using a PCOS mouse model. Forty-eight prepubertal female BALB C mice aged 25-30 days and weighing 12-14 g were studied. The PCOS model was created by subcutaneous injection of the dehydroepiandrosterone (DHEA) hormone in 8 mice of BALB C for 20 consecutive days. Apoptosis and the amount of ROS were evaluated in GCs of the ovaries via flow cytometry. The activity of AKT protein was measured by western blot, and the viability of GCs was investigated using spectrophotometry. Ovarian tissue sections were prepared, stained with H&E, and the morphology of the sections was examined. Statistical analysis was performed by SPSS v22.0 software using one-way ANOVA. We found that AST administration leads to a significant reduction in oxidative stress ($P < 0.01$) and consequently a significant decrease in the rate of apoptosis ($P < 0.01$). While the expression of AKT in the AST group revealed a significant increase ($P < 0.05$), it decreased in the metformin group. However, it was still significantly higher than the control and PCOS groups. Ovulation was confirmed in both metformin and AST groups. Further studies are warranted to prove the efficacy of AST and to introduce it as a complementary therapeutic agent in PCOS.

Marine Carotenoids: Bioactivities and Potential Benefits to Human Health.

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Author information

Abstract

Among natural pigments, carotenoids play important roles in physiological functions. The characteristics of carotenoids and their effects on human health have been reported for a long time, but most studies have focused on carotenoids from vegetables, fruits, and other parts of higher plants. Few reports are available on carotenoids from marine sources, such as seaweeds, microalgae, and marine animals, which have attracted attention in recent decades. Hundreds of carotenoids have been identified and isolated from marine organisms and their beneficial physiological functions, such as anti-cancer, anti-obesity, anti-diabetic, anti-inflammatory, and cardioprotective activities have been reported. The purpose of this review is to discuss the literature on the beneficial bioactivities of some of the most abundant marine carotenoids, including fucoxanthin, astaxanthin, cantaxanthin, peridinin, fucoxanthinol, and halocynthiaxanthin.

KEYWORDS:

Biological activity; astaxanthin; cantaxanthin; fucoxanthin

PMID:

26565683

[PubMed - as supplied by publisher]

[Carcinogenesis](#). 1994 Jan;15(1):15-9.

Chemoprevention of mouse urinary bladder carcinogenesis by the naturally occurring carotenoid astaxanthin.

[Tanaka T](#), [Morishita Y](#), [Suzui M](#), [Kojima T](#), [Okumura A](#), [Mori H](#).

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The chemopreventive effects of two xanthophylls, astaxanthin (AX) and canthaxanthin (CX), on urinary bladder carcinogenesis induced by N-butyl-N(4-hydroxybutyl)nitrosamine (OH-BBN) was investigated in male ICR mice. Mice were given 250 p.p.m. OH-BBN in drinking water for 20 weeks and after a 1 week interval with tap water, water containing AX or CX at a concentration of 50 p.p.m. was administered during subsequent 20 weeks. Other groups of mice were treated with AX or CX alone or untreated. At the end of the study (week 41), the incidences of preneoplastic lesions and neoplasms in the bladder of mice treated with OH-BBN and AX or CX were smaller than those of mice given OH-BBN. In particular, AX administration after OH-BBN exposure significantly reduced the incidence of bladder cancer (transitional cell carcinoma) ($P < 0.003$). However, the inhibition of the frequencies of such lesions in mice treated with OH-BBN and CX was not significant. Treatment with AX or CX also decreased the number/nucleus of silver-stained nucleolar organizer region proteins (AgNORs), a new index of cell proliferation, in the transitional epithelium exposed to OH-BBN. Preneoplasms and neoplasms induced by OH-BBN, and the antiproliferative potential, was greater for AX than CX. These results indicate that AX is a possible chemopreventive agent for bladder carcinogenesis and such an effect of AX may be partly due to suppression of cell proliferation.

Publication Types:

PMID: 8293542 [PubMed - indexed for MEDLINE]

[Autoimmunity](#). 1993;16(2):95-102.

Preventive action of carotenoids on the development of lymphadenopathy and proteinuria in MRL-lpr/lpr mice.

[Tomita Y](#), [Jyonouchi H](#), [Engelman RW](#), [Day NK](#), [Good RA](#).

Department of Public Health, School of Medicine, Kurume University, Japan.

The chemopreventive action of carotenoids on proteinuria and lymphadenopathy were examined in autoimmune-prone MRL-lpr/lpr (MRL/l) mice. They were fed a synthetic full-fed diet (16-18 kcal/mouse/day) with supplementation of beta-carotene or astaxanthin (0.19 mumoles/mouse, 3 times a week), and the development of lymphadenopathy and proteinuria were examined. MRL/l mice fed a full-fed diet without the supplementation of carotenoids or those fed a calorie-restricted (CR) diet (10-11 kcal/mouse/day, 60% calorie intake of full-fed mice) were employed as controls. CR dramatically delayed the development of proteinuria and lymphadenopathy, as reported previously. Carotenoids also significantly delayed the onset of these symptoms in MRL/l mice fed a full-fed diet. Carotenoids were half as effective as CR and astaxanthin, a carotenoid without provitamin A activity, which appeared to exert more significant preventive actions than beta-carotene in delaying the development of these symptoms. Similar chemopreventive actions of carotenoids were also demonstrated in MRL/l mice fed a regular diet (Lab Chow). CR has been shown to augment IL-2 production and to decrease serum prolactin levels in this strain, which may be related to its dramatic preventive action of autoimmunity. However, carotenoids did not affect IL-2 production nor prolactin levels in full-fed MRL/l mice. The chemopreventive actions of carotenoids observed in autoimmune-prone MRL/l mice may be attributed to yet unknown mechanisms, apart from their provitamin A activity or oxygen-quenching activity.

Publication Types:

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Inhibition of benzo(a)pyrene-induced mouse forestomach neoplasia by astaxanthin containing egg yolks

Anticarcinogenic activity of astaxanthin-containing egg yolks (designate AEY) was investigated for benzo(a)pyrene (BP)-induced mouse forestomach tumorigenesis initiating regimen. Female ICR mouse (6-7 weeks of age) were housed in polycarbonated cages (5 mice/cage; 20 mice/treatment) in a humidity-and-temperature-controlled facility and permitted free access to water and food. One week later, four and 2 days prior to p.o. treatment with BP (2 mg/0.2 ml corn oil), mice were given 0.2 ml PBS containing 50 mg AEY, 100 mg AEY, 150 mg AEY, or 150 mg CEY. Control mice were only given 0.2 ml PBS. Three days later this sequence was repeated for a total of 4 times. Beginning with the first intubation and continuing thereafter, body weight and food intake were recorded once weekly. All surviving mice were sacrificed 24 weeks after the first dose of BP. Mice treated with AEY developed only about one third as many neoplasms/animal as mice in control or CEY-treated group ($p < 0.05$). Reduction effect of tumor development by AEY was dependent upon doses applied. Tumor incidence was also reduced by AEY treatments, but significantly reduced only by 150 mg AEY treatment when compared to that by control or CEY. Food intake and body weight were not affected by AEY treatment. These results indicate that AEY inhibits tumorigenesis of mouse forestomach induced by BP.

[Cancer prevention by astaxanthin, a natural carotenoid](#)

[MOU X Y](#) (Kyoto Prefectural Univ. Medicine Graduate School Of Medical Sci.)

Astaxanthin is a natural carotenoid. The anticarcinogenic effect of astaxanthin was shown in mouse lung and liver models. The effect of astaxanthin on cell proliferation, cell cycle progression and apoptosis was examined in the HepG2 human liver cancer cell line. Astaxanthin significantly inhibited the proliferation of liver cancer cells in a dose-dependent manner. Flow cytometric analysis demonstrated that astaxanthin restrained the cell cycle progression at G1, and induced apoptosis. Further examinations by real-time quantitative RT-PCR revealed that astaxanthin enhanced the expression of p21CIP1/WAF1, GADD153 and c-myc genes. These results suggest that astaxanthin will be a promising agent for use in chemopreventive or therapeutics against cancer.

Lee, S et al. (1998). J Kor Soc food Sci Nutr 27(1): 163-167, 1998.
Language: Korean

Inhibition of Sarcoma-180 Cell-induced Mouse Ascites Cancer by Astaxanthin-containing Egg Yolk

Sang-Ho Lee, Cherl-Woo Park, Kyung-Ah Park, Young-Choon Lee, Eui-Sung Choi,
Yeong Lae Ha

Abstract

Anticarcinogenic activity of astaxanthin-containing egg yolk(designate AEY) was investigated for mouse ascites carcinogenesis induced by mouse Sarcoma-180(S-180) cells. Female ICR mice (8 mice/treatment, 7~8 weeks of age, 25±1g) were injected, i.p. with S-180 cells (1×10^7 cell/ml PBS). Two days later, each mouse was given 0.1ml PBS containing AEY(10, 25 or 50µg/g body weight) or control egg yolk (CEY: 50µg/g body weight) every other day for 7 times. Control mice were only given 0.1ml S-180 cells and 0.1ml PBS. Mice treated with 25µg/g body weight of AEY showed 24.8 days of life, which was equivalent to 138% of control mice's life (18.0 days). Based on dose-dependant experiment of AEY, mice treated with 10µg/g body weight showed slightly longer life (19.4 days) relative to mice treated with control mice, and mice treated with 50µg/g body weight exhibited 21.9 days of life. Mice treated with any dose of AEY exhibited longer life than mice with CEY 50µg/g body weight. Body weight of mice treated with AEY was reduced relative to that of control mice or CEY-treated mice. These results suggest that AEY inhibits the carcinogenesis of mouse ascites induced by S-180 cells.

The protective effects of astaxanthin against cisplatin-induced retinal toxicity.

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[Author information](#)

Abstract

This study investigated the toxic effects of an antineoplastic agent, Cisplatin (CIS), on retinal cells and the potential capacity of Astaxanthin(ASTA) to elicit a future therapeutic protocol in CIS-induced retinal toxicity. Six groups were formed for the assessment; control (healthy; Group 1), olive oil (olive oil only; Group 2), ASTA control group (ASTA only, Group 3), the single intraperitoneal (IP) dose of 16 mg/kg CIS (CIS only group; Group 4), 16 mg/kg CIS + 25 mg/kg (IP) ASTA (Group 5) and 16 mg/kg CIS + 75 mg/kg (IP) ASTA (Group 6). On the third day after cisplatin administration, rats in all groups were sacrificed under anesthesia and the analysis of the biochemical parameters and histopathological levels were performed. A significant decrease in GSH levels and increases in MDA, eNOS, 8-OHdG expressions were recorded. Additionally, CIS treatment had caused acidophilic staining in retinal histological appearance. ASTA treatment reduced the increases in MDA, eNOS, and 8-OHdG levels following CIS administration and increased the levels of GSH expressions, as well. These results may suggest the ASTA molecule as a promising option to prevent retinal toxicity in patients receiving CIS treatment for malignant tumors.

KEYWORDS:

Astaxanthin; chemotherapy; cisplatin toxicity; eNOS; oxidative stress; retina

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DOI: [10.1080/15569527.2018.1518330](https://doi.org/10.1080/15569527.2018.1518330)

Astaxanthin-alpha tocopherol nanoemulsion formulation by emulsification methods: Investigation on anticancer, wound healing, and antibacterial effects.

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Author information

Abstract

Emulsion-based delivery systems have been fabricated and developed to increase the bioavailability of astaxanthin and alpha-tocopherol as active compounds for various biomedical applications. Astaxanthin-alpha tocopherol nanoemulsion (ATNE) is well known for its potential 6.-6.30 effect. The current study investigated ATNE by spontaneous (SENE) and ultrasonication emulsification (USNE) methods to optimally fabricate oil/water nanoemulsion characterized for biomedical applications. The two methods were compared by using a response surface method of 3-level Box-Behnken design (BBD) with significant factors. Transmission electron microscopy (TEM) confirmed spherical-shaped nanoemulsion from SENE and USNE methods and dynamic light scattering (DLS) proved the good stability of the fabricated nanoemulsion. Cytotoxicity studies on three different cancer cells confirmed that the nanoemulsion at higher concentrations was more toxic than one at lower concentrations by accompanying a significant decrease in the cellular viability after 24 and 48 h of exposure. The wound-healing potential using scratch assay evidenced faster healing effect of the nanoemulsion. Both minimal inhibitory concentration (MIC) and minimum bactericidal concentrations (MBC) methods confirmed significant antibacterial activity to disrupt the integrity of the bacterial cell membrane. The current results suggested that ATNE act as effectively targeted drug delivery vehicles in the future for cancer treatment applications due to its significant results of anticancer, wound healing, and antimicrobial effects.

KEYWORDS:

Antimicrobial; Astaxanthin; Nanoemulsion; Spontaneous emulsification; Toxicity; Ultrasonication; Wound healing

PMID: 30172200 DOI: [10.1016/j.colsurfb.2018.08.042](#)

Astaxanthin inhibits gemcitabine-resistant human pancreatic cancer progression through EMT inhibition and gemcitabine resensitization.

[Yan T](#)¹, [Li HY](#)¹, [Wu JS](#)¹, [Niu Q](#)¹, [Duan WH](#)¹, [Han QZ](#)², [Ji WM](#)¹, [Zhang T](#)¹, [Lv W](#)¹.

Author information

Abstract

Pancreatic cancer rapidly acquires resistance to chemotherapy resulting in its being difficult to treat. Gemcitabine is the current clinical chemotherapy strategy; however, owing to gemcitabine resistance, it is only able to prolong the life of patients with pancreatic cancer for a limited number of months. Understanding the underlying molecular mechanisms of gemcitabine resistance and selecting a suitable combination of agents for the treatment of pancreatic cancer is required. Astaxanthin (ASX) is able to resensitize gemcitabine-resistant human pancreatic cancer cells (GR-HPCCs) to gemcitabine. ASX was identified to upregulate human equilibrative nucleoside transporter 1 (hENT1) and downregulate ribonucleoside diphosphate reductase (RRM) 1 and 2 to enhance gemcitabine-induced cell death in GR-HPCCs treated with gemcitabine, and also downregulates TWIST1 and ZEB1 to inhibit the gemcitabine-induced epithelial-mesenchymal transition (EMT) phenotype in GR-HPCCs and to mediate hENT1, RRM1 and RRM2. Furthermore, ASX acts through the hypoxia-inducible factor 1 α /signal transducer and activator of transcription 3 signaling pathway to mediate TWIST1, ZEB1, hENT1, RRM1 and RRM2, regulating the gemcitabine-induced EMT phenotype and gemcitabine-induced cell death. Co-treatment with ASX and gemcitabine in a tumor xenograft model induced by GR-HPCCs supported the *in vitro* results. The results of the present study provide a novel therapeutic strategy for the treatment of gemcitabine-resistant pancreatic cancer.

KEYWORDS:

astaxanthin; epithelial-mesenchymal transition; gemcitabine; gemcitabine-resistance human pancreatic cancer cells

PMID: 29098031

PMCID: [PMC5652142](#)

DOI: [10.3892/ol.2017.6836](#)

[Free PMC Article](#)

[Dis Esophagus](#). 2017 Jun 1;30(6):1-7. doi: 10.1093/dote/dox027.

Astaxanthin increases radiosensitivity in esophageal squamous cell carcinoma through inducing apoptosis and G2/M arrest.

[Qian X](#), [Tan C](#), [Yang B](#), [Wang F](#), [Ge Y](#), [Guan Z](#), [Cai J](#).

Abstract

Nowadays esophageal squamous cell carcinoma (ESCC) is primarily treated by a comprehensive approach combining surgical resection and neoadjuvant chemo- or radiotherapy. However, ESCC is resistant to radiation therapy, resulting in its invasion, infiltration, and metastasis. It usually has rapidly progressed and has a poor outcome clinically. The purpose of this study is to determine the potential radiosensitizing effect of astaxanthin (ATX) and explore the underlying mechanisms in ESCC cells in vitro. ESCC cell lines were exposure to irradiation, in the presence or absence of ATX treatment. Cell viability and radiosensitization were tested by CCK8 assay and clonogenic survival assay, respectively. Cell apoptosis and the changes of cell cycle distribution were observed by flow cytometry. The protein expression of Bcl2, Bax, CyclinB1, and Cdc2 was examined by western blot analysis. It was shown that ATX improved radiosensitivity of ESCC cells and induced apoptosis and G2/M arrest via inhibiting Bcl2, CyclinB1, Cdc2, and promoting Bax expression. In conclusion, ATX might function as a promising radiosensitizer in ESCC cells by leading to apoptosis and G2/M arrest.

KEYWORDS:

apoptosis; astaxanthin; cell cycle; esophageal squamous cell carcinoma; radiosensitization

PMID: 28475750

DOI: [10.1093/dote/dox027](#)

[Indexed for MEDLINE]

Astaxanthin down-regulates Rad51 expression via inactivation of AKT kinase to enhance mitomycin C-induced cytotoxicity in human non-small cell lung cancer cells.

[Ko JC](#)¹, [Chen JC](#)², [Wang TJ](#)³, [Zheng HY](#)³, [Chen WC](#)³, [Chang PY](#)³, [Lin YW](#)⁴.

Author information

Abstract

Astaxanthin has been demonstrated to exhibit a wide range of beneficial effects, including anti-inflammatory and anti-cancer properties. However, the molecular mechanism of astaxanthin-induced cytotoxicity in non-small cell lung cancer (NSCLC) cells has not been identified. Rad51 plays a central role in homologous recombination, and studies show that chemo-resistant carcinomas exhibit high levels of Rad51 expression. In this study, astaxanthin treatment inhibited cell viability and proliferation of two NSCLC cells, A549 and H1703. Astaxanthin treatment (2.5-20 μ M) decreased Rad51 expression and phospho-AKT(Ser473) protein level in a time and dose-dependent manner. Furthermore, expression of constitutively active AKT (AKT-CA) vector rescued the decreased Rad51 mRNA and protein levels in astaxanthin-treated NSCLC cells. Combined treatment with phosphatidylinositol 3-kinase (PI3K) inhibitors (LY294002 or wortmannin) further decreased the Rad51 expression in astaxanthin-exposed A549 and H1703 cells. Knockdown of Rad51 expression by transfection with si-Rad51 RNA or cotreatment with LY294002 further enhanced the cytotoxicity and cell growth inhibition of astaxanthin. Additionally, mitomycin C (MMC) as an anti-tumor antibiotic is widely used in clinical NSCLC chemotherapy. Combination of MMC and astaxanthin synergistically resulted in cytotoxicity and cell growth inhibition in NSCLC cells, accompanied with reduced phospho-AKT(Ser473) level and Rad51 expression. Overexpression of AKT-CA or Flag-tagged Rad51 reversed the astaxanthin and MMC-induced synergistic cytotoxicity. In contrast, pretreatment with LY294002 further decreased the cell viability in astaxanthin and MMC co-treated cells. In conclusion, astaxanthin enhances MMC-induced cytotoxicity by decreasing Rad51 expression and AKT activation. These findings may provide rationale to combine astaxanthin with MMC for the treatment of NSCLC.

PMID: 26921637 DOI: [10.1016/j.bcp.2016.02.016](#) [Indexed for MEDLINE]

Biocompatible astaxanthin as a novel marine-oriented agent for dual chemo-photothermal therapy.

[Nguyen VP](#)¹, [Kim SW](#)², [Kim H](#)¹, [Kim H](#)¹, [Seok KH](#)³, [Jung MJ](#)⁴, [Ahn YC](#)^{1,5}, [Kang HW](#)^{1,5}.

Author information

Abstract

The photothermal effect of a marine-oriented xanthophyll carotenoid, astaxanthin (AXT), was characterized based on its potential absorption of visible laser light and conversion of optical light energy into heat for thermal treatment. As an antioxidant and anticancer agent, AXT extracted from marine material can be utilized for photothermal therapy due to its strong light absorption. The current study investigated the feasibility of the marine-based material AXT to increase the therapeutic efficacy of chemo-photothermal therapy (PTT) by assessing photothermal sessions in both cells and tumor tissues. A quasi-cw Q-switched 80 W 532 nm laser system was utilized to induce thermal necrosis in in vitro and in vivo models. An in vitro cytotoxicity study of AXT was implemented using squamous cell carcinoma (VX2) and macrophage (246.7) cell lines. In vivo PTT experiments were performed on 17 rabbits bearing VX2 tumors on their eyes that were treated with or without intratumoral injection of AXT at a dose of 100 μ l (300 μ g/ml) followed by laser irradiation at a low irradiance of 0.11 W/cm². Fluorescence microscopy images revealed cellular death via apoptosis and necrosis owing to the dual chemo-photothermal effects induced by AXT. In vivo experimental results demonstrated that the AXT-assisted irradiation entailed a temperature increase by 30.4°C after tumor treatment for 4 min. The relative variations in tumor volume confirmed that the tumors treated with both AXT and laser irradiation completely disappeared 14 days after treatment, but the tumors treated under other conditions gradually grew. Due to selective light absorption, AXT-assisted laser treatment could be an effective thermal therapy for various drug-resistant cancers.

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PMCID: [PMC5378353](#)

DOI: [10.1371/journal.pone.0174687](#)

[Indexed for MEDLINE]

[Free PMC Article](#)

Astaxanthin Inhibits PC-3 Xenograft Prostate Tumor Growth in Nude Mice.

[Ni X](#)¹, [Yu H](#)², [Wang S](#)³, [Zhang C](#)⁴, [Shen S](#)⁵.

Author information

Abstract

Prostate cancer (PCa), the most common malignancy in men, is a major cause of cancer deaths. A better understanding of the mechanisms that drive tumor initiation and progression may identify actionable targets to improve treatment of this patient group. As a dietary carotenoid, astaxanthin has been demonstrated to exert beneficial effects against inflammation, cardiovascular disease, oxidative damage, or different cancer sites. This study used intragastric administration of astaxanthin to detect its role on tumor proliferation, apoptosis, microRNA (miRNA) overexpression, and microbacteria composition change by establishing androgen-independent PCa cell PC-3 xenograft nude mice. Nude mice were inoculated with androgen-independent prostate cancer PC-3 cells subcutaneously. The intervention was started when tumors reached 0.5-0.6 cm in diameter. Mice were intragastrically administered 100 mg/kg astaxanthin (HA), 25 mg/kg astaxanthin (LA), or olive oil (TC). The results showed that 100 mg/kg astaxanthin significantly inhibited tumor growth compared to the TC group, with an inhibitory rate of 41.7%. A decrease of Ki67 and proliferating cell nuclear antigen (PCNA) as well as an increase of cleaved caspase-3 were observed in HA-treated tumors, along with increasing apoptotic cells, obtained by TUNEL assay. The HA significantly elevated the levels of tumor suppressors miR-375 and miR-487b in tumor tissues and the amount of *Lactobacillus* sp. and *Lachnospiraceae* in mice stools, while there was no significant difference between LA and TC groups. These results provide a promising regimen to enhance the therapeutic effect in a dietary supplement manner.

KEYWORDS:

PCR-DGGE; astaxanthin; immunohistochemistry; miRNA; prostate cancer

PMID: 28282880

PMCID: [PMC5367023](#)

DOI: [10.3390/md15030066](#)

[Indexed for MEDLINE]

[Free PMC Article](#)

Astaxanthin modifies clastogenic effects of ionizing radiation in vitro in peripheral blood lymphocytes of the persons recovered from acute radiation sickness.

[Kurinyi DA](#)¹, [Rushkovsky SR](#)², [Dybska OB](#)¹, [Dubrovina GV](#)¹, [Pilinska MA](#)¹.

Author information

Abstract

AIM:

To assess radioprotective activity of astaxanthin toward radiation-induced in vitro cytogenetic effects in human peripheral blood lymphocytes (PBL).

MATERIALS AND METHODS:

PBL from the cleanup workers exposed to ionizing radiation at high doses in 1986 during accident on Chornobyl nuclear power plant and who were diagnosed with acute radiation sickness of the first and second degrees, were cultured in vitro. Astaxanthin was added into the culture medium at a final concentration of 20.0 µg/ml, prior to γ-irradiation of PBL in vitro at a dose of 1 Gy. The slides of metaphase chromosomes were analyzed.

RESULTS:

Astaxanthin demonstrated considerable radioprotective effect in irradiated PBL manifested in significantly decreased levels of unstable cytogenetic markers of radiation exposure (dicentric and centric rings).

CONCLUSION:

The data evidence on radioprotective capacity of astaxanthin toward radiation-induced cytogenetic effects in vitro in PBL of liquidators irradiated during Chornobyl nuclear power plant accident. This article is a part of a Special Issue entitled "The Chornobyl Nuclear Accident: Thirty Years After".

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[Indexed for MEDLINE]

Genoprotective properties of astaxanthin revealed by ionizing radiation exposure in vitro on human peripheral blood lymphocytes.

[Article in English, Ukrainian; Abstract available in Ukrainian from the publisher]

[Pilinska MA](#)¹, [Kurinnyi DA](#)¹, [Rushkovsky SR](#)², [Dybska OB](#)¹.

[Author information](#)

Abstract

in [English](#), [Ukrainian](#)

OBJECTIVE: to identify possible radioprotective properties of astaxanthin by means of cytogenetic criteria.

METHODS: Cultivation of peripheral blood lymphocytes from five apparently healthy volunteers; treatment of lymphocytes' cultures by astaxanthin in final concentrations 20 µg/ml in G₀ phase of mitotic cycle, prior to irradiation in vitro in a dose 1 Gy; cytogenetic analysis the uniformly stained slides of metaphase chromosomes. The electrophoresis of individual cells (Comet assay); visualization of results under fluorescent microscope; accounting the number of nucleoid the fourth grade that correspond to apoptosis of the cells.

RESULTS: Established that astaxanthin in final concentration 20.0 µg/ml exposed to the culture of human peripheral blood lymphocytes in the early G₀ phase of mitotic cycle leads to significant reduction of cytogenetic effects induced by gamma irradiation in vitro in dose 1.0 Gy (from 26.05 ± 1.81 to 9.08 ± 0.78 per 100 cells, respectively) and to significant increase the frequency of apoptotic cells at the 48 hour of cultivation (from (3.78 ± 0.24) to (8.26 ± 0.91) %, respectively).

CONCLUSIONS: The results obtained show the ability of astaxanthin to considerable weakening of radioinduced mutagenic effect in human peripheral blood lymphocytes, which testify its powerful radioprotective potential.

M. A. Pilinska, D. A. Kurinnyi, S. R. Rushkovsky, O. B. Dybska.

KEYWORDS: apoptosis; astaxanthin; chromosome aberrations; culture of human peripheral blood lymphocytes; radioprotective effect

PMID: 28027548

[Indexed for MEDLINE]

Cancer prevention by carotenoids

Nishino, et al,

A review with 13 refs. Various natural carotenoids have been proven to have anticarcinogenic activity. Epidemiol. investigations have shown that cancer risk is inversely related to the consumption of green and yellow vegetables and fruits. As b-carotene is present in abundance in these vegetables and fruits, it has been investigated extensively as a possible cancer preventive agent. However, various carotenoids which coexist with b-carotene in vegetables and fruits also have anticarcinogenic activity, and some of these, such as a-carotene, lutein and lycopene, show a higher potency than b-carotene in suppressing exptl. carcinogenesis. Thus, we have carried out more extensive studies on cancer preventive activities of natural carotenoids in foods. For example, we found that b-cryptoxanthin showed antitumor initiating activity, as well as antitumor promoting activity. It is of interest that not only carotenoids distributed in vegetables and fruits, but also animal carotenoids, such as astaxanthin, are promising as cancer preventive agents. In the present study, the cancer preventive potential of phytoene was also confirmed. The establishment of NIH3T3 cells that produce phytoene by introducing the crtB gene provides evidence that resistance against transformation, imposed by transfection of activated H-ras oncogene, was acquired by phytoene prodn. Anal. of the action mechanism of these natural carotenoids is now in progress, and some interesting results have already been obtained; for example, various carotenoids were suggested to stimulate the expression of RB gene, an antioncogene.

Phytopharmaceuticals in Cancer Chemoprevention CRC press D Bagchi and H. Preuss Ed. 2005.

Astaxanthin and Cancer Chemoprevention

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Introduction

There are clear links between human cancers and diet.^{1,2} By some estimates, dietary risk factors rank higher than tobacco usage and much higher than pollution or occupational hazards in their association with cancer deaths.³ In addition to avoidance of tobacco smoke and carcinogenic food items, regular intake of chemopreventive compounds is a promising approach for reducing cancer incidence.^{3,4} A number of substances naturally occurring in foodstuffs, particularly antioxidant compounds in plant products, have shown promise as potential chemopreventive agents.³⁻⁶ Among these phytonutrients, the yellow, orange and red carotenoid pigments have recently sparked much interest. In epidemiological studies, vegetable and fruit consumption has consistently been associated with reduced incidence of various cancers,⁵⁻⁷ and dietary carotenoid intake from these sources has similarly been correlated with reduced cancer risk.⁸⁻¹⁰ However, several recent large-scale intervention trials failed to find any chemopreventive effect of long-term supplementation with β -carotene, the most abundant dietary carotenoid.¹¹⁻¹³ Several naturally occurring carotenoids other than β -carotene have exhibited anticancer activity,¹⁴⁻¹⁷ and are being considered further as potential chemopreventive agents. Among these carotenoids, the red pigment astaxanthin is of particular interest in health management due to its unique structural and chemical properties.¹⁸⁻²⁰ This chapter will review the evidence for anticarcinogenic behavior of selected carotenoids, with an emphasis on the chemopreventive activities of astaxanthin.

A preliminary investigation of the enzymatic inhibition of 5alpha-reduction and growth of prostatic carcinoma cell line LNCap-FGC by natural astaxanthin and Saw Palmetto lipid extract in vitro.

Anderson ML.

Inhibition of 5alpha-reductase has been reported to decrease the symptoms of benign prostate hyperplasia (BPH) and possibly inhibit or help treat prostate cancer. Saw Palmetto berry lipid extract (SPLE) is reported to inhibit 5alpha-reductase and decrease the clinical symptoms of BPH. Epidemiologic studies report that carotenoids such as lycopene may inhibit prostate cancer. In this investigation the effect of the carotenoid astaxanthin, and SPLE were examined for their effect on 5alpha-reductase inhibition as well as the growth of prostatic carcinoma cells in vitro. The results show astaxanthin demonstrated 98% inhibition of 5alpha-reductase at 300 microg/mL in vitro. Alphastat, the combination of astaxanthin and SPLE, showed a 20% greater inhibition of 5alpha-reductase than SPLE alone in vitro. CONCLUSIONS: Low levels of carotenoid astaxanthin inhibit 5alpha-reductase and decrease the growth of human prostatic cancer cells in vitro. Astaxanthin added to SPLE shows greater inhibition of 5alpha-reductase than SPLE alone in vitro.

[Invest New Drugs](#). 2009 Oct 30. [Epub ahead of print]

Astaxanthin inhibits tumor invasion by decreasing extracellular matrix production and induces apoptosis in experimental rat colon carcinogenesis by modulating the expressions of ERK-2, NFkB and COX-2.

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Abstract

Colon cancer is the third most malignant neoplasm in the world and it remains an important cause of mortality in Asian and Western countries. Astaxanthin (AST), a major component of carotenoids possesses attractive remedial features. The purpose of this study is to investigate the possible mechanism of action of astaxanthin against 1, 2 dimethyl hydrazine (DMH)-induced rat colon carcinogenesis. Wistar male rats were randomized into five groups, group 1 were control rats, group 2 were rats that received AST (15 mg/kg body wt p.o. everyday), rats in group 3 were induced with DMH (40 mg/kg body wt, s.c.), DMH-induced rats in groups 4 and 5 were either pre or post initiated with AST, respectively as in group 2. DMH-induced rats exhibited elevated expressions of Nuclear factor kappa B-p65 (NF-kappaB-p65), Cyclooxygenase-2 (COX-2), Matrixmetallo proteinases (MMP) 2/9, Proliferating cell nuclear antigen (PCNA), and Extracellular signal-regulated kinase-2 (ERK-2) as confirmed by immunofluorescence. Further, Westernblot analysis of MMPs-2/9, ERK-2 and Protein kinase B (Akt) revealed increased expressions of these proteins in DMH-induced groups of rats. AST-treatment decreased the expressions of all these vital proteins, involved in colon carcinogenesis. The ability of AST to induce apoptosis in the colon of DMH-induced rats was confirmed by Annexin-V/PI staining in a confocal microscopy, DNA fragmentation analysis and expression of caspase-3 by Western blotting. In conclusion, astaxanthin exhibits anti-inflammatory and anti-cancer effects by inducing apoptosis in DMH-induced rat colon carcinogenesis by modulating the expressions of NFkB, COX-2, MMPs-2/9, Akt and ERK-2.

PMID: 19876598 [PubMed - as supplied by publisher]

[Chem Biol Interact.](#) 2009 Aug 14;180(3):398-406. Epub 2009 Apr 2.

Intervention of astaxanthin against cyclophosphamide-induced oxidative stress and DNA damage: a study in mice.

[Tripathi DN](#), [Jena GB](#).

Department of Pharmacology and Toxicology, National Institute of Pharmaceutical Education and Research, Sector-67, S.A.S. Nagar, Punjab 160062, India.

Abstract

Astaxanthin, a natural and nutritional red carotenoid pigment, is used as a dietary supplement. The intention of the present study was to investigate the beneficial effects of dietary pigment astaxanthin, against cyclophosphamide-induced oxidative stress and DNA damage. The end points of evaluation of the study included: (a) malondialdehyde, glutathione and superoxide dismutase concentration in liver to detect oxidative stress; (b) normal and modified alkaline comet assays (the latter includes lesion-specific enzymes formamidopyrimidine-DNA glycosylase and endonuclease-III) to detect normal and oxidative stress-induced DNA damage by cyclophosphamide in the mouse bone marrow and the peripheral blood lymphocytes. In addition, micronucleus assay and chromosomal aberration test capable of detecting the DNA damage were also carried out in peripheral blood and bone marrow of mice. Cyclophosphamide (100 mg/kg intra-peritoneal) treatment led to significant increase in liver malondialdehyde and decreased the antioxidant enzymes glutathione and superoxide dismutase. Further, cyclophosphamide also significantly increased the DNA damage as observed from normal and modified comet assays as well as micronucleus and chromosomal aberration assay. Pre-treatment with astaxanthin (12.5, 25 and 50 mg/kg/day for 5 days per oral) resulted in the restoration of oxidative stress markers such as malondialdehyde, glutathione and superoxide dismutase in liver. The amelioration of oxidative stress with astaxanthin pre-treatment correlated well with the decreased DNA damage as evident from normal and modified alkaline comet assays of bone marrow cells and peripheral blood lymphocytes. Further astaxanthin pre-treatment also reduced the frequency of chromosomal breakage and micronucleus formation in the mouse bone marrow cells and peripheral blood reticulocytes. It is thus concluded that pre-treatment with astaxanthin attenuates cyclophosphamide-induced oxidative stress and subsequent DNA damage in mice and it can be used as a chemoprotective agent against the toxicity of anticancer drug cyclophosphamide.

PMID: 19539803 [PubMed - indexed for MEDLINE]

[Cancer Lett.](#) 2009 Sep 28;283(1):108-17. Epub 2009 May 6.

Growth-inhibitory effects of the astaxanthin-rich alga *Haematococcus pluvialis* in human colon cancer cells.

[Palozza P](#), [Torelli C](#), [Boninsegna A](#), [Simone R](#), [Catalano A](#), [Mele MC](#), [Picci N](#).

Institute of General Pathology, Catholic University School of Medicine, L. Go F. Vito, 1 00168 Rome, Italy. p.palozza@rm.unicatt.it

Abstract

The growth-inhibitory effects of the astaxanthin-rich *Haematococcus pluvialis* were studied in HCT-116 colon cancer cells. *H. pluvialis* extract (5-25 microg/ml) inhibited cell growth in a dose- and time-dependent manner, by arresting cell cycle progression and by promoting apoptosis. At 25 microg/ml of *H. pluvialis* extract, an increase of p53, p21(WAF-1/CIP-1) and p27 expression (220%, 160%, 250%, respectively) was observed, concomitantly with a decrease of cyclin D1 expression (58%) and AKT phosphorylation (21%). Moreover, the extract, at the same concentration, strongly up-regulated apoptosis by modifying the ratio of Bax/Bcl-2 and Bcl-XL, and increased the phosphorylation of p38, JNK, and ERK1/2 by 160%, 242%, 280%, respectively. Growth-inhibitory effects by *H. pluvialis* were also observed in HT-29, LS-174, WiDr, SW-480 cells. This study suggests that *H. pluvialis* may protect from colon cancer.

PMID: 19423215 [PubMed - indexed for MEDLINE]

[Fundam Clin Pharmacol](#). 2009 Apr;23(2):225-34.

Antioxidative and antiproliferative effects of astaxanthin during the initiation stages of 1,2-dimethyl hydrazine-induced experimental colon carcinogenesis.

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Department of Biochemistry, University of Madras, Guindy campus, Chennai - 600 025, Tamil Nadu, India.

Abstract

Colon cancer is one of the major causes of cancer mortality worldwide. Several carotenoids with antioxidant properties are reported for their chemopreventive nature. In this study, we have evaluated the chemopreventive efficacy of astaxanthin on lipid peroxidation, antioxidant status, total number of aberrant crypt foci (ACF), and cell proliferation in 1,2 dimethylhydrazine (DMH)-induced colon carcinogenesis using a rat model. DMH was induced subcutaneously at a dosage of 40 mg/kg body weight, twice a week for 2 weeks. Astaxanthin was administered before and after the DMH induction, orally at a concentration of 15 mg/kg body weight throughout the experimental period. At the end of 16 weeks, pre-treatment with astaxanthin markedly reduced the degree of histological lesions, ACF development and also lowered the number of argyrophilic nucleolar organizer regions. Our results also showed the decreased levels of colon enzymic and non-enzymic antioxidants and increased levels of lipid peroxidation marker levels in DMH-induced rats, which were significantly reversed on astaxanthin administration. In conclusion, the results of this study suggest that astaxanthin has an affirmative and beneficial effect against chemically induced colonic pre-neoplastic progression in rats induced by DMH.

PMID: 19645817 [PubMed - indexed for MEDLINE]

[Anticancer Res.](#) 2010 Jun;30(6):2171-5.

Effect of dietary astaxanthin at different stages of mammary tumor initiation in BALB/c mice.

[Nakao R](#), [Nelson OL](#), [Park JS](#), [Mathison BD](#), [Thompson PA](#), [Chew BP](#).

School of Food Science, Washington State University, Pullman, WA 99164, USA.

Abstract

The effects of astaxanthin on tumor growth, cardiac function and immune response in mice were studied. Female BALB/c mice were fed a control diet (diet C) for 8 weeks, 0.005% astaxanthin for 8 weeks (diet A), or diet C for weeks 1-5 followed by diet A thereafter (diet CA). Mice were injected with a mammary tumor cell line on day 7 and tumor growth was measured daily. Mice fed diet A had extended tumor latency and lower tumor volume ($p < 0.05$). Interestingly, those fed diet CA showed the fastest tumor growth. Astaxanthin feeding elevated plasma astaxanthin concentrations; there was no difference in plasma astaxanthin between mice fed CA and those fed A. Mice fed diet A, but not CA, had a higher ($p < 0.05$) natural killer cell subpopulation and plasma interferon-gamma concentration compared to those fed diet C. Astaxanthin delayed tumor growth and modulated immune response, but only when astaxanthin was given before tumor initiation. This suggests that an adequate blood astaxanthin status is needed to protect against tumor initiation; conversely, astaxanthin supplementation after tumor initiation may be contraindicated.

PMID: 20651366 [PubMed - indexed for MEDLINE]

ASTAXANTHIN SHOWS POTENTIAL TO ACTIVATE CANCER CELL DEATH IN-VITRO.

Artif Cells Nanomed Biotechnol. 2019 Dec;47(1):891-895.
doi: 10.1080/21691401.2019.1580286.

Astaxanthin induces apoptosis and increases activity of antioxidant enzymes in LS-180 cells

[Maryam Hormozi](#)¹, [Shadi Ghoreishi](#)², [Parasto Baharvand](#)³

- PMID: **30873887**
- DOI: [10.1080/21691401.2019.1580286](https://doi.org/10.1080/21691401.2019.1580286)

Abstract

Astaxanthin, a Xanthophyll carotenoid, has strong antioxidant properties. Some studies have shown the effectiveness of this compound on the prevention and treatment of cancer. Therefore, the aim of this study was to evaluate the effects of astaxanthin on induction of apoptosis and antioxidant activity in the LS-180 cell line. In this experimental study, after the treatment of LS-180 50, 100 and 150 μm of Astaxanthin for 24 h, the expression levels of Bax, Bcl2 and Caspase3 genes were investigated by Real-time PCR. Also, the level of malondialdehyde, as an indicator of oxidative stress and activity of anti-superoxide dismutase enzymes, catalase and glutathione peroxidase was investigated by colorimetric methods. The results showed that astaxanthin increases the expression of Bax and Caspase3 genes and decreases that of Bcl2, thereby, inducing apoptosis and inhibiting growth and proliferation of the cells. Additionally, reduction in the levels of malondialdehyde was evident with a significant elevation in antioxidant activity mediated by the action of superoxide dismutase, catalase and glutathione peroxidase. These results suggest that astaxanthin has the potency to induce apoptosis in LS-180 cells by increasing the expression of apoptotic genes and activity of antioxidant enzymes. Thus, astaxanthin has potential in the prevention and treatment of cancer.

ASTAXANTHIN COMBINED WITH HUMAN SERUM ALBUMIN SHOW POTENTIAL TO TREAT OVARIAN CANCER IN CELL STUDY.

Anticancer Agents Med Chem. 2019;19(6):792-801.

doi: 10.2174/1871520619666190225123003.

Astaxanthin Combine with Human Serum Albumin to Abrogate Cell Proliferation, Migration, and Drug-resistant in Human Ovarian Carcinoma SKOV3 Cells

[Xiu-Zhen Su](#)¹, [Ran Chen](#)¹, [Cai-Bing Wang](#)¹, [Xi-Lin Ouyang](#)¹, [Yan Jiang](#)¹, [Ming-Yi Zhu](#)¹

PMID: 30799797 DOI: [10.2174/1871520619666190225123003](https://doi.org/10.2174/1871520619666190225123003)

Abstract

Background: Astaxanthin (AST) shows a large range of beneficial effects together with anti-cancer and antioxidation properties. Human Serum Albumin (HSA) is the most abundant protein in blood plasma which plays the role of a depot and transport protein for many exogenous compounds. However, whether HSA could enhance AST-induced cytotoxic effects in human ovarian cancer cells has not been examined to date.

Objective: This study aims to explore the anticancer effect and the molecular mechanism of AST combine with HSA induced cytotoxicity in ovarian cancer SKOV3 cells.

Methods: The ovarian cancer SKOV3 cells were treated by AST combined with HSA to study the effects of cell proliferation, cell morphology, cell cycle arrest, related protein expression, nuclear transfer, cell migration, and drug-resistant.

Results: Our data confirmed that AST+HSA treatment enhanced the anticancer effects of AST, arrested G1 phase cell cycle and induced apoptosis in SKOV3 cells. AST+HSA induced apoptosis via mitochondrial apoptotic pathways was related to the increased ratio of Bcl-2/Bax and activation of caspase-3. Besides, exposure of cells to AST+HSA triggered the inactivation of NF- κ B and activation p53 and MAPKs signaling pathways. Furthermore, AST+HSA significantly overcome the drug-resistant and inhibited the migration of SKOV3 cells.

Conclusion: AST combined treatment with HSA considerably inhibited NF- κ B expression and translocation to nucleus, thereby improving the AST-induced cytotoxic effect on SKOV3 cells. These findings may provide rationale to combine AST with HSA for the treatment of ovarian cancer.

ASTAXANTHIN SHOWS PROMISE AS A COLON CANCER TREATMENT IN CELL STUDY.

Sci Rep. 2019 Jul 1;9(1):9457.
doi: 10.1038/s41598-019-45924-3.

Astaxanthin suppresses the metastasis of colon cancer by inhibiting the MYC-mediated downregulation of microRNA-29a-3p and microRNA-200a

[Hye-Youn Kim](#)¹, [Young-Mi Kim](#)², [Suntaek Hong](#)^{3,4}

- PMID: [31263239](#) PMCID: [PMC6603017](#) DOI: [10.1038/s41598-019-45924-3](#) **Free PMC article**

Abstract

Colorectal cancer (CRC) is the third most common cancer, and is associated with a high percentage of cancer-related death globally. Furthermore, the success rate of therapeutic treatment for CRC patients mainly depends on the status of metastasis. Therefore, novel drugs or therapeutic techniques should be discovered for the treatment of metastatic CRC. In this study, we selected Astaxanthin (AXT), one of the most common carotenoids, as a novel metastasis inhibitor through high-throughput drug screening based on invadopodia staining, and confirmed the anti-migratory and anti-invasive activity of AXT. We demonstrated that AXT increases miR-29a-3p and miR-200a expression, and thereby suppresses the expression of MMP2 and ZEB1, respectively. As a result, AXT represses the epithelial-mesenchymal transition (EMT) of CRC cells. Through the mechanistic study, we identified that AXT shows anti-metastatic activity through the transcriptional repression of MYC transcription factor. Finally, we also confirmed that AXT suppresses the *in vivo* metastatic capacity of colon cancer cell using mouse model. Collectively, we uncovered the novel function of AXT in the inhibition of EMT and invadopodia formation, implicating the novel therapeutic potential for AXT in metastatic CRC patients.

ASTAXANTHIN INHIBITS THE PROLIFERATION OF PROSTATE CANCER CELLS IN-VITRO.

Mar Drugs. 2020 Aug 7;18(8):415.
doi: 10.3390/md18080415.

Anti-Tumor Effects of Astaxanthin by Inhibition of the Expression of STAT3 in Prostate Cancer

[Shao-Qian Sun](#)¹, [You-Xi Zhao](#)¹, [Si-Yu Li](#)¹, [Jing-Wen Qiang](#)¹, [Yi-Zhi Ji](#)¹

- PMID: [32784629](#)
- PMCID: [PMC7459748](#)
- DOI: [10.3390/md18080415](#)

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Abstract

Astaxanthin is a natural product gaining increasing attention due to its safety and anti-cancer properties. In this study, we investigated the mechanisms of the anti-cancer effects of astaxanthin on prostate cancer (PCa) cell lines using aggressive PCa DU145 cells. Also an instantaneous silenced cell line (si-STAT3) derived from DU145 and a control cell line (si-NK) were used for the MTT and colony formation assays to determine the role of astaxanthin in proliferation and colony formation abilities. Flow cytometry assays were used to detect the apoptosis of tumor cells. Migration and invasion assays detected the weakening of the respective abilities. Western blot and RT-PCR tests detected the levels of STAT3 protein and mRNA. Astaxanthin resulted in suppression of the proliferation of DU145 cells and the level of STAT3. The treatment of DU145 cells with astaxanthin decreased the cloning ability, increased the apoptosis percentage and weakened the abilities of migration and invasion of the cells. Furthermore, astaxanthin reduced the expression of STAT3 at protein and mRNA levels. The effects were enhanced when astaxanthin and si-STAT3 were combined. The results of animal experiments were consistent with the results in cells. Thus, astaxanthin inhibits the proliferation of DU145 cells by reducing the expression of STAT3.

ASTAXANTHIN REPRESSES CANCER STEM CELLS AND MAY BE USEFUL IN SUPPORTING OTHER THERAPIES AGAINST BREAST CANCER.

Mar Drugs. 2020 Nov 20;18(11):577.
doi: 10.3390/md18110577.

Astaxanthin Reduces Stemness Markers in BT20 and T47D Breast Cancer Stem Cells by Inhibiting Expression of Pontin and Mutant p53

[Yong Tae Ahn](#)¹, [Min Sung Kim](#)², [Youn Sook Kim](#)³, [Won Gun An](#)²

- PMID: [33233699](#)
- PMCID: [PMC7699712](#)
- DOI: [10.3390/md18110577](#)

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Abstract

Astaxanthin (AST) is a product made from marine organisms that has been used as an anti-cancer supplement. It reduces pontin expression and induces apoptosis in SKBR3, a breast cancer cell line. Using Western blotting and qRT-PCR analyses, this study revealed that in the T47D and BT20 breast cancer cell lines, AST inhibits expression of pontin and mutp53, as well as the Oct4 and Nanog cancer stem cell (CSC) stemness genes. In addition, we explored the mechanism by which AST eradicates breast cancer cells using pontin siRNAs. Pontin knockdown by pontin siRNA reduced proliferation, Oct4 and Nanog expression, colony and spheroid formation, and migration and invasion abilities in breast cancer cells. In addition, reductions in Oct4, Nanog, and mutp53 expression following rottlerin treatment confirmed the role of pontin in these cells. Therefore, pontin may play a central role in the regulation of CSC properties and in cell proliferation following AST treatment. Taken together, these findings demonstrate that AST can repress CSC stemness genes in breast cancer cells, which implies that AST therapy could be used to improve the efficacy of other anti-cancer therapies against breast cancer cells.

ASTAXANTHIN POSITIVELY AFFECTS PROSTATE CANCER CELLS IN-VITRO.

J Food Biochem. 2021 Apr;45(4):e13702.

doi: 10.1111/jfbc.13702. Epub 2021 Mar 10.

Anti-androgenic effect of astaxanthin in LNCaP cells is mediated through the aryl hydrocarbon-androgen receptors cross talk

[Nima Montazeri-Najafabady¹](#), [Nazanin Chatrabnous¹](#), [Mohammad-Reza Arabnezhad²](#), [Negar Azarpira³](#)

- PMID: 33694182 DOI: [10.1111/jfbc.13702](https://doi.org/10.1111/jfbc.13702)

Abstract

The aim of this study was to investigate the anti-androgenic effects of astaxanthin (AST) on human prostatic cancer cell growth, and its impact on androgen receptor (AR) signaling using prostate cancer (PCa) cell line LNCaP. LNCaP cells were treated with AST alone and in combination with CH223191 and flutamide (Flu) in the presence and absence of testosterone. MTT assay, cellular prostate-specific antigen (PSA) and dihydrotestosterone (DHT) production, mRNA levels of CYP1A1, PSA, Kallikrein-Related Peptidase 2 (KLK2), Transmembrane Serine Protease 2 (TMPRSS2), and AR genes were measured as endpoints. The expression of CYP1A1, PSA, KLK2, TMPRSS2, and AR mRNA levels was decreased which results in reducing the production of PSA and DHT in the presence of testosterone. Our data clearly demonstrate that AST has a potential ability to suppress the human prostate LNCaP cells growth at high concentrations. AST was able to repress the testosterone-induced transcription of AR-target genes. PRACTICAL APPLICATIONS: Astaxanthin is a natural compound with the most potent antioxidant activity among other antioxidants. In the current study, ASX suppressed the LNCaP cells at high concentrations. Furthermore, AST inhibited testosterone-induced transcriptional activation of androgen-related genes. AST induced the expression of CYP1A1, which is able to metabolize the steroid hormones. It seems that AST can act as AhR exogenous ligand by induction of CYP1A1, which results in testosterone metabolism and consequent suppression of AR genes. So that, AST could prevent the growth of testosterone-dependent PCa cells, downregulate downstream genes in testosterone pathways, and enhance the metabolism of testosterone via AhR pathway. Collectively, AST could be considered as a potential candidate for the treatment of PCa.

Astaxanthin inhibits tumor invasion by decreasing extracellular matrix production and induces apoptosis in experimental rat colon carcinogenesis by modulating the expressions of ERK-2, NFkB and COX-2.

[Nagendraprabhu P](#), [Sudhandiran G](#).

Source

Department of Biochemistry, University of Madras, Chennai, Tamil nadu, India.

Abstract

Colon cancer is the third most malignant neoplasm in the world and it remains an important cause of mortality in Asian and Western countries. Astaxanthin (AST), a major component of carotenoids possesses attractive remedial features. The purpose of this study is to investigate the possible mechanism of action of astaxanthin against 1, 2 dimethyl hydrazine (DMH)-induced rat colon carcinogenesis. Wistar male rats were randomized into five groups, group 1 were control rats, group 2 were rats that received AST (15 mg/kg body wt p.o. everyday), rats in group 3 were induced with DMH (40 mg/kg body wt, s.c.), DMH-induced rats in groups 4 and 5 were either pre or post initiated with AST, respectively as in group 2. DMH-induced rats exhibited elevated expressions of Nuclear factor kappa B-p65 (NF- κ B-p65), Cyclooxygenase-2 (COX-2), Matrixmetallo proteinases (MMP) 2/9, Proliferating cell nuclear antigen (PCNA), and Extracellular signal-regulated kinase-2 (ERK-2) as confirmed by immunofluorescence. Further, Westernblot analysis of MMPs-2/9, ERK-2 and Protein kinase B (Akt) revealed increased expressions of these proteins in DMH-induced groups of rats. AST-treatment decreased the expressions of all these vital proteins, involved in colon carcinogenesis. The ability of AST to induce apoptosis in the colon of DMH-induced rats was confirmed by Annexin-V/PI staining in a confocal microscopy, DNA fragmentation analysis and expression of caspase-3 by Western blotting. In conclusion, astaxanthin exhibits anti-inflammatory and anti-cancer effects by inducing apoptosis in DMH-induced rat colon carcinogenesis by modulating the expressions of NFkB, COX-2, MMPs-2/9, Akt and ERK-2.

PMID: 19876598 [PubMed - indexed for MEDLINE]

Astaxanthin induces mitochondria-mediated apoptosis in rat hepatocellular carcinoma CBRH-7919 cells.

[Song XD](#), [Zhang JJ](#), [Wang MR](#), [Liu WB](#), [Gu XB](#), [Lv CJ](#).

Source

Medicine Research Center, Binzhou Medical University, Yantai, China.

Abstract

We designed to study the role of mitochondria in astaxanthin-induced apoptosis in hepatocellular carcinoma cells. Effect of astaxanthin on cell proliferation was studied by using methyl thiazolyl tetrazolium (MTT) in three tumor cell lines (CBRH-7919, SHZ-88 and Lewis) and normal human hepatocyte HL-7702 cell. Cell apoptosis rate, changes of mitochondrial morphology, mitochondrial transmembrane potential and electron transport chain were evaluated respectively. Expressions of B cell lymphoma/leukemia-2 (Bcl-2) and Bcl-2 associated X protein (Bax) were detected by Western blot. Results as following, astaxanthin had little effect on HL-7702 cell, however its inhibition was most pronounced in CBRH-7919 cell line with an IC_{50} of 39 μ M. This dose of astaxanthin and CBRH-7919 cell line were chosen for further studies. Astaxanthin could induce cell apoptosis and mitochondrial membrane damage. The mitochondrial transmembrane potential and function of electron transport chain were decreased. The expression of Bcl-2 protein was down-regulated but that of Bax protein was up-regulated. In conclusion, astaxanthin showed anticancer effect by inducing cell apoptosis through the regulation of mitochondrial-dependent manner.

PMID: 21628881 [PubMed - indexed for MEDLINE]

[Am J Vet Res.](#) 2010 Jan;71(1):89-96.

Evaluation of the protective effects of all-trans-astaxanthin on canine osteosarcoma cell lines.

[Wakshlag JJ](#), [Balkman CA](#), [Morgan SK](#), [McEntee MC](#).

Source

Department of Clinical Sciences, College of Veterinary Medicine, Cornell University, Ithaca, NY 14853, USA. jw37@cornell.edu

Abstract

OBJECTIVE: To determine the effects of the antioxidant astaxanthin on growth of canine osteosarcoma cells with and without concurrent chemotherapeutic or irradiation insult.

SAMPLE POPULATION: Cells from 3 established canine osteosarcoma cell lines (D17, OS 2.4, and HMPOS).

PROCEDURES: Growth-curve kinetics and cell cytotoxic effects were assessed by means of various treatment combinations and a 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide assay. Western blotting was performed to examine previously identified signaling pathways that astaxanthin reportedly affects. Additionally, cell-cycle kinetic evaluations, soft agar colony-forming assays, and antioxidant assays were performed to better understand the effect of astaxanthin on cell growth and function.

RESULTS: Exposure to astaxanthin alone resulted in a mild to pronounced attenuation of cell proliferation in vitro, depending on the cell line, and did not interfere with the cell-death response to doxorubicin, irradiation, or peroxide-mediated insult. In some instances, astaxanthin acted in an additive fashion to augment cell death. Astaxanthin exposure increased the antioxidant potential of cells, whereas peroxide-mediated cell stress increased the antioxidant potential to the same degree as astaxanthin exposure or greater. No dramatic changes in phosphorylation of protein kinase B or upregulation of connexin 43 were detected.

CONCLUSIONS AND CLINICAL RELEVANCE: Findings suggested that astaxanthin administration may be beneficial in treatment of dogs for osteosarcoma. Its actions as an antioxidant did not improve osteosarcoma cell survival during chemotherapeutic or irradiation insults, warranting further research into this natural compound as an adjuvant, antiproliferative treatment for osteosarcoma in dogs.

PMID: 20043787 [PubMed - indexed for MEDLINE]

ASTAXANTHIN REVIEWED FOR ITS POTENT PHOTOPROTECTIVE EFFECTS IN THE SUPPRESSION OF INFLAMMATION AND CANCER.

Mar Drugs. 2020 Oct 30;18(11):544.

doi: 10.3390/md18110544.

On a Beam of Light: Photoprotective Activities of the Marine Carotenoids Astaxanthin and Fucoxanthin in Suppression of Inflammation and Cancer

[Elena Catanzaro](#)¹, [Anupam Bishayee](#)², [Carmela Fimognari](#)¹

- PMID: [33143013](#)
- PMCID: [PMC7692561](#)
- DOI: [10.3390/md18110544](#)

Free PMC article

Abstract

Every day, we come into contact with ultraviolet radiation (UVR). If under medical supervision, small amounts of UVR could be beneficial, the detrimental and hazardous effects of UVR exposure dictate an unbalance towards the risks on the risk-benefit ratio. Acute and chronic effects of ultraviolet-A and ultraviolet-B involve mainly the skin, the immune system, and the eyes. Photodamage is an umbrella term that includes general phototoxicity, photoaging, and cancer caused by UVR. All these phenomena are mediated by direct or indirect oxidative stress and inflammation and are strictly connected one to the other. Astaxanthin (ASX) and fucoxanthin (FX) are peculiar marine carotenoids characterized by outstanding antioxidant properties. In particular, ASX showed exceptional efficacy in counteracting all categories of photodamages, in vitro and in vivo, thanks to both antioxidant potential and activation of alternative pathways. Less evidence has been produced about FX, but it still represents an interesting promise to prevent the detrimental effect of UVR. Altogether, these results highlight the importance of digging into the marine ecosystem to look for new compounds that could be beneficial for human health and confirm that the marine environment is as much as full of active compounds as the terrestrial one, it just needs to be more explored.

Astaxanthin anticancer effects are mediated through multiple molecular mechanisms: A systematic review

[Immacolata Faraone¹](#), [Chiara Sinisgalli¹](#), [Angela Ostuni¹](#), [Maria Francesca Armentano¹](#), [Monica Carmosino¹](#), [Luigi Milella²](#), [Daniela Russo¹](#), [Fabiana Labanca³](#), [Haroon Khan⁴](#)

- PMID: 32057895
- DOI: [10.1016/j.phrs.2020.104689](https://doi.org/10.1016/j.phrs.2020.104689)

Abstract

During the latest decades, the interest on the effectiveness of natural compounds and their impact on human health constantly increased, especially on those demonstrating to be effective on cancer. Molecules coming from nature are currently used in chemotherapy like Taxol, Vincristine or Vinblastine, and several other natural substances have been showed to be active in reducing cancer cell progression and migration. Among them, astaxanthin, a xanthophyll red colored carotenoid, displayed different biological activities including, antiinflammatory, antioxidant, proapoptotic, and anticancer effects. It can induce apoptosis through downregulation of antiapoptotic protein (Bcl-2, p-Bad, and survivin) expression and upregulation of proapoptotic ones (Bax/Bad and PARP). Thanks to these mechanisms, it can exert anticancer effects towards colorectal cancer, melanoma, or gastric carcinoma cell lines. Moreover, it possesses antiproliferative activity in many experimental models and enhances the effectiveness of conventional chemotherapeutic drugs on tumor cells underling its potential future use. This review provides an overview of the current knowledge on the anticancer potential of astaxanthin by modulating several molecular targets. While it has been clearly demonstrated its multitarget activity in the prevention and regression of malignant cells in in vitro or in preclinical investigations, further clinical studies are needed to assess its real potential as anticancer in humans.

Diabetes

Astaxanthin reduces blood pressure, improves glucose metabolism and reduces visceral body fat mass in placebo-controlled randomized study on patients with Type-2 diabetes.

[Asia Pac J Clin Nutr.](#) 2018;27(2):341-346. doi: 10.6133/apjcn.052017.11.

Astaxanthin improves glucose metabolism and reduces blood pressure in patients with type 2 diabetes mellitus.

[Mashhadi NS¹](#), [Zakerkish M²](#), [Mohammadiasl J³](#), [Zarei M⁴](#), [Mohammadshahi M⁵](#), [Haghighizadeh MH⁶](#).

[Author information](#)

Abstract

BACKGROUND AND OBJECTIVES:

This randomized, placebo-controlled trial was performed for 8 weeks to investigate the potential effects of astaxanthin (AST) supplementation on the adiponectin concentration, lipid peroxidation, glycemic control, insulin sensitivity, and anthropometric indices in participants with type 2 diabetes mellitus.

METHODS AND STUDY DESIGN:

We enrolled 44 participants with type 2 diabetes who met our inclusion criteria. Eight milligrams of AST supplementation or a placebo were randomly administered once daily for 8 weeks to these participants.

RESULTS:

The 8-week administration of AST supplementation increased the serum adiponectin concentration and reduced visceral body fat mass ($p < 0.01$), serum triglyceride and very-low-density lipoprotein cholesterol concentrations, and systolic blood pressure ($p < 0.05$). Furthermore, AST significantly reduced the fructosamine concentration ($p < 0.05$) and marginally reduced the plasma glucose concentration ($p = 0.057$).

CONCLUSIONS:

We demonstrated that because participants with type 2 diabetes often have hypertriglycemia and uncontrolled glucose metabolism; our findings of dual beneficial effects are clinically valuable. Our results may provide a novel complementary treatment with potential impacts on diabetic complications without adverse effects.

PMID: 29384321 DOI: [10.6133/apjcn.052017.11](#) [Free full text](#)

ASTAXANTHIN DECREASES LEVELS OF OXIDATIVE STRESS MARKER MALONDIALDEHYDE AND INFLAMMATORY CYTOKINE INTERLEUKIN-6 IN PATIENTS WITH TYPE-2 DIABETES IN RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED HUMAN CLINICAL TRIAL.

Int J Clin Pract. 2021 May;75(5):e14022.

doi: 10.1111/ijcp.14022. Epub 2021 Feb 2.

The antioxidant and anti-inflammatory effects of astaxanthin supplementation on the expression of miR-146a and miR-126 in patients with type 2 diabetes mellitus: A randomised, double-blind, placebo-controlled clinical trial

[Nafiseh Shokri-Mashhadi^{1,2}](#), [Maryam Tahmasebi^{3,4}](#), [Javad Mohammadi-Asl⁵](#), [Mehrnoosh Zakerkish⁶](#), [Majid Mohammadshahi²](#)

- PMID: 33445213 DOI: [10.1111/ijcp.14022](https://doi.org/10.1111/ijcp.14022)

Abstract

Background: The pathogenesis of type 2 diabetes mellitus (T2DM) is associated with chronic oxidative stress and inflammation. It is well known that the expression of some miRNAs such as miRNA-146a is upregulated in diabetic and hyperglycaemic patients, whereas circulating miRNA-126 is reduced. Therefore, we aimed to determine the effects of astaxanthin (AST) supplementation on the circulating malondialdehyde (MDA) and interleukin 6 (IL-6) levels, and the expression of miR-146a and miR-126 in patients with T2DM.

Methods: This randomised, double-blind, placebo-controlled clinical trial was conducted in 44 patients with T2DM randomly receiving 8 mg/d of oral AST (n = 22) or placebo (n = 22) for 8 weeks.

Results: We observed that AST supplementation could decrease plasma levels of MDA and IL-6 (P < .05) and decrease the expression level of miR-146a over time (fold change: -1/388) (P < .05).

Conclusion: AST supplementation might be beneficial for improving circulating MDA and IL-6 and the down-regulation of miR-146a. However, future investigations are suggested to confirm these results.

Astaxanthin ameliorates experimental diabetes-induced renal oxidative stress and fibronectin by upregulating connexin43 in glomerular mesangial cells and diabetic mice.

[Chen Q](#)¹, [Tao J](#)¹, [Li G](#)², [Zheng D](#)³, [Tan Y](#)³, [Li R](#)³, [Tian L](#)³, [Li Z](#)³, [Cheng H](#)³, [Xie X](#)⁴.

Author information

Abstract

Oxidative stress is the major cause of renal fibrosis in the progression of DN. Connexin43 (Cx43) exerts an anti-fibrosis effect on diabetic kidneys. The current study aimed to investigate whether astaxanthin (AST) could ameliorate the pathological progression of DN by upregulating Cx43 and activating the Nrf2/ARE signaling, which is a pivotal anti-oxidative stress system, to strengthen the cellular anti-oxidative capacity and diminish fibronectin (FN) accumulation in HG-induced glomerular mesangial cells (GMCs). Our hypothesis was verified in GMCs and the kidneys from db/db mice by western blot, immunofluorescence, immunohistochemistry, immunoprecipitation, dual luciferase reporter assay and reactive oxygen related detection kits. Results showed that AST simultaneously upregulated the Cx43 protein level and promoted the Nrf2/ARE signaling activity in the kidney of db/db mice and HG-treated GMCs. However, Cx43 depletion abrogated the Nrf2/ARE signaling activation induced by AST. AST reduced the interaction between c-Src and Nrf2 in the nuclei of GMCs cultured with HG, thereby enhancing the Nrf2 accumulation in the nuclei of GMCs. Our data suggested that AST promoted the Nrf2/ARE signaling by upregulating the Cx43 protein level to prevent renal fibrosis triggered by HG in GMCs and db/db mice. c-Src acted as a mediator in these processes.

KEYWORDS:

Astaxanthin; Connexin43; Diabetic nephropathy; Nrf2/ARE signaling; Renal fibrosis

PMID: 30268666

DOI: [10.1016/j.ejphar.2018.09.028](https://doi.org/10.1016/j.ejphar.2018.09.028)

Short-Term Administration of Astaxanthin Attenuates Retinal Changes in Diet-Induced Diabetic *Psammomys obesus*.

[Baccouche B](#)^{1,2}, [Benlarbi M](#)¹, [Barber AJ](#)³, [Ben Chaouacha-Chekir R](#)¹.

[Author information](#)

Abstract

OBJECTIVES: *Psammomys obesus* is a high-fat diet (HFD)-fed animal model of obesity and type 2 diabetes recently explored as a model of non-proliferative diabetic retinopathy. This study tested the protective effect of the pigment astaxanthin (AST) in the *P. obesus* diabetic retina.

METHODS: Young adult *P. obesus* were randomly assigned to two groups. The control group received a normal diet consisting of a plant-based regimen, and the HFD group received an enriched laboratory chow. After 3 months, control and diabetic rodents were administered vehicle or AST, daily for 7 days. Body weight, blood glucose, and plasma pentosidine were assessed. Frozen sections of retinas were immunolabeled for markers of oxidative stress, glial reactivity and retinal ganglion cell bodies, and imaged by confocal microscopy.

RESULTS: Retinal tissue from AST-treated control and HFD-diabetic *P. obesus* showed a greater expression of the antioxidant enzyme heme oxygenase-1 (HO-1). In retinas of HFD-diabetic AST-treated *P. obesus*, cellular retinaldehyde binding protein and glutamine synthetase in Müller cells were more intense compared to the untreated HFD-diabetic group. HFD-induced diabetes downregulated the expression of glial fibrillary acidic protein in astrocytes, the POU domain protein 3A in retinal ganglion cells, and synaptophysin throughout the plexiform layers.

DISCUSSION: Our results show that type 2-like diabetes induced by HFD affected glial and neuronal retinal cell homeostasis. AST treatment induced the antioxidant enzyme HO-1 and reduced glial reactivity. These findings suggest that diabetic *P. obesus* is a useful model of HFD-induced obesity and diabetes to evaluate early neuroglial retinal alterations and antioxidant neuroprotection mechanisms in DR.

KEYWORDS: Diabetic retinopathy; high-fat diet; neurodegeneration; neuroprotection; oxidative stress

Astaxanthin Promotes Nrf2/ARE Signaling to Alleviate Renal Fibronectin and Collagen IV Accumulation in Diabetic Rats.

[Zhu X](#)^{1,2}, [Chen Y](#)^{3,4}, [Chen Q](#)⁵, [Yang H](#)², [Xie X](#)^{1,2,3}.

Author information

Abstract

Astaxanthin (AST), a natural keto-carotenoid classified as a xanthophyll, is well known for its antioxidant properties. AST can ameliorate the pathological characteristics of diabetic nephropathy (DN). However, the underlying mechanisms remain to be explored. This study was aimed at exploring whether AST exerts a protective effect on DN via activating nuclear factor erythroid 2-related factor 2- (Nrf2-) antioxidative response element (ARE) signaling. Streptozotocin-induced diabetic rats were treated with AST for 12 weeks. We found that AST treatment ameliorated renal morphological injury. Reduced fibronectin and collagen IV protein expression were found in the kidneys of diabetic rats. Furthermore, AST promoted the nuclear translocation of Nrf2 and increased its downstream protein heme oxygenase-1 and superoxide dismutase 1 expression. AST also increased the activity of SOD and decreased malondialdehyde generation in the serum of diabetic rats. These results suggest that the renoprotective effect of AST on DN partly depends on Nrf2-ARE signaling. The antioxidative stress effect of AST is responsible for the activation of Nrf2-ARE signaling in DN.

PMID: 29744366

PMCID: [PMC5884145](#)

DOI: [10.1155/2018/6730315](#)

[Indexed for MEDLINE]

[Free PMC Article](#)

Astaxanthin and Corni Fructus protect against diabetes-induced oxidative stress, inflammation, and advanced glycation end product in livers of streptozotocin-induced diabetic rats.

[Park CH¹](#), [Xu FH](#), [Roh SS](#), [Song YO](#), [Uebaba K](#), [Noh JS](#), [Yokozawa T](#).

Author information

Abstract

This study was conducted to compare the protective effects of astaxanthin (ASX) with Corni Fructus (CF) against diabetes-induced pathologies such as oxidative stress-induced inflammation and advanced glycation end product (AGE) formation in the liver of type 1 diabetic rats. ASX (50 mg/kg body weight/day) or CF (200 mg/kg body weight/day) was orally administered every day for 18 days to streptozotocin (STZ)-induced diabetic rats, and their effects were compared with nondiabetic and diabetic control rats. The administration of CF, but not ASX, decreased both the elevated serum and hepatic glucose concentration in diabetic rats. In diabetic rats, increased levels of AGE, reactive oxygen species, and lipid peroxidation were significantly decreased by treatment with both ASX and CF in the liver of diabetic rats. STZ treatment markedly augmented the protein expressions of AGE, and both ASX and CF efficiently attenuated these increases in hepatic protein expressions. In addition, oxidative stress and proinflammatory protein expressions were upregulated in the diabetic rats. On the contrary, these upregulations of protein expressions were decreased by the administration of ASX or CF. These results suggest that the inhibitory effect of ASX on diabetes-induced hepatic dysfunction could be derived from the blocking of AGE formation and further anti-inflammation and that CF exhibited beneficial effects through the attenuation of hyperglycemia, and thus the inhibition of AGE formation and the inflammatory responses. Therefore, ASX as well as CF may help prevent ongoing diabetes-induced hepatic injury.

KEYWORDS:

AGE; Corni Fructus; astaxanthin; inflammation; oxidative stress; streptozotocin-induced diabetes

PMID:

25569034

[PubMed - indexed for MEDLINE]

[Mar Drugs](#). 2013 Mar 21;11(3):960-74. doi: 10.3390/md11030960.

Astaxanthin attenuates the apoptosis of retinal ganglion cells in db/db mice by inhibition of oxidative stress.

[Dong LY](#)¹, [Jin J](#), [Lu G](#), [Kang XL](#).

[Author information](#)

Abstract

Diabetic retinopathy is a common diabetic eye disease caused by changes in retinal ganglion cells (RGCs). It is an ocular manifestation of systemic disease, which affects up to 80% of all patients who have had diabetes for 10 years or more. The genetically diabetic db/db mouse, as a model of type-2 diabetes, shows diabetic retinopathy induced by apoptosis of RGCs. Astaxanthin is a carotenoid with powerful antioxidant properties that exists naturally in various plants, algae and seafood. Here, astaxanthin was shown to reduce the apoptosis of RGCs and improve the levels of oxidative stress markers, including superoxide anion, malondialdehyde (MDA, a marker of lipid peroxidation), 8-hydroxy-2-deoxyguanosine (8-OHdG, indicator of oxidative DNA damage) and MnSOD (manganese superoxide dismutase) activity in the retinal tissue of db/db mouse. In addition, astaxanthin attenuated hydrogen peroxide(H₂O₂)-induced apoptosis in the transformed rat retinal ganglion cell line RGC-5. Therefore, astaxanthin may be developed as an antioxidant drug to treat diabetic retinopathy.

PMID:

23519150

[PubMed - indexed for MEDLINE]

PMCID:

PMC3705382

[Free PMC Article](#)

ASTAXANTHIN SHOWS POTENTIAL TO REGULATE INSULIN RESISTANCE AND INFLAMMATION IN GESTATIONAL DIABETES IN MOUSE MODEL.

Dose Response. 2020 May 20;18(2):1559325820926765.

doi: 10.1177/1559325820926765. eCollection Apr-Jun 2020.

Effects of Astaxanthin on Inflammation and Insulin Resistance in a Mouse Model of Gestational Diabetes Mellitus

[Weihong Feng¹](#), [Yanxia Wang¹](#), [Na Guo¹](#), [Pu Huang²](#), [Yang Mi¹](#)

- PMID: [32501299](#)
- PMCID: [PMC7241269](#)
- DOI: [10.1177/1559325820926765](#)

Free PMC article

Abstract

Gestational diabetes mellitus (GDM) is a condition in which a hormone made by the placenta prevents the body from using insulin effectively. It is important to find an effective treatment. A mouse model of GDM was used to testify the effects of astaxanthin on glucose tolerance and insulin sensitivity. Production of inflammatory cytokines, reactive oxygen species (ROS), and glucose transporter type 4 (GLUT4) translocation and insulin-related signaling were measured in the presence of astaxanthin both in vivo and in vitro. It was found that astaxanthin improved insulin sensitivity, glucose tolerance, and litter size of offspring and reduced birth weight of offspring and inflammation in GDM mouse. Moreover, astaxanthin increased GLUT4 translocating to membrane without altering its secretion/expression and glucose uptake and consumption in C2C12 skeletal muscle cells. Furthermore, ROS generation and insulin-related signaling inhibited by tumor necrosis factor α was restored by astaxanthin. It is concluded that astaxanthin has the potential to attenuate GDM symptoms by regulating inflammation and insulin resistance in skeletal muscle of pregnant mice. Our findings suggest that astaxanthin could be a promising and effective molecule to treat GDM.

ASTAXANTHIN SHOWS PROMISE AS A PREVENTIVE AND THERAPEUTIC TREATMENT FOR CO-MORBIDITY OF DIABETES AND DEPRESSION IN RATS.

Front Pharmacol. 2020 Jan 30;10:1621.

doi: 10.3389/fphar.2019.01621. eCollection 2019.

Preventive and Therapeutic Effects of Astaxanthin on Depressive-Like Behaviors in High-Fat Diet and Streptozotocin-Treated Rats

[Yuting Ke](#)^{1,2,3}, [Shizhong Bu](#)⁴, [Hong Ma](#)¹, [Lei Gao](#)¹, [Yujia Cai](#)¹, [Yisheng Zhang](#)⁵, [Wenhua Zhou](#)¹

PMID: [32082151](#) PMCID: [PMC7003134](#) DOI: [10.3389/fphar.2019.01621](#) [Free PMC article](#)

Abstract

The comorbidity of diabetes and depression has a negative impact on both lifestyle and quality of life. Astaxanthin (AST) has been demonstrated to improve glucose metabolism and has antidepressant-like effects, but it is not clear whether AST has potential for preventing depression in diabetes. The aim of this study is to observe the preventive and therapeutic effects of AST on glucose metabolism or depressive-like behaviors in a diabetic rat model produced by feeding with a high-fat diet for 10 weeks followed by injection of 25 mg/kg streptozotocin (STZ). Preventive treatment with AST at doses of 7.5, 15, and 25 mg/kg/day was given by intragastric gavage 4 weeks before STZ injection. Preventive plus therapeutic treatment also involved therapeutic AST treatments for 6 more weeks after STZ injection, whereas therapeutic-only treatment involved only the 6-week post-STZ treatment. Depressive-like behaviors were evaluated at the end of the treatment by using open field, locomotor activity, elevated plus maze, and forced swimming tests. Preventive and therapeutic treatment with AST both reduced the level of fasting glucose, improved glucose tolerance, and decreased total TCh and TG in diabetic rats. Preventive or preventative plus therapeutic treatment with AST decreased the immobility time and increased the time spent in the open arms of an elevated plus maze and locomotor activity in diabetic rats. However, therapeutic treatment with AST alone failed to affect the depressive-like behaviors. Preventive or preventative plus therapeutic treatment with AST at doses of 15 or 25 mg/kg significantly increased the expression of pERK, pAKT, pCREB, and BDNF in the prefrontal cortex (PFC) in diabetic rats. In contrast, therapeutic treatment with 25 mg/kg AST alone increased the expression of pERK in the PFC. This study indicates that AST may be used as a preventive or therapeutic approach for co-morbidity of diabetes and depression.

ASTAXANTHIN SHOWS POTENTIAL IN TREATING DIABETES AS WELL AS GESTATIONAL DIABETES (WHICH INCREASES THE RISK OF BOTH DIABETES AND CARDIOVASCULAR DISEASE IN PREGNANT MAMMALS AND THEIR FETUSES) IN MOUSE MODEL.

Naunyn Schmiedebergs Arch Pharmacol. 2020 Dec;393(12):2517-2527.
doi: 10.1007/s00210-020-01861-x. Epub 2020 Apr 11.

Astaxanthin alleviates gestational diabetes mellitus in mice through suppression of oxidative stress

[Yangyang Chen](#)¹, [Jichun Tang](#)², [Yinghong Zhang](#)¹, [Juan Du](#)³, [Yuanli Wang](#)¹, [Hui Yu](#)¹, [Yanling He](#)⁴

- PMID: **32279084**
- DOI: [10.1007/s00210-020-01861-x](https://doi.org/10.1007/s00210-020-01861-x)

Abstract

Gestational diabetes mellitus (GDM) affects 7% of pregnant women worldwide, which increases the risk of diabetes and cardiovascular disease for both the mother and the fetus. Natural compound Astaxanthin has been reported to have benefits in obesity and diabetes. A pregnant C57BL/KsJ db/+ mouse was used as a genetic GDM model to investigate the effect of Astaxanthin on GDM symptoms and reproductive outcomes. Blood glucose, plasma insulin, glucose intolerance, insulin sensitivity, biochemical indexes of plasma, and the liver were measured; Nrf2 and HO-1 protein levels were detected by Western blotting. Astaxanthin significantly alleviated the glucose intolerance and β cell insufficiency, inhibited in vivo oxidative stress, enhanced the activity of antioxidant enzymes, and improved reproductive outcomes. Mechanistically, the effect of Astaxanthin was mediated by restoring the Nrf2/HO-1 antioxidant pathway in the liver of GDM mice. Our findings supported that Astaxanthin was a potential therapeutic reagent for not only diabetes but also GDM symptomology.

ASTAXANTHIN DEMONSTRATES ANTI-DIABETIC EFFECTS IN RAT MODEL AND MAY BE DEVELOPED AS AN ANTI-DIABETIC THERAPY FOR HUMANS.

Endocr J. 2020 Dec 2.

doi: [10.1507/endocrj.EJ20-0699](https://doi.org/10.1507/endocrj.EJ20-0699). Online ahead of print.

Anti-diabetic effects of astaxanthin on an STZ-induced diabetic model in rats

[Fen Zhuge](#)¹, [Yinhua Ni](#)², [Chunyan Wan](#)², [Fen Liu](#)², [Zhengwei Fu](#)²

- PMID: **33268598**
- DOI: [10.1507/endocrj.EJ20-0699](https://doi.org/10.1507/endocrj.EJ20-0699)

Abstract

Type 2 diabetes mellitus (T2DM), which is characterized by insulin resistance and relative insulin insufficiency, has become the most common chronic metabolic disease threatening global health. The preferred therapies for T2DM include lifestyle interventions and the use of anti-diabetic drugs. However, considering their adverse reactions, it is important to find a low-toxicity and effective functional food or drug for diabetes prevention and treatment. Astaxanthin is a potent antioxidant carotenoid found in marine organisms has been reported to prevent diet-induced insulin resistance and hepatic steatosis. To investigate the anti-diabetic effects of astaxanthin, male Wistar rats were fed a high-energy diet for 4 weeks, followed by a low dose streptozotocin (STZ) injection to induce the diabetes model, and the rats were then fed an astaxanthin-containing diet for another 3 weeks. Astaxanthin significantly decreased blood glucose and total cholesterol (TC) levels, and increased blood levels of high density lipoprotein cholesterol (HDL-C) in STZ-induced diabetic rats in a dose dependent manner. These results were associated with increased expression of insulin sensitivity related genes (adiponectin, adipoR1, and adipoR2) in vivo, thereby attenuating STZ-induced diabetes. In addition, we also compared the anti-diabetic effects of astaxanthin and monacolin K, which has been reported to downregulate hyperlipidemia and hyperglycemia. The results revealed that astaxanthin and monacolin K showed similar anti-diabetic effects in STZ-induced diabetic rats. Therefore, astaxanthin may be developed as an anti-diabetic agent in the future.

ASTAXANTHIN NANOEMULSION REDUCES GLUCOSE LEVELS IN DIABETIC RABBITS.

J Adv Pharm Technol Res. Oct-Dec 2020;11(4):189-193.

doi: 10.4103/japtr.JAPTR_55_20. Epub 2020 Oct 10.

Antidiabetic activity of thin film containing astaxanthin-loaded nanoemulsion using carboxymethylcellulose sodium polymer on alloxan-induced diabetic rabbit

[Lusi Nurdianti^{1,2}](#), [Taofik Rusdiana¹](#), [Iyan Sopyan¹](#)

PMID: 33425703 PMCID: [PMC7784939](#) DOI: [10.4103/japtr.JAPTR_55_20](#) **Free PMC article**

Abstract

The present study was conducted to evaluate the potency of thin film containing astaxanthin-loaded nanoemulsion (FDT-As-NE) in lowering blood glucose levels on alloxan-induced diabetic rabbit (ADR). Astaxanthin nanoemulsion (As-NE) was prepared using self-nanoemulsifying method, followed by incorporated into the carboxymethylcellulose sodium matrix polymer using a solvent casting method to form a thin film. The evaluation of FDT-As-NE was performed by chemical, physical, and mechanical characterizations. The administration of thin film was done by an intraoral route. New Zealand albino rabbits were induced with alloxan to get experimental diabetic animals. The antidiabetic activity was carried out in three groups of treatment. Group I was ADR treated by FDT-As-NE, Group II was ADR treated by pure astaxanthin, while Group III was normal control. The measurement of fasting means blood glucose levels was carried out in 0 days (before treatment) and after 14 days of treatment. The histopathological analysis of the pancreas was also examined. Data were statistically evaluated using Kruskal-Wallis statistical test. $P < 0.05$ was considered statistically significant. FDT-As-NE had good physical and mechanical characteristics that suitable for intraoral administration. Group I reduced elevated blood glucose levels compared to Group II ($P < 0.01$). Histopathological examination of pancreatic tissue for a Group I showed the normal condition of pancreatic β -cell, suggesting the absence of any pathological lesions. These results suggest that thin film containing astaxanthin-loaded nanoemulsion administered by an intraoral route potentially useful for reducing glucose levels.

ASTAXANTHIN DOSE-DEPENDENTLY REDUCES BLOOD GLUCOSE LEVELS AND IMPROVES BLOOD LIPID PROFILE IN DIABETIC RAT MODEL AND MAY BE DEVELOPED INTO A THERAPEUTIC CLINICAL TREATMENT FOR DIABETES.

Endocr J. 2021 Apr 28;68(4):451-459.

doi: 10.1507/endocrj.EJ20-0699. Epub 2020 Dec 2.

Anti-diabetic effects of astaxanthin on an STZ-induced diabetic model in rats

[Fen Zhuge](#)¹, [Yinhua Ni](#)², [Chunyan Wan](#)², [Fen Liu](#)², [Zhengwei Fu](#)²

- PMID: 33268598 DOI: [10.1507/endocrj.EJ20-0699](https://doi.org/10.1507/endocrj.EJ20-0699) **Free article**

Abstract

Type 2 diabetes mellitus (T2DM), which is characterized by insulin resistance and relative insulin insufficiency, has become the most common chronic metabolic disease threatening global health. The preferred therapies for T2DM include lifestyle interventions and the use of anti-diabetic drugs. However, considering their adverse reactions, it is important to find a low-toxicity and effective functional food or drug for diabetes prevention and treatment. Astaxanthin is a potent antioxidant carotenoid found in marine organisms has been reported to prevent diet-induced insulin resistance and hepatic steatosis. To investigate the anti-diabetic effects of astaxanthin, male Wistar rats were fed a high-energy diet for 4 weeks, followed by a low dose streptozotocin (STZ) injection to induce the diabetes model, and the rats were then fed an astaxanthin-containing diet for another 3 weeks. Astaxanthin significantly decreased blood glucose and total cholesterol (TC) levels, and increased blood levels of high density lipoprotein cholesterol (HDL-C) in STZ-induced diabetic rats in a dose dependent manner. These results were associated with increased expression of insulin sensitivity related genes (adiponectin, adipoR1, and adipoR2) in vivo, thereby attenuating STZ-induced diabetes. In addition, we also compared the anti-diabetic effects of astaxanthin and monacolin K, which has been reported to downregulate hyperlipidemia and hyperglycemia. The results revealed that astaxanthin and monacolin K showed similar anti-diabetic effects in STZ-induced diabetic rats. Therefore, astaxanthin may be developed as an anti-diabetic agent in the future.

Inhibition of inflammation by astaxanthin alleviates cognition deficits in diabetic mice.

[Zhou X¹](#), [Zhang F¹](#), [Hu X¹](#), [Chen J¹](#), [Wen X²](#), [Sun Y³](#), [Liu Y³](#), [Tang R⁴](#), [Zheng K⁵](#), [Song Y⁶](#).

Author information

Abstract

Neurons in the hippocampal and cortical functional regions are more susceptible to damage induced by hyperglycemia, which can result in severe spatial learning and memory impairment. Neuroprotection ameliorates cognitive impairment induced by hyperglycemia in diabetic encephalopathy (DE). Astaxanthin has been widely studied in diabetes mellitus and diabetic complications due to its hypoglycemic, antioxidant and anti-apoptotic effects. However, whether astaxanthin can alleviate cognition deficits induced by DE and its precise mechanisms remain undetermined. In this study, DE was induced by streptozotocin (STZ, 150 mg/kg) in ICR mice. We observed the effect of astaxanthin on cognition and investigated its potential mechanisms in DE mice. Results showed that astaxanthin treatment significantly decreased the latency and enhanced the distance and time spent in the target quadrant in the Morris water maze test. Furthermore, neuronal survival was significantly increased in the hippocampal CA3 region and the frontal cortex following treatment with astaxanthin. Meanwhile, immunoblotting was used to observe the nuclear translocation of nuclear factor-kappaB (NF- κ B) p65 and the expression of tumor necrosis factor- α (TNF- α) in the hippocampus and frontal cortex. The results indicated that astaxanthin could inhibit NF- κ B nuclear translocation and downregulate TNF- α expression in the hippocampus and frontal cortex. Overall, the present study implied that astaxanthin could improve cognition by protecting neurons against inflammation injury potentially through inhibiting the nuclear translocation of NF- κ B and down-regulating TNF- α .

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KEYWORDS:

Astaxanthin; Cognition deficits; Diabetic encephalopathy; Inflammation; Nuclear factor- κ B; Tumor necrosis factor- α

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26272354

[PubMed - in process]

Astaxanthin Inhibits Expression of Retinal Oxidative Stress and Inflammatory Mediators in Streptozotocin-Induced Diabetic Rats.

[Yeh PT](#)^{1,2}, [Huang HW](#)³, [Yang CM](#)^{1,4}, [Yang WS](#)^{5,6}, [Yang CH](#)^{1,4}.

Abstract

PURPOSE: We evaluated whether orally administered astaxanthin (AST) protects against oxidative damage in the ocular tissues of streptozotocin (STZ)-induced diabetic rats.

METHODS AND RESULTS: Fifty 6-week-old female Wistar rats were randomly assigned to receive an injection of STZ to induce diabetes (n = 40) or to remain uninduced (n = 10). The diabetic rats were randomly selected into four groups and they were separately administered normal saline, 0.6 mg/kg AST, 3 mg/kg AST, or 0.5 mg/kg lutein daily for eight weeks. Retinal functions of each group were evaluated by electroretinography. The expression of oxidative stress and inflammatory mediators in the ocular tissues was then assessed by immunohistochemistry, western blot analysis, ELISA, RT-PCR, and electrophoretic mobility shift assay (EMSA). Retinal functions were preserved by AST and lutein in different levels. Ocular tissues from AST- and lutein-treated rats had significantly reduced levels of oxidative stress mediators (8-hydroxy-2'-deoxyguanosine, nitrotyrosine, and acrolein) and inflammatory mediators (intercellular adhesion molecule-1, monocyte chemoattractant protein-1, and fractalkine), increased levels of antioxidant enzymes (heme oxygenase-1 and peroxiredoxin), and reduced activity of the transcription factor nuclear factor-kappaB (NF-κB).

CONCLUSION: The xanthophyll carotenoids AST and lutein have neuroprotective effects and reduce ocular oxidative stress, and inflammation in the STZ diabetic rat model, which may be mediated by downregulation of NF-κB activity.

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PMCID: [PMC4713224](#)

DOI: [10.1371/journal.pone.0146438](#)

[Indexed for MEDLINE]

[Free PMC Article](#)

Potential of Dietary Non-Provitamin A Carotenoids in the Prevention and Treatment of Diabetic Microvascular Complications.

[Murillo AG](#)¹, [Fernandez ML](#)².

Author information

Abstract

Diabetes is a chronic metabolic disease that affects a substantial part of the population around the world. Whether type I or type II, this disease has serious macro- and microvascular complications that constitute the primary cause of death in diabetic patients. Microvascular complications include diabetic retinopathy, nephropathy, and neuropathy. Although these complications are clinically and etiologically diverse, they share a common factor: glucose-induced damage. In the progression of diabetic complications, oxidative stress, inflammation, and the formation of glycation end products play an important role. Previous studies have shown that a healthy diet is vital in preventing these complications; in particular, the intake of antioxidants has been studied for their potential effect in ameliorating hyperglycemic injuries. Carotenoids are lipid-soluble pigments synthesized by plants, bacteria, and some kinds of algae that are responsible for the yellow, red, and orange colors in food. These compounds are part of the antioxidant machinery in plants and have also shown their efficacy in quenching free radicals, scavenging reactive oxygen species, modulating gene expression, and reducing inflammation in vitro and in vivo, showing that they can potentially be used as part of a preventive strategy for metabolic disorders, including diabetes and its related complications. This review highlights the potential protective effects of 4 non-provitamin A carotenoids--lutein, zeaxanthin, lycopene, and astaxanthin--in the development and progression of diabetic microvascular complications.

KEYWORDS:

carotenoids; diabetes; inflammation; microvascular complications; oxidative stress

PMID: 26773012

PMCID: [PMC4717886](#)

DOI: [10.3945/an.115.009803](#)

[Indexed for MEDLINE]

[Free PMC Article](#)

Depression can be prevented by astaxanthin through inhibition of hippocampal inflammation in diabetic mice.

[Zhou XY](#)¹, [Zhang F](#)¹, [Hu XT](#)¹, [Chen J](#)¹, [Tang RX](#)², [Zheng KY](#)³, [Song YJ](#)⁴.

Author information

Abstract

The critical factor considered in a depression induced by diabetes is the inflammation eliciting hippocampal, amygdala and thalamic neuronal injury. Therefore, inhibiting inflammatory reactions in the brain and reducing neuronal injury can alleviate depression in rodents suffering from diabetes mellitus. The oral administration of astaxanthin has been employed in emotional disorders and diabetic complications due to its anti-depressant, anti-inflammatory and anti-apoptotic functions. However, it has not been reported whether astaxanthin can improve diabetes-related depression-like behavior, and its potential mechanisms have not been elucidated. The objective of the present study is to elucidate the effect of astaxanthin on depression in diabetic mice and to understand the underlying molecular mechanisms. In this study, experimental diabetic mice were given a single intraperitoneal injection of streptozotocin (STZ, 150mg/kg, dissolved in citrate buffer) after fasting for 12h. The diabetic model was assessed 72h after STZ injection, and mice with a fasting blood glucose level more than or equal to 16.7mmol/L were used in this study, and oral astaxanthin (25mg/kg) was provided uninterrupted for ten weeks. Depression-like behavior was evaluated by the tail suspension test (TST) and forced swimming test (FST). The glial fibrillary acidic protein (GFAP) and cleaved caspase-3-positive cells were measured by immunohistochemistry, and the western blotting was used to test the protein levels of interleukin-6 (IL-6), interleukin-1 β (IL-1 β) and cyclooxygenase (COX-2). The results showed that astaxanthin had an anti-depressant effect on diabetic mice. Furthermore, we observed that astaxanthin significantly reduced the number of GFAP-positive cells in the hippocampus and hypothalamus, and also the expression of cleaved caspase-3 in the hippocampus, amygdala and hypothalamus was decreased as well. Moreover, astaxanthin could down-regulate the expression of IL-6, IL-1 β and COX-2 in the hippocampus. These findings suggest that the mechanism of astaxanthin in preventing depression in diabetic mice involves the inhibition of inflammation/inflammation inhibition, thereby protecting neurons in hippocampus, amygdala and hypothalamus against hyperglycemic damage.

KEYWORDS: Astaxanthin; Depression; Diabetes; Inflammation; Injury

PMID: 28017669 DOI: [10.1016/j.brainres.2016.12.018](#) [Indexed for MEDLINE]

Impact of divergent effects of astaxanthin on insulin signaling in L6 cells.

[Ishiki M¹](#), [Nishida Y](#), [Ishibashi H](#), [Wada T](#), [Fujisaka S](#), [Takikawa A](#), [Urakaze M](#), [Sasaoka T](#), [Usui I](#), [Tobe K](#).

[Author information](#)

Abstract

Because oxidative stress promotes insulin resistance in obesity and type 2 diabetes, it is crucial to find effective antioxidant for the purpose of decreasing this threat. In this study, we explored the effect of astaxanthin, a carotenoid antioxidant, on insulin signaling and investigated whether astaxanthin improves cytokine- and free fatty acid-induced insulin resistance in vitro. We examined the effect of astaxanthin on insulin-stimulated glucose transporter 4 (GLUT4) translocation, glucose uptake, and insulin signaling in cultured rat L6 muscle cells using plasma membrane lawn assay, 2-deoxyglucose uptake, and Western blot analysis. Next, we examined the effect of astaxanthin on TNF α - and palmitate-induced insulin resistance. The amount of reactive oxygen species generated by TNF α or palmitate with or without astaxanthin was evaluated by dichlorofluorescein staining. We also compared the effect of astaxanthin on insulin signaling with that of other antioxidants, α -lipoic acid and α -tocopherol. We observed astaxanthin enhanced insulin-stimulated GLUT4 translocation and glucose uptake, which was associated with an increase in insulin receptor substrate-1 tyrosine and Akt phosphorylation and a decrease in c-Jun N-terminal kinase (JNK) and insulin receptor substrate-1 serine 307 phosphorylation. Furthermore, astaxanthin restored TNF α - and palmitate-induced decreases in insulin-stimulated GLUT4 translocation or glucose uptake with a concomitant decrease in reactive oxygen species generation. α -Lipoic acid enhanced Akt phosphorylation and decreased ERK and JNK phosphorylation, whereas α -tocopherol enhanced ERK and JNK phosphorylation but had little effect on Akt phosphorylation. Collectively these findings indicate astaxanthin is a very effective antioxidant for ameliorating insulin resistance by protecting cells from oxidative stress generated by various stimuli including TNF α and palmitate.

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23715867

[PubMed - indexed for MEDLINE]

Astaxanthin reduces type 2 diabetic-associated cognitive decline in rats via activation of PI3K/Akt and attenuation of oxidative stress.

[Li X](#)¹, [Qi Z](#)², [Zhao L](#)³, [Yu Z](#)⁴.

Author information

Abstract

Astaxanthin (AST) is an oxygenated derivative of carotenoid, which possesses a strong antioxidant activity. AST can effectively remove active oxygen from the body, and is thus considered to have an important role in disease prevention and treatment. The present study aimed to determine the effects of AST on type 2 diabetic-associated cognitive decline (DACD) in rats. Rats were intraperitoneally injected with streptozotocin (STZ), in order to establish a model of diabetes mellitus (DM). A total of 40 rats were randomly divided into five groups: The control group, the DM group, the AST (50 mg/kg) group, the AST (100 mg/kg) group, and the AST+LY294002 group (AST, 50 mg/kg and LY, 0.25 µg/100 g). Following a 14-day treatment with AST, the body weight, blood glucose levels and cognitive function were determined. In addition, the protein expression levels of phosphatidylinositol 3-kinase (PI3K)/Akt, glutathione peroxidase and superoxide dismutase activity, glutathione and malondialdehyde content, and inducible nitric oxide synthase (iNOS), caspase-3 and caspase-9 activity were detected in the rats with DM. AST clearly augmented body weight and reduced blood glucose levels in rats with DM. Furthermore, treatment with AST significantly improved the cognitive function of rats with DM. Treatment with AST activated the PI3K/Akt pathway, and suppressed oxidative stress in the DM rats. In the cerebral cortex and hippocampus of the rats with DM, the activities of iNOS, caspase-3 and caspase-9 were markedly reduced. Furthermore, treatment with the Akt inhibitor LY294002 reduced the effectiveness of AST on DACD in rats. In conclusion, AST may reduce type 2 DACD in rats via activation of PI3K/Akt and attenuation of oxidative stress.

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26648531

[PubMed - in process]

[Life Sci.](#) 2007 Jan 16;80(6):522-9. Epub 2006 Oct 12.

Astaxanthin ameliorates features of metabolic syndrome in SHR/NDmcr-cp.

[Hussein G](#), [Nakagawa T](#), [Goto H](#), [Shimada Y](#), [Matsumoto K](#), [Sankawa U](#), [Watanabe H](#).

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Glucose and lipid metabolic parameters play crucial roles in metabolic syndrome and its major feature of insulin resistance. This study was designed to investigate whether dietary astaxanthin oil (ASX-O) has potential effects on metabolic syndrome features in an SHR/NDmcr-cp (cp/cp) rat model. Oral administration of ASX (50 mg/kg/day) for 22 weeks induced a significant reduction in arterial blood pressure in SHRcp. It also significantly reduced the fasting blood glucose level, homeostasis index of insulin resistance (HOMA-IR), and improved insulin sensitivity. The results also showed an improved adiponectin level, a significant increase in high-density lipoprotein cholesterol, a significant decrease in plasma levels of triglycerides, and non-esterified fatty acids. Additionally, ASX showed significant effects on the white adipose tissue by decreasing the size of the fat cells. These results suggest that ASX ameliorates insulin resistance by mechanisms involving the increase of glucose uptake, and by modulating the level of circulating lipid metabolites and adiponectin.

Publication Types:

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ASTAXANTHIN REDUCES OXIDATIVE STRESS IN DIABETIC RATS BY REGULATING A VARIETY OF TARGETS.

Diabetes Metab Syndr Obes. 2020 Nov 11;13:4281-4295.
doi: 10.2147/DMSO.S274315. eCollection 2020.

Network Pharmacology Combined with Transcriptional Analysis to Unveil the Biological Basis of Astaxanthin in Reducing the Oxidative Stress Induced by Diabetes Mellitus

[Xueliang Sun](#)^{1,2}, [Yanbin Ji](#)², [Ayesha Tahir](#)³, [Jun Kang](#)¹

- PMID: [33204134](#)
- PMCID: [PMC7667204](#)
- DOI: [10.2147/DMSO.S274315](#)

Abstract

Purpose: Astaxanthin (Ast) has been reported to reduce oxidative stress induced by diabetes mellitus (DM). The aim of this research was to give a systematic overview of the biological basis for this process.

Methods: Ast-targeted proteins were collected from the BATMAN database, Comparative Toxicogenomics Database, and STITCH database. Putative DM-related protein targets were collected from the GeneCards database. A DM-rat model was then built with streptozotocin (STZ) combined with a high-sugar, high-fat diet for 30 days. Total cholesterol (TC), triglycerides (TGs), and insulin levels were examined using whole tail-vein blood from overnight-fasted rats. SOD, GSH, and MDA activity was detected in liver tissue ($p < 0.05$). In addition, we used RNA-sequencing analysis to detect gene-transcription level in liver tissue of rats and GO biological process analysis to show all the $\log_2FC \geq 2$ genes in the Ast-fed DM rats compared with the DM group using the STRING database. Ast-intersecting targets were collected with Venn analysis. Docking analysis between Ast and targeted proteins was done with the SwissDock server. Ast targets-pathway networks were built using Cytoscape 3.7.2 software.

J Agric Food Chem. 2020 Mar 18;68(11):3649-3655.

doi: 10.1021/acs.jafc.0c00784. Epub 2020 Mar 6.

Hydrophilic Astaxanthin: PEGylated Astaxanthin Fights Diabetes by Enhancing the Solubility and Oral Absorbability

[Yanjun Liu](#)¹, [Lu Yang](#)¹, [Yongli Guo](#)¹, [Ting Zhang](#)¹, [Xing Qiao](#)¹, [Jingfeng Wang](#)¹, [Jie Xu](#)¹, [Changhu Xue](#)^{1,2}

- PMID: [32118432](#)
- DOI: [10.1021/acs.jafc.0c00784](#)

Abstract

To develop hydrophilic astaxanthin with significantly enhanced solubility and stability, astaxanthin polyethylene glycol succinate (APGS) was synthesized by esterification of an astaxanthin succinate diester with polyethylene glycol 1000. The chemical structure of the hydrophilic derivative was confirmed by ¹H nuclear magnetic resonance and mass spectra. APGS showed better solubility than free astaxanthin in water and enhanced bioavailability compared to that of free astaxanthin. Additionally, testing the effects on diabetes and inflammation in a high-fat- and high-sucrose-diet-induced insulin-resistant mouse model demonstrated its benefits, suggesting that APGS maintains the health-promoting properties of astaxanthin. These results suggest that APGS could be a better source of hydrophilic astaxanthin.

ASTAXANTHIN SHOWS POTENTIAL FOR THE TREATMENT OF DIABETIC NEPHROPATHY IN RAT STUDY.

Eur J Pharm Biopharm. 2020 Nov;156:143-154.
doi: 10.1016/j.ejpb.2020.09.005. Epub 2020 Sep 13.

Kidney-targeted astaxanthin natural antioxidant nanosystem for diabetic nephropathy therapy

[Zhong Chen](#)¹, [Wenhua Li](#)¹, [Liwang Shi](#)¹, [Lei Jiang](#)¹, [Minghui Li](#)¹, [Changmei Zhang](#)², [Haisheng Peng](#)³

- PMID: **32937179**
- DOI: [10.1016/j.ejpb.2020.09.005](https://doi.org/10.1016/j.ejpb.2020.09.005)

Abstract

Diabetic nephropathy (DN) is a frequent and severe microvascular complication associated with oxidative stress of diabetes mellitus. A novel astaxanthin-based natural antioxidant nanosystem, namely AST-GLU-LIP, with preferential renal uptake and bioavailability were prepared and applied for treatment of diabetic nephropathy in rats. Our results of kidney-targeted evaluation showed that glucose-PEG₆₀₀-DSPE ligand modified AST liposomes could be specifically transported by overexpressed GLUT1 on the membrane of glomerular mesangial cells and achieved excellent kidney-targeted drug delivery. In addition, the results of pharmacodynamics and therapeutics in DN rats demonstrated that AST-GLU-LIP could improve the bioavailability and antioxidant capacity of AST to scavenge redundant ROS induced by oxidative stress. AST-GLU-LIP could also significantly improve the renal pathological morphology to protect the kidney as a therapeutic drug for diabetic nephropathy.

Astaxanthin from shrimp by-products ameliorates nephropathy in diabetic rats.

[Sila A¹](#), [Ghlyssi Z](#), [Kamoun Z](#), [Makni M](#), [Nasri M](#), [Bougatef A](#), [Sahnoun Z](#).

Author information

Abstract

AIM:

This study investigated the hypoglycemic and antioxidant effects of shrimp astaxanthin on the kidney of alloxan-induced diabetic rats.

METHODS:

Animals were distributed into four groups of six rats each: a control group (C), a diabetic group (D), a diabetic group supplemented with Astaxanthin (D+As) dissolved in olive oil and a diabetic group supplemented with olive oil (D+OO). In vitro antidiabetic effect was tested in plasma and kidney tissue.

RESULTS:

The group D of rats showed significant ($P < 0.05$) increase of glycemia, creatinine, urea and uric acid levels compared to those of the control group (C). Moreover, plasma and kidney malondialdehyde (MDA) and protein carbonyl (PCO) levels for the rats of the group D were significantly increased compared to the control group. Contrariwise, antioxidant enzyme activities, such as catalase (EC 1.11.1.6), superoxide dismutase (EC 1.15.1.1) and non-enzymatic levels of reduced glutathione, were significantly ($P < 0.05$) decreased in the plasma and kidney of diabetic rats compared to the control ones.

The astaxanthin supplementation in rats diet improved the antioxidant enzyme activities and significantly decreased the MDA and PCO levels compared to diabetic rats. Indeed, no significant ($P \geq 0.05$) improvement was observed for the fourth group (D+OO) compared to the control group (C). Histological analysis of kidney showed glomerular hypertrophy and tubular dilatation for the diabetic rats. For D+As rats, these histopathological changes were less prominent.

CONCLUSIONS:

Our results suggest that shrimp astaxanthin may play an important role in reduction of oxidative damage and could prevent pathological changes in diabetic rats suggesting promising application of shrimp astaxanthin in diabetes treatment.

PMID:

24821271

[PubMed - indexed for MEDLINE]

Astaxanthin improves cognitive deficits from oxidative stress, nitric oxide synthase and inflammation through upregulation of PI3K/Akt in diabetes rat.

[Xu L](#)¹, [Zhu J](#)², [Yin W](#)³, [Ding X](#)³.

Author information

Abstract

Diabetes-induced cognitive deficit (DICD) is a prevalent disease with substantial morbidity and mortality and as a global health problem with serious economic burdens. Astaxanthin (AST) has a good prospect in production of nutritional, medical, and particularly functional health drug. The present study was aimed to study the effect of AST on DICD in diabetes mellitus (DM) rat through suppression of oxidative stress, nitric oxide synthase (NOS) pathway, inflammatory reaction and upregulation of PI3K/Akt. In the study, Morris water maze test was used to detect the cognitive function of DM rat. Afterwards, we measured the body weight and blood glucose levels of DM rats. Then, oxidative stress, the activities of eNOS and iNOS, and inflammatory factors were analyzed using a commercial kit in cerebral cortex and hippocampus. Finally, the caspase-3/9 and phosphoinositide 3-kinase (PI3K)/Akt expressions were also checked out with Real Time PCR and immunoblotting, respectively. In this experiment, AST could available enhance the body weight and reduce blood glucose levels of DM rats. Moreover, AST could observably perfect cognitive function of DM rat. Next, the activities of oxidative stress, nitric oxide synthase and inflammation were distinctly diminution in DM rat, after the treatment of AST. Furthermore, our present results demonstrated that AST had the protective effect on the brain cell of DM rat, decreased the caspase-3/9 expression and promoted the expression of PI3K/Akt in cerebral cortex and hippocampus.

KEYWORDS:

Diabetes-induced cognitive deficit; PI3K/Akt; astaxanthin; inflammatory; nitric oxide synthase; oxidative stress

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Anti-inflammatory Effect of Astaxanthin on the Sickness Behavior Induced by Diabetes Mellitus.

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Author information

Abstract

Chronic inflammation appears to play a critical role in sickness behavior caused by diabetes mellitus. Astaxanthin has been used in treating diabetes mellitus and diabetic complications because of its neuroprotective and anti-inflammatory actions. However, whether astaxanthin can improve sickness behavior induced by diabetes and its potential mechanisms are still unknown. The aim of this study was to investigate the effects of astaxanthin on diabetes-elicited abnormal behavior in mice and its corresponding mechanisms. An experimental diabetic model was induced by streptozotocin (150 mg/kg) and astaxanthin (25 mg/kg/day) was provided orally for 10 weeks. Body weight and water consumption were measured, and the sickness behavior was evaluated by the open field test (OFT) and closed field test (CFT). The expression of glial fibrillary acidic protein (GFAP) was measured, and the frontal cortical cleaved caspase-3 positive cells, interleukin-6 (IL-6), and interleukin-1 β (IL-1 β) expression levels were also investigated. Furthermore, cystathionine β -synthase (CBS) in the frontal cortex was detected to determine whether the protective effect of astaxanthin on sickness behavior in diabetic mice is closely related to CBS. As expected, we observed that astaxanthin improved general symptoms and significantly increase horizontal distance and the number of crossings in the OFT and CFT. Furthermore, data showed that astaxanthin could decrease GFAP-positive cells in the brain and down-regulate the cleaved caspase-3, IL-6, and IL-1 β , and up-regulate CBS in the frontal cortex. These results suggest that astaxanthin provides neuroprotection against diabetes-induced sickness behavior through inhibiting inflammation, and the protective effects may involve CBS expression in the brain.

KEYWORDS:

Astaxanthin; Cystathionine β -synthase; Diabetes; Inflammation

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Astaxanthin protects mesangial cells from hyperglycemia-induced oxidative signaling.

[Manabe E](#), [Handa O](#), [Naito Y](#), [Mizushima K](#), [Akagiri S](#), [Adachi S](#), [Takagi T](#), [Kokura S](#), [Maoka T](#), [Yoshikawa T](#).

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Astaxanthin (ASX) is a carotenoid that has potent protective effects on diabetic nephropathy in mice model of type 2 diabetes. In this study, we investigated the protective mechanism of ASX on the progression of diabetic nephropathy using an in vitro model of hyperglycemia, focusing on mesangial cells. Normal human mesangial cells (NHMCs) were cultured in the medium containing normal (5 mM) or high (25 mM) concentrations of D-glucose. Reactive oxygen species (ROS) production, the activation of nuclear transcription factors such as nuclear factor kappa B (NFkappaB) and activator protein-1 (AP-1), and the expression/production of transforming growth factor-beta 1 (TGFbeta(1)) and monocyte chemoattractant protein-1 (MCP-1) were evaluated in the presence or absence of ASX. High glucose (HG) exposure induced significant ROS production in mitochondria of NHMCs, which resulted in the activation of transcription factors, and subsequent expression/production of cytokines that plays an important role in the mesangial expansion, an important event in the pathogenesis of diabetic nephropathy. ASX significantly suppressed HG-induced ROS production, the activation of transcription factors, and cytokine expression/production by NHMCs. In addition, ASX accumulated in the mitochondria of NHMCs and reduced the production of ROS-modified proteins in mitochondria. ASX may prevent the progression of diabetic nephropathy mainly through ROS scavenging effect in mitochondria of mesangial cells and thus is expected to be very useful for the prevention of diabetic nephropathy.

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Inhibitory effect of astaxanthin combined with Flavangenol on oxidative stress biomarkers in streptozotocin-induced diabetic rats.

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In this study, the effect of dietary antioxidants, such as astaxanthin and Flavangenol, and a combination of both, in counteracting oxidative stress in streptozotocin-induced diabetes was investigated. Streptozotocin-induced diabetic rats were divided into four groups: control, astaxanthin, Flavangenol, and combined astaxanthin and Flavangenol (mix group). Each group other than the control group was fed with an astaxanthin diet (0.1 g/kg), Flavangenol diet (2.0 g/kg), or an astaxanthin (0.1 g/kg)-Flavangenol (2.0 g/kg) mixture diet, respectively. After 12 weeks of feeding, the results showed that the lipid peroxide levels of plasma and lens and the plasma triglyceride (TG) level in the mix group were significantly decreased by 44%, 20%, and 20%, respectively, compared with the control group. In the mix group, lipid peroxidation was also significantly reduced by 70% in the liver and 20% in the kidney compared with the control group. Furthermore, the level of urinary 8-hydroxy-2'-deoxyguanosine (8-OHdG) in the mix group was significantly lower, 36%, than the control group. The alpha-tocopherol concentrations in the plasma, liver, and kidney in the astaxanthin and mix groups were significantly higher, 3-9 times, than in the control group. The degree of cataract formation in the Flavangenol and mix groups tended to be lower than the control group. These results indicate that the combination of astaxanthin with Flavangenol has an improved protective effect on oxidative stress associated with streptozotocin-induced diabetes than either agent used alone. Thus, this combination may be beneficial in preventing the progression of diabetic complications.

PMID: 19326340 [PubMed - indexed for MEDLINE]

Effect of astaxanthin in combination with alpha-tocopherol or ascorbic acid against oxidative damage in diabetic ODS rats.

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The present study was performed to investigate the effect of astaxanthin in combination with other antioxidants against oxidative damage in streptozotocin (STZ)-induced diabetic Osteogenic Disorder Shionogi (ODS) rats. Diabetic-ODS rats were divided into five groups: control, astaxanthin, ascorbic acid, alpha-tocopherol, and tocotrienol. Each of the four experimental groups was administered a diet containing astaxanthin (0.1 g/kg), in combination with ascorbic acid (3.0 g/kg), alpha-tocopherol (0.1 g/kg), or tocotrienol (0.1 g/kg) for 20 wk. The effects of astaxanthin with other antioxidants on lipid peroxidation, urinary 8-hydroxy-2-deoxyguanosine (8-OHdG) excretion, serum creatinine (Cr) level, creatinine clearance (Ccr), and urinary protein content were assessed. The serum lipid peroxide levels and chemiluminescent (CL) intensity in the liver of the alpha-tocopherol and tocotrienol groups were significantly reduced in comparison to that of the control group. In the alpha-tocopherol group, urinary 8-OHdG excretion, serum Cr level, Ccr, urinary albumin excretion, and urinary protein concentration were significantly decreased as compared with those in the control group. Additionally, the CL intensity in the kidney of the alpha-tocopherol group was significantly lower, but that of the ascorbic acid group was significantly higher than that in the control group. These results indicate that dietary astaxanthin in combination with alpha-tocopherol has an inhibitory effect on oxidative stress. On the other hand, our study suggests that excessive ascorbic acid intake increases lipid peroxidation in diabetic rats.

PMID: 18797156 [PubMed - indexed for MEDLINE]

[Int J Mol Med](#). 2006 Oct;18(4):685-95.

Microarray profiling of gene expression patterns in glomerular cells of astaxanthin-treated diabetic mice: a nutrigenomic approach.

[Naito Y](#), [Uchiyama K](#), [Mizushima K](#), [Kuroda M](#), [Akagiri S](#), [Takagi T](#), [Handa O](#), [Kokura S](#), [Yoshida N](#), [Ichikawa H](#), [Takahashi J](#), [Yoshikawa T](#).

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We have demonstrated that astaxanthin reduces glomerular oxidative stress as well as inhibits the increase in urinary albumin in diabetic db/db mice. The aim of the present study was to determine the gene expression patterns in the glomerular cells of the diabetic mouse kidney, and to investigate the effects of astaxanthin on the expression of these genes using a high-density DNA microarray. The diet administered to the astaxanthin-supplementation group was prepared by mixing a control powder with astaxanthin at a concentration of 0.02%. Glomerular cells were obtained from the kidneys of mice by laser capture microdissection. Preparation of cRNA and target hybridization were performed according to the Affymetrix GeneChip eukaryotic small sample target labeling assay protocol. The gene expression profile was evaluated by the mouse expression set 430A GeneChip. Array data analysis was carried out using Affymetrix GeneChip operating and Ingenuity Pathway analysis software. Comparison between diabetic db/db and non-diabetic db/m mice revealed that 779 probes (3.1%) were significantly affected, i.e. 550 probes were up-regulated, and 229 probes were down-regulated, both at levels of ≥ 1.5 -fold in the diabetic mice. Ingenuity signal analysis of 550 up-regulated probes revealed the mitochondrial oxidative phosphorylation pathway as the most significantly affected canonical pathway. The affected genes were associated with complexes I, III, and IV located on the mitochondrial inner membrane, and the expression levels of these genes were decreased in mice treated with astaxanthin as compared to the levels in the control mice. In addition, the expression of many genes associated with oxidative stress, collagen synthesis, and transforming growth factor-beta signaling was enhanced in the diabetic mice, and this enhancement was slightly inhibited in the astaxanthin-treated mice. In conclusion, this genome-wide nutrigenomics approach provided insight into genes and putative genetic pathways that are thought to be affected by stimulation by high-glucose concentrations. In addition, the present approach may help us gain a better understanding of the genes and pathways involved in the anti-diabetic mechanism of astaxanthin.

Publication Types:

PMID: 16964424 [PubMed - indexed for MEDLINE]

[Biofactors](#). 2004;20(1):49-59.

Prevention of diabetic nephropathy by treatment with astaxanthin in diabetic db/db mice.

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Oxidative stress is implicated as an important mechanism by which diabetes causes nephropathy. Astaxanthin, which is found as a common pigment in algae, fish, and birds, is a carotenoid with significant potential for antioxidative activity. In this study, we examined whether chronic administration of astaxanthin could prevent the progression of diabetic nephropathy induced by oxidative stress in mice. We used female db/db mice, a rodent model of type 2 diabetes, and their non-diabetic db/m littermates. The mice were divided into three groups as follows: non-diabetic db/m, diabetic db/db, and diabetic db/db treated with astaxanthin. Blood glucose level, body weight, urinary albumin, and urinary 8-hydroxydeoxyguanosine (8-OHdG) were measured during the experiments. Histological and 8-OHdG immunohistochemical studies were performed for 12 weeks from the beginning of treatment. After 12 weeks of treatment, the astaxanthin-treated group showed a lower level of blood glucose compared with the non-treated db/db group; however, both groups had a significantly high level compared with the db/m mice. The relative mesangial area calculated by the mesangial area/total glomerular area ratio was significantly ameliorated in the astaxanthin-treated group compared with the non-treated db/db group. The increases in urinary albumin and 8-OHdG at 12 weeks of treatment were significantly inhibited by chronic treatment with astaxanthin. The 8-OHdG immunoreactive cells in glomeruli of non-treated db/db mice were more numerous than in the astaxanthin-treated db/db mice. In this study, treatment with astaxanthin ameliorated the progression and acceleration of diabetic nephropathy in the rodent model of type 2 diabetes. The results suggested that the antioxidative activity of astaxanthin reduced the oxidative stress on the kidneys and prevented renal cell damage. In conclusion, administration of astaxanthin might be a novel approach for the prevention of diabetes nephropathy.

PMID: 15096660 [PubMed - indexed for MEDLINE]

Astaxanthin protects beta-cells against glucose toxicity in diabetic db/db mice.

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Oxidative stress induced by hyperglycemia possibly causes the dysfunction of pancreatic beta-cells and various forms of tissue damage in patients with diabetes mellitus. Astaxanthin, a carotenoid of marine microalgae, is reported as a strong anti-oxidant inhibiting lipid peroxidation and scavenging reactive oxygen species. The aim of the present study was to examine whether astaxanthin can elicit beneficial effects on the progressive destruction of pancreatic beta-cells in db/db mice--a well-known obese model of type 2 diabetes. We used diabetic C57BL/KsJ-db/db mice and db/m for the control. Astaxanthin treatment was started at 6 weeks of age and its effects were evaluated at 10, 14, and 18 weeks of age by non-fasting blood glucose levels, intraperitoneal glucose tolerance test including insulin secretion, and beta-cell histology. The non-fasting blood glucose level in db/db mice was significantly higher than that of db/m mice, and the higher level of blood glucose in db/db mice was significantly decreased after treatment with astaxanthin. The ability of islet cells to secrete insulin, as determined by the intraperitoneal glucose tolerance test, was preserved in the astaxanthin-treated group. Histology of the pancreas revealed no significant differences in the beta-cell mass between astaxanthin-treated and -untreated db/db mice. In conclusion, these results indicate that astaxanthin can exert beneficial effects in diabetes, with preservation of beta-cell function. This finding suggests that anti-oxidants may be potentially useful for reducing glucose toxicity.

PMID: 12688512 [PubMed - indexed for MEDLINE]

Astaxanthin protects β -cells against glucose toxicity in diabetic db/db mice

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Oxidative stress induced by hyperglycemia possibly causes the dysfunction of pancreatic β -cells and various forms of tissue damage in patients with diabetes mellitus.

Astaxanthin, a carotenoid of marine microalgae, is reported as a strong anti-oxidant inhibiting lipid peroxidation and scavenging reactive oxygen species. The aim of the present study was to examine whether astaxanthin can elicit beneficial effects on the progressive destruction of pancreatic β -cells in db/db mice β – a well-known obese model of type 2 diabetes. We used diabetic C57BL/KsJ-db/db mice and db/m for the control. Astaxanthin treatment was started at 6 weeks of age and its effects were evaluated at 10, 14, and 18 weeks of age by non-fasting blood glucose levels, intraperitoneal glucose tolerance test including insulin secretion, and β -cell histology. The non-fasting blood glucose level in db/db mice was significantly higher than that of db/m mice, and the higher level of blood glucose in db/db mice was significantly decreased after treatment with astaxanthin. The ability of islet cells to secrete insulin, as determined by the intraperitoneal glucose tolerance test, was preserved in the astaxanthin-treated group. Histology of the pancreas revealed no significant differences in the β -cell mass between astaxanthin-treated and -untreated db/db mice. In conclusion, these results indicate that astaxanthin can exert beneficial effects in diabetes, with preservation of β -cell function. This finding suggests that anti-oxidants may be potentially useful for reducing glucose toxicity.

[J Am Geriatr Soc.](#) 2015 Jun;63(6):1271-3. doi: 10.1111/jgs.13505.

Astaxanthin Improves Nonalcoholic Fatty Liver Disease in Werner Syndrome with Diabetes Mellitus.

[Takemoto M](#)^{1,2}, [Yamaga M](#)^{1,2}, [Furuichi Y](#)³, [Yokote K](#)^{1,2}.

[Author information](#)

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26096415

[PubMed - indexed for MEDLINE]

[Chem Biol Interact.](#) 2010 Aug 5;186(3):306-15. Epub 2010 May 31.

Astaxanthin ameliorates the redox imbalance in lymphocytes of experimental diabetic rats.

[Otton R](#), [Marin DP](#), [Bolin AP](#), [Santos Rde C](#), [Polotow TG](#), [Sampaio SC](#), [de Barros MP](#).

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Abstract

Diabetes mellitus is a syndrome of impaired insulin secretion/sensitivity and frequently diagnosed by hyperglycemia, lipid abnormalities, and vascular complications. The diabetic 'glucolipotoxicity' also induces immunodepression in patients by redox impairment of immune cells. Astaxanthin (ASTA) is a pinkish-orange carotenoid found in many marine foods (e.g. shrimp, crabs, salmon), which has powerful antioxidant, photoprotective, antitumor, and cardioprotective properties. Aiming for an antioxidant therapy against diabetic immunodepression, we here tested the ability of prophylactic ASTA supplementation (30 days, 20 mg ASTA/kg BW) to oppose the redox impairment observed in isolated lymphocytes from alloxan-induced diabetic Wistar rats. The redox status of lymphocytes were thoroughly screened by measuring: (i) production of superoxide ($O_2^{\cdot-}$), nitric oxide (NO), and hydrogen peroxide (H_2O_2); (ii) cytosolic Ca^{2+} ; (iii) indexes of oxidative injury; and (iv) activities of major antioxidant enzymes. Hypolipidemic and antioxidant effects of ASTA in plasma of ASTA-fed/diabetic rats were apparently reflected in the circulating lymphocytes, since lower activities of catalase, restored ratio between glutathione peroxidase and glutathione reductase activities and lower scores of lipid oxidation were concomitantly measured in those immune cells. Noteworthy, lower production of NO and $O_2^{\cdot-}$ (precursors of peroxynitrite), and lower cytosolic Ca^{2+} indicate a hypothetical antiapoptotic effect of ASTA in diabetic lymphocytes. However, questions are still open regarding the proper ASTA supplementation dose needed to balance efficient antioxidant protection and essential NO/ H_2O_2 -mediated proliferative capacities of diabetic lymphocytes.

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ASTAXANTHIN'S MECHANISM OF ACTION IN SENSITIZING INSULIN SIGNALING DEMONSTRATED IN CELL STUDY.

Mar Drugs. 2020 Sep 28;18(10):495.
doi: 10.3390/md18100495.

Astaxanthin Inhibits p70 S6 Kinase 1 Activity to Sensitize Insulin Signaling

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- PMCID: [PMC7600478](#)
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Abstract

Astaxanthin (AST) is a carotenoid with therapeutic values on hyperglycemia and diabetic complications. The mechanisms of action of AST remain incompletely understood. p70 S6 kinase 1 (S6K1) is a serine/threonine kinase that phosphorylates insulin receptor substrate 1 (IRS-1)^{S1101} and desensitizes the insulin receptor (IR). Our present study aims to determine if AST improves glucose metabolisms by targeting S6K1. Western blot analysis revealed that AST inhibited the phosphorylation of two S6K1 substrates, S6^{S235/236} and IRS-1^{S1101}, but enhanced the phosphorylation of AKT^{T308}, AKT^{S473}, and S6K1^{T389} by feedback activation of the phosphatidylinositol-3 (PI-3) kinase in 3T3-L1 adipocytes and L6 myotubes. In vitro kinase assays revealed that AST inhibited S6K1 activity with an IC₅₀ value of approximately 13.8 μM. AST increased insulin-induced IR tyrosine phosphorylation and IRS-1 binding to the p85 subunit of PI-3 kinase. Confocal microscopy revealed that AST increased the translocation of the glucose transporter 4 (GLUT4) to the plasma membrane in L6 cells. Glucose uptake assays using a fluorescent dye, 2-NBDG (2-N-(Nitrobenz-2-oxa-1,3-diazol-4-yl)amino)-2-deoxyglucose), revealed that AST increased glucose uptake in 3T3-L1 adipocytes and L6 myotubes under insulin resistance conditions. Our study identifies S6K1 as a previously unrecognized molecular target of AST and provides novel insights into the mechanisms of action of AST on IR sensitization.

[Int Endod J.](#) 2010 Jun 8. [Epub ahead of print]

In vivo astaxanthin treatment partially prevents antioxidant alterations in dental pulp from alloxan-induced diabetic rats.

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Abstract

Leite MF, de Lima A, Massuyama MM, Otton R. In vivo astaxanthin treatment partially prevents antioxidant alterations in dental pulp from alloxan-induced diabetic rats. *International Endodontic Journal*. Abstract Aim To evaluate the effect of astaxanthin on antioxidant parameters of dental pulp from diabetic rats. The hypothesis tested was that supplementation of diabetic rats with astaxanthin might eliminate, or at least attenuate, the defect in their antioxidative status. Methodology Wistar rats (n = 32) were divided into four groups: untreated control, treated control, untreated diabetic and treated diabetic rats. A prophylactic dose of astaxanthin (20 mg kg⁻¹ body weight) was administered daily by gavage for 30 days. On day 23, diabetes was induced by injection of alloxan (60 mg kg⁻¹ body weight). After 7 days of diabetes induction, the rats were killed, and pulp tissue from incisor teeth removed. Superoxide dismutase (SOD), catalase, glutathione peroxidase (GPx) and reductase activities were determined. Data were compared by anova and the Newman-Keuls test (P < 0.05). Results Diabetes caused a reduction in SOD, GPx and reductase activity in dental pulp tissue. Astaxanthin had no effect on SOD and catalase activities; however, it stimulated GPx in control and diabetic rats. Conclusions Diabetes altered the antioxidant system in dental pulp tissue; astaxanthin partially improved the diabetic complications.

PMID: 20546046 [PubMed - as supplied by publisher]

[Arch Oral Biol.](#) 2010 Jul;55(7):479-85.

Astaxanthin restores the enzymatic antioxidant profile in salivary gland of alloxan-induced diabetic rats.

[Leite MF](#), [Lima AM](#), [Massuyama MM](#), [Otton R](#).

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Abstract

OBJECTIVE: To evaluate the effect of astaxanthin on antioxidant parameters of salivary gland from diabetic rats. The hypothesis of the study was whether the supplementation of diabetic rats with astaxanthin might antagonize, or at least prevent, the defect in their antioxidative status.

DESIGN: Wistar rats (n=32) were divided in 4 groups: untreated control, treated control, untreated diabetic and treated diabetic rats. Astaxanthin (20mg/kg body weight) was administered daily by gavage for 30 days. On day 23, diabetes was induced by injection of alloxan (60 mg/kg body weight). After 7 days of diabetes induction, the rats were killed and submandibular and parotid removed. Superoxide dismutase (SOD), catalase, glutathione peroxidase and reductase activities and the content of thiol groups were determined. Data were compared by ANOVA and the Tukey test ($p<0.05$).

RESULTS: Diabetes caused a reduction of SOD, and thiol content and increase of catalase and glutathione peroxidase activities of submandibular gland whilst in the parotid gland diabetes caused an increase of thiol content and no effect in the antioxidant system. The astaxanthin restores the enzymatic activities in the salivary gland, however does not prevent its oxidative damage.

CONCLUSION: The submandibular gland presented more susceptibility to oxidative alterations induced by diabetes. Astaxanthin presented a positive effect on the oxidative protection of the salivary gland from diabetic rats.

PMID: 20510163 [PubMed - in process]

[J Agric Food Chem.](#) 2009 Oct 14;57(19):8793-7.

Protection against oxidative stress, inflammation, and apoptosis of high-glucose-exposed proximal tubular epithelial cells by astaxanthin.

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Abstract

Astaxanthin is a carotenoid with powerful antioxidant properties that exists naturally in various plants, algae, and seafood. The purpose of the present study is to examine the protective action of astaxanthin against high-glucose-induced oxidative stress, inflammation, and apoptosis in proximal tubular epithelial cells (PTECs). To assess the efficacy of astaxanthin, several key markers and activities were measured, including lipid peroxidation, total reactive species (RS), superoxide (*O(2)), nitric oxide (NO*), and peroxynitrite (ONOO(-)), as well as expressions of inflammatory proteins, inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2), nuclear factor-kappa B (NF-kappaB) nuclear translocation, and levels of Bcl2/Bax protein. Results showed that astaxanthin effectively suppressed lipid peroxidation, total RS, *O(2) , NO* , ONOO(-) , iNOS and COX-2 protein levels, NF-kappaB nuclear translocation, and pro-apoptotic Bax, whereas it increased anti-apoptotic Bcl2 protein levels. On the basis of these findings, it was concluded that in PTECs, astaxanthin has a protective efficacy against several deleterious effects caused by high glucose exposure and proposed that astaxanthin should be explored further as a potential antidiabetic remedy for the treatment of diabetic nephropathy.

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Ameliorative effect of astaxanthin on endothelial dysfunction in streptozotocin-induced diabetes in male rats.

[Zhao ZW](#), [Cai W](#), [Lin YL](#), [Lin QF](#), [Jiang Q](#), [Lin Z](#), [Chen LL](#).

Source

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Abstract

The present study was designed to examine whether astaxanthin (ASX, 3,3-dihydroxybeta, beta-carotene-4,4-dione, CAS 472-61-7), a dietary antioxidant carotenoid that is naturally present in algae, crustaceans, and fish, has a protective effect on endothelial dysfunction of aortas in diabetic rats and the possible molecular mechanism involved. Male Wistar rats were randomly divided into four groups: control rats, diabetic rats, diabetic rats treated with ASX (10 mg/kg/d), and control rats treated with ASX. Type 1 diabetes was induced by a single intraperitoneal injection of streptozotocin (STZ; 60 mg/kg). STZ-induced diabetes in rats was complicated with excessive oxidative stress and endothelial dysfunction, increased serum oxidized low-density lipoprotein (ox-LDL) and aortic malondialdehyde (MDA) levels, inhibited endothelium-dependent vasorelaxation to acetylcholine (ACh) and unaffected endothelium-dependent vasorelaxation to sodium nitroprusside (SNP). Simultaneously, lectin-like oxLDL receptor-1 (LOX-1) expression was enhanced and endothelial nitric oxide (NO) synthase (eNOS) expression was reduced in the aortas of diabetic rats. ASX treatment could significantly decrease serum oxLDL and aortic MDA levels, attenuate blunted endothelium-dependent vasodilator responses to ACh, upregulate eNOS expression, and decrease LOX-1 expression. These results indicated that ASX could ameliorate diabetic endothelial dysfunction by inhibiting the ox-LDL/LOX-1-eNOS pathway. Treatment with ASX might be clinically useful for diabetic complications associated with endothelial dysfunction.

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High dose astaxanthin lowers blood pressure and increases insulin sensitivity in rats: are these effects interdependent?

[Preuss HG](#), [Echard B](#), [Yamashita E](#), [Perricone NV](#).

Source

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Abstract

The present investigation in Sprague-Dawley rats (SD) was designed to examine effects of astaxanthin (Asta) at different doses on elevated blood pressure (BP) and glucose-insulin perturbations produced by heavy sucrose ingestion. We also examined effects of Asta on BP during restraint stress. SD were divided into six groups each containing eight rats. All SD ate a basic diet of ground regular rat chow with sucrose added at 30% w/w. The Control group received only the basic diet containing added sucrose, while the other five groups each received the same diet with added test material: captopril, (30 mg/Kg), pioglitazone (15.0 mg/Kg), low Asta (25 mg/Kg), medium Asta (50 mg/kg) or high Asta (100 mg/Kg). Many tests were carried out to examine the mechanisms behind the effects of Asta on BP (serum ACE activity, losartan challenge, and LNAME challenge) and the glucose-insulin system (glucose tolerance, HOMA measurement, and insulin challenge). In SD, a relatively low dose of Asta decreased SBP, but produced no major changes in the glucose-insulin system simulating results from a previous study using Zucker Fatty Rats. Increasing the dose of Asta resulted in both a lowering of elevated systolic BP and enhanced insulin sensitivity determined by many different estimations. BP lowering was consistent with changes in the renin-angiotensin (RAS) and nitric oxide (NO) systems. At the examined doses of each, captopril lowered BP in SD without influencing glucose-insulin metabolism, whereas pioglitazone favorably affected glucose-insulin metabolism while showing essentially no effects on BP. Accordingly, Asta beneficially affects both sucrose-induced elevations of BP and insulin resistance at relatively high doses in SD. Also, Asta at higher doses lessens restraint stress, whereas, captopril and pioglitazone did not at the doses examined, even though they influenced the BP and glucose-insulin systems respectively.

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PMCID: PMC3039228

ROS production in neutrophils from alloxan-induced diabetic rats treated in vivo with astaxanthin.

[Marin DP](#), [Bolin AP](#), [Macedo Rde C](#), [Sampaio SC](#), [Otton R](#).

Source

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Abstract

BACKGROUND: *Astaxanthin (ASTA) is a carotenoid which has powerful antioxidant, anti-tumor, anti-diabetic, anti-inflammatory and cardioprotective properties. The present study investigated the effect of daily ASTA intake on oxidative stress and the functional properties of neutrophils from alloxan-induced diabetic rats.*

METHODS: *Neutrophils isolated from ASTA-fed rats (30days, 20mg ASTA/kg of body weight - BW) induced to diabetes by alloxan treatment (i.p. 75mg/BW) were assessed by: production of superoxide and hydrogen peroxide, nitric oxide, basal calcium release, oxidative damage (TBARS and carbonyls content), and activities of major antioxidant enzymes.*

RESULTS: *Our results show that diabetes promotes a significant oxidative stress in neutrophils. The production of superoxide was significantly increased in neutrophils from diabetic rats and treatment with ASTA was not effective in reducing superoxide levels. At the same time, a reduction in the activity of total superoxide dismutase enzyme was observed, which was not restored after treatment with ASTA. At resting conditions, neutrophils have a higher basal production of hydrogen peroxide, which is enhanced following PMA-stimulation. Treatment with ASTA does not restore values to the basal levels. The indicators of oxidative damage to biomolecules showed that diabetic rats significantly increased the lipid and protein damage, but this change was reversed after treatment with ASTA.*

CONCLUSION: *Our results show that diabetes condition promotes a marked oxidative stress in neutrophils and treatment with ASTA for 30days at a dose of 20mg/kg of BW partially reverses those deleterious effects.*

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Protective actions of microalgae against endogenous and exogenous advanced glycation endproducts (AGEs) in human retinal pigment epithelial cells.

[Sun Z](#), [Liu J](#), [Zeng X](#), [Huangfu J](#), [Jiang Y](#), [Wang M](#), [Chen F](#).

Source

School of Biological Sciences, The University of Hong Kong, Pokfulam Road, Hong Kong, P. R. China.

Abstract

The formation and accumulation of advanced glycation endproducts (AGEs) is a key pathophysiological process involved in various diabetic complications such as diabetic retinopathy. In the present study, for the first time, protective effects of three microalgal strains, including their extracts and active compounds, against both endogenous and exogenous AGEs in cell-based models were investigated. Results showed that in cultured human-derived retinal pigment epithelial ARPE-19 cells, the extract of *Chlorella zofingiensis* and its nutritional ingredient astaxanthin exhibited significant inhibitory effects on the formation of endogenous N(ϵ)-carboxymethyllysine (CML), a key AGE representative, through the suppression of intracellular oxidative stress. On the other hand, extracts of *Chlorella zofingiensis*, *Chlorella protothecoides* and *Nitzschia laevis* as well as their nutritional ingredients, namely astaxanthin, lutein and eicosapentaenoic acid (EPA), attenuated the deleterious effects induced by exogenous AGEs, such as cell proliferation and mRNA upregulation of vascular endothelial growth factor (VEGF) and matrix metalloproteinases (MMP)-2, which are critical steps involved in the pathogenesis of diabetic retinopathy. These results suggested the positive roles of astaxanthin, lutein and EPA in controlling the development of diabetes. These microalgae, therefore, might be regarded as beneficial foods and preventive agent choices for patients with diabetic retinopathy.

PMID: 21779563 [PubMed - in process]

Mar Drugs. 2020 Jul 9;18(7):357.

doi: 10.3390/md18070357.

Impact of Astaxanthin on Diabetes Pathogenesis and Chronic Complications

[Rebecca Landon](#)¹, [Virginie Gueguen](#)², [Hervé Petite](#)¹, [Didier Letourneur](#)², [Graciela Pavon-Djavid](#)², [Fani Anagnostou](#)^{1,3}

- PMID: **32660119**
- PMCID: [PMC7401277](#)
- DOI: [10.3390/md18070357](#)

Free PMC article

Abstract

Oxidative stress (OS) plays a pivotal role in diabetes mellitus (DM) onset, progression, and chronic complications. Hyperglycemia-induced reactive oxygen species (ROS) have been shown to reduce insulin secretion from pancreatic β -cells, to impair insulin sensitivity and signaling in insulin-responsive tissues, and to alter endothelial cells function in both type 1 and type 2 DM. As a powerful antioxidant without side effects, astaxanthin (ASX), a xanthophyll carotenoid, has been suggested to contribute to the prevention and treatment of DM-associated pathologies. ASX reduces inflammation, OS, and apoptosis by regulating different OS pathways though the exact mechanism remains elusive. Based on several studies conducted on type 1 and type 2 DM animal models, orally or parenterally administrated ASX improves insulin resistance and insulin secretion; reduces hyperglycemia; and exerts protective effects against retinopathy, nephropathy, and neuropathy. However, more experimental support is needed to define conditions for its use. Moreover, its efficacy in diabetic patients is poorly explored. In the present review, we aimed to identify the up-to-date biological effects and underlying mechanisms of ASX on the ROS-induced DM-associated metabolic disorders and subsequent complications. The development of an in-depth research to better understand the biological mechanisms involved and to identify the most effective ASX dosage and route of administration is deemed necessary.

Ulcers and Gastrointestinal Health

Astaxanthin at high dosage decreases gastric inflammation in patients with *H. pylori* bacteria present in their gut and increases immunity marker CD4 in randomized, placebo-controlled human clinical study.

[FEMS Immunol Med Microbiol.](#) 2007 Jul;50(2):244-8. Epub 2007 May 23.

Gastric inflammatory markers and interleukins in patients with functional dyspepsia treated with astaxanthin.

[Andersen LP](#), [Holck S](#), [Kupcinskas L](#), [Kiudelis G](#), [Jonaitis L](#), [Janciauskas D](#), [Permin H](#), [Wadström T](#).

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The chronic active inflammation caused by *Helicobacter pylori* is dominated by neutrophils, macrophages, lymphocytes and plasma cells. Several interleukins are involved in the inflammatory process. The aim of this study was to investigate the effect of astaxanthin on gastric inflammation in patients with functional dyspepsia. Forty-four consecutive patients were included, and biopsies were examined for IL-4, IL-6, IL-8, IL-10, interferon-gamma, CD4, CD8, CD14, CD19, CD25 and CD30. Patients were randomized: 21 patients were treated with 40 mg of astaxanthin daily, and 23 patients were treated with a placebo. There was a significant decrease in gastric inflammation in *H. pylori*-positive patients from both groups. There were no significant changes in the density of *H. pylori* or in any of the interleukins during or after treatment. There was a significant up-regulation of CD4 and down-regulation of CD8 in patients with *H. pylori* treated with astaxanthin. Astaxanthin had an effect on the inflammation and on the density of *H. pylori* in mice in a study where the diet could be standardized without antioxidants (Bennedsen et al., 1999). These dietary conditions are impossible in studies involving humans, and may be due to the minor effect when the host have access to antioxidants in their diet.

Publication Types: PMID: 17521392 [PubMed - indexed for MEDLINE]

ASTAXANTHIN SHOWS POTENTIAL FOR GASTROINTESTINAL HEALTH IN NORMAL AND OBESE MICE.

[Nutrients](#). 2018 Sep 18;10(9). pii: E1320. doi: 10.3390/nu10091320.

Front Microbiol . 2021 Sep 6;12:671271. doi: 10.3389/fmicb.2021.671271. eCollection 2021.

Microbial Composition and Co-occurrence Patterns in the Gut Microbial Community of Normal and Obese Mice in Response to Astaxanthin

[Yuan Gao](#)¹, [Fang Liu](#)¹, [Robert W Li](#)², [Chunjun Li](#)¹, [Changhu Xue](#)^{1,3}, [Qingjuan Tang](#)¹

- PMID: 34552567 PMCID: [PMC8450573](#) DOI: [10.3389/fmicb.2021.671271](#)

Abstract

The changes and interaction of gut microbiota, which respond to dietary supplements, play critical roles on improving human health. The modulating effect of astaxanthin on gut microbiota has been reported. However, little is known about the co-occurrence patterns among microbial taxa in response to astaxanthin. In this study, the gut microbial composition, co-occurrence patterns, and microbial correlations with physiological parameters in astaxanthin-fed normal and obese mice were studied. Astaxanthin altered the microbial composition and co-occurrence patterns in normal and obese mice. Furthermore, astaxanthin gave more profound impacts on microbiota in obesity when compared with normal mice. In group A (normal or obese mice supplemented with astaxanthin), the abundance of *Acinetobacter* was decreased, and *Alistipes* was increased by astaxanthin, which also occurred in the MA group (obese mice supplemented with astaxanthin). An operational taxonomic unit (OTU) (GreenGenID# 4029632) assigned to the genus *Bacteroides* acted as a connector in the global network of A and MA groups. It may play critical roles in bridging intimate interactions between the host and other bacteria intervened by astaxanthin. Several modules correlated with physiological parameters were detected. For example, modules A12 and MA10 were significantly and negatively correlated with lipopolysaccharide (LPS) and fasting blood glucose (FBG) levels, respectively. A positive correlation was found between the node connectivity of the OTUs belonging to Clostridiaceae with LPS in obese mice, which indicated the role of Clostridiales as a potential pathological marker. Our findings provided a new interpretation of the role of astaxanthin in health and may contribute to further research on microbial community engineering.

Astaxanthin Inhibits Mitochondrial Dysfunction and Interleukin-8 Expression in *Helicobacter pylori*-Infected Gastric Epithelial Cells.

Kim SH¹, Lim JW², Kim H³.

Author information

Abstract

Helicobacter pylori (*H. pylori*) infection leads to gastric inflammation, peptic ulcer and gastric carcinoma. *H. pylori* activates NADPH oxidase and increases reactive oxygen species (ROS), which induce NF- κ B activation and IL-8 expression in gastric epithelial cells.

Dysfunctional mitochondria trigger inflammatory cytokine production. Peroxisome proliferator-activated receptors- γ (PPAR- γ) regulate inflammatory response. Astaxanthin is a powerful antioxidant that protects cells against oxidative stress. The present study was aimed at determining whether astaxanthin inhibits *H. pylori*-induced mitochondrial dysfunction, NF- κ B activation, and IL-8 expression via PPAR- γ activation in gastric epithelial cells. Gastric epithelial AGS cells were treated with astaxanthin, NADPH oxidase inhibitor apocynin and PPAR- γ antagonist GW9662, and infected with *H. pylori*. As a result, *H. pylori* caused an increase in intracellular and mitochondrial ROS, NF- κ B activation and IL-8 expression, but decreased mitochondrial membrane potential and ATP level. Astaxanthin inhibited *H. pylori*-induced alterations (increased ROS, mitochondrial dysfunction, NF- κ B activation, and IL-8 expression). Astaxanthin activated PPAR- γ and its target gene catalase in *H. pylori*-infected cells. Apocynin reduced ROS and inhibited IL-8 expression while astaxanthin did not affect NADPH oxidase activity. Inhibitory effects of astaxanthin on ROS levels and IL-8 expression were suppressed by addition of GW9662. In conclusion, astaxanthin inhibits *H. pylori*-induced mitochondrial dysfunction and ROS-mediated IL-8 expression by activating PPAR- γ and catalase in gastric epithelial cells. Astaxanthin may be beneficial for preventing oxidative stress-mediated gastric inflammation-associated *H. pylori* infection.

KEYWORDS:

Helicobacter pylori; astaxanthin; gastric epithelial cells; mitochondrial dysfunction; reactive oxygen species

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Free PMC Article

[Phytother Res.](#) 2012 Aug;26(8):1126-32. doi: 10.1002/ptr.3681. Epub 2011 Dec 14.

Protective effects of astaxanthin from *Paracoccus carotinifaciens* on murine gastric ulcer models.

[Murata K¹](#), [Oyagi A](#), [Takahira D](#), [Tsuruma K](#), [Shimazawa M](#), [Ishibashi T](#), [Hara H](#).

Author information

Abstract

The purpose of this study was to investigate the effect of astaxanthin extracted from *Paracoccus carotinifaciens* on gastric mucosal damage in murine gastric ulcer models. Mice were pretreated with astaxanthin for 1 h before ulcer induction. Gastric ulcers were induced in mice by oral administration of hydrochloride (HCl)/ethanol or acidified aspirin. The effect of astaxanthin on lipid peroxidation in murine stomach homogenates was also evaluated by measuring the level of thiobarbituric acid reactive substance (TBARS). The free radical scavenging activities of astaxanthin were also measured by electron spin resonance (ESR) measurements. Astaxanthin significantly decreased the extent of HCl/ethanol- and acidified aspirin-induced gastric ulcers. Astaxanthin also decreased the level of TBARS. The ESR measurement showed that astaxanthin had radical scavenging activities against the 1,1-diphenyl-2-picrylhydrazyl radical and the superoxide anion radical. These results suggest that astaxanthin has antioxidant properties and exerts a protective effect against ulcer formation in murine models.

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PMID:

22170791

[PubMed - indexed for MEDLINE]

[Eur J Pharmacol.](#) 2005 May 2;514(1):53-9. Epub 2005 Apr 20.

Protective effect of astaxanthin on naproxen-induced gastric antral ulceration in rats.

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Department of Biotechnology, School of Life Sciences and Biotechnology, Korea University, Seoul 136-701, South Korea.

Frequently used for humans as non-steroidal anti-inflammatory drug, naproxen has been known to induce ulcerative gastric lesion. The present study investigated the in vivo protective effect of astaxanthin isolated from *Xanthophyllomyces dendrorhous* against naproxen-induced gastric antral ulceration in rats. The oral administration of astaxanthin (1, 5, and 25 mg/kg of body weight) showed a significant protection against naproxen (80 mg/kg of body weight)-induced gastric antral ulcer and inhibited elevation of the lipid peroxide level in gastric mucosa. In addition, pretreatment of astaxanthin resulted in a significant increase in the activities of radical scavenging enzymes such as superoxide dismutase, catalase, and glutathione peroxidase. A histologic examination clearly proved that the acute gastric mucosal lesion induced by naproxen nearly disappeared after the pretreatment of astaxanthin. These results suggest that astaxanthin removes the lipid peroxides and free radicals induced by naproxen, and it may offer potential remedy of gastric ulceration.

PMID: 15878324 [PubMed - indexed for MEDLINE]

[Yao Xue Xue Bao](#). 2009 May;44(5):558-60.

[Therapeutic effect of astaxanthin on acetic acid-induced gastric ulcer in rats].

[Article in Chinese]

[Yang Q](#)¹, [Zhang Z](#), [Zhu X](#), [Ruan H](#), [Fu Y](#).

[Author information](#)

Abstract

This study is to investigate therapeutic effect of astaxanthin on acetic acid-induced gastric ulcer in rats. Rats were divided into control group, ulcercontrol group, and astaxanthin (5, 10, and 25 mg x kg⁻¹) groups at random, 8 rats in each group. After administered for 10 days consecutively, all the rats were sacrificed. The area of ulcer and the levels of MDA, SOD, CAT and GSH-Px in gastric mucosa were measured. Compared with ulcercontrol group, in astaxanthin (5, 10, and 25 mg x kg⁻¹) groups, the area of ulcer was decreased significantly. Level of MDA decreased while activities of SOD, CAT and GSH-Px increased (P < 0.05). Astaxanthin has good therapeutic effect on acetic acid-induced gastric ulcer in rats. Eliminating free radical and improving local blood circulation of the ulcer may be the mechanism of action.

PMID:

19618736

[PubMed - indexed for MEDLINE]

Ulcer preventive and antioxidative properties of astaxanthin from *Haematococcus pluvialis*.

[Kamath BS](#), [Srikanta BM](#), [Dharmesh SM](#), [Sarada R](#), [Ravishankar GA](#).

Plant Cell Biotechnology Department, Central Food Technological Research Institute, Mysore, 570 020, India.

The anti-ulcer properties of astaxanthin fractions such as total carotenoid and astaxanthin esters from *Haematococcus pluvialis* were evaluated in ethanol-induced gastric ulcers in rats. Since oxygen radical release is a pathogenic factor of ethanol-induced gastric damage, astaxanthin - a free radical scavenger, was investigated as a potential ulcer preventive agent. Astaxanthin fractions - total carotenoid and astaxanthin esters were orally administered to experimental rats at 100, 250 and 500 microg/kg b.w. prior to ulcer induction. Alcian blue binding assay indicates that, total carotenoid and astaxanthin esters at 500 microg/kg b.w could protect gastric mucin approximately 40% and 67% respectively. Pre-treatment with astaxanthin esters, also resulted in significant increase in antioxidant enzyme levels - catalase, superoxide dismutase, and glutathione peroxidase in stomach homogenate. Histopathological examination substantiated the protective effect of astaxanthin in pre-treated rats. The increased antioxidant potencies such as free radical scavenging activity with an IC(50) of approximately 8 microg/ml and reducing power abilities (59×10^3 U/g) in vitro, reveal that *H. pluvialis* astaxanthin may protect gastric mucosal injury by antioxidative mechanism. In addition, approximately 23 fold increased lipoxygenase-inhibitory property, in comparison with standard astaxanthin and significant H(+), K(+)-ATPase-inhibitory activity of astaxanthin esters, in comparison with known proton pump blocking anti-ulcer drug - omeprazole, may envisage the potential gastroprotective effect by regulating the gastric mucosal injury and gastric acid secretion by the gastric cell during ulcer disease.

Publication Types:

PMID: 18602387 [PubMed - indexed for MEDLINE]

[Phytomedicine](#). 2008 Jun;15(6-7):391-9. Epub 2008 May 7.

Efficacy of the natural antioxidant astaxanthin in the treatment of functional dyspepsia in patients with or without *Helicobacter pylori* infection: A prospective, randomized, double blind, and placebo-controlled study.

[Kupcinskas L](#), [Lafolie P](#), [Lignell A](#), [Kiudelis G](#), [Jonaitis L](#), [Adamonis K](#), [Andersen LP](#), [Wadström T](#).

Kaunas University of Medicine, 50009 Kaunas, Lithuania. limas.kupcinskas@kmu.lt

OBJECTIVES: The aim of this study was to evaluate the efficacy of the natural antioxidant astaxanthin in functional dyspepsia in different doses and compared with placebo. **DESIGN:** The study was a controlled, prospective, randomized, and double blind trial. **PARTICIPANTS:** Patients with functional dyspepsia, divided into three groups with 44 individuals in each group (placebo, 16mg, or 40mg astaxanthin, respectively). **INTERVENTIONS:** Participants were asked to accept gastroscopy before treatment, together with questionnaires: GSRS and SF-36. Urea breath test (UBT) was done before the treatment. **MAIN OUTCOME:** The primary objective was to test the hypothesis that the antioxidant astaxanthin at two doses regimens compared to placebo should ameliorate gastrointestinal discomfort measured as GSRS in patients with functional dyspepsia, who were either positive or negative for *Helicobacter pylori*, after 4 weeks of treatment. **RESULTS:** At the end of therapy (week 4) no difference between the three treatment groups was observed regarding mean Gastrointestinal Symptom Rating Scale (GSRS) scores of abdominal pain, indigestion and reflux syndromes. The same results were observed at the end of follow-up. However reduction of reflux syndrome before treatment to week 4 was significantly pronounced in the higher (40mg) dose compared to the other treatment groups (16mg and placebo, $p=0.04$). **CONCLUSION:** In general, no curative effect of astaxanthin was found in functional dyspepsia patients. Significantly greater reduction of reflux symptoms were detected in patients treated with the highest dose of the natural antioxidant astaxanthin. The response was more pronounced in *H. pylori*-infected patients.

Publication Types:

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Oral Astaxanthin Supplementation Prevents Peritoneal Fibrosis in Rats.

[Wakabayashi K](#)¹, [Hamada C](#)¹, [Kanda R](#)¹, [Nakano T](#)¹, [Ito H](#)¹, [Horikoshi S](#)¹, [Tomino Y](#)².

Author information

Abstract

BACKGROUND: Preventing peritoneal damage during peritoneal dialysis is critical. Reactive oxygen species (ROS) have an important role in peritoneal damage; however, few studies have investigated this. We aimed to determine the effects of oral astaxanthin (AST) supplementation in a peritoneal fibrosis (PF) rat model.

METHODS: Thirty-seven Sprague-Dawley rats were divided into 5 groups: Control 1 (fed a normal diet without stimulation), Control 2 (fed an AST-supplemented diet without stimulation), Group 1 (fed a normal diet with 8% chlorhexidine gluconate [CG] stimulation for 3 weeks), Group 2 (fed a 0.06% AST-supplemented diet with CG stimulation), and Group 3 (fed a 0.06% AST-supplemented diet that was initiated 4 weeks before CG stimulation). Peritoneal fibrosis, vascular proliferation, and fibrosis-related factor expression were examined.

RESULTS: Peritoneal thickness was significantly suppressed by AST supplementation. Astaxanthin diminished the number of CD68-, 8-hydroxy-2'-deoxyguanosine (8-OHdG)-, and monocyte chemoattractant protein-1 (MCP-1)-positive cells. Type 3 collagen, tumor necrosis factor- α (TNF- α), interleukin-1 β (IL-1 β), and MCP-1 mRNA expression was significantly lower in Group 3 than in Group 1. Increased transforming growth factor- β (TGF- β) and Snail mRNA expression, vascular density, and the number of α -smooth muscle actin (α -SMA)-positive cells were also decreased in Group 3.

CONCLUSION: Astaxanthin suppressed PF development through the inhibition of inflammation and oxidation in PF rats. It appears that the anti-oxidative agent AST may be useful for the prevention of peritoneal damage.

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KEYWORDS: Anti-inflammation; anti-oxidant; astax-anthin; peritoneal fibrosis

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DOI: [10.3747/pdi.2013.00317](#)

[Indexed for MEDLINE]

[Free PMC Article](#)

Effects of Dietary Supplementation with Astaxanthin on Histamine Induced Lesions in the Gizzard and Proventriculus of Broiler Chicks.

[Ohh MH](#)¹, [Kim S](#)², [Pak SC](#)³, [Chee KM](#)¹.

[Author information](#)

Abstract

Astaxanthin (ASX) is a xanthophyll pigment isolated from crustaceans and salmonids. Owing to its powerful antioxidant activity, ASX has been reported to have the potential to protect against gastric ulcers and a variety of other illnesses. Histamine (His) is a dietary factor that causes gastric erosion and ulceration in young chicks. In this study, we examined whether ASX had protective effects on dietary histamine-induced lesions in the gizzard and proventriculus of broiler chickens. Four experimental treatment groups were planned: basal diet (BD), BD+His, BD+ASX, and BD+ASX+His, with four chicks (5 days old) in each group and three replications (i.e., a total of 12 chicks per group). The BD was supplemented with either 0.4% His or 100 ppm ASX. The birds were fed ad libitum for 3 weeks, and diets contained no antimicrobial compounds. Supplementing the diet with His significantly decreased body weight gain, but increased the weights of the gizzard and proventriculus of the chicks as compared with those of chicks in the BD group ($p < 0.05$). ASX did not affect His-dependent changes in chick body weight or weights of the gizzard and proventriculus. The loss of gastric glands in the proventriculus, which was observed in His-treated chicks, was not prevented by ASX administration. The frequency of proventricular ulceration, however, was lowered by treatment with ASX, without significant differences between the two supplementation levels. In conclusion, our data showed that ASX might be helpful for alleviating structural damage to the digestive system in poultry under certain stressful conditions.

KEYWORDS:

Antioxidant; Astaxanthin; Histamine; Immunohistochemistry; Lesion; Proventriculitis

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PMCID: [PMC4852255](#)

DOI: [10.5713/ajas.15.1020](#)

[Free PMC Article](#)

Astaxanthin and β -carotene in *Helicobacter pylori*-induced Gastric Inflammation: A Mini-review on Action Mechanisms.

[Kang H¹](#), [Kim H¹](#).

Author information

Abstract

Helicobacter pylori is a dominant bacterium living in the human gastric tissues. In *H. pylori*-infected tissues, the infiltrated inflammatory cells produce reactive oxygen species (ROS), leading to gastric inflammation with production of various mediators. According to numerous epidemiological studies, dietary carotenoids may prevent gastric inflammation due to their antioxidant properties. Recent studies showed that antioxidant and anti-inflammatory effects of astaxanthin and β -carotene may contribute to inhibition of *H. pylori*-induced gastric inflammation. Astaxanthin changes *H. pylori*-induced activation of T helper cell type 1 response towards T helper cell type 2 response in the infected tissues. Astaxanthin inhibits the growth of *H. pylori*. Even though astaxanthin reduces *H. pylori*-induced gastric inflammation, it does not reduce cytokine levels in the infected tissues. β -Carotene suppresses ROS-mediated inflammatory signaling, including mitogen-activated protein kinases and redox-sensitive transcription factors, and reduces expression of inflammatory mediators, including interleukin-8, inducible nitric oxide synthase, and cyclooxygenase-2 in the infected tissues. Therefore, consumption of astaxanthin- and β -carotene-rich foods may be beneficial to prevent *H. pylori*-induced gastric inflammation. This review will summarize anti-inflammatory mechanisms of astaxanthin and β -carotene in *H. pylori*-mediated gastric inflammation.

KEYWORDS:

Astaxanthine; Beta-carotene; *Helicobacter pylori*; Inflammation

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PMCID: [PMC5503216](#)

DOI: [10.15430/JCP.2017.22.2.57](#)

[Free PMC Article](#)

Bioaccessibility, Cellular Uptake, and Transport of Astaxanthin Isomers and their Antioxidative Effects in Human Intestinal Epithelial Caco-2 Cells.

[Yang C](#)¹, [Zhang H](#)¹, [Liu R](#)¹, [Zhu H](#)¹, [Zhang L](#), [Tsao R](#)¹.

Author information

Abstract

The bioaccessibility, bioavailability, and antioxidative activities of three astaxanthin geometric isomers were investigated using an in vitro digestion model and human intestinal Caco-2 cells. This study demonstrated that the trans-cis isomerization of all-E-astaxanthin and the cis-trans isomerization of Z-astaxanthins could happen both during in vitro gastrointestinal digestion and cellular uptake processes. 13Z-Astaxanthin showed higher bioaccessibility than 9Z- and all-E-astaxanthins during in vitro digestion, and 9Z-astaxanthin exhibited higher transport efficiency than all-E- and 13Z-astaxanthins. These might explain why 13Z- and 9Z-astaxanthins are found at higher concentrations in human plasma than all-E-astaxanthin in reported studies. All three astaxanthin isomers were effective in maintaining cellular redox homeostasis as seen in the antioxidant enzyme (CAT, SOD) activities; 9Z- and 13Z-astaxanthins exhibited a higher protective effect than all-E-astaxanthin against oxidative stress as demonstrated by the lower cellular uptake of Z-astaxanthins and lower secretion and gene expression of the pro-inflammatory cytokine IL-8 in Caco-2 cells treated with H₂O₂. We conclude, for the first time, that Z-astaxanthin isomers may play a more important role in preventing oxidative stress induced intestinal diseases.

KEYWORDS:

13Z-astaxanthin; 9Z-astaxanthin; Caco-2 cells; all-E-astaxanthin; bioaccessibility; cellular uptake; cis-isomers; in vitro digestion

PMID: 29083169

DOI: [10.1021/acs.jafc.7b04254](https://doi.org/10.1021/acs.jafc.7b04254)

[Indexed for MEDLINE]

Astaxanthin Inhibits Mitochondrial Dysfunction and Interleukin-8 Expression in *Helicobacter pylori*-Infected Gastric Epithelial Cells.

Kim SH¹, Lim JW², Kim H³.

Author information

Abstract

Helicobacter pylori (*H. pylori*) infection leads to gastric inflammation, peptic ulcer and gastric carcinoma. *H. pylori* activates NADPH oxidase and increases reactive oxygen species (ROS), which induce NF- κ B activation and IL-8 expression in gastric epithelial cells. Dysfunctional mitochondria trigger inflammatory cytokine production. Peroxisome proliferator-activated receptors- γ (PPAR- γ) regulate inflammatory response. Astaxanthin is a powerful antioxidant that protects cells against oxidative stress. The present study was aimed at determining whether astaxanthin inhibits *H. pylori*-induced mitochondrial dysfunction, NF- κ B activation, and IL-8 expression via PPAR- γ activation in gastric epithelial cells. Gastric epithelial AGS cells were treated with astaxanthin, NADPH oxidase inhibitor apocynin and PPAR- γ antagonist GW9662, and infected with *H. pylori*. As a result, *H. pylori* caused an increase in intracellular and mitochondrial ROS, NF- κ B activation and IL-8 expression, but decreased mitochondrial membrane potential and ATP level. Astaxanthin inhibited *H. pylori*-induced alterations (increased ROS, mitochondrial dysfunction, NF- κ B activation, and IL-8 expression). Astaxanthin activated PPAR- γ and its target gene catalase in *H. pylori*-infected cells. Apocynin reduced ROS and inhibited IL-8 expression while astaxanthin did not affect NADPH oxidase activity. Inhibitory effects of astaxanthin on ROS levels and IL-8 expression were suppressed by addition of GW9662. In conclusion, astaxanthin inhibits *H. pylori*-induced mitochondrial dysfunction and ROS-mediated IL-8 expression by activating PPAR- γ and catalase in gastric epithelial cells. Astaxanthin may be beneficial for preventing oxidative stress-mediated gastric inflammation-associated *H. pylori* infection.

KEYWORDS:

Helicobacter pylori; astaxanthin; gastric epithelial cells; mitochondrial dysfunction; reactive oxygen species

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[Indexed for MEDLINE]

[Free PMC Article](#)

Effects of astaxanthin and vitamin C on the prevention of gastric ulcerations in stressed rats.

[Nishikawa Y](#), [Minenaka Y](#), [Ichimura M](#), [Tatsumi K](#), [Nadamoto T](#), [Urabe K](#).

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Astaxanthin (Asx), one of the carotenoids, is a red pigment in fish and Crustaceans, and possesses stronger reduction properties than conventional carotenoids, like beta-carotene. However, little is known about the biochemical properties and physiological functions of astaxanthin. The effects of astaxanthin and vitamin C on stressed rats were studied physiologically and biochemically. beta-Carotene and three kinds of astaxanthins, which were extracted from *Haematococcus* and *Phaffia*, and synthesized chemically, were used in these experiments. These rats given astaxanthins or beta-carotene had stress induced on the 12th day by immersing the rats in chest-level water at 20 degrees C for 24 h after fasting for 24 h. Rats given astaxanthins or beta-carotene prior to stressing were appreciably protected against the evolution of gastric ulcerations in relation to control rats. Ulcer indexes in particular were smaller with the rat group fed astaxanthin extracted from *Haematococcus* than the other groups. Next, the effects of Asx and/or vitamin C on the protection of evolution of gastric ulcer in stressed rats were pursued by the same methods as described above. The results showed that rats given Asx or vitamin C were appreciably protected against the evolution of gastric ulcerations in relation to control rats. The effects were more intense, especially in rats simultaneously supplied Asx and vitamin C than in rats taking either Asx or vitamin C. It was suggested that the simultaneous supplementation of food substances with astaxanthin and vitamin C would supply enough antioxidants to offset stress-related injuries.

PMID: 16161762 [PubMed - indexed for MEDLINE]

Suppressive effect of astaxanthin isolated from the *Xanthophyllomyces dendrorhous* mutant on ethanol-induced gastric mucosal injury in rats.

[Kim JH](#), [Choi SK](#), [Choi SY](#), [Kim HK](#), [Chang HI](#).

Department of Biotechnology, School of Life Sciences and Biotechnology, Korea University, Seoul 136-701, South Korea.

Ethanol has been found to induce ulcerative gastric lesion in humans. The present study investigated the in vivo protective effect of astaxanthin isolated from the *Xanthophyllomyces dendrorhous* mutant against ethanol-induced gastric mucosal injury in rats. The rats were treated with 80% ethanol for 3 d after pretreatment with two doses of astaxanthin (5 and 25 mg/kg of body weight respectively) for 3 d, while the control rats received only 80% ethanol for 3 d. The oral administration of astaxanthin (5 and 25 mg/kg of body weight) showed significant protection against ethanol-induced gastric lesion and inhibited elevation of the lipid peroxide level in gastric mucosa. In addition, pretreatment with astaxanthin resulted in a significant increase in the activities of radical scavenging enzymes such as superoxide dismutase, catalase, and glutathione peroxidase. A histologic examination clearly indicated that the acute gastric mucosal lesion induced by ethanol nearly disappeared after pretreatment with astaxanthin.

PMID: 16041134 [PubMed - indexed for MEDLINE]

ASTAXANTHIN SHOWS POTENTIAL TO PREVENT INFLAMMATORY BOWEL DISEASE IN MOUSE MODEL.

J Clin Biochem Nutr. 2019 Jan;64(1):66-72.
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Astaxanthin, a xanthophyll carotenoid, prevents development of dextran sulphate sodium-induced murine colitis

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PMID: **30705514** PMCID: [PMC6348411](#) DOI: [10.3164/jcfn.18-47](#) [Free PMC article](#)

Abstract

Astaxanthin is a xanthophyll carotenoid, which possesses strong scavenging effect on reactive oxygen species. In this study, we examined the effect of astaxanthin on dextran sulfate sodium (DSS)-induced colitis in mice. Experimental colitis was induced by the oral administration of 4% w/v DSS in tap water in C57BL/6J mice. Astaxanthin was mixed with a normal rodent diet (0.02 or 0.04%). Astaxanthin significantly ameliorated DSS-induced body weight loss and reduced the disease activity index. The ameliorating effects was observed in a dose-dependent manner. Immunochemical analyses showed that astaxanthin markedly suppressed DSS-induced histological inflammatory changes (inflammatory cell infiltration, edematous changes and goblet cell depletion). Plasma levels of malondialdehyde and 8-hydroxy-2-deoxyguanosine were significantly reduced by the administration of 0.04% astaxanthin. Astaxanthin significantly suppressed the mucosal mRNA expression of IL-1 β , IL-6, TNF- α , IL-36 α and IL-36 γ . Astaxanthin blocked the DSS-induced translocation of NF- κ B p65 and AP-1 (c-Jun) into the nucleus of mucosal epithelial cells, and also suppressed DSS-induced mucosal activation of MAPKs (ERK1/2, p38 and JNK). In conclusion, astaxanthin prevented the development of DSS-induced colitis via the direct suppression of NF- κ B, AP-1 and MAPK activation. These findings suggest that astaxanthin is a novel candidate as a therapeutic option for the treatment of inflammatory bowel disease.

ASTAXANTHIN REDUCES INTESTINAL INJURY IN MICE.

Oxid Med Cell Longev. 2021 Jan 5;2021:8894491.

doi: 10.1155/2021/8894491. eCollection 2021.

Astaxanthin Alleviates Ochratoxin A-Induced Cecum Injury and Inflammation in Mice by Regulating the Diversity of Cecal Microbiota and TLR4/MyD88/NF- κ B Signaling Pathway

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PMID: 33505592 PMCID: [PMC7806395](#) DOI: [10.1155/2021/8894491](#) **Free PMC article**

Abstract

Ochratoxin A (OTA) is a common environmental pollutant found in a variety of foods and grains, and excessive OTA consumption causes serious global health effects on animals and humans. Astaxanthin (AST) is a natural carotenoid that has anti-inflammatory, antiapoptotic, immunomodulatory, antitumor, antidiabetes, and other biological activities. The present study is aimed at investigating the effects of AST on OTA-induced cecum injury and its mechanism of action. Eighty C57 mice were randomly divided into four groups, including the control group, OTA group (5 mg/kg body weight), AST group (100 mg/kg body weight), and AST intervention group (100 mg/kg body weight AST+5 mg/kg body weight OTA). It was found that AST decreased the endotoxin content, effectively prevented the shortening of mouse cecum villi, and increased the expression levels of tight junction (TJ) proteins, consisting of occludin, claudin-1, and zonula occludens-1 (ZO-1). AST increased the number of goblet cells, the contents of mucin-2 (MUC2), and defensins (Defa5 and β -pD2) significantly, while the expression of mucin-1 (MUC1) decreased significantly. The 16S rRNA sequencing showed that AST affected the richness and diversity of cecum flora, decreased the proportion of lactobacillus, and also decreased the contents of short-chain fatty acids (SCFAs) (acetate and butyrate). In addition, AST significantly decreased the expression of TLR4, MyD88, and p-p65, while increasing the expression of p65. Meanwhile, the expression of inflammatory factors including TNF- α and INF- γ decreased, while the expression of IL-10 increased. In conclusion, AST reduced OTA-induced cecum injury by regulating the cecum barrier function and TLR4/MyD88/NF- κ B signaling pathway.

ASTAXANTHIN SHOWS POTENTIAL TO TREAT ALCOHOL-INDUCED GUT DAMAGE IN FISH MODEL.

Nat Prod Res. 2020 Oct 9;1-7.

doi: 10.1080/14786419.2020.1830396. Online ahead of print.

Biological effect of astaxanthin on alcohol-induced gut damage in *Carassius auratus* used as experimental model

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- PMID: **33032453**
- DOI: [10.1080/14786419.2020.1830396](https://doi.org/10.1080/14786419.2020.1830396)

Abstract

Alcohol and its metabolites are responsible for damage both within the gastrointestinal tract and other organs. Alcohol abuse promote intestinal inflammation, that may be the cause of multiple organ dysfunctions and chronic disorders. In this research, the effect of astaxanthin, a powerful antioxidant with several biological effects, on alcohol damage-induced in the intestine of *Carassius auratus*, was investigated. In the fishes exposed to ethanol, an increase of the intestinal epithelium mucous cells and circulating macrophages, with intestinal mucosa disorganization was observed. In contrast, in the fishes treated with astaxanthin intestinal morphology was restored. By immunohistochemical analysis, using α -Smooth Muscle Actin (α -SMA) and Vasoactive intestinal polypeptide (VIP) antibodies, a reduction of inflammatory states alcohol-induced was evident, with more regular muscularis submucosa and more organized intestinal mucosa without inflammatory cells. The results suggest that astaxanthin treatments can be a good candidate for preventing damage within the gastrointestinal associated with excessive alcohol consumption.

Effect of antioxidants on the immune response of *Helicobacter pylori*.

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Antioxidants are substances capable of inhibiting oxidation. In chronic diseases, inflammatory response cells produce oxygen free radicals. Oxygen free radicals cause DNA damage, and this may lead to gene modifications that might be carcinogenic. Chronic *Helicobacter pylori* infection causes the production of DNA-damaging free radicals. In recent years, various groups have studied the effects of antioxidants, especially on *H. pylori*-associated gastric cancer. In most of the studies, it has been shown that *H. pylori* infection does affect the level of antioxidants measured in the gastric juice, but there are also controversial results. Recent experimental studies, both in vivo and in vitro, have shown that vitamin C and astaxanthin, a carotenoid, are not only free radical scavengers but also show antimicrobial activity against *H. pylori*. It has been shown that astaxanthin changes the immune response to *H. pylori* by shifting the Th1 response towards a Th2 T-cell response. Very few experimental studies support the epidemiologic studies, and further studies are needed to describe the effect and the mechanism of antioxidants in the *H. pylori* immune response.

Publication Types:

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Astaxanthin-rich algal meal and vitamin C inhibit *Helicobacter pylori* infection in BALB/cA mice.

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Helicobacter pylori infection in humans is associated with chronic type B gastritis, peptic ulcer disease, and gastric carcinoma. A high intake of carotenoids and vitamin C has been proposed to prevent development of gastric malignancies. The aim of this study was to explore if the microalga *Haematococcus pluvialis* rich in the carotenoid astaxanthin and vitamin C can inhibit experimental *H. pylori* infection in a BALB/cA mouse model. Six-week-old BALB/cA mice were infected with the mouse-passaged *H. pylori* strain 119/95. At 2 weeks postinoculation mice were treated orally once daily for 10 days (i) with different doses of algal meal rich in astaxanthin (0.4, 2, and 4 g/kg of body weight, with the astaxanthin content at 10, 50, and 100 mg/kg, respectively), (ii) with a control meal (algal meal without astaxanthin, 4 g/kg), or (iii) with vitamin C (400 mg/kg). Five mice from each group were sacrificed 1 day after the cessation of treatment, and the other five animals were sacrificed 10 days after the cessation of treatment. Culture of *H. pylori* and determination of the inflammation score of the gastric mucosae were used to determine the outcome of the treatment. Mice treated with astaxanthin-rich algal meal or vitamin C showed significantly lower colonization levels and lower inflammation scores than those of untreated or control-meal-treated animals at 1 day and 10 days after the cessation of treatment. Lipid peroxidation was significantly decreased in mice treated with the astaxanthin-rich algal meal and vitamin C compared with that of animals not treated or treated with the control meal. Both astaxanthin-rich algal meal and vitamin C showed an inhibitory effect on *H. pylori* growth in vitro. In conclusion, antioxidants may be a new strategy for treating *H. pylori* infection in humans.

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PMCID: PMC90084

ASTAXANTHIN HUMAN CELL STUDY FINDS THAT IT MAY INHIBIT GASTRIC DISEASES ASSOCIATED WITH *H. PYLORI*.

Nutrients. 2020 Jun 11;12(6):1750.
doi: 10.3390/nu12061750.

Effect of Astaxanthin on Activation of Autophagy and Inhibition of Apoptosis in *Helicobacter pylori*-Infected Gastric Epithelial Cell Line AGS

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PMID: 32545395 PMCID: [PMC7353244](#) DOI: [10.3390/nu12061750](#) [Free PMC article](#)

Abstract

Helicobacter pylori (*H. pylori*) infection leads to the massive apoptosis of the gastric epithelial cells, causing gastric ulcers, gastritis, and gastric adenocarcinoma. Autophagy is a cellular recycling process that plays important roles in cell death decisions and can protect cells by preventing apoptosis. Upon the induction of autophagy, the level of the autophagy substrate p62 is reduced and the autophagy-related ratio of microtubule-associated proteins 1A/1B light chain 3B (LC3B)-II/LC3B-I is heightened. AMP-activated protein kinase (AMPK) and mammalian target of rapamycin (mTOR) are involved in the regulation of autophagy. Astaxanthin (AST) is a potent anti-oxidant that plays anti-inflammatory and anti-cancer roles in various cells. In the present study, we examined whether AST inhibits *H. pylori*-induced apoptosis through AMPK-mediated autophagy in the human gastric epithelial cell line AGS (adenocarcinoma gastric) in vitro. In this study, *H. pylori* induced apoptosis. Compound C, an AMPK inhibitor, enhanced the *H. pylori*-induced apoptosis of AGS cells. In contrast, metformin, an AMPK activator, suppressed *H. pylori*-induced apoptosis, showing that AMPK activation inhibits *H. pylori*-induced apoptosis. AST inhibited *H. pylori*-induced apoptosis by increasing the phosphorylation of AMPK and decreasing the phosphorylation of RAC-alpha serine/threonine-protein kinase (Akt) and mTOR in *H. pylori*-stimulated cells. The number of LC3B puncta in *H. pylori*-stimulated cells increased with AST. These results suggest that AST suppresses the *H. pylori*-induced apoptosis of AGS cells by inducing autophagy through the activation of AMPK and the downregulation of its downstream target, mTOR. In conclusion, AST may inhibit gastric diseases associated with *H. pylori* infection by increasing autophagy through the activation of the AMPK pathway.

ASTAXANTHIN SUPPRESSES GASTRIC CANCER INDUCED BY H. PYLORI IN HUMAN CELL STUDY.

Mar Drugs. 2020 Jul 15;18(7):365.
doi: 10.3390/md18070365.

Transcriptome Analysis of the Inhibitory Effect of Astaxanthin on *Helicobacter pylori*-Induced Gastric Carcinoma Cell Motility

[Suhn Hyung Kim](#)[‡], [Hyeyoung Kim](#)[‡]

PMID: 32679742 PMCID: [PMC7404279](#) DOI: [10.3390/md18070365](#) [Free PMC article](#)

Abstract

Helicobacter pylori (*H. pylori*) infection promotes the metastasis of gastric carcinoma cells by modulating signal transduction pathways that regulate cell proliferation, motility, and invasion. Astaxanthin (ASTX), a xanthophyll carotenoid, is known to inhibit cancer cell migration and invasion, however the mechanism of action of ASTX in *H. pylori*-infected gastric epithelial cells is not well understood. To gain insight into this process, we carried out a comparative RNA sequencing (RNA-Seq) analysis of human gastric cancer AGS (adenocarcinoma gastric) cells as a function of *H. pylori* infection and ASTX administration. The results were used to identify genes that are differently expressed in response to *H. pylori* and ASTX. Gene ontology (GO) analysis identified differentially expressed genes (DEGs) to be associated with cell cytoskeleton remodeling, motility, and/or migration. Among the 20 genes identified, those encoding c-MET, PI3KC2, PLC γ 1, Cdc42, and ROCK1 were selected for verification by real-time PCR analysis. The verified genes were mapped, using signaling networks contained in the KEGG database, to create a signaling pathway through which ASTX might mitigate the effects of *H. pylori*-infection. We propose that *H. pylori*-induced upregulation of the upstream regulator c-MET, and hence, its downstream targets Cdc42 and ROCK1, is suppressed by ASTX. ASTX is also suggested to counteract *H. pylori*-induced activation of PI3K and PLC γ . In conclusion, ASTX can suppress *H. pylori*-induced gastric cancer progression by inhibiting cytoskeleton reorganization and reducing cell motility through downregulation of c-MET, EGFR, PI3KC2, PLC γ 1, Cdc42, and ROCK1.

ASTAXANTHIN MAY PREVENT H. PYLORI-INDUCED GASTRIC DISORDERS BY PREVENTING OXIDATIVE STRESS OF MITOCHONDRIA.

J Cancer Prev. 2019 Mar;24(1):54-58.

doi: 10.15430/JCP.2019.24.1.54. Epub 2019 Mar 30.

Astaxanthin Prevents Decreases in Superoxide Dismutase 2 Level and Superoxide Dismutase Activity in *Helicobacter pylori*-infected Gastric Epithelial Cells

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PMID: 30993096 PMCID: [PMC6453584](#) DOI: [10.15430/JCP.2019.24.1.54](#) [Free PMC article](#)

Abstract

Background: *Helicobacter pylori* increases production of reactive oxygen species (ROS), which activates inflammatory and carcinogenesis-related signaling pathways in gastric epithelial cells. Therefore, reducing ROS, by upregulating antioxidant enzyme, such as superoxide dismutase (SOD), may be a novel strategy to prevent *H. pylori*-associated gastric diseases. Astaxanthin is an antioxidant carotenoid that prevents oxidative stress-induced cell injury. The present study was aimed to determine whether *H. pylori* decreases SOD activity by changing the levels of SOD1/SOD2 and whether astaxanthin prevents changes in SOD levels and activity in *H. pylori*-infected gastric epithelial AGS cells.

Methods: AGS cells were pre-treated with astaxanthin for 3 hours prior to *H. pylori* infection and cultured for 1 hour in the presence of *H. pylori*. SOD levels and activity were assessed by Western blot analysis and a commercial assay kit, respectively. Mitochondrial ROS was determined using MitoSOX fluorescence.

Results: *H. pylori* decreased SOD activity and the SOD2 level, but increased mitochondrial ROS in AGS cells. The SOD1 level was not changed by *H. pylori* infection. Astaxanthin prevented *H. pylori*-induced decreases in the SOD2 level and SOD activity and reduced mitochondrial ROS in AGS cells.

Conclusions: Consumption of astaxanthin-rich food may prevent the development of *H. pylori*-associated gastric disorders by suppressing mitochondrial oxidative stress.

Astaxanthin Inhibits *Helicobacter pylori*-induced Inflammatory and Oncogenic Responses in Gastric Mucosal Tissues of Mice

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- PMID: [33409257](#)
- PMCID: [PMC7783239](#)
- DOI: [10.15430/JCP.2020.25.4.244](#)

Abstract

Helicobacter pylori is recognized as a risk factor for gastric carcinogenesis. The chronic exposure of gastric epithelium to *H. pylori* induces a prolonged inflammatory state that may progress to gastric cancer. Astaxanthin, a pinkish antioxidant carotenoid, abundant in marine organisms, is known for its protective effect against inflammation and multiple types of cancer. The purpose of this study was to examine the effect of astaxanthin on *H. pylori*-induced oxidative injury, inflammation, and oncogene expression in gastric mucosal tissues of the infected mice. Mice were inoculated using oral gavage with *H. pylori* suspension (10^8 colony forming unit of *H. pylori*/0.1 mL) for three days, after which they were fed astaxanthin-supplemented diet (5 mg/kg body weight/day for seven weeks). The effects of astaxanthin on *H. pylori*-induced increase in lipid peroxide (LPO) production, myeloperoxidase (MPO) activity, expression of the inflammatory cytokine IFN- γ and oncogenes (c-myc and cyclin D1), and the accompanying histologic changes in gastric mucosal tissues were evaluated. *H. pylori* infection increased the level of LPO, MPO activity, and the expression of IFN- γ , c-myc, and cyclin D1 in gastric mucosal tissues of mice. *H. pylori* infection induced neutrophil infiltration and hyperplasia of gastric mucosa. Astaxanthin supplementation attenuated these effects. In conclusion, consumption of astaxanthin-rich foods may prevent *H. pylori*-associated oxidative damage and inflammatory and oncogenic responses in gastric mucosal tissues.

ASTAXANTHIN REDUCES INTESTINAL DAMAGE IN RAT MODEL OF NECROTIZING ENTEROCOLITIS.

Am J Perinatol. 2021 Apr 14.

doi: 10.1055/s-0041-1727156. Online ahead of print.

Astaxanthin Reduces the Severity of Intestinal Damage in a Neonatal Rat Model of Necrotizing Enterocolitis

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- PMID: 33853144 DOI: [10.1055/s-0041-1727156](https://doi.org/10.1055/s-0041-1727156)

Objective: This study aimed to ascertain the effects of astaxanthin (ASX) in an experimental necrotizing enterocolitis (NEC) model using rat pups.

Study design: Forty-two pups born from five Wistar albino rats were randomly divided into three groups as the control group, NEC + placebo (saline), and NEC + ASX. Pups in the NEC + ASX group were given 100 mg/kg/day oral ASX from day 1 to day 4 of the study. Saline of 2 mL/kg was given to the NEC + placebo group. Histopathological, immunohistochemical (caspase-3), and biochemical evaluations including the total antioxidant status (TAS), total oxidant status (TOS), superoxide dismutase (SOD), glutathione (GSH), lipid hydroperoxide (LPO), 8-hydroxydeoxyguanosine (8-OHdG), advanced oxidation protein products (AOPP), myeloperoxidase (MPO), tumor necrosis factor- α (TNF- α), interleukin-1 β (IL-1 β), and nuclear factor erythroid 2-related factor 2 (Nfr-2) activities were all performed.

Results: A better survival rate and weight gain were demonstrated in the NEC + ASX group ($p < 0.05$). In the histopathological evaluation, the severity of intestinal damage was significantly reduced in the NEC + ASX group, as well as decreased apoptosis (enzyme-linked immunosorbent assay [ELISA] for caspase-3; $p = 0.001$). The biochemical analyses of intestinal tissue TOS, oxidative stress index (OSI; TOS/TAS), IL-1 β , LPO, 8-OHdG, AOPP, caspase-3 ($p < 0.001$ for all), and TNF- α and MPO ($p = 0.001$ for both parameters) levels were lower in the NEC + ASX group than in the NEC + placebo group. Nrf-2, TAS, GSH, and SOD levels were higher in the NEC + ASX group than in the NEC + placebo group ($p = 0.001, 0.001, <0.001, \text{ and } 0.01$, respectively).

Conclusion: ASX treatment has been shown to effectively reduce the severity of intestinal damage in NEC due to its antioxidant, anti-inflammatory, and antiapoptotic properties.

[Immunol Lett.](#) 1999 Dec 1;70(3):185-9.

Treatment of *H. pylori* infected mice with antioxidant astaxanthin reduces gastric inflammation, bacterial load and modulates cytokine release by splenocytes.

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Helicobacter pylori is a gram-negative bacterium affecting about half of the world population, causing chronic gastritis type B dominated by activated phagocytes. In some patients the disease evolves into gastric ulcer, duodenal ulcer, gastric cancer or MALT lymphoma. The pathogenesis is in part caused by the immunological response. In mouse models and in human disease, the mucosal immune response is characterized by activated phagocytes. Mucosal T-lymphocytes are producing IFN-gamma thus increasing mucosal inflammation and mucosal damage. A low dietary intake of antioxidants such as carotenoids and vitamin C may be an important factor for acquisition of *H. pylori* by humans. Dietary antioxidants may also affect both acquisition of the infection and the bacterial load of *H. pylori* infected mice. Antioxidants, including carotenoids, have anti-inflammatory effects. The aim of the present study was to investigate whether dietary antioxidant induced modulation of *H. pylori* in mice affected the cytokines produced by *H. pylori* specific T-cells. We found that treatment of *H. pylori* infected mice with an algal cell extract containing the antioxidant astaxanthin reduces bacterial load and gastric inflammation. These changes are associated with a shift of the T-lymphocyte response from a predominant Th1-response dominated by IFN-gamma to a Th1/Th2-response with IFN-gamma and IL-4. To our knowledge, a switch from a Th1-response to a mixed Th1/Th2-response during an ongoing infection has not been reported previously.

Publication Types:

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Astaxanthin-rich algal meal and vitamin C inhibit *Helicobacter pylori* infection in BALB/cA mice.

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Helicobacter pylori infection in humans is associated with chronic type B gastritis, peptic ulcer disease, and gastric carcinoma. A high intake of carotenoids and vitamin C has been proposed to prevent development of gastric malignancies. The aim of this study was to explore if the microalga *Haematococcus pluvialis* rich in the carotenoid astaxanthin and vitamin C can inhibit experimental *H. pylori* infection in a BALB/cA mouse model. Six-week-old BALB/cA mice were infected with the mouse-passaged *H. pylori* strain 119/95. At 2 weeks postinoculation mice were treated orally once daily for 10 days (i) with different doses of algal meal rich in astaxanthin (0.4, 2, and 4 g/kg of body weight, with the astaxanthin content at 10, 50, and 100 mg/kg, respectively), (ii) with a control meal (algal meal without astaxanthin, 4 g/kg), or (iii) with vitamin C (400 mg/kg). Five mice from each group were sacrificed 1 day after the cessation of treatment, and the other five animals were sacrificed 10 days after the cessation of treatment. Culture of *H. pylori* and determination of the inflammation score of the gastric mucosae were used to determine the outcome of the treatment. Mice treated with astaxanthin-rich algal meal or vitamin C showed significantly lower colonization levels and lower inflammation scores than those of untreated or control-meal-treated animals at 1 day and 10 days after the cessation of treatment. Lipid peroxidation was significantly decreased in mice treated with the astaxanthin-rich algal meal and vitamin C compared with that of animals not treated or treated with the control meal. Both astaxanthin-rich algal meal and vitamin C showed an inhibitory effect on *H. pylori* growth in vitro. In conclusion, antioxidants may be a new strategy for treating *H. pylori* infection in humans.

[Chem Biol Interact.](#) 2011 Aug 15;193(1):79-87. Epub 2011 May 20.

Dietary astaxanthin inhibits colitis and colitis-associated colon carcinogenesis in mice via modulation of the inflammatory cytokines.

[Yasui Y](#), [Hosokawa M](#), [Mikami N](#), [Miyashita K](#), [Tanaka T](#).

Source

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Abstract

Astaxanthin (AX) is one of the marine carotenoid pigments, which possess powerful biological antioxidant, anti-inflammatory and anti-cancer properties. The purpose of this study is to investigate possible inhibitory effect of AX against inflammation-related mouse colon carcinogenesis and dextran sulfate sodium (DSS)-induced colitis in male ICR mice. We conducted two different experiments. In the first experiment, we evaluated the effects of AX at three dose levels, 50, 100 and 200 ppm in diet, on colitis-associated colon carcinogenesis induced by azoxymethane (AOM)/DSS in mice. In the second, the effects of the AX (100 and 200 ppm) in diet on DSS-induced colitis were determined. We found that dietary AX significantly inhibited the occurrence of colonic mucosal ulcers, dysplastic crypts, and colonic adenocarcinoma at week 20. AX-feeding suppressed expression of inflammatory cytokines, including nuclear factor (NF)- κ B, tumor necrosis factor (TNF)- α and interleukin (IL)-1 β , inhibited proliferation, and induced apoptosis in the colonic adenocarcinomas. Feeding with 200 ppm AX, but not 100 ppm, significantly inhibited the development of DSS-induced colitis. AX feeding (200 ppm in diet) also lowered the protein expression of NF- κ B, and the mRNA expression of inflammatory cytokines, including IL-1 β , IL-6, and cyclooxygenase (COX)-2. Our results suggest that the dietary AX suppresses the colitis and colitis-related colon carcinogenesis in mice, partly through inhibition of the expression of inflammatory cytokine and proliferation. Our findings suggest that AX is one of the candidates for prevention of colitis and inflammation-associated colon carcinogenesis in humans.

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Respiratory Health and Asthma

ASTAXANTHIN IMPROVES PERFORMANCE; ENHANCES WHOLE-BODY FAT OXIDATION RATES; AND REDUCES RESPIRATORY EXCHANGE RATIO IN RECREATIONAL CYCLISTS IN ONLY SEVEN DAYS OF SUPPLEMENTATION IN HUMAN CLINICAL TRIAL.

J Sci Med Sport. 2021 Jan;24(1):92-97.

doi: 10.1016/j.jsams.2020.06.017. Epub 2020 Jul 3.

The effect of astaxanthin supplementation on performance and fat oxidation during a 40 km cycling time trial

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PMID: 32660833 DOI: [10.1016/j.jsams.2020.06.017](https://doi.org/10.1016/j.jsams.2020.06.017)

Abstract

Objectives: This study aimed to investigate whether supplementation with 12 mg·day⁻¹ astaxanthin for 7 days can improve exercise performance and metabolism during a 40 km cycling time trial.

Design: A randomised, double-blind, crossover design was employed.

Methods: Twelve recreationally trained male cyclists (VO_{2peak} : 56.5 ± 5.5 mL·kg⁻¹·min⁻¹, W_{max} : 346.8 ± 38.4 W) were recruited. Prior to each experimental trial, participants were supplemented with either 12 mg·day⁻¹ astaxanthin or an appearance-matched placebo for 7 days (separated by 14 days of washout). On day 7 of supplementation, participants completed a 40 km cycling time trial on a cycle ergometer, with indices of exercise metabolism measured throughout.

Results: Time to complete the 40 km cycling time trial was improved by $1.2 \pm 1.7\%$ following astaxanthin supplementation, from 70.76 ± 3.93 min in the placebo condition to 69.90 ± 3.78 min in the astaxanthin condition (mean improvement = 51 ± 71 s, $p = 0.029$, $g = 0.21$). Whole-body fat oxidation rates were also greater ($+0.09 \pm 0.13$ g·min⁻¹,

$p = 0.044$, $g = 0.52$), and the respiratory exchange ratio lower (-0.03 ± 0.04 , $p = 0.024$, $g = 0.60$) between 39-40 km in the astaxanthin condition.

Conclusions: Supplementation with $12 \text{ mg}\cdot\text{day}^{-1}$ astaxanthin for 7 days provided an ergogenic benefit to 40 km cycling time trial performance in recreationally trained male cyclists and enhanced whole-body fat oxidation rates in the final stages of this endurance-type performance event.

In vitro suppression of lymphocyte activation in patients with seasonal allergic rhinitis and pollen-related asthma by cetirizine or azelastine in combination with ginkgolide B or astaxanthin.

[Mahmoud FF¹](#), [Haines D](#), [Al-Awadhi R](#), [Arifhodzic N](#), [Abal A](#), [Azeamouzi C](#), [Al-Sharah S](#), [Tosaki A](#).

Author information

Abstract

Novel strategies are evaluated for management of allergic rhinitis and asthma in patients co-afflicted with both disorders. It is hypothesized that the platelet activating factor receptor antagonist ginkgolide B (GB) and the carotenoid antioxidant astaxanthin (ASX) interact with antihistamines cetirizine dihydrochloride (CTZ) and azelastine (AZE) to potentiate their ability to downregulate potentially pathological immune activation. Peripheral blood mononuclear cells from asthmatics and healthy subjects, cultured 24 hours with 50 µg/ml phytohemagglutinin (PHA) or PHA plus each drug are analyzed by flow cytometry for expression of CD25+ or HLA-DR+ by CD3+ (T cells). Results are reported as stimulation indices for CD3+CD25+ (SICD3+CD25+) and CD3+HLA-DR+ (SICD3+HLADR+) cells in cultures treated with PHA alone, versus cultures treated with both PHA and drugs. Optimal suppression of activated cells was observed in cultures stimulated with ASX 10⁻⁶ M + CTZ 10⁻⁶ M (SICD3+CD25+, p = 0.016; SICD3+HLADR, p = 0.012); ASX 10⁻⁶ M + AZE 10⁻⁶ M (SICD3+CD25+, p = 0.012; SICD3+HLADR, p = 0.015); GB 10⁻⁶ M + CTZ 10⁻⁶ M (SICD3+CD25+, p = 0.024, SICD3+HLADR+, p = 0.019). Results demonstrate improved activity of antihistamines by 2 phytochemicals, suggesting dosing strategies for animal trials of ASX- or GB-augmented formulations for seasonal allergic rhinitis and asthma.

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22849842

[PubMed - indexed for MEDLINE]

ASTAXANTHIN SHOWS THERAPEUTIC EFFECT FOR ACUTE LUNG INJURY AND ACUTE RESPIRATORY DISTRESS SYNDROME IN META-ANALYSIS OF FIVE MOUSE MODELS.

Aging (Albany NY). 2020 Sep 23;12(18):18716-18740.
doi: 10.18632/aging.104042. Online ahead of print.

Identification of robust genetic signatures associated with lipopolysaccharide-induced acute lung injury onset and astaxanthin therapeutic effects by integrative analysis of RNA sequencing data and GEO datasets

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Abstract

Acute lung injury (ALI) and acute respiratory distress syndrome (ARDS) are life-threatening clinical conditions predominantly arising from uncontrolled inflammatory reactions. It has been found that the administration of astaxanthin (AST) can exert protective effects against lipopolysaccharide (LPS)-induced ALI; however, the robust genetic signatures underlying LPS induction and AST treatment remain obscure. Here we performed a statistical meta-analysis of five publicly available gene expression datasets from LPS-induced ALI mouse models, conducted RNA-sequencing (RNA-seq) to screen differentially expressed genes (DEGs) in response to LPS administration and AST treatment, and integrative analysis to determine robust genetic signatures associated with LPS-induced ALI onset and AST administration. Both the meta-analyses and our experimental data identified a total of 198 DEGs in response to LPS administration, and 11 core DEGs (*Timp1*, *Ly6i*, *Cxcl13*, *Irf7*, *Cxcl5*, *Ccl7*, *Isg15*, *Saa3*, *Saa1*, *Tgtp1*, and *Gbp11*) were identified to be associated with AST therapeutic effects. Further, the 11 core DEGs were verified by quantitative real-time PCR (qRT-PCR) and immunohistochemistry (IHC), and functional enrichment analysis revealed that these genes are primarily associated with neutrophils and chemokines. Collectively, these findings unearthed the robust genetic signatures underlying LPS administration and the molecular targets of AST for ameliorating ALI/ARDS which provide directions for further research.

Astaxanthin prevents pulmonary fibrosis (scarring of lung tissue) in rats and in-vitro.

[J Cell Mol Med.](#) 2015 Sep;19(9):2215-31. doi: 10.1111/jcmm.12609. Epub 2015 Jun 27.

Astaxanthin prevents pulmonary fibrosis by promoting myofibroblast apoptosis dependent on Drp1-mediated mitochondrial fission.

[Zhang J¹](#), [Xu P²](#), [Wang Y³](#), [Wang M⁴](#), [Li H²](#), [Lin S⁵](#), [Mao C¹](#), [Wang B¹](#), [Song X¹](#), [Lv C^{1,2}](#).

Author information

Abstract

Promotion of myofibroblast apoptosis is a potential therapeutic strategy for pulmonary fibrosis. This study investigated the antifibrotic effect of astaxanthin on the promotion of myofibroblast apoptosis based on dynamin-related protein-1 (Drp1)-mediated mitochondrial fission in vivo and in vitro. Results showed that astaxanthin can inhibit lung parenchymal distortion and collagen deposition, as well as promote myofibroblast apoptosis. Astaxanthin demonstrated pro-apoptotic function in myofibroblasts by contributing to mitochondrial fission, thereby leading to apoptosis by increasing the Drp1 expression and enhancing Drp1 translocation into the mitochondria. Two specific siRNAs were used to demonstrate that Drp1 is necessary to promote astaxanthin-induced mitochondrial fission and apoptosis in myofibroblasts. Drp1-associated genes, such as Bcl-2-associated X protein, cytochrome c, tumour suppressor gene p53 and p53-up-regulated modulator of apoptosis, were highly up-regulated in the astaxanthin group compared with those in the sham group. This study revealed that astaxanthin can prevent pulmonary fibrosis by promoting myofibroblast apoptosis through a Drp1-dependent molecular pathway. Furthermore, astaxanthin provides a potential therapeutic value in pulmonary fibrosis treatment.

KEYWORDS: astaxanthin; mitochondrial fission; myofibroblast apoptosis; pulmonary fibrosis

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Toxins (Basel). 2019 Sep 17;11(9):540.
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Astaxanthin Protects OTA-Induced Lung Injury in Mice through the Nrf2/NF- κ B Pathway

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- DOI: [10.3390/toxins11090540](#)

Free PMC article

Abstract

The aim of this research was to evaluate the potential protective mechanism of astaxanthin (ASTA) against oxidative damage and inflammation caused by ochratoxin (OTA) in mouse lung. We divided mice into a control group (CG), an OTA group (PG), an astaxanthin group (AG), and an OTA+ASTA group (JG). Oxidative indices (malondialdehyde (MDA), total superoxide dismutase (T-SOD), and reduced glutathione (GSH)) and inflammatory markers (interleukin 1 β (IL-1 β), interleukin 6 (IL-6), and tumor necrosis factor α (TNF- α)) were assayed in the lung, and the lung-weight-to-body-weight ratio was calculated. Apoptosis was detected in pathological sections by the TdT-mediated dUTP nick-end labeling (TUNEL) assay. Oxidative damage and inflammation were detected in the lung of mice after exposure to OTA. Besides, Nrf2- and NF- κ B-pathway-associated proteins were detected by Western blot. In contrast with OTA, ASTA significantly raised the expression of Nrf2, HO-1, and MnSOD, while the expression of other proteins (Keap1, TLR4, and NF- κ B) was significantly decreased. These results indicate that ASTA exerted protective effects against OTA-induced oxidative damage and inflammation in the lung by regulating the Nrf2 and NF- κ B pathways.

ASTAXANTHIN INHIBITS TOBACCO SMOKE-INDUCED EMPHYSEMA IN MICE AND MAY BE A THERAPY FOR CHRONIC OBSTRUCTIVE PULMONARY DISEASE.

Mar Drugs. 2019 Nov 28;17(12):673.

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Astaxanthin Suppresses Cigarette Smoke-Induced Emphysema through Nrf2 Activation in Mice

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- DOI: [10.3390/md17120673](#)

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Abstract

Oxidative stress plays an important role in the pathogenesis of chronic obstructive pulmonary disease (COPD). The activation of nuclear factor erythroid 2-related factor 2 (Nrf2) is a key cellular defense mechanism against oxidative stress. Recent studies have shown that astaxanthin protects against oxidative stress via Nrf2. In this study, we investigated the emphysema suppression effect of astaxanthin via Nrf2 in mice. Mice were divided into four groups: control, smoking, astaxanthin, and astaxanthin + smoking. The mice in the smoking and astaxanthin + smoking groups were exposed to cigarette smoke for 12 weeks, and the mice in the astaxanthin and astaxanthin + smoking groups were fed a diet containing astaxanthin. Significantly increased expression levels of Nrf2 and its target gene, heme oxygenase-1 (HO-1), were found in the lung homogenates of astaxanthin-fed mice. The number of inflammatory cells in the bronchoalveolar lavage fluid (BALF) was significantly decreased, and emphysema was significantly suppressed. In conclusion, astaxanthin protects against oxidative stress via Nrf2 and ameliorates cigarette smoke-induced emphysema. Therapy with astaxanthin directed toward activating the Nrf2 pathway has the potential to be a novel preventive and therapeutic strategy for COPD.

ASTAXANTHIN PREVENTS LUNG DAMAGE CAUSED BY INFLAMMATION AND HYPEROXIA IN RAT MODEL.

Comb Chem High Throughput Screen. 2020 Sep 14.

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Astaxanthin prevents lung injury due to hyperoxia and inflammation

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[Türkmenoğlu](#)⁴, [Ataman Gönel](#)⁵

PMID: 32933455 DOI: [10.2174/1386207323666200915092012](https://doi.org/10.2174/1386207323666200915092012)

Background/Aim: We aimed to ascertain the effects of astaxanthin on the lungs of rat pups with bronchopulmonary dysplasia (BPD) induced by hyperoxia and lipopolysaccharide (LPS).

Materials and Methods: Forty-two newborn Wistar rats born to spontaneous pregnant rats were divided into three groups: Hyperoxia (95% O₂) + lipopolysaccharide (LPS) group, hyperoxia + LPS + astaxanthin group and control: no treatment group (21% O₂). Pups in the hyperoxia + LPS + astaxanthin group were given 100 mg/kg/day oral astaxanthin from the first day to the fifth day. Histopathologic and biochemical evaluations including glutathione (GSH), total antioxidant status (TAS), total oxidant status (TOS), lipid hydroperoxide (LPO), 8-hydroxydeoxyguanosine (8-OHdG), advanced oxidation protein products (AOPP), myeloperoxidase (MPO), total thiol, tumor necrosis factor-alpha (TNF- α), interleukin 1 beta (IL1 β) and caspase-3 activities were performed.

Results: A better survival rates and weight gain were demonstrated in the hyperoxia + LPS + astaxanthin group ($p < 0.001$). In the histopathologic evaluation, the severity of lung damage was significantly reduced in the hyperoxia+LPS+astaxanthin group, as well as decreased apoptosis (ELISA for caspase-3) ($p < 0.001$). The biochemical analyses of lung tissues TAS, GSH, Total thiol levels were significantly higher in the astaxanthin treated group compared to hyperoxia + LPS group ($p < 0.05$) while TOS, AOPP, LPO, 8-OHdG, MPO levels were significantly lower ($p < 0.001$). In addition, unlike the hyperoxia + LPS group, TNF- α and IL-1 β levels in lung tissue were significantly lower in the astaxanthin-treated group ($p < 0.001$).

Conclusion: Astaxanthin was shown to reduce lung damage caused by inflammation and hyperoxia with its anti-inflammatory, anti-oxidant, anti-apoptotic properties and to protect the lung from severe destruction.

Astaxanthin alleviated acute lung injury by inhibiting oxidative/nitrative stress and the inflammatory response in mice.

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Author information

Abstract

The purpose of the present study was to assess the effect of astaxanthin (ASX) treatment on the acute lung injury (ALI) induced by cecal ligation and puncture (CLP) in mice. Mice were randomly allocated into the following groups: (1) the saline control group, in which mice were given saline before sham operation; (2) the ASX control group, in which mice received ASX before sham operation; (3) the ALI group, in which mice were given saline before CLP operation; and (4) the ALI+ASX group, in which mice received ASX before CLP operation. ASX was dissolved in olive oil and administrated by oral gavage for 14 days consecutively before the CLP or sham operation. In experiment 1, Kaplan-Meier survival analysis was conducted for 72 h after CLP. In experiment 2, blood, bronchoalveolar lavage fluid (BALF) and lung tissues were collected at 24 h after the CLP or sham operation to determine the severity of lung injury. The results showed that ASX treatment could significantly decrease the CLP-induced mortality rate in mice. Meanwhile, ASX treatment significantly attenuated CLP-induced lung histopathological injury, inflammatory infiltration, total protein and albumin concentration, and total cell and neutrophil counts in the BALF. Furthermore, ASX treatment alleviated oxidative/nitrative stress, inflammation levels and pulmonary apoptosis in lung tissues. In addition, ASX treatment markedly down-regulated the expression of inducible nitric oxide synthase (i-NOS), nitrotyrosine (NT) and nuclear factor-kappa B (NF- κ B) P65 in the lung tissues compared with that in the ALI group. Astaxanthin treatment had markedly protective effect against ALI in mice, and the potential mechanism is associated with its ability to inhibit the inflammatory response, oxidative/nitrative stress, and pulmonary apoptosis, as well as down-regulate NF- κ B P65 expression.

KEYWORDS:

Acute lung injury; Astaxanthin; Inflammatory response; NF- κ B P65; Oxidative stress; Pulmonary apoptosis

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ASTAXANTHIN SHOWS POTENTIAL TO REDUCE PULMONARY FIBROSIS BY ACTIVATING FIBROBLAST PROLIFERATION AND MIGRATION IN MOUSE MODEL.

J Cell Mol Med. 2020 Sep;24(17):10245-10250.
doi: 10.1111/jcmm.15477. Epub 2020 Aug 19.

Astaxanthin attenuates pulmonary fibrosis through lncITPF and mitochondria-mediated signal pathways

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Abstract

Pulmonary fibrosis is a chronic interstitial lung disease characterized by pulmonary epithelial injury, fibroblast activation, extracellular matrix deposition, and tissue structure destruction. However, an effective drug treatment remains unavailable. Therefore, studying the mechanism of pulmonary fibrogenesis and finding effective drugs have become important problems in the field of respiratory diseases. Pulmonary fibrosis is typically characterized by activated fibroblast proliferation and migration. Hence, abnormality in activated fibroblast proliferation and migration is a major concern for treating pulmonary fibrosis. Long noncoding RNA (lncRNA) is an enigmatic subclass of ncRNA that regulates various fundamental biological processes and participates in disease occurrence and development. However, studies on lncRNA as the therapeutic target of drug action are rarely reported. Our group first identified differentially expressed lncRNAs and revealed that lncITPF is a highly upregulated lncRNA in lung fibrosis. In particular, lncITPF is detected in the blood of patients with idiopathic pulmonary fibrosis. Clinical analysis shows that lncITPF is positively correlated with the degree of fibrosis. The receiver operating characteristic (ROC) curve indicates that the specificity and sensitivity values are 95.0 and 64.3, respectively. The area under the ROC curve is 0.804, indicating that lncITPF can be a diagnostic biomarker for IPF. However, whether lncITPF is effective as a therapeutic target of drug action against pulmonary fibrosis remains unclear. In this study, lncITPF acting as the therapeutic target of astaxanthin was explored in depth. The findings elucidated that astaxanthin blocks the activated fibroblast proliferation and migration through lncITPF and mitochondria-mediated signal pathways to alleviate pulmonary fibrogenesis.

[Phytother Res.](#) 2010 Jul 14. [Epub ahead of print]

Summative interaction between astaxanthin, Ginkgo biloba extract (EGb761) and vitamin C in Suppression of respiratory inflammation: a comparison with ibuprofen.

[Haines DD](#), [Varga B](#), [Bak I](#), [Juhasz B](#), [Mahmoud FF](#), [Kalantari H](#), [Gesztelyi R](#), [Lekli I](#), [Czompa A](#), [Tosaki A](#).

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Abstract

In this study, combinations of Ginkgo biloba leaf extract (EGb761) plus the carotenoid antioxidant astaxanthin (ASX) and vitamin C were evaluated for a summative dose effect in the inhibition of asthma-associated inflammation in asthmatic guinea-pigs. Ovalbumin-sensitized Hartley guinea-pigs challenged with ovalbumin aerosol to induce asthma, were administered EGb761, ASX, vitamin C or ibuprofen. Following killing, bronchoalveolar lavage (BAL) fluid was evaluated for inflammatory cell infiltrates and lung tissue cyclic nucleotide content. Each parameter measured was significantly altered to a greater degree by drug combinations, than by each component acting independently. An optimal combination was identified that included astaxanthin (10 mg/kg), vitamin C (200 mg/kg) and EGb761 (10 mg/kg), resulting in counts of eosinophils and neutrophils each 1.6-fold lower; macrophages 1.8-fold lower, cAMP 1.4-fold higher; and cGMP 2.04-fold higher than levels in untreated, asthmatic animals ($p < 0.05$). In conclusion, EGb761, ASX and vitamin C are shown here to interact summatively to suppress inflammation with efficacy equal to or better than ibuprofen, a widely used non-steroidal antiinflammatory drug (NSAID). Such combinations of non-toxic phytochemicals constitute powerful tools for the prevention of onset of acute and chronic inflammatory disease if consumed regularly by healthy individuals; and may also augment the effectiveness of therapy for those with established illness. Copyright (c) 2010 John Wiley & Sons, Ltd.

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ASTAXANTHIN PREVENTS LUNG INJURY INDUCED BY LIPOPOLYSACCHARIDES IN-VITRO.

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eCollection 2019.

Astaxanthin prevents against lipopolysaccharide-induced acute lung injury and sepsis via inhibiting activation of MAPK/NF- κ B

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- PMID: [30972212](#)
- PMCID: [PMC6456544](#)

[Free PMC article](#)

Abstract

Background: Endotoxin-induced acute inflammatory diseases such as sepsis, mediated by excessive production of various pro-inflammatory cytokines remain the leading cause of mortality in critically ill patients. Lipopolysaccharide (LPS), the characteristic endotoxin found in the outer membrane of Gram-negative bacteria, can induce the innate immunity system and through Mitogen activated protein kinase (MAPK) and Nuclear Factor- κ B (NF- κ B), increase the production of inflammatory mediators. Astaxanthin (ASX), a xanthophyll carotenoid, exerts beneficial effects against oxidation, inflammation, and cancer. But poor evidence has been reported that whether it has protective effects on LPS-induced injury. This study aims to investigate the effects of ASX on LPS-induced sepsis and acute lung injury and to demonstrate its mechanisms.

Methods: Mouse prime macrophage (MPM) challenged with LPS were used for in vitro pharmacological activity and mechanistic studies. Inflammatory factors (tumor necrosis factor- α and interleukin-6 levels) in MPM were determined. The mouse models of LPS-induced sepsis and acute lung injury administrated with or without the compound were used for in vivo studies.

Results: Pre-treatment of MPM with ASX inhibited MAPK/NF- κ B signaling pathway, and attenuated LPS-increased inflammatory factors *in vitro*. In animal models of LPS-induced sepsis and acute lung injury, administration of ASX significantly improved survival and protected lung injury. Subsequently, ASX was shown to suppress LPS-induced inflammatory factors increase, MAPK phosphorylation, and NF- κ B activation *in vivo*.

Conclusions: ASX exerts impressively protective effects on LPS-induced injury *in vitro* and *in vivo*. Taken together, it might be used as a potential candidate for clinical sepsis.

In vitro effects of astaxanthin combined with ginkgolide B on T lymphocyte activation in peripheral blood mononuclear cells from asthmatic subjects.

[Mahmoud FF¹](#), [Haines DD](#), [Abul HT](#), [Abal AT](#), [Onadeko BO](#), [Wise JA](#).

Author information

Abstract

This study was undertaken to identify novel approaches to pharmacological treatment of asthma. Here we hypothesize that the platelet-activating factor receptor antagonist ginkgolide B (GB) in combination with the antioxidant carotenoid astaxanthin (ASX) suppresses T cell activation comparably to two commonly-used antihistamines: cetirizine dihydrochloride (CTZ) and azelastine (AZE). Peripheral blood mononuclear cells from asthmatics, cultured 24 h with either 50 microg/ml phytohemagglutinin (PHA) or PHA plus selected dosages of each drug are analyzed by flow cytometry for CD25+ or HLA-DR+ on CD3+ (T cells). Results are reported as stimulation indices (SI) of %CD3+CD25+ cells or %CD3+HLA-DR+ cells in cultures treated with PHA alone versus these subpopulations in cultures treated with both PHA and drugs. Combinations of ASX and GB exhibited optimal suppression at 10(-7) M GB + 10(-8) M ASX for CD3+CD25+ (SI = 0.79 +/- 0.04, P = 0.001) and 10(-7) M GB + 10(-7) M ASX for CD3+HLA-DR+ (SI = 0.82 +/- 0.05, P = 0.004). In conclusion, suppression of T cell activation below fully stimulated values by GB, ASX, and their combinations was comparable and for some combinations better than that mediated by CTZ and AZE. These results suggest that ASX and GB may have application as novel antiasthmatic formulations.

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14978350

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The Protective Effects of Astaxanthin on the OVA-Induced Asthma Mice Model.

[Hwang YH](#)¹, [Hong SG](#)², [Mun SK](#)³, [Kim SJ](#)⁴, [Lee SJ](#)⁵, [Kim JJ](#)⁶, [Kang KY](#)⁷, [Yee ST](#)⁸.

Author information

Abstract

Although astaxanthin has a variety of biological activities such as anti-oxidant effects, inhibitory effects on skin deterioration and anti-inflammatory effects, its effect on asthma has not been studied. In this paper, the inhibitory effect of astaxanthin on airway inflammation in a mouse model of ovalbumin (OVA)-induced asthma was investigated. We evaluated the number of total cells, Th1/2 mediated inflammatory cytokines in bronchoalveolar lavage fluid (BALF) and airway hyperresponsiveness as well as histological structure. The level of total IgE, IgG1, IgG2a, OVA-specific IgG1, and OVA-specific IgG2a were also examined. The oral administration of 50 mg/mL astaxanthin inhibited the respiratory system resistance, elastance, newtonian resistance, tissue damping, and tissue elastance. Also, astaxanthin suppressed the total cell number, IL-4, and IL-5, and increased the IFN- γ in the BALF. In the sera, total IgE, IgG1, and OVA-specific IgG1 were reduced by astaxanthin exposure and IgG2a and OVA-specific IgG2a were enhanced via oral administration of astaxanthin. Infiltration of inflammatory cells in the lung, production of mucus, lung fibrosis, and expression of caspase-1 or caspase-3 were suppressed in OVA-induced asthmatic animal treated with astaxanthin. These results suggest that astaxanthin may have therapeutic potential for treating asthma via inhibiting Th2-mediated cytokine and enhancing Th1-mediated cytokine.

KEYWORDS:

airway hyperresponsiveness (AHR); astaxanthin; asthma; helper T cells (Th cells)

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The effects of oral Cardax (disodium disuccinate astaxanthin) on multiple independent oxidative stress markers in a mouse peritoneal inflammation model: influence on 5-lipoxygenase in vitro and in vivo.

[Lockwood SF](#)¹, [Penn MS](#), [Hazen SL](#), [Bikádi Z](#), [Zsila F](#).

Author information

Abstract

Disodium disuccinate astaxanthin ('rac'-dAST; Cardax) is a water-dispersible C40 carotenoid derivative under development for oral and parenteral administration for cardioprotection of the at-risk ischemic cardiovascular patient. In experimental infarction models in animals (rats, rabbits, and dogs), significant myocardial salvage has been obtained, up to 100% at the appropriate dose in dogs. The documented mechanism of action in vitro includes direct scavenging of biologically produced superoxide anion; in vivo in rabbits, modulation of the complement activity of serum has also been shown. A direct correlation between administration of the test compound in animals and reductions of multiple, independent markers of oxidative stress in serum was recently obtained in a rat experimental infarction model. For the current study, it was hypothesized that oral Cardax administration would inhibit oxidative damage of multiple relevant biological targets in a representative, well-characterized murine peritoneal inflammation model. A previously developed mass spectrometry-based (LC/ESI/MS/MS) approach was used to interrogate multiple distinct pathways of oxidation in a black mouse (C57/BL6) model system. In vivo markers of oxidant stress from peritoneal lavage samples (supernatants) were evaluated in mice on day eight (8) after treatment with either Cardax or vehicle (lipophilic emulsion without drug) orally by gavage at 500 mg/kg once per day for seven (7) days at five (5) time points: (1) baseline prior to treatment (t=0); (2) 16 h following intraperitoneal (i.p.) injection with thioglycollate to elicit a neutrophilic infiltrate; (3) 4 h following i.p. injection of yeast cell wall (zymosan; t=16 h/4 h thioglycollate+zymosan); (4) 72 h following i.p. injection with thioglycollate to elicit monocyte/macrophage infiltration; and (5) 72 h/4 h thioglycollate+zymosan. A statistically significant sparing effect on the arachidonic acid (AA) and linoleic acid (LA) substrates was observed at time points two and five. When normalized to the concentration of the oxidative substrates, statistically significant reductions of 8-isoprostane-F(2alpha) (8-iso-F(2alpha)) at time point three (maximal neutrophil recruitment/activation), and 5-HETE, 5-oxo-EET, 11-HETE, 9-HODE, and PGF(2alpha) at time point five (maximal monocyte/macrophage recruitment/activation) were observed. Subsequently, the direct interaction of the optically inactive stereoisomer of Cardax (meso-dAST) with human 5-lipoxygenase (5-LOX) was evaluated in vitro with circular dichroism (CD) and electronic absorption (UV/Vis) spectroscopy, and subsequent molecular docking calculations were made using mammalian 15-LOX as a surrogate (for which XRC data has been reported). The results suggested that the meso-compound was capable of interaction with, and binding to, the solvent-exposed surface of the enzyme. These preliminary studies provide the foundation for more detailed evaluation of the therapeutic effects of this compound on the 5-LOX enzyme, important in chronic diseases such as atherosclerosis, asthma, and prostate cancer in humans.

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The Promising Effects of Astaxanthin on Lung Diseases

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- PMID: **33179051**
- DOI: [10.1093/advances/nmaa143](https://doi.org/10.1093/advances/nmaa143)

Abstract

Astaxanthin (ASX) is a naturally occurring xanthophyll carotenoid. Both in vitro and in vivo studies have shown that it is a potent antioxidant with anti-inflammatory properties. Lung cancer is the leading cause of cancer death worldwide, whereas other lung diseases such as chronic obstructive pulmonary disease, emphysema, and asthma are of high prevalence. In the past decade, mounting evidence has suggested a protective role for ASX against lung diseases. This article reviews the potential role of ASX in protecting against lung diseases, including lung cancer. It also summarizes the underlying molecular mechanisms by which ASX protects against pulmonary diseases, including regulating the nuclear factor erythroid 2-related factor/heme oxygenase-1 pathway, NF- κ B signaling, mitogen-activated protein kinase signaling, Janus kinase-signal transducers and activators of transcription-3 signaling, the phosphoinositide 3-kinase/Akt pathway, and modulating immune response. Several future directions are proposed in this review. However, most in vitro and in vivo studies have used ASX at concentrations that are not achievable by humans. Also, no clinical trials have been conducted and/or reported. Thus, preclinical studies with ASX treatment within physiological concentrations as well as human studies are required to examine the health benefits of ASX with respect to lung diseases.

Liver and Kidney Health

ASTAXANTHIN REDUCED KIDNEY AGING IN RATS DOING AEROBIC EXERCISE.

Zhongguo Ying Yong Sheng Li Xue Za Zhi 2021 Jul;37(4):433-438. doi:
10.12047/j.cjap.6064.2021.034.

[Effects of astaxanthin combined with aerobic exercise on renal aging of rat induced by D-galactose and its mechanism]

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- PMID: 34374266 DOI: [10.12047/j.cjap.6064.2021.034](https://doi.org/10.12047/j.cjap.6064.2021.034)

Abstract

Objective: To study the effects and mechanisms of astaxanthin combined with aerobic exercise on renal senescence of rat induced by D-galactose. **Methods:** Sixty 3-month-old SPF SD rats were divided into control group (C group), acute senescence group (S group), astaxanthin+acute senescence group (AS group), aerobic exercise+acute senescence group (ES group), astaxanthin+aerobic exercise+acute senescence group (AES group), by two-factor two-level 2×2 factorial design with 12 rats in each group. Acute senescence model of rat was established by intraperitoneal injection with 100 mg/(kg·d) D-galactose, and the intervention was conducted with 20 mg/(kg·d) astaxanthin and/or aerobic exercise with 60% VO_{2max} for 6 weeks. The histopathological/ultrastructural changes of the kidney were observed by light microscope/electron microscope; the levels of SOD, γ-GCS and MDA were detected by ELISA, and LDF in kidney was determined by fluorescence colorimetry; the protein expression of Nrf2 signaling pathway was detected by immunohistochemistry. **Results:** Compared with AS and ES group, in AES group, the improvement of renal tissue morphology/ultrastructure was more significant; LDF was

decreased significantly ($P < 0.01$); SOD activity was significantly increased ($P < 0.01$); γ -GCS was significantly higher than that of AS group, but not significantly different from that of ES group ($P > 0.05$); there was no significant difference in MDA between groups ($P > 0.05$); the levels of Nrf2 and p-Nrf2 were increased significantly ($P < 0.05$, $P < 0.01$); HO-1 was significantly higher than that of ES group ($P < 0.05$), but not significantly different compared with that of AS group ($P > 0.05$). **Conclusion:** Astaxanthin combined with aerobic exercise can delay aging process of kidney, its mechanism may be that the combination regulate the protein expression in Nrf2 signaling pathway, \uparrow detoxifying enzymes and antioxidant enzyme activity, and improve oxidative stress in kidney of rat induced by D-galactose.

Protective effects of astaxanthin on ConA-induced autoimmune hepatitis by the JNK/p-JNK pathway-mediated inhibition of autophagy and apoptosis.

[Li J](#)¹, [Xia Y](#)¹, [Liu T](#)¹, [Wang J](#)¹, [Dai W](#)¹, [Wang F](#)¹, [Zheng Y](#)¹, [Chen K](#)¹, [Li S](#)¹, [Abudumijiti H](#)¹, [Zhou Z](#)², [Wang J](#)², [Lu W](#)², [Zhu R](#)², [Yang J](#)¹, [Zhang H](#)³, [Yin Q](#)³, [Wang C](#)¹, [Zhou Y](#)³, [Lu J](#)¹, [Zhou Y](#)¹, [Guo C](#)¹.

[Author information](#)

Abstract

OBJECTIVE:

Astaxanthin, a potent antioxidant, exhibits a wide range of biological activities, including antioxidant, atherosclerosis and antitumor activities. However, its effect on concanavalin A (ConA)-induced autoimmune hepatitis remains unclear. The aim of this study was to investigate the protective effects of astaxanthin on ConA-induced hepatitis in mice, and to elucidate the mechanisms of regulation.

MATERIALS AND METHODS:

Autoimmune hepatitis was induced in Balb/C mice using ConA (25 mg/kg), and astaxanthin was orally administered daily at two doses (20 mg/kg and 40 mg/kg) for 14 days before ConA injection. Levels of serum liver enzymes and the histopathology of inflammatory cytokines and other marker proteins were determined at three time points (2, 8 and 24 h). Primary hepatocytes were pretreated with astaxanthin (80 μ M) in vitro 24 h before stimulation with TNF- α (10 ng/ml). The apoptosis rate and related protein expression were determined 24 h after the administration of TNF- α .

RESULTS:

Astaxanthin attenuated serum liver enzymes and pathological damage by reducing the release of inflammatory factors. It performed anti-apoptotic effects via the descending phosphorylation of Bcl-2 through the down-regulation of the JNK/p-JNK pathway.

CONCLUSION:

This research firstly expounded that astaxanthin reduced immune liver injury in ConA-induced autoimmune hepatitis. The mode of action appears to be downregulation of JNK/p-JNK-mediated apoptosis and autophagy.

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25761053

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Astaxanthin prevents and reverses diet-induced insulin resistance and steatohepatitis in mice: A comparison with vitamin E.

[Ni Y](#)^{1,2}, [Nagashimada M](#)¹, [Zhuge F](#)¹, [Zhan L](#)¹, [Nagata N](#)¹, [Tsutsui A](#)³, [Nakanuma Y](#)³, [Kaneko S](#)², [Ota T](#)^{1,2}.

Author information

Abstract

Hepatic insulin resistance and nonalcoholic steatohepatitis (NASH) could be caused by excessive hepatic lipid accumulation and peroxidation. Vitamin E has become a standard treatment for NASH. However, astaxanthin, an antioxidant carotenoid, inhibits lipid peroxidation more potently than vitamin E. Here, we compared the effects of astaxanthin and vitamin E in NASH. We first demonstrated that astaxanthin ameliorated hepatic steatosis in both genetically (ob/ob) and high-fat-diet-induced obese mice. In a lipotoxic model of NASH: mice fed a high-cholesterol and high-fat diet, astaxanthin alleviated excessive hepatic lipid accumulation and peroxidation, increased the proportion of M1-type macrophages/Kupffer cells, and activated stellate cells to improve hepatic inflammation and fibrosis. Moreover, astaxanthin caused an M2-dominant shift in macrophages/Kupffer cells and a subsequent reduction in CD4(+) and CD8(+) T cell recruitment in the liver, which contributed to improved insulin resistance and hepatic inflammation. Importantly, astaxanthin reversed insulin resistance, as well as hepatic inflammation and fibrosis, in pre-existing NASH. Overall, astaxanthin was more effective at both preventing and treating NASH compared with vitamin E in mice. Furthermore, astaxanthin improved hepatic steatosis and tended to ameliorate the progression of NASH in biopsy-proven human subjects. These results suggest that astaxanthin might be a novel and promising treatment for NASH.

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26603489

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PMC4658633

[Free PMC Article](#)

Effects of Antioxidants in Reducing Accumulation of Fat in Hepatocyte.

[Yang JP](#)¹, [Shin JH](#)², [Seo SH](#)³, [Kim SG](#)⁴, [Lee SH](#)⁵, [Shin EH](#)^{6,7}.

Author information

Abstract

The progress of the hepatic steatosis (HS), a clinicopathological status, is influenced by cellular oxidative stress, lipogenesis, fatty acid (FA) oxidation, and inflammatory responses. Because antioxidants are gaining attention as potent preventive agents for HS, we aimed to investigate anti-lipogenic effects of the antioxidants vitamin C (VC), N-acetylcysteine (NAC), and astaxanthin (ATX) using hepatocytes. For this, we established an in vitro model using 1 mM oleic acid (OA) and human liver hepatocellular carcinoma (HepG2) cells; 10 μ M antioxidants were evaluated for their ability to reduce fat accumulation in hepatocytes. Our results showed that all three antioxidants were effective to reduce fat accumulation for the molecular targets such as reduction in lipid droplets, triglyceride (TG) concentration, reactive oxygen species (ROS) production, and cell apoptosis, as well as in gene expressions of endoplasmic reticulum (ER) stress-related effectors, lipogenesis, and inflammatory cytokines. There were simultaneous increases in diphenyl-1-picrylhydrazyl (DPPH) radical scavenging effect, cell survival, AMPK phosphorylation, NRF2-related gene expression for cellular defense, and FA β -oxidation. However, among these, ATX more effectively inhibited ER stress and lipogenesis at the intracellular level than VC or NAC. Consequently, ATX was also more effective in inhibiting cell death, lipotoxicity, and inflammation. Our result emphasizes that ATX achieved greater lipotoxicity reduction than VC and NAC.

KEYWORDS:

N-acetyl-L-cysteine; astaxanthin; free radical scavenging; lipogenesis; oleic acid; vitamin C

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[Indexed for MEDLINE]

[Free PMC Article](#)

Astaxanthin Promotes Nrf2/ARE Signaling to Alleviate Renal Fibronectin and Collagen IV Accumulation in Diabetic Rats.

[Zhu X](#)^{1,2}, [Chen Y](#)^{3,4}, [Chen Q](#)⁵, [Yang H](#)², [Xie X](#)^{1,2,3}.

Author information

Abstract

Astaxanthin (AST), a natural keto-carotenoid classified as a xanthophyll, is well known for its antioxidant properties. AST can ameliorate the pathological characteristics of diabetic nephropathy (DN). However, the underlying mechanisms remain to be explored. This study was aimed at exploring whether AST exerts a protective effect on DN via activating nuclear factor erythroid 2-related factor 2- (Nrf2-) antioxidative response element (ARE) signaling. Streptozotocin-induced diabetic rats were treated with AST for 12 weeks. We found that AST treatment ameliorated renal morphological injury. Reduced fibronectin and collagen IV protein expression were found in the kidneys of diabetic rats. Furthermore, AST promoted the nuclear translocation of Nrf2 and increased its downstream protein heme oxygenase-1 and superoxide dismutase 1 expression. AST also increased the activity of SOD and decreased malondialdehyde generation in the serum of diabetic rats. These results suggest that the renoprotective effect of AST on DN partly depends on Nrf2-ARE signaling. The antioxidative stress effect of AST is responsible for the activation of Nrf2-ARE signaling in DN.

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[Indexed for MEDLINE]

[Free PMC Article](#)

Reparative Effects of Astaxanthin-Hyaluronan Nanoaggregates against Retrorsine-CCl₄-Induced Liver Fibrosis and Necrosis.

[Wu YJ](#)¹, [Wu YC](#)^{2,3}, [Chen IF](#)⁴, [Wu YL](#)⁵, [Chuang CW](#)⁶, [Huang HH](#)⁷, [Kuo SM](#)⁸.

Author information

Abstract

Astaxanthin (Asta), a xanthophyll carotenoid, has been reported to be a strong antioxidative agent and has anti-inflammatory, antitumor and free radical-scavenging activities. However, inadequate stability and water solubility results in its low bioavailability. This study incorporated Asta into hydrophilic hyaluronan nanoparticles (HAN) to produce Asta-HAN aggregates (AHANA) using an electrostatic field system and investigated the restorative effects of AHANA on retrorsine-CCl₄-induced liver fibrosis in rats in vivo. Transmission electron microscopy (TEM) revealed that the prepared HAN were approximately 15 ± 2.1 nm in diameter and after the incorporation of Asta into HAN, the size increased to 210-500 nm. The incorporation efficiency of Asta was approximately 93% and approximately 54% of Asta was released after incubation for 18 h. Significant reductions in alanine aminotransferase and aspartate aminotransferase levels were observed after the rats were intraperitoneally injected with AHANA. Histopathological findings revealed the greatest reduction in hepatic fibrosis and hepatocyte necrosis in the rats after 2 weeks of intraperitoneal injection with AHANA, which is consistent with the data acquired from serum biochemical analysis. The restorative effects on liver damage displayed by AHANA in vivo demonstrated that Asta aggregated through HAN incorporation exerts therapeutic effects on liver fibrosis and necrosis.

KEYWORDS:

astaxanthin; astaxanthin-hyaluronan nanoparticles-aggregate; hyaluronan nanoparticle; liver fibrosis and necrosis

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[Free PMC Article](#)

Astaxanthin attenuates contrast agent-induced acute kidney injury in vitro and in vivo via the regulation of SIRT1/FOXO3a expression.

[Liu N](#)¹, [Chen J](#)², [Gao D](#)¹, [Li W](#)^{3,4}, [Zheng D](#)⁵.

Author information

Abstract

PURPOSE: The study was processed to investigate the effect of astaxanthin (AST; 3,3-dihydroxybeta, beta-carotene-4,4-dione) on the acute kidney injury induced by iohexol and the relationship with SIRT1/FOXO3a signal pathway.

METHODS: Thirty male Sprague Dawley rats were randomly divided into five groups as follows: control group (CON; olive oil only), contrast media group, astaxanthin control group (100 mg/kg), low astaxanthin dose group (LAG, 50 mg/kg) and high astaxanthin dose group (HAG, 100 mg/kg). As followed, serum creatinine (SCr), blood urea nitrogen (BUN), the oxidative stress markers and apoptosis-related proteins were detected. Human proximal tubular epithelial cells (HK-2) were cultured in DMEM/F12 medium in vitro and then randomly divided into appropriate experimental groups: normal group (N), dimethyl sulfoxide (DMSO), iohexol group (I), iohexol + (1.0, 10.0 $\mu\text{mol/L}$) astaxanthin group (I + LAST; I + HAST), iohexol + SIRT1 inhibitors (nicotinamide) group (NA) and iohexol + si-RNA FOXO3a group (si-RNA FOXO3a); when cultured for 24 h, cell proliferation ability was tested by cell counting kit (CCK-8), reactive oxygen species (ROS) were detected by flow cytometry and the expression of SIRT1 and FOXO3a were observed using western blot.

RESULTS: At the end of the experiment, the levels of SCr, BUN and malondialdehyde (MDA) were all increased in the CM group. The LAG and HAG reduce superoxide anion (SOD) activity, catalase (CAT) activity, glutathione peroxidase (GPx) activity and glutathione (GSH) content, as well as SCr and BUN level. Moreover, apoptosis-associated proteins, caspase 3 p17, bax and bcl-2 were upregulated. In HK-2 cells, after adding iohexol, proliferation and intracellular ROS levels were significantly increased. Using astaxanthin in advance after the intervention, the result is opposite. SIRT1 inhibitors NA can reduce the expression of SIRT1 and decrease the expression of FOXO3a protein. Si-RNA FOXO3a reduces the expression of FOXO3a but had no significant effect on the expression of SIRT1.

CONCLUSIONS: Our study demonstrates that the intervention of astaxanthin could attenuate the oxidative stress and apoptosis in contrast-induced acute kidney injury (CI-AKI), and the SIRT1/FOXO3a pathway participates in the contrast-induced apoptosis of HK-2 cells. Finally, astaxanthin reduces CI-AKI by suppression of apoptosis, which may be through inhibition of SIRT1/FOXO3a pathways.

Astaxanthin Ameliorates Hepatic Damage and Oxidative Stress in Carbon Tetrachloride-administered Rats.

[Islam MA¹](#), [Al Mamun MA¹](#), [Faruk M¹](#), [Ul Islam MT¹](#), [Rahman MM¹](#), [Alam MN¹](#), [Rahman AFMT¹](#), [Reza HM¹](#), [Alam MA¹](#).

Author information

Abstract

BACKGROUND: Astaxanthin is of carotenoids group which possess strong antioxidant properties. The present study was conducted to evaluate the hepatoprotective effects of astaxanthin in carbon tetrachloride (CCl₄)-treated rats.

MATERIALS AND METHODS: Female Long-Evans rats were administered with CCl₄ orally (1 ml/kg) twice a week for 2 weeks and were treated with astaxanthin (10 mg/kg) every day for 2 weeks. Blood plasma samples were isolated from each group and were analyzed for alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase activities. Oxidative stress parameters such as malondialdehyde (MDA), nitric oxide (NO), and advanced protein oxidation product (APOP) were measured. Several enzyme functions such as myeloperoxidase (MPO), superoxide dismutase (SOD), and catalase (CAT) activities in the plasma and liver tissues were also analyzed. Moreover, inflammation and tissue fibrosis were also confirmed by histological staining of liver tissues.

RESULTS: This investigation revealed that CCl₄ administration in rats increased plasma AST, ALT, and ALP activities which were normalized by astaxanthin treatment. Moreover, CCl₄ administration increased as MDA, NO, and APOP level both in plasma and tissues compared to control rats. Astaxanthin also exhibited a significant reduction of those parameters in CCl₄-administered rats. Astaxanthin treatment also restored the CAT and SOD activities and lowered MPO activity in CCl₄-administered rats. Histological assessment also revealed that the astaxanthin prevented the inflammatory cells infiltration, decreased free iron deposition, and fibrosis in liver of CCl₄-administered rats.

CONCLUSION: These results suggest that astaxanthin protects liver damage induced by CCl₄ by inhibiting lipid peroxidation and stimulating the cellular antioxidant system.

SUMMARY: Carbon tetrachloride (CCl₄) administration increased oxidative stress-mediated hepatic damage and inflammation in rats. Astaxanthin, a potent antioxidant, prevents oxidative stress and inflammatory cells infiltration in CCl₄-administered rats. Astaxanthin also ameliorated the progression of hepatic fibrosis in CCl₄-administered rats. **Abbreviations Used:** APOP: Advanced protein oxidation product; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; ALP: Alkaline phosphatase; CAT: Catalase; CCl₄: Carbon tetrachloride; CVD: Cardiovascular disease; HSCs: Hepatic stellate cells; H₂O₂: Hydrogen peroxide; MDA: Malondialdehyde; MMP2: Matrix

metalloproteinase2; MPO: Myeloperoxidase; NF- κ B: Nuclear factor kappa B; NO: Nitric oxide; Nrf2: Nuclear factor erythroid 2-related factor 2; \cdot ONOO \cdot : Peroxynitrate; ROS: Reactive oxygen species; SOD: superoxide dismutase; TCA: Trichloroacetic acid; TBA: Thiobarbituric acid; TGF-1: Transforming growth factor 1, TGF- β : Transforming growth factor- β ; TIMP1: Tissue inhibitor of metalloproteinase 1; TNF- α : Tumor necrosis factor-alpha; \cdot CCl3: Trichloromethyl free radical; CCl3O2 \cdot : Trichloroperoxyl radical.

KEYWORDS:

Carbon tetrachloride; fibrosis; inflammation; lipid peroxidation

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PMCID: [PMC5757332](#)

DOI: [10.4103/pr.pr_26_17](#)

[Free PMC Article](#)

Astaxanthin prevents ischemia-reperfusion injury of the steatotic liver in mice.

[Li S](#)^{1,2,3,4}, [Takahara T](#)⁵, [Fujino M](#)^{1,6}, [Fukuhara Y](#)⁷, [Sugiyama T](#)⁵, [Li XK](#)¹, [Takahara S](#)².

Author information

Abstract

Steatosis has a low tolerance against ischemia-reperfusion injury (IRI). To prevent IRI in the steatotic liver, we attempted to elucidate the protective effect of astaxanthin (ASTX) in the steatotic liver model by giving mice a methionine and choline-deficient high fat (MCDHF) diet. Levels of lipid peroxidation and apoptosis, the expression of inflammatory cytokines and heme oxygenase (HO)-1, in the liver were assessed. Reactive oxygen species (ROS), inflammatory cytokines, apoptosis-related proteins and members of the signaling pathway were also examined in isolated Kupffer cells and/or hepatocytes from the steatotic liver. ASTX decreased serum ALT and AST levels, the amount of TUNEL, F4/80, or 4HNE-positive cells and the mRNA levels of inflammatory cytokines in MCDHF mice by IRI. Moreover, HO-1 and HIF-1 α , phosphorylation of Akt and mTOR expressions were increased by ASTX. The inflammatory cytokines produced by Kupffer, which were subjected to hypoxia and reoxygenation (HR), were inhibited by ASTX. Expressions of Bcl-2, HO-1 and Nrf2 in hepatocytes by HR were increased, whereas Caspases activation, Bax and phosphorylation of ERK, MAPK, and JNK were suppressed by ASTX. Pretreatment with ASTX has a protective effect and is a safe therapeutic treatment for IRI, including for liver transplantation of the steatotic liver.

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PMCID: [PMC5679630](#)

DOI: [10.1371/journal.pone.0187810](#)

[Indexed for MEDLINE]

[Free PMC Article](#)

Astaxanthin pretreatment attenuates acetaminophen-induced liver injury in mice.

[Zhang J¹](#), [Zhang S¹](#), [Bi J¹](#), [Gu J¹](#), [Deng Y¹](#), [Liu C²](#).

Author information

Abstract

BACKGROUND: Acetaminophen (APAP) is a conventional drug widely used in the clinic because of its antipyretic-analgesic effects. However, accidental or intentional APAP overdoses induce liver injury and even acute liver failure (ALF). Astaxanthin (ASX) is the strongest antioxidant in nature that shows preventive and therapeutic properties, such as ocular protection, anti-tumor, anti-diabetes, anti-inflammatory, and immunomodulatory effects. The aim of present study was to determine whether ASX pretreatment provides protection against APAP-induced liver failure.

METHODS: Male C57BL/6 mice were randomly divided into 7 groups, including control, oil, ASX (30mg/kg or 60mg/kg), APAP and APAP+ASX (30mg/kg or 60mg/kg) groups. Saline, olive oil and ASX were administered for 14days. The APAP and APAP+ASX groups were given a peritoneal injection of 700mg/kg or 300mg/kg APAP to determine the 5-day survival rate and for further observation, respectively. Blood and liver samples were collected to detect alanine transaminase (ALT), aspartate transaminase (AST), inflammation, oxidative stress and antioxidant systems, and to observe histopathologic changes and key proteins in the mitogen-activated protein kinase (MAPK) family.

RESULTS: ASX pretreatment before APAP increased the 5-day survival rate in a dose-dependent manner and reduced the ALT, AST, hepatic necrosis, reactive oxygen species (ROS) generation, lipid peroxidation (LPO), oxidative stress and pro-inflammatory factors. ASX protected against APAP toxicity by inhibiting the depletion of glutathione (GSH) and superoxide dismutase (SOD). Administration of ASX did not change the expression of c-Jun N-terminal kinase (JNK), extracellular signal-regulated kinase (ERK) and P38. However, phosphorylation of JNK, ERK and P38 was reduced, consistent with the level of tumor necrosis factor alpha (TNF- α) and TNF receptor-associated factor 2 (TRAF2).

CONCLUSION: ASX provided protection for the liver against APAP hepatotoxicity by alleviating hepatocyte necrosis, blocking ROS generation, inhibiting oxidative stress, and reducing apoptosis by inhibiting the TNF- α -mediated JNK signal pathway and by phosphorylation of ERK and P38, which made sense in preventing and treating liver damage.

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KEYWORDS: Acetaminophen; Apoptosis; Astaxanthin; JNK pathway; Liver injury; Oxidative stress

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Evaluation of efficacy of natural astaxanthin and vitamin E in prevention of colistin-induced nephrotoxicity in the rat model.

[Ghissi Z](#)¹, [Hakim A](#)², [Sila A](#)³, [Mnif H](#)⁴, [Zeghal K](#)², [Rebai T](#)⁵, [Bougatef A](#)³, [Sahnoun Z](#)².

Author information

Abstract

OBJECTIVE: We evaluated the effect of astaxanthin (ASX) and vitamin E (vit E) on colistin methanesulfonate (CMS) induced-nephrotoxicity in rats.

METHODS: Animals were treated with sterile saline, 300000 or 450 000 IU/kg/day of CMS, CMS + ASX (20 mg/kg), CMS + vit E (100 mg/kg), or CMS + 1 ml/kg olive oil (OO) for 7 days. The plasma/urine creatinine (Cr) level, urine γ -glutamyl-transferase (GGT) level, and renal tissue activities in malondialdehyde (MDA), superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx) and reductase (GSH), as well as renal histology were performed.

RESULTS: CMS induced a tubular damage, increased the GGT and MDA levels, and decreased the activities of SOD, CAT, GPx and GSH. Co-treatment with ASX or vit E restored all biochemical parameters cited above and improved the histopathological damage.

CONCLUSION: Nephrotoxicity induced by CMS might be due to oxidative damage. The improvement by ASX or vit E seems to be related to their antioxidant properties.

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KEYWORDS: Astaxanthin; Colistin; Nephrotoxicity; Oxidative damage; Vitamin E

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[Indexed for MEDLINE]

Astaxanthin reduces hepatic lipid accumulations in high-fat-fed C57BL/6J mice via activation of peroxisome proliferator-activated receptor (PPAR) alpha and inhibition of PPAR gamma and Akt.

[Jia Y¹](#), [Wu C¹](#), [Kim J¹](#), [Kim B¹](#), [Lee SJ²](#).

Author information

Abstract

We have previously reported that astaxanthin (AX), a dietary carotenoid, directly interacts with peroxisome proliferator-activated receptors PPAR α and PPAR γ , activating PPAR α while inhibiting PPAR γ , and thus reduces lipid accumulation in hepatocytes in vitro. To investigate the effects of AX in vivo, high-fat diet (HFD)-fed C57BL/6J mice were orally administered AX (6 or 30mg/kg body weight) or vehicle for 8weeks. AX significantly reduced the levels of triglyceride both in plasma and in liver compared with the control HFD mice. AX significantly improved liver histology and thus reduced both steatosis and inflammation scores of livers with hematoxylin and eosin staining. The number of inflammatory macrophages and Kupffer cells were reduced in livers by AX administration assessed with F4/80 staining. Hepatic PPAR α -responsive genes involved in fatty acid uptake and β -oxidation were upregulated, whereas inflammatory genes were downregulated by AX administration. In vitro radiolabeled assays revealed that hepatic fatty acid oxidation was induced by AX administration, whereas fatty acid synthesis was not changed in hepatocytes. In mechanism studies, AX inhibited Akt activity and thus decreased SREBP1 phosphorylation and induced Insig-2a expression, both of which delayed nuclear translocation of SREBP1 and subsequent hepatic lipogenesis. Additionally, inhibition of the Akt-mTORC1 signaling axis by AX stimulated hepatic autophagy that could promote degradation of lipid droplets. These suggest that AX lowers hepatic lipid accumulation in HFD-fed mice via multiple mechanisms. In addition to the previously reported differential regulation of PPAR α and PPAR γ , inhibition of Akt activity and activation of hepatic autophagy reduced hepatic steatosis in mouse livers.

KEYWORDS:

Akt; Astaxanthin; Autophagy; PPAR; SREBP1

PMID: 26878778

DOI: [10.1016/j.jnutbio.2015.09.015](#)

[Indexed for MEDLINE]

Astaxanthin Inhibits Proliferation and Induces Apoptosis and Cell Cycle Arrest of Mice H22 Hepatoma Cells.

[Shao Y](#)¹, [Ni Y](#)², [Yang J](#)³, [Lin X](#)⁴, [Li J](#)⁵, [Zhang L](#)⁶.

Author information

Abstract

BACKGROUND It is widely recognized that astaxanthin (ASX), a member of the carotenoid family, has strong biological activities including antioxidant, anti-inflammation, and immune-modulation activities. Previous studies have confirmed that ASX can effectively inhibit hepatoma cells in vitro.

MATERIAL AND METHODS MTT was used to assay proliferation of mice H22 cells, and flow cytometry was used to determine apoptosis and cell cycle arrest of H22 cells in vitro and in vivo.

Moreover, anti-tumor activity of ASX was observed in mice. **RESULTS** ASX inhibited the proliferation of H22 cells, promoted cell necrosis, and induced cell cycle arrest in G2 phase in vitro and in vivo.

CONCLUSIONS This study indicated that ASX can inhibit proliferation and induce apoptosis and cell cycle arrest in mice H22 hepatoma cells in vitro and in vivo.

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[Free PMC Article](#)

Improved Hepatoprotective Effect of Liposome-Encapsulated Astaxanthin in Lipopolysaccharide-Induced Acute Hepatotoxicity.

[Chiu CH](#)¹, [Chang CC](#)^{2,3}, [Lin ST](#)⁴, [Chyau CC](#)⁵, [Peng RY](#)^{6,7}.

[Author information](#)

Abstract

Lipopolysaccharide (LPS)-induced acute hepatotoxicity is significantly associated with oxidative stress. Astaxanthin (AST), a xanthophyll carotenoid, is well known for its potent antioxidant capacity. However, its drawbacks of poor aqueous solubility and low bioavailability have limited its utility. Liposome encapsulation is considered as an effective alternative use for the improvement of bioavailability of the hydrophobic compound. We hypothesized that AST encapsulated within liposomes (LA) apparently shows improved stability and transportability compared to that of free AST. To investigate whether LA administration can efficiently prevent the LPS-induced acute hepatotoxicity, male Sprague-Dawley rats (n = six per group) were orally administered liposome-encapsulated AST at 2, 5 or 10 mg/kg-day (LA-2, LA-5, and LA-10) for seven days and then were LPS-challenged (i.p., 5 mg/kg). The LA-10 administered group, but not the other groups, exhibited a significant amelioration of serum glutamic pyruvic transaminase (GPT), glutamic oxaloacetic transaminase (GOT), blood urea nitrogen (BUN), creatinine (CRE), hepatic malondialdehyde (MDA) and glutathione peroxidase (GSH-Px), IL-6, and hepatic nuclear NF-κB and inducible nitric oxide synthase (iNOS), suggesting that LA at a 10 mg/kg-day dosage renders hepatoprotective effects. Moreover, the protective effects were even superior to that of positive control N-acetylcysteine (NAC, 200 mg/kg-day). Histopathologically, NAC, free AST, LA-2 and LA-5 partially, but LA-10 completely, alleviated the acute inflammatory status. These results indicate that hydrophobic AST after being properly encapsulated by liposomes improves bioavailability and can also function as potential drug delivery system in treating hepatotoxicity.

KEYWORDS: Astaxanthin; antioxidant enzymes; hepatotoxicity; inflammation; liposome encapsulation

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PMCID: [PMC4964502](#)

DOI: [10.3390/ijms17071128](#)

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[Free PMC Article](#)

ASTAXANTHIN IMPROVES LIVER FUNCTION AND REDUCES OXIDATIVE STRESS BY IMPROVING LIPID METABOLISM IN BOTH HEALTHY AND OBESE DOGS.

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Effects of astaxanthin supplementation in healthy and obese dogs

[Tae Murai](#)¹, [Koh Kawasumi](#)¹, [Kumi Tominaga](#)², [Yuki Okada](#)¹, [Motoo Kobayashi](#)¹, [Toshiro Arai](#)¹

PMID: 30859086 PMCID: [PMC6385744](#) DOI: [10.2147/VMRR.S186202](#) [Free PMC article](#)

Abstract

Background: Since astaxanthin (ASX) has potent anti-oxidative effects with inhibitory action of lipid peroxidation and singlet oxygen quenching activity, it is widely used as a functional food for keeping good health in human. Obesity is a risk factor for various metabolic disorders. It is characterized by low-grade chronic inflammation based on oxidative stress by excessively produced ROS. From the point of preventive medicine, natural compounds have been proposed as potential therapeutic agents in the prevention of metabolic disorder in companion animals. The purpose of this study is to evaluate the effects of ASX supplementation in healthy and obese dogs.

Materials and Methods: Ten healthy beagle dogs and 5 clinically obese dogs were used in this study. The healthy beagle dogs were randomly divided into 2 groups as follows: control and test groups. The test group dogs received ASX supplementation mixed with the food for 6 weeks. Five clinically obese dogs received ASX supplementation for 8 weeks. Metabolites, hormones and enzymes were measured before and after ASX supplementation.

Results: In the healthy dog groups, after 6 weeks, plasma triglyceride (TG) and malondialdehyde concentrations and lactate dehydrogenase (LDH) values significantly decreased in the test group. There was no significant difference in the control group. In clinically obese dogs, plasma TG concentration decreased after 8 weeks of ASX supplementation. Plasma alanine aminotransferase and LDH values clearly decreased in all 5 dogs and 4 dogs out of 5 dogs, respectively.

Conclusion: ASX supplementation (0.3 mg/kg body weight/day) for 6 weeks in healthy dogs and 8 weeks in obese dogs induced the elevation of antioxidant function and of liver function by ameliorating lipid metabolism.

ASTAXANTHIN SHOWS LIVER-PROTECTIVE PROPERTIES IN SHRIMP.

Mar Drugs. 2020 Apr 17;18(4):218.

doi: 10.3390/md18040218.

Astaxanthin Attenuates Fish Oil-Related Hepatotoxicity and Oxidative Insult in Juvenile Pacific White Shrimp (*Litopenaeus vannamei*)

[Yingying Yu](#)^{1,2,3}, [Yang Liu](#)², [Peng Yin](#)¹, [Weiwen Zhou](#)¹, [Lixia Tian](#)¹, [Yongjian Liu](#)¹, [Donghui Xu](#)³, [Jin Niu](#)¹

PMID: [32316590](#) PMCID: [PMC7230248](#) DOI: [10.3390/md18040218](#) [Free PMC article](#)

Abstract

The present study investigated the effect of dietary astaxanthin (AX) on the growth performance, antioxidant parameters, and repair of hepatopancreas damage in Pacific white shrimp (*Litopenaeus vannamei*). To evaluate the hepatopancreas protective function of AX in shrimps, we compared the effect of five isonitrogenous and isoenergetic diets under oxidized fish oil conditions with varying AX levels during the 50-day experimental period. The formulated diets were as follows: (i) OFO (oxidized fish oil); (ii) OFO/AX150 (oxidized fish oil + AX150 mg/kg); (iii) OFO/AX250 (oxidized fish oil + AX250 mg/kg); (iv) OFO/AX450 (oxidized fish oil + AX450 mg/kg); and, (v) control group (fresh fish oil). Results showed that the oxidized fish oil with 275.2 meq/kg peroxide value (POV) resulted in a substantial decrease in the final body weight of *L. vannamei* ($P > 0.05$) and induced some visible histopathological alterations in the hepatopancreas. Growth performance was significantly higher in shrimps fed with the OFO/AX450 diet than those fed with the OFO diet ($p < 0.05$). However, no significant difference was observed when the OFO/AX450 diet was compared to the control diet containing fresh fish oil ($p > 0.05$). Moreover, shrimps under the OFO/AX450 diet displayed a significant improvement in hepatopancreatic health and showed a reduction of malondialdehyde (MDA) compared to those under the OFO diet ($p < 0.05$). Dietary AX improved the antioxidant capacity of *L. vannamei* by increasing the catalase (CAT) activity in the hemolymph. Acute salinity change test showed a higher shrimp survival rate under OFO/AX450 diet than the OFO diet ($p < 0.05$), suggesting that AX can contribute to enhanced stress tolerance. In conclusion, our data suggest that AX confers dose-dependent protection against OFO-induced oxidative insults and hepatopancreatic damage in shrimp.

ASTAXANTHIN REDUCES LIVER DAMAGE IN RATS EXPOSED TO ARSENIC.

Food Funct. 2020 Oct 21;11(10):9252-9262.

doi: 10.1039/d0fo01223h.

Inflammation response after the cessation of chronic arsenic exposure and post-treatment of natural astaxanthin in liver: potential role of cytokine-mediated cell-cell interactions

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Abstract

Ongoing groundwater arsenic contamination throughout China was first recognized in the 1960s. Groundwater arsenic contamination is a high risk for human and animal health worldwide. Apart from drinking water, diet is the second pathway for arsenic to enter the human body and eventually cause liver injury. Natural astaxanthin extracted from the green algae *Haematococcus pluvialis* has dominated the nutraceutical market for potential health benefits. Nevertheless, the molecular mechanism underlying the protective effect post astaxanthin against arsenic-induced hepatotoxicity remains largely obscure. In this study, we investigate the effect of natural astaxanthin (derived from *Haematococcus pluvialis*) on oxidative stress and liver inflammatory response in rats after the cessation of chronic arsenic exposure. Wistar rats were given astaxanthin (250 mg kg⁻¹) daily for 2 weeks after the cessation of exposure to sodium arsenite (300 µg L⁻¹, drinking water, 24 weeks) by intragastric administration. The results showed that post treatment with astaxanthin attenuated liver injury induced by long-term exposure to arsenic in rats. Most importantly, post treatment with astaxanthin decreased the increasing of inflammatory cytokine NF-κB, tumor necrosis factor-α, interleukin-1β, oxidative stress level, and total arsenic content in livers of rats exposed to arsenic. In addition, post treatment with astaxanthin reversed the increasing of protein levels of alpha-smooth muscle actin and collagen Iα1, which are the activation markers of hepatic stellate cells (HSCs). Collectively, these data demonstrate that post astaxanthin treatment attenuates inflammation response in the liver after the cessation of chronic arsenic exposure via inhibition of cytokine-mediated cell-cell interactions. Daily ingestion of natural astaxanthin might be a potential and beneficial candidate for the treatment of liver damage after the cessation of chronic exposure to sodium arsenite.

ASTAXANTHIN ALLEVIATES INDUCED LIVER DAMAGE IN RATS IN A DOSE-DEPENDENT MANNER.

J Vet Med Sci. 2019 Aug 24;81(8):1162-1172.
doi: 10.1292/jvms.18-0690. Epub 2019 Jul 3.

The effects of astaxanthin on liver histopathology and expression of superoxide dismutase in rat aflatoxicosis

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PMID: 31270307 PMCID: [PMC6715921](#) DOI: [10.1292/jvms.18-0690](#) [Free PMC article](#)

Abstract

The metabolism of aflatoxin B₁ (AFB₁) generates reactive oxygen species (ROS) that destroys hepatocytes. Meanwhile, astaxanthin (AX) is known to have stronger antioxidative activity than other carotenoids. This study aimed to investigate hepatoprotective role of AX from AFB₁-induced toxicity in rat by histopathological study and immunohistochemistry of Cu/Zn-SOD (SOD1) which acts as the first enzyme in antioxidative reaction against cell injury from ROS. Twenty Wistar rats were randomly divided into 4 groups. The control and AFB₁ groups were gavaged by water for 7 days followed by a single DMSO and 1 mg/kg AFB₁, respectively. The AXL+ AFB₁ and AXH+ AFB₁ groups were given of 5 mg/kg and 100 mg/kg AX for 7 days before 1 mg/kg AFB₁ administration. The result showed significantly elevated liver weight per 100 g body weight in AFB₁ group. The histopathological finding revealed vacuolar degeneration, necrosis, megalocytosis and binucleation of hepatocytes with bile duct hyperplasia in AFB₁ group. The severities of pathological changes were sequentially reduced in AXL+AFB₁ and AXH+AFB₁ groups. Most rats in AXH+AFB₁ group owned hypertrophic hepatocytes and atypical proliferation of cholangiocytes which are adaptive responses to severe hepatocyte damage. The SOD1 expression was also significantly higher in AXH+AFB₁ group than solely treated AFB₁ and AXL+AFB₁ groups. In conclusion, AX alleviated AFB₁-induced liver damage in rat by stimulating SOD1 expression and transdifferentiation of cholangiocytes in dose dependent manner.

ASTAXANTHIN IMPROVES MULTIPLE MARKERS IN LIVER AND KIDNEYS SUBJECTED TO ISCHAEMIA IN RAT STUDY.

Prz Gastroenterol. 2020;15(2):161-172.
doi: 10.5114/pg.2019.88620. Epub 2019 Oct 9.

Evaluation with endothelial nitric oxide synthase (eNOS) immunoreactivity of the protective role of astaxanthin on hepatorenal injury of remote organs caused by ischaemia reperfusion of the lower extremities

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- PMID: [32550950](#)
- PMCID: [PMC7294969](#)
- DOI: [10.5114/pg.2019.88620](#)

Free PMC article

Abstract

Introduction: Ischemia and following reperfusion triggers local and systemic damage with the involvement of free oxygen radicals and inflammatory mediators. Although blood flow saves extremity from necrosis, multi organ dysfunction may progress and cause death of the patient.

Aim: The study aims to examine the effect of astaxanthin (AST) on the prevention of remote tissue injury resulting from lower extremity ischaemia-reperfusion (I/R). To elucidate the potential hepatoprotective and renoprotective effects of AST, in addition to histopathological findings, the intrahepatic and intrarenal kinetics of endothelial nitric oxide synthase (eNOS) during I/R were determined by using the immunohistochemical method.

Material and Methods: Twenty-eight male Wistar albino rats were divided into four groups. For the control group, only the anaesthesia procedure (2 h) was conducted without I/R. In the I/R group, 2 h of reperfusion was conducted following ischaemia under anaesthesia. For the I/R group + AST, 7 days prior to ischaemia, 125 mg/kg AST was given with gavage, and 2 h of ischaemia and 2 h of reperfusion were conducted under anaesthesia. Following necropsy, liver and kidney tissue samples were fixed in 10% buffered formalin for 48 h for histopathological and immunohistochemical investigation.

Results: The histological analysis revealed that severe I/R hepatorenal injury such as inflammatory cell infiltration, dilatation in sinusoids and lumen of tubuli, congestion in glomerular capillaries, degeneration in hepatocyte and epithelial cells of tubuli, and necrosis was ameliorated by AST. Immunohistochemical studies showed that the I/R-induced elevation in eNOS expression was reduced by AST treatment.

Conclusions: In the case of acute lower extremity I/R, AST decreased the ischaemic injury in liver and renal tissues by protecting the microcirculation and providing a cytoprotective effect with vasodilatation.

ASTAXANTHIN FOUND SUPERIOR TO OTHER CAROTENOIDS (LYCOPENE, LUTEIN, ZEAXANTHIN AND CANTHAXANTHIN) AGAINST LIVER FIBROSIS IN VITRO.

Lipids. 2019 Jun;54(6-7):401-410.

doi: 10.1002/lipd.12157. Epub 2019 May 29.

Comparison of Carotenoids for Their Antifibrogenic Effects in Hepatic Stellate Cells

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PMID: [31140624](#) PMCID: [PMC6591040](#) DOI: [10.1002/lipd.12157](#) [Free PMC article](#)

Abstract

Hepatic stellate cells (HSC) have an important role in the development of liver fibrosis by producing extracellular matrix proteins when they are activated upon liver injury. We previously demonstrated that astaxanthin (ASTX), a xanthophyll carotenoid, attenuates HSC activation. The objective of this study was to compare the anti-fibrogenic effects of ASTX with those of other common carotenoids. LX-2 cells, a human HSC cell line, were treated with ASTX, lycopene, lutein (LT), zeaxanthin, or canthaxanthin, to measure messenger RNA (mRNA) and protein expression of pro-fibrogenic genes. Pro-fibrogenic gene expressions were also measured in ASTX- or LT-treated primary mouse HSC. To determine the underlying mechanisms of the anti-fibrogenic effect of ASTX and LT, SMA-related and MAD-related protein 3 (SMAD3) pathways and the accumulation of reactive oxygen species (ROS) were measured in LX-2 cells. Among five carotenoids tested, ASTX and LT attenuated HSC activation in LX-2 cells by reducing the mRNA and protein levels of pro-fibrogenic genes, such as smooth muscle α actin and procollagen type I α 1 (COL1A1). In addition, both ASTX and LT significantly decreased the expression of pro-fibrogenic genes, including COL1A1, COL3A1, and COL6A1, in activated primary mouse HSC, with ASTX being more potent than LT. The anti-fibrogenic effect of ASTX was mediated by inhibiting the phosphorylation of SMAD3 and cellular ROS accumulation, while LT only prevented the accumulation of ROS in LX-2 cells. In conclusion, ASTX showed the most potent anti-fibrogenic effect among the five carotenoids via inhibition of SMAD3 phosphorylation and cellular ROS accumulation while LT only prevented ROS levels in HSC.

Astaxanthin as a Potential Protector of Liver Function: A Review.

[Chen JT¹](#), [Kotani K²](#).

Author information

Abstract

Protecting against liver damage, such as non-alcoholic fatty liver disease, is currently considered to be important for the prevention of adverse conditions, such as cardiovascular and cancerous diseases. Liver damage often occurs in relation to oxidative stress with metabolic disorders, including cellular lipid accumulation. Astaxanthin (3,3'-dihydroxy- β,β -carotene-4,4'dione), a xanthophyll carotenoid, is a candidate for liver protection. Here, we briefly review astaxanthin as a potential protector against liver damage. In particular, studies have reported antioxidative effects of astaxanthin in liver tissues. Astaxanthin treatment is also reported to improve hyperlipidemia, which indirectly induces the antioxidative effects of astaxanthin on liver pathologies.

Furthermore, astaxanthin may alleviate liver damage independent of its antioxidative effects. Of note, there are still insufficient human data to observe the effect of astaxanthin treatment on liver function in clinical conditions. More studies investigating the relevance of astaxanthin on liver protection are necessary.

KEYWORDS:

Alanine aminotransferase; Antioxidant; Aspartate aminotransferase; Liver function; Oxidative stress; Reactive oxygen species; γ -glutamyltransferase

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PMCID: [PMC5012237](#)

DOI: [10.14740/jocmr2672w](#)

[Free PMC Article](#)

Astaxanthin; a Promising Protector Against Gentamicin-Induced Nephrotoxicity in Rats.

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Author information

Abstract

Gentamicin is an aminoglycoside antibiotic widely used against infections caused by Gram-negative microorganisms. Nephrotoxicity is the main limitation to its therapeutic use. The objective of this study was to evaluate the potential protective effect of astaxanthin on the renal damage generated by gentamicin in rats, in an attempt to understand its mechanism of action, which may pave the way for possible therapeutic applications. The daily oral administration of the astaxanthin at a concentration of 50 mg/kg for 15 days to gentamicin (80 mg/kg.b.w) treated rats showed a significant decrease ($p < 0.05$) in plasma creatinine, urea, TNF- α as well as plasma and renal MDA and HP. The treatment also resulted in a significant increase in hemoglobin, plasma sodium, potassium and TAS as well as renal total protein, GSH, Pr-SHs, G6PD, SOD, GPx, CAT and GR levels. The histological examinations of renal tissues in this study revealed damage and glomerular infiltration in gentamicin treated rats. The presented data suggest that astaxanthin has a significant prophylactic action against gentamicin-induced nephrotoxicity in rats. The effect was more pronounced in case of astaxanthin pre-treatment compared with administration of astaxanthin post-treatment. Taken together, astaxanthin has a potential as a protective and therapeutic agent for nephrotoxicity and deserves clinical trial in the near future as an adjuvant therapy in patients treated with gentamicin.

PMID:

27658618

[Indexed for MEDLINE]

Astaxanthin inhibits inflammation and fibrosis in the liver and adipose tissue of mouse models of diet-induced obesity and nonalcoholic steatohepatitis.

[Kim B¹](#), [Farruggia C¹](#), [Ku CS¹](#), [Pham TX¹](#), [Yang Y¹](#), [Bae M¹](#), [Wegner CJ¹](#), [Farrell NJ¹](#), [Harness E¹](#), [Park YK¹](#), [Koo SI¹](#), [Lee JY²](#).

Author information

Abstract

The objective of this study was to determine if astaxanthin (ASTX), a xanthophyll carotenoid, can prevent obesity-associated metabolic abnormalities, inflammation and fibrosis in diet-induced obesity (DIO) and nonalcoholic steatohepatitis (NASH) mouse models. Male C57BL/6J mice were fed a low-fat (6% fat, w/w), a high-fat/high-sucrose control (HF/HS; 35% fat, 35% sucrose, w/w), or a HF/HS containing ASTX (AHF/HS; 0.03% ASTX, w/w) for 30 weeks. To induce NASH, another set of mice was fed a HF/HS diet containing 2% cholesterol (HF/HS/HC) a HF/HS/HC with 0.015% ASTX (AHF/HS/HC) for 18 weeks. Compared to LF, HF/HS significantly increased plasma total cholesterol, triglyceride and glucose, which were lowered by ASTX. ASTX decreased hepatic mRNA levels of markers of macrophages and fibrosis in both models. The effect of ASTX was more prominent in NASH than DIO mice. In epididymal fat, ASTX also decreased macrophage infiltration and M1 macrophage marker expression, and inhibited hypoxia-inducible factor 1- α and its downstream fibrogenic genes in both mouse models. ASTX significantly decreased tumor necrosis factor α mRNA in the splenocytes from DIO mice upon lipopolysaccharides stimulation compared with those from control mice fed an HF/HS diet. Additionally, ASTX significantly elevated the levels of genes that regulate fatty acid β -oxidation and mitochondrial biogenesis in the skeletal muscle compared with control obese mice, whereas no differences were noted in adipose lipogenic genes. Our results indicate that ASTX inhibits inflammation and fibrosis in the liver and adipose tissue and enhances the skeletal muscle's capacity for mitochondrial fatty acid oxidation in obese mice.

KEYWORDS:

Astaxanthin; Fibrosis; Inflammation; Macrophage infiltration; Macrophage phenotypes; Obesity

PMID: 28193580 DOI: [10.1016/j.jnutbio.2016.01.006](#) [Indexed for MEDLINE]

[Int J Mol Sci](#). 2017 Mar 8;18(3). pii: E593. doi: 10.3390/ijms18030593.

Hepatic Transcriptome Profiles of Mice with Diet-Induced Nonalcoholic Steatohepatitis Treated with Astaxanthin and Vitamin E.

[Kobori M](#)¹, [Takahashi Y](#)², [Sakurai M](#)³, [Ni Y](#)⁴, [Chen G](#)⁵, [Nagashimada M](#)⁶, [Kaneko S](#)⁷, [Ota T](#)⁸.

[Author information](#)

Abstract

Astaxanthin alleviates hepatic lipid accumulation and peroxidation, inflammation, and fibrosis in mice with high-cholesterol, high-cholelate, and high-fat (CL) diet-induced nonalcoholic steatohepatitis (NASH) [...].

KEYWORDS:

astaxanthin; comprehensive gene expression analysis; eukaryotic initiation factor-2 (EIF2); nonalcoholic steatohepatitis (NASH); peroxisome proliferator-activated receptor α (PPARA); vitamin E

PMID: 28282876

PMCID: [PMC5372609](#)

DOI: [10.3390/ijms18030593](#)

[Indexed for MEDLINE]

[Free PMC Article](#)

[Nutrients](#). 2017 Mar 13;9(3). pii: E271. doi: 10.3390/nu9030271.

A Combination of Flaxseed Oil and Astaxanthin Improves Hepatic Lipid Accumulation and Reduces Oxidative Stress in High Fat-Diet Fed Rats.

[Xu J](#)^{1,2,3}, [Rong S](#)⁴, [Gao H](#)⁵, [Chen C](#)^{6,7}, [Yang W](#)⁸, [Deng Q](#)^{9,10,11}, [Huang Q](#)^{12,13,14}, [Xiao L](#)¹⁵, [Huang F](#)^{16,17,18}.

Author information

Abstract

Hepatic lipid accumulation and oxidative stress are crucial pathophysiological mechanisms for non-alcoholic fatty liver disease (NAFLD). Thus, we examined the effect of a combination of flaxseed oil (FO) and astaxanthin (ASX) on hepatic lipid accumulation and oxidative stress in rats fed a high-fat diet. ASX was dissolved in flaxseed oil (1 g/kg; FO + ASX). Animals were fed diets containing 20% fat, where the source was lard, or 75% lard and 25% FO + ASX, or 50% lard and 50% FO + ASX, or FO + ASX, for 10 weeks. Substitution of lard with FO + ASX reduced steatosis and reduced hepatic triacylglycerol and cholesterol. The combination of FO and ASX significantly decreased hepatic sterol regulatory element-binding transcription factor 1 and 3-hydroxy-3-methylglutaryl-CoA reductase but increased peroxisome proliferator activated receptor expression. FO + ASX significantly suppressed fatty acid synthase and acetyl CoA carboxylase but induced carnitine palmitoyl transferase-1 and acyl CoA oxidase expression. FO + ASX also significantly elevated hepatic SOD, CAT and GPx activity and GSH, and markedly reduced hepatic lipid peroxidation. Thus, FO and ASX may reduce NAFLD by reversing hepatic steatosis and reducing lipid accumulation and oxidative stress.

KEYWORDS:

astaxanthin; flaxseed oil; high fat diet; lipid accumulation; oxidant stress

PMID: 28335388

PMCID: [PMC5372934](#)

DOI: [10.3390/nu9030271](#)

[Indexed for MEDLINE]

[Free PMC Article](#)

Astaxanthin Prevented Oxidative Stress in Heart and Kidneys of Isoproterenol-Administered Aged Rats.

[Alam MN¹](#), [Hossain MM¹](#), [Rahman MM¹](#), [Subhan N¹](#), [Mamun MAA¹](#), [Ulla A¹](#), [Reza HM¹](#), [Alam MA¹](#).

Author information

Abstract

The objective of this study was to investigate the effect of astaxanthin on isoproterenol (ISO)-induced myocardial infarction and cardiac hypertrophy in rats. To evaluate the effect of astaxanthin on ISO-induced cardiac dysfunction, 18 aged Long Evans male rats were evenly divided into three groups. Group I (Control group) was given only the laboratory-ground food and normal water. Group II (ISO group) was administered ISO at a dose of 50 mg/kg subcutaneously (SC) twice a week for two weeks. Group III (Astaxanthin + ISO group) was treated with astaxanthin (25 mg/kg) orally every day and ISO 50 mg/kg SC twice a week for two weeks. ISO administration in rats increased the heart and left ventricular wet weights and increased inflammatory cell infiltration and fibrosis. Moreover, ISO administration increased the lipid peroxidation and decreased antioxidant enzyme activities in heart tissues. Astaxanthin treatment prevented the increased wet weight of heart and decreased inflammatory cell infiltration and fibrosis. The protective effect of astaxanthin was associated with reduction of free radicals by improving antioxidant enzyme function, as well as normalization and/or suppression of elevated oxidative stress markers, such as malondialdehyde (MDA), nitric oxide (NO), and advanced protein oxidation product (APOP) in ISO-administered rats. Furthermore, astaxanthin decreased the elevated activities of aspartate transaminase (AST), alanine transaminase (ALT), and creatinin kinase muscle/brain (CK-MB) in ISO-administered rats. In conclusion, astaxanthin may protect cardiac tissues in ISO-administered rats through suppression of oxidative stress and enhancement of antioxidant enzyme functions.

KEYWORDS:

antioxidant enzymes; astaxanthin; free radicals; heart, fibrosis; oxidative stress

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[Indexed for MEDLINE]

Astaxanthin ameliorates ferric nitrilotriacetate-induced renal oxidative injury in rats.

[Okazaki Y](#)^{1,2}, [Okada S](#)^{1,3}, [Toyokuni S](#)².

Author information

Abstract

Daily intake of vegetables can reduce the risk of cancer and lifestyle-related diseases. However, supplementary intake of β -carotene alone has been reported to increase the risk of lung cancer in male cigarette smokers and people who were exposed to asbestos. The mechanism of the antioxidative properties of carotenoids *in vivo*, especially under oxidative stress conditions, still remains unclear. To investigate the antioxidant properties of dietary compounds, we examined the effects of chemically modified astaxanthin (Ax-C-8) using a rat model of ferric nitrilotriacetate (Fe-NTA)-induced renal oxidative injury. Ax-C-8 demonstrated lethally toxic effects on the rats in a dose-dependent manner. Following supplementation with Ax-C-8 (0.02%, w/w) for 30 days, the rats were euthanized 1, 4 and 24 h after injection of Fe-NTA. After 4 h, Ax-C-8 pretreatment suppressed the elevation of creatinine and blood urea nitrogen and protected the rats from renal tubular necrosis and the formation of 4-hydroxy-2-nonenal-modified proteins. After 24 h, pretreatment with Ax-C-8 maintained the renal antioxidant enzyme levels and renal tubules. Here, we demonstrate the antioxidant effects of Ax-C-8 against Fe-NTA-induced oxidative injury in rats receiving a regular diet. These data suggest that dietary intake of astaxanthin may be useful for the prevention of renal tubular oxidative damage.

KEYWORDS:

astaxanthin; ferric nitrilotriacetate; oxidative stress; vitamin E

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PMCID: [PMC5525010](#)

DOI: [10.3164/jcbn.16-114](#)

[Free PMC Article](#)

ASTAXANTHIN ALLEVIATES SELENIUM TOXICITY IN FISH BY REDUCING INFLAMMATION AND OXIDATION IN THE LIVER.

Chemosphere. 2020 Apr;244:125546.

doi: 10.1016/j.chemosphere.2019.125546. Epub 2019 Dec 4.

Effect of sub-chronic exposure to selenium and astaxanthin on *Channa argus*: Bioaccumulation, oxidative stress and inflammatory response

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- PMID: [32050342](#)
- DOI: [10.1016/j.chemosphere.2019.125546](#)

Abstract

Selenium (Se) is the most common micronutrient and that becomes toxic when present at higher concentrations in aquatic environments. Astaxanthin (AST) has been documented to possess antioxidant and anti-inflammatory properties. The aim of this study was to explore the potential of dietary AST and Se exposure on oxidative stress, and inflammatory response in *Channa argus*. After acclimation, 540 fish were randomly distributed into nine groups housed in twenty-seven glass tanks. The fish were exposed for 8 weeks to waterborne Se at 0, 100 and 200 $\mu\text{g L}^{-1}$ or dietary AST at 0, 50 and 100 mg kg^{-1} . The results shown that Se accumulation in the kidney, liver, spleen, intestine and gill were significantly increased following Se exposure, dietary 50 and 100 mg kg^{-1} AST supplementation decreased the accumulation of Se in the kidney, liver, spleen, and intestine. In addition, AST supplementation can decrease oxidative stress and inflammatory response in the liver and spleen following exposure to waterborne Se. These results indicate that AST has the potential to alleviate the effects of Se toxicity in *C. argus*.

ASTAXANTHIN IMPROVES DIABETES-INDUCED OXIDATIVE STRESS IN KIDNEY OF DIBETIC MICE.

Eur J Pharmacol. 2018 Dec 5;840:33-43.

doi: 10.1016/j.ejphar.2018.09.028. Epub 2018 Sep 27.

Astaxanthin ameliorates experimental diabetes-induced renal oxidative stress and fibronectin by upregulating connexin43 in glomerular mesangial cells and diabetic mice

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- PMID: [30268666](#)
- DOI: [10.1016/j.ejphar.2018.09.028](#)

Abstract

Oxidative stress is the major cause of renal fibrosis in the progression of DN. Connexin43 (Cx43) exerts an anti-fibrosis effect on diabetic kidneys. The current study aimed to investigate whether astaxanthin (AST) could ameliorate the pathological progression of DN by upregulating Cx43 and activating the Nrf2/ARE signaling, which is a pivotal anti-oxidative stress system, to strengthen the cellular anti-oxidative capacity and diminish fibronectin (FN) accumulation in HG-induced glomerular mesangial cells (GMCs). Our hypothesis was verified in GMCs and the kidneys from db/db mice by western blot, immunofluorescence, immunohistochemistry, immunoprecipitation, dual luciferase reporter assay and reactive oxygen related detection kits. Results showed that AST simultaneously upregulated the Cx43 protein level and promoted the Nrf2/ARE signaling activity in the kidney of db/db mice and HG-treated GMCs. However, Cx43 depletion abrogated the Nrf2/ARE signaling activation induced by AST. AST reduced the interaction between c-Src and Nrf2 in the nuclei of GMCs cultured with HG, thereby enhancing the Nrf2 accumulation in the nuclei of GMCs. Our data suggested that AST promoted the Nrf2/ARE signaling by upregulating the Cx43 protein level to prevent renal fibrosis triggered by HG in GMCs and db/db mice. c-Src acted as a mediator in these processes.

ASTAXANTHIN DEMONSTRATES PROTECTIVE EFFECT AGAINST INDUCED KIDNEY INJURY IN RATS.

Int Urol Nephrol. 2019 Feb;51(2):351-358.

doi: 10.1007/s11255-018-2027-2. Epub 2018 Nov 19.

Protective effect of astaxanthin against contrast-induced acute kidney injury via SIRT1-p53 pathway in rats

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- PMID: [30456546](#)
- DOI: [10.1007/s11255-018-2027-2](#)

Abstract

Purpose: The present study was designed to further investigate the protective effect of astaxanthin (AST) on contrast-induced acute kidney injury (CI-AKI) in rats and the relationship between SIRT1-p53 pathway and astaxanthin.

Methods: 40 adult male Sprague Dawley (SD) rats were randomly divided into five groups (n = 8/group): control (CON), normal rats treated with AST (AST), CM-treated (CM), CM rats treated with isoform of nitric oxide synthase (iNOS) inhibitor (iNOS + CM), and CM rats treated with AST (AST + CM). Serum creatinine (Scr) and blood urea nitrogen (BUN) values were measured at 72 h following the procedure. Hematoxylin and eosin (H-E) staining was used to observe the pathologic changes of kidney. Tunel staining was used to test apoptosis of kidney tubules. Oxidative stress, SIRT1 activity, nitric oxide (NO), and 3-nitrotyrosine (3-NT) content were individually measured with the commercial available kits.

Results: Compared with the CON group, Scr and BUN levels significantly increased in the CM group (P < 0.05), and the values in two pre-treatment groups (iNOS + CM and AST + CM) had significantly decreased (P < 0.05). H-E and Tunel staining had shown that renal tubular injury was severe in CM group. The renal injury score and apoptosis index in the two pre-treatment groups also decreased (P < 0.05). The present study showed that in CM group the levels of oxidative stress indicators significantly increased, and the activities of antioxidant stress indicators significantly decreased. These

indicators in two pre-treatment groups significantly improved ($P < 0.05$). In the CM group the expression levels of SIRT1 significantly increased, and the ac-p53/p53 significantly increased ($P < 0.05$). Compared with the CM group, in AST + CM group the expression levels of SIRT1 increased, the expression levels of p53 and ac-p53/p53 decreased ($P < 0.05$). The levels of NO and 3-NT in CM group significantly increased ($P < 0.05$). Compared the CM group, the levels in the two pre-treatment groups significantly decreased ($P < 0.05$).

Conclusions: Astaxanthin has a protective effect on CI-AKI, the mechanism may be related to the SIRT1-p53 pathway. Astaxanthin can reduce the content of NO and 3-NT in renal tissue of CI-AKI, and alleviate the renal injury induced by contrast agents.

ASTAXANTHIN IMPROVES KIDNEY FIBROSIS IN MOUSE MODEL.

Mol Med Rep. 2019 Apr;19(4):3168-3178.

doi: 10.3892/mmr.2019.9970. Epub 2019 Feb 19.

Astaxanthin ameliorates renal interstitial fibrosis and peritubular capillary rarefaction in unilateral ureteral obstruction

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PMID: 30816496 PMCID: [PMC6423568](#) DOI: [10.3892/mmr.2019.9970](#) [Free PMC article](#)

Abstract

Loss of peritubular capillaries is a notable feature of progressive renal interstitial fibrosis. Astaxanthin (ASX) is a natural carotenoid with various biological activities. The present study aimed to evaluate the effect of ASX on unilateral ureteral obstruction (UUO)-induced renal fibrosis in mice. For that purpose, mice were randomly divided into five treatment groups: Sham, ASX 100 mg/kg, UUO, UUO + ASX 50 mg/kg and UUO + ASX 100 mg/kg. ASX was administered to the mice for 7 or 14 days following UUO. The results demonstrated that UUO-induced histopathological changes in the kidney tissue were prevented by ASX. Renal function was improved by ASX treatment, as evidenced by decreased blood urea nitrogen and serum creatinine levels. Furthermore, the extent of renal fibrosis and collagen deposition induced by UUO was suppressed by ASX. The levels of collagen I, fibronectin and α -smooth muscle actin were increased by UUO in mice or by transforming growth factor (TGF)- β 1 treatment in NRK-52E cells, and were reduced by ASX administration. In addition, ASX inhibited the UUO-induced decrease in peritubular capillary density by upregulating vascular endothelial growth factor and downregulating thrombospondin 1 levels. Inactivation of the TGF- β 1/Smad signaling pathway was involved in the anti-fibrotic mechanism of ASX in UUO mice and TGF- β 1-treated NRK-52E cells. In conclusion, ASX attenuated renal interstitial fibrosis and peritubular capillary rarefaction via inactivation of the TGF- β 1/Smad signaling pathway.

ASTAXANTHIN PROTECTS AGAINST ALCOHOLIC LIVER DISEASE IN MICE.

Mar Drugs. 2019 Mar 19;17(3):181.

doi: 10.3390/md17030181.

Comparative Transcriptome Analyses Provide Potential Insights into the Molecular Mechanisms of Astaxanthin in the Protection against Alcoholic Liver Disease in Mice

[Huilin Liu](#)¹, [Huimin Liu](#)^{2,3}, [Lingyu Zhu](#)⁴, [Ziqi Zhang](#)⁵, [Xin Zheng](#)⁶, [Jingsheng Liu](#)^{7,8}, [Xueqi Fu](#)⁹

PMID: **30893931** PMCID: [PMC6471478](#) DOI: [10.3390/md17030181](#) **Free PMC article**

Abstract

Alcoholic liver disease (ALD) is a major cause of chronic liver disease worldwide. It is a complex process, including a broad spectrum of hepatic lesions from fibrosis to cirrhosis. Our previous study suggested that astaxanthin (AST) could alleviate the hepatic inflammation and lipid dysmetabolism induced by ethanol administration. In this study, a total of 48 male C57BL/6J mice were divided into 4 groups: a Con group (fed with a Lieber–DeCarli liquid diet), an AST group (fed with a Lieber–DeCarli liquid diet and AST), an Et group (fed with an ethanol-containing Lieber–DeCarli liquid diet), and an EtAST group (fed with an ethanol-containing Lieber–DeCarli liquid diet and AST). Then, comparative hepatic transcriptome analysis among the groups was performed by Illumina RNA sequencing. Gene enrichment analysis was conducted to identify pathways affected by the differentially expressed genes. Changes of the top genes were verified by quantitative real-time PCR (qRT-PCR) and Western blot. A total of 514.95 ± 6.89 , 546.02 ± 15.93 , 576.06 ± 21.01 , and 690.85 ± 54.14 million clean reads were obtained for the Con, AST, Et, and EtAST groups, respectively. Compared with the Et group, 1892 differentially expressed genes (DEGs) (including 351 upregulated and 1541 downregulated genes) were identified in the AST group, 1724 differentially expressed genes (including 233 upregulated and 1491 downregulated genes) were identified in the Con group, and 1718 DEGs (including 1380 upregulated and 338 downregulated genes) were identified in the EtAST group. The enrichment analyses revealed that the chemokine signaling, the antigen processing and presentation, the nucleotide-binding and oligomerization domain (NOD)-like receptor signaling, and the Toll-like receptor signaling pathways enriched the most differentially expressed genes. The findings of this study provide insights for the development of nutrition-related therapeutics for ALD.

ASTAXANTHIN PROTECTS AGAINST KIDNEY FIBROSIS IN MICE.

Biochim Biophys Acta Gen Subj. 2019 Sep;1863(9):1360-1370.

doi: 10.1016/j.bbagen.2019.05.020. Epub 2019 Jun 3.

Astaxanthin protects against renal fibrosis through inhibiting myofibroblast activation and promoting CD8⁺ T cell recruitment

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PMID: 31170498 DOI: [10.1016/j.bbagen.2019.05.020](https://doi.org/10.1016/j.bbagen.2019.05.020)

Abstract

Background: Renal fibrosis is a common pathological hallmark of chronic kidney disease, and no effective treatment is clinically available to manage its progression. Astaxanthin was recently found to be anti-fibrotic, but its effect on renal fibrosis remains unclear.

Methods: C57BL/6J mice were subjected to unilateral ureteral obstruction and intragastrically administered astaxanthin. Histopathology and immunohistochemistry were performed to evaluate renal fibrosis. Flow cytometry was used to examine lymphocyte accumulation in the fibrotic kidneys. Western blotting, real-time qPCR, and immunofluorescence were performed to cover the underlying mechanism concerning astaxanthin treatment during renal fibrosis.

Results: Oral administration of astaxanthin effectively alleviates renal fibrosis in mice. In vitro, astaxanthin inhibited fibroblast activation by modulating Smad2, Akt and STAT3 pathways and suppressed epithelial-to-mesenchymal transition in renal tubular epithelial cells through Smad2, snail, and β -catenin. Moreover, astaxanthin significantly induced the rapid accumulation of CD8⁺ T cells in fibrotic kidneys, which was accompanied by elevated expression of IFN- γ . Accordingly, the depletion of CD8⁺ T cells strongly diminished the protective effect of astaxanthin. Further investigation showed that astaxanthin increased the population of CD8⁺ T cells by upregulating the expression of CCL5 in macrophages.

Conclusions: These findings highlight the beneficial effect of astaxanthin on fibroblast activation, epithelial-to-mesenchymal transition, and CD8⁺ T cell recruitment during renal fibrosis.

General Significance: These data indicate that astaxanthin could serve as a therapeutic strategy to treat renal fibrotic conditions.

ASTAXANTHIN SHOWS EFFECT ON APOPTOSIS OF RAT RENAL TUBULAR EPITHELIAL CELLS AND MAY PROVIDE A NEW TREATMENT FOR ACUTE KIDNEY INJURY.

Am J Transl Res. 2019 May 15;11(5):3039-3047.

eCollection 2019.

Effect of astaxanthin on apoptosis of rat renal tubular epithelial cells induced by iohexol

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- PMID: [31217873](#)
- PMCID: [PMC6556630](#)

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Abstract

Contrast acute kidney injury refers to acute renal failure due to the application of contrast agents. Astaxanthin, as an antioxidant, can improve early acute kidney injury in severely burned rats. However, the mechanism of astaxanthin for renal protection is still unclear. In this study, the rat renal tubular epithelial cells (NRK-52E) were treated with iohexol, astaxanthin, astaxanthin plus nicotinamide and nicotinamide. Subsequently, the nuclear morphology was observed by fluorescence staining of DAPI DNA, the apoptosis was detected by flow cytometry, the mitochondrial membrane potential was detected by JC-1 and the SIRT1, P53, Bax, Bcl-2 protein expression level was detected by Western blotting. We found that astaxanthin can reduce nuclear pyknosis and nuclear deep staining, decrease the number of apoptotic cells, up-regulate the expression of proapoptotic proteins P53 and Bax and up-regulate the expression of anti-apoptotic protein Bcl-2 by increasing SIRT1 expression level, thereby exerting protective effects on renal tubular epithelial cells. At the same time, nicotinamide has the opposite effect on the NRK-52E compared with astaxanthin. These results indicated that astaxanthin may provide a new option for the prevention of contrast-induced acute kidney injury.

ASTAXANTHIN SHOWS BOTH THERAPEUTIC AND PROTECTIVE EFFECTS AGAINST ALCOHOL-INDUCED LIVER FIBROSIS IN MICE.

Int J Mol Sci. 2019 Aug 20;20(16):4057.

doi: 10.3390/ijms20164057.

Therapeutic and Protective Effects of Liposomal Encapsulation of Astaxanthin in Mice with Alcoholic Liver Fibrosis

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PMID: [31434227](#) PMCID: [PMC6718996](#) DOI: [10.3390/ijms20164057](#) [Free PMC article](#)

Abstract

Astaxanthin (Asta) has been demonstrated to possess anti-inflammatory, antitumor, and free radical-clearing activities. However, the poor stability and low water solubility of Asta hamper its bioavailability. The objectives of this study were to fabricate Asta-loaded liposomes (Asta-lipo) and investigate the therapeutic effects of Asta-lipo on alcoholic liver fibrosis in mice. The mice were administered with Asta-lipo or liposomes alone prior to a 3-week dose containing 30% alcohol with or without feeding with a second dose of 30% alcohol. The prepared Asta-lipo of 225.0 ± 58.3 nm in diameter, had an encapsulation efficiency of 98%. A slow release profile of 16.2% Asta from Asta-lipo was observed after a 24-h incubation. Restorative actions against alcoholic liver fibrosis were observed after oral administration of Asta-lipo for 4 weeks. Hepatic repair, followed by a second dose of 30% alcohol, suggested that Asta-lipo exerted protective and reparative effects against liver injuries induced by repeated consumption of alcohol. The changes of serum ALT and AST values were principally in consistence with the histopathologic findings. Asta-lipo exerted rapid and direct effects against repeated alcohol-induced liver disease, whereas Asta-lipo given orally could boost recovery from liver injuries obtained due to previous long-term alcohol use. These data demonstrate that Asta-lipo has applicable protective and therapeutic potential to treat alcohol-induced liver diseases.

ASTAXANTHIN AMELIORATES MITOCHONDRIAL FUNCTION THEREBY PROTECTING AGAINST INDUCED KIDNEY TOXICITY IN RATS.

Biomed Pharmacother. 2020 Jan;121:109629.

doi: 10.1016/j.biopha.2019.109629. Epub 2019 Nov 13.

Maintenance of mitochondrial function by astaxanthin protects against bisphenol A-induced kidney toxicity in rats

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- DOI: [10.1016/j.biopha.2019.109629](https://doi.org/10.1016/j.biopha.2019.109629)

Free article

Abstract

Bisphenol A (BPA), a global environmental pollutant, has been reported to have the potential to induced organs toxicity. This study explored the potential benefits of astaxanthin (ATX), a natural antioxidant, against BPA toxicity in the kidney, and explored whether mitochondria are involved in this condition. Male Wistar rats were fed with a vehicle, BPA, BPA plus ATX, ATX and were evaluated after five weeks. ATX treatment significantly reversed BPA-induced changes in body weight, kidney/body weight, and renal function related markers. When treated simultaneously with ATX, the imbalance of the oxidative-antioxidant status caused by BPA was also alleviated. The high expression of BPA-induced pro-inflammatory cytokines were inhibited by ATX treatment. ATX treatment also lessened the effects of BPA-induced caspase-3, -8, -9 and -10 gene expression and enzyme activity. The benefits of ATX were associated with enhanced mitochondrial function, which led to increased mitochondrial-encoded gene expression, mitochondrial copy number, and increased mitochondrial respiratory chain complex enzyme activity. Our results demonstrate the efficacy of ATX in protecting BPA-induced kidney damage, in part by regulating oxidative imbalance and improving mitochondrial function. Collectively, these findings provide a new perspective for the rational use of ATX in the treatment of BPA-induced kidney disease.

Molecules. 2020 Mar 18;25(6):1386.

doi: 10.3390/molecules25061386.

Protective Effect of Astaxanthin on Ochratoxin A-Induced Kidney Injury to Mice by Regulating Oxidative Stress-Related NRF2/KEAP1 Pathway

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PMID: 32197464 PMCID: [PMC7144393](#) DOI: [10.3390/molecules25061386](#) **Free PMC article**

Abstract

The present study aimed to investigate the effects of astaxanthin (ASX) on ochratoxin A (OTA)-induced renal oxidative stress and its mechanism of action. Serum kidney markers, histomorphology, ultrastructural observation, and oxidative stress indicators were assessed. Meanwhile, quantitative real-time reverse transcription PCR and western blotting detection of NRF2 (encoding nuclear factor, erythroid 2 like) and members of the NRF2/KEAP1 signaling pathway (KEAP1 (encoding Kelch-like ECH-associated protein), NQO1 (encoding NAD(P)H quinone dehydrogenase), HO-1 (encoding heme oxygenase 1), γ -GCS (gamma-glutamylcysteine synthetase), and GSH-Px (glutathione peroxidase 1)) were performed. Compared with the control group, the OTA-treated group showed significantly increased levels of serum UA (uric acid) and BUN (blood urea nitrogen), tubular epithelial cells were swollen and degenerated, and the levels of antioxidant enzymes decreased significantly, and the expression of NRF2 (cytoplasm), NQO1, HO-1, γ -GCS, and GSH-Px decreased significantly. More importantly, after ASX pretreatment, compared with the OTA group, serum markers were decreased, epithelial cells appeared normal; the expression of antioxidant enzymes increased significantly, NQO1, HO-1, γ -GCS and GSH-Px levels increased significantly, and ASX promoted the transfer of NRF2 from the cytoplasm to the nucleus. These results highlight the protective ability of ASX in renal injury caused by OTA exposure, and provide theoretical support for ASX's role in other mycotoxin-induced damage.

ASTAXANTHIN REDUCES LIVER DAMAGE AND MITOCHONDRIAL DYSFUNCTION IN MICE WITH NON-ALCOHOLIC FATTY LIVER DISEASE.

Br J Pharmacol. 2020 Aug;177(16):3760-3777.
doi: 10.1111/bph.15099. Epub 2020 Jun 27.

Astaxanthin attenuates hepatic damage and mitochondrial dysfunction in non-alcoholic fatty liver disease by up-regulating the FGF21/PGC-1 α pathway

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PMID: 32446270 PMCID: PMC7393201 (available on 2021-08-01) DOI: [10.1111/bph.15099](https://doi.org/10.1111/bph.15099)

Abstract

Background and Purpose: Non-alcoholic fatty liver disease (NAFLD) is considered to be one of the most common chronic liver diseases across worldwide. Astaxanthin (Ax) is a carotenoid, and beneficial effects of astaxanthin, including anti-oxidative, anti-inflammatory, and anti-tumour activity, have been identified. The present study aimed to elucidate the protective effect of astaxanthin against NAFLD and its underlying mechanism.

Experimental approach: Mice were fed either a high fat or chow diet, with or without astaxanthin, for up to 12 weeks. L02 cells were treated with free fatty acids combined with different doses of astaxanthin for 48 h. Histopathology, expression of lipid metabolism, inflammation, apoptosis, and fibrosis-related gene expression were assessed. And the function of mitochondria was also evaluated.

Key Results: The results indicated that astaxanthin attenuated HFD- and FFA-induced lipid accumulation and its associated oxidative stress, cell apoptosis, inflammation, and fibrosis both in vivo and in vitro. Astaxanthin up-regulated FGF21 and PGC-1 α expression in damaged hepatocytes, which suggested an unrecognized mechanism of astaxanthin on ameliorating NAFLD.

Conclusion and implications: Astaxanthin attenuated hepatocyte damage and mitochondrial dysfunction in NAFLD by up-regulating FGF21/PGC-1 α pathway. Our results suggest that astaxanthin may become a promising drug to treat or relieve NAFLD.

ASTAXANTHIN AMELIORATES INDUCED LIVER FIBROSIS IN RATS.

Biomed Res Int. 2021 Feb 11;2021:6631415.
doi: 10.1155/2021/6631415. eCollection 2021.

***Haematococcus pluvialis* Carotenoids Enrich Fractions Ameliorate Liver Fibrosis Induced by Thioacetamide in Rats: Modulation of Metalloproteinase and Its Inhibitor**

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PMID: 33628797 PMCID: [PMC7895575](#) DOI: [10.1155/2021/6631415](#) **Free PMC article**

Abstract

Hepatic fibrosis is a consequence of chronic liver diseases. Metalloproteinase and its inhibitor have crucial roles in the resolution of liver fibrosis. The current relevant study is aimed to evaluate the therapeutic effect of *Haematococcus pluvialis* (*H. pluvialis*) extract, astaxanthin-rich fraction, astaxanthin ester-rich fraction, and β -carotene-rich fraction as well as their mechanisms of action in curing hepatic fibrosis induced by thioacetamide (TAA). Liver fibrosis was induced using TAA (intraperitoneal injection, two times a week for 6 weeks), in a rat model and *H. pluvialis* extract (200 mg/kg), and other fractions (30 mg/kg) were orally administered daily for 4 weeks after the last TAA injection. Based on HPLC analysis, *H. pluvialis* extract contains β -carotene (12.95 mg/g, extract) and free astaxanthin (10.85 mg/g, extract), while HPLC/ESI-MS analysis revealed that *H. pluvialis* extract contains 28 carotenoid compounds including three isomers of free astaxanthin, α or β -carotene, lutein, 14 astaxanthin mono-esters, 5 astaxanthin di-esters, and other carotenoids. *H. pluvialis* and its fractions reduced liver enzymes, nitric oxide, collagen 1, alpha-smooth muscle actin, and transforming growth factor-beta as well as elevated catalase antioxidant activity compared to the TAA group. Also, *H. pluvialis* extract and its fractions exceedingly controlled the balance between metalloproteinase and its inhibitor, activated Kupffer cells proliferation, and suppressed liver apoptosis, necrobiosis, and fibrosis. These findings conclude that *H. pluvialis* extract and its fractions have an antifibrotic effect against TAA-induced liver fibrosis by regulating the oxidative stress and proinflammatory mediators, suppressing multiple profibrogenic factors, and modulating the metalloproteinase and its inhibitor pathway, recommending *H. pluvialis* extract and its fractions for the development of new effective medicine for treating hepatic fibrosis disorders.

ASTAXANTHIN PROTECTS AGAINST KIDNEY DAMAGE IN RATS WITH INDUCED RENOVASCULAR OCCLUSION.

Comb Chem High Throughput Screen. 2020 Sep 13.

doi: 10.2174/1386207323666200914104432. Online ahead of print.

Protective Effects of Astaxanthin on Nephrotoxicity in Rats with Induced Renovascular Occlusion

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PMID: 32928081 DOI: [10.2174/1386207323666200914104432](https://doi.org/10.2174/1386207323666200914104432)

Abstract

Background: Various effects of Astaxanthin was shown in the studies including its antioxidant, anti-inflammatory, anti-tumor and immunoregulator effects.

Objective: The aim of this study was to evaluate the beneficial effects of Astaxanthin on renovascular occlusion induced renal injury and to investigate the possible mechanisms.

Methods: The rats were randomly assigned into three groups as follows: Group 1: control group (n=12), Group 2: renal ischemiareperfusion injury group (n=12), Group 3: renal ischemia-reperfusion + asthaxantine treated group (n=12). The control group and the renal ischemia-reperfusion group were given 2cc/kg/g olive oil for 7 days before establishing ischemia to renal tissue. Astaxanthin dissolved in olive oil was given orally to the renal ischemia+astaxanthin group for 7 days before inducing renal ischemia. Caspase-(3, 8, 9), GSH, SOD, Total Thiol, TNF- α , IL-6, 8-OHdG were performed for each group.

Results: Renal IRI was verified by analysing the pathological changes of renal tissues and the renal functions after renal reperfusion. Much less renal tubular damage was determined the IRI+ASX group in comparison to the IRI group. Caspase-8, -9 and -3 immunoreactivity was observed to be minimal in the control group. Apoptosis was observed to be significantly reduced in the IRI + ASX group with respect to IRI group and close to the level of the control group (p <0.05). Caspase-3 levels of tissue samples

were significantly increased in IRI group compared to other groups, but significantly lower in IRI+ASX group with respect to the IRI group ($p < 0.05$). The TOS and OSI levels, indicating increased oxidative stress, were significantly lower in the IRI+ASX group with respect to the IRI group ($p < 0.001$), but still higher than the control group ($p < 0.001$). In addition to GSH, SOD and Total Thiol levels, TAS levels were also significantly higher in IRI + ASX group in comparison to the IRI group ($p < 0.05$). TNF- α , IL-6, lipid hydroperoxide, AOPP and 8-OHdG levels were lower in the IRI+ASX group than the IRI group ($p < 0.001$). MPO, IL-6, TNF- α levels, representing the parameters indicating neutrophil infiltration and inflammation of the renal tissues, significantly increased in IRI group with respect to the other groups ($p < 0.005$).

Conclusion: When all the data obtained in our study were evaluated, ASX was determined to prevent renal damage due to renovascular occlusion to a great extent, through complex mechanisms involving antioxidant, anti-inflammatory and antiapoptotic effects. Biochemical, histological and oxidative stress parameters were improved due to ASX.

ASTAXANTHIN INCREASES MITOCHONDRIAL RESPIRATION AND SHOWS POTENTIAL AGAINST LIVER FIBROSIS IN MOUSE MODEL.

J Nutr Biochem. 2019 Sep;71:82-89.

doi: 10.1016/j.jnutbio.2019.06.001. Epub 2019 Jun 20.

Astaxanthin attenuates the increase in mitochondrial respiration during the activation of hepatic stellate cells

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PMID: 31302374 PMCID: [PMC6707861](#) DOI: [10.1016/j.jnutbio.2019.06.001](#) [Free PMC article](#)

Abstract

Upon liver injury, quiescent hepatic stellate cells (qHSCs) transdifferentiate to myofibroblast-like activated HSCs (aHSCs), which are primarily responsible for the accumulation of extracellular matrix proteins during the development of liver fibrosis. Therefore, aHSCs may exhibit different energy metabolism from that of qHSCs to meet their high energy demand. We previously demonstrated that astaxanthin (ASTX), a xanthophyll carotenoid, prevents the activation of HSCs. The objective of this study was to determine if ASTX can exert its antifibrogenic effect by attenuating any changes in energy metabolism during HSC activation. To characterize the energy metabolism of qHSCs and aHSCs, mouse primary HSCs were cultured on uncoated plastic dishes for 7 days for spontaneous activation in the presence or absence of 25 μ M ASTX. qHSCs (1 day after isolation) and aHSCs treated with or without ASTX for 7 days were used to determine parameters related to mitochondrial respiration using a Seahorse XFe24 Extracellular Flux analyzer. aHSCs had significantly higher basal respiration, maximal respiration, ATP production, spare respiratory capacity and proton leak than those of qHSCs. However, ASTX prevented most of the changes occurring during HSC activation and improved mitochondrial cristae structure with decreased cristae junction width, lumen width and the area in primary mouse aHSCs. Furthermore, qHSCs isolated from ASTX-fed mice had lower mitochondrial respiration and glycolysis than control qHSCs. Our findings suggest that ASTX may exert its antifibrogenic effect by attenuating the changes in energy metabolism during HSC activation.

Protective effects of astaxanthin on a combination of D-galactose and jet lag-induced aging model in mice.

[Ni Y](#)¹, [Wu T](#)¹, [Yang L](#)¹, [Xu Y](#)¹, [Ota T](#)², [Fu Z](#)¹.

[Author information](#)

Abstract

Oxidative stress caused free radical and mitochondrial damage plays a critical role in the progression of aging and age-related damage at the cellular and tissue levels. Antioxidant supplementation has received growing attention and the effects of antioxidant on aging are increasingly assessed in both animal and human studies. However, additional and more promising treatments that contribute to the expansion of anti-aging therapies are needed. Astaxanthin, a super antioxidant carotenoid and free radical scavenger, inhibits lipid peroxidation more potently than vitamin E. In the present study, we investigated the preventative effects of astaxanthin on aging using an accelerated aging model: mice chronically treated with a combination of D-galactose and jet lag. After 6 weeks of treatment, astaxanthin administration tended to protect the liver weight loss in aged mice. It is probably by upregulating the mRNA expression of galactose-1-phosphate uridylyltransferase, which contribute to the enhancement of D-galactose metabolism. Astaxanthin supplementation also improved muscle endurance of aged mice in a swimming test. These results were associated with reduced oxidative stress in serum and increased anti-oxidative enzymes activities and mRNA expression in vivo. Moreover, astaxanthin reversed the dysregulation of aging-related gene expression caused by the combination of D-galactose and jet lag in the liver and kidney of mice. In conclusion, astaxanthin prevents liver weight loss, ameliorates locomotive muscular function, exerts significant anti-aging effects by reducing oxidative stress and improving the expression of age-related genes in D-galactose and jet lag-induced aging model.

KEYWORDS:

Aging; Antioxidant; Astaxanthin; D-galactose; Jet lag

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DOI: [10.1507/endocrj.EJ17-0500](https://doi.org/10.1507/endocrj.EJ17-0500)

[Indexed for MEDLINE]

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The protective effect of astaxanthin against cisplatin-induced nephrotoxicity in rats.

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Author information

Abstract

PURPOSE: The aim of this experimental study was to investigate the antioxidant effects of astaxanthin against cisplatin-induced nephrotoxicity in rats.

METHODS: Forty-eight male Sprague-Dawley rats weighing 264.83 ± 7.39 g were randomly divided into six groups of eight animals each. These were constituted as control, olive oil control, astaxanthin control, cisplatin control, 16 mg/kg cisplatin & 25 mg/kg astaxanthin and 16 mg/kg cisplatin & 75 mg/kg astaxanthin groups. Biochemical evaluation was performed by measuring blood urea nitrogen, serum creatinine, total oxidant status and total antioxidant status. Renal corpuscle, proximal and distal tubules areas (μm^2) were calculated for histopathological evaluation, and Caspase-3 staining was performed for immunohistochemical evaluation.

RESULTS: Cisplatin reduced total antioxidant status levels and increased blood urea nitrogen, serum creatinine, total oxidant status, and Caspase-3 levels. It also caused dilatation, vacuolization, and loss of tubular epithelial cells in the proximal and distal tubules, and glomerular degeneration and edema were determined in kidney tissue ($p < 0.05$). Administration of 25 mg and 75 mg astaxanthin increased total antioxidant status levels, reduced blood urea nitrogen, serum creatinine, total oxidant status, and Caspase-3, and ameliorated degenerative distal and proximal tubules, glomerular degeneration and edema in kidney tissue ($p < 0.05$).

CONCLUSIONS: The nephrotoxic effect of cisplatin was diminished by the antioxidant effect of astaxanthin.

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KEYWORDS: Antioxidant; Astaxanthin; Cisplatin; Nephrotoxicity; Oxidant

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[Indexed for MEDLINE]

Astaxanthin Promotes Nrf2/ARE Signaling to Inhibit HG-Induced Renal Fibrosis in GMCs.

[Xie X](#)^{1,2}, [Chen Q](#)^{3,4}, [Tao J](#)^{5,6}.

Author information

Abstract

Oxidative stress is the main cause of diabetic nephropathy (DN) progression. Nuclear factor-erythroid 2-related factor 2 (Nrf2)/antioxidant response element (ARE) signaling is a crucial cellular defense system to cope with oxidative stress. Astaxanthin (AST) is a fat-soluble xanthophyll carotenoid with remarkable antioxidative capacity. AST exerted renal protective in diabetic rats. This study aimed to determine whether AST could alleviate the pathological progress of DN by activating Nrf2/ARE signaling and diminishing the excessive oxidative stress and fibronectin (FN) accumulation in glomerular mesangial cells (GMCs) challenged with high glucose (HG). In the current study, we found that AST treatment alleviated the metabolic parameters, renal morphology and extracellular matrix (ECM) accumulation in streptozotocin-induced diabetic rats. Additionally, HG induced the adaptively activated Nrf2/ARE signaling and increased the expression of FN, intercellular adhesion molecule-1 (ICAM-1) and transforming growth factor- β ;1 (TGF- β ;1), as well as the intracellular reactive oxygen species (ROS) generation in GMCs. However, AST treatment strongly promoted the nuclear translocation and transcriptional activity of Nrf2 as well as upregulated the expression of superoxide dismutase (SOD1), NAD(P)H: quinone oxidoreductase (NQO1) and heme oxygenase-1 (HO-1), ultimately quenching the higher level of ROS and inhibiting the FN, ICAM-1 and TGF- β ;1 expression induced by HG. Collectively, our data suggest that the renoprotective effect of AST on DN depends on Nrf2/ARE signaling activation, which could be a potentially therapeutic strategy in the treatment of DN.

KEYWORDS:

Nrf2/ARE signaling; astaxanthin; diabetic nephropathy; oxidative stress; renal fibrosis

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DOI: [10.3390/md16040117](#)

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Astaxanthin alleviates renal damage of rats on high fructose diet through modulating NFκB/SIRT1 pathway and mitigating oxidative stress.

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Author information

Abstract

This study was conducted to determine the effect of astaxanthin (ASX) treatment on alleviation of renal damage in high fructose induced nephrotoxicity in rats. Treatments were arranged in a 2 × 2 factorial fashion: administrations of fructose (30%, via drinking water) and ASX (1 mg/kg/day, within 0.2 ml olive oil) for 8 weeks. Data were analyzed by two-way ANOVA. The ASX treatment decreased serum urea ($p < .01$) and blood urea-N concentrations ($p < .02$) at a lower extent in rats receiving fructose than those not receiving fructose. Moreover, the ASX treatment reversed the increases in malondialdehyde (MDA) ($p < .0001$) and nuclear factor kappa B (NF-κB) ($p < .0003$) levels and the decreases in superoxide dismutase (SOD) activity ($p < .0001$) and sirtuin-1 (SIRT1) level ($p < .0004$), in the kidney upon high fructose consumption. The data suggest that ASX supplementation alleviates renal damage induced by high fructose consumption through modulating NF-κB/SIRT1 pathway and mitigating oxidative stress.

KEYWORDS:

Astaxanthin; NF-κB; SIRT1; fructose; oxidative stress

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DOI: [10.1080/13813455.2018.1493609](https://doi.org/10.1080/13813455.2018.1493609)

Astaxanthin Prevents Alcoholic Fatty Liver Disease by Modulating Mouse Gut Microbiota.

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[Author information](#)

Abstract

The development and progression of alcoholic fatty liver disease (AFLD) is influenced by the intestinal microbiota. Astaxanthin, a type of oxygenated carotenoid with strong antioxidant and anti-inflammatory properties, has been proven to relieve liver injury. However, the relationship between the gut microbiota regulation effect of astaxanthin and AFLD improvement remains unclear. The effects of astaxanthin on the AFLD phenotype, overall structure, and composition of gut microbiota were assessed in ethanol-fed C57BL/6J mice. The results showed that astaxanthin treatment significantly relieves inflammation and decreases excessive lipid accumulation and serum markers of liver injury. Furthermore, astaxanthin was shown to significantly decrease species from the phyla Bacteroidetes and Proteobacteria and the genera *Butyrivimonas*, *Bilophila*, and *Parabacteroides*, as well as increase species from Verrucomicrobia and *Akkermansia* compared with the Et (ethanol) group. Thirteen phylotypes related to inflammation as well as correlated with metabolic parameters were significantly altered by ethanol, and then notably reversed by astaxanthin. Additionally, astaxanthin altered 18 and 128 KEGG (Kyoto Encyclopedia of Genes and Genomes) pathways involved in lipid metabolism and xenobiotic biodegradation and metabolism at levels 2 and 3, respectively. These findings suggest that *Akkermansia* may be a potential target for the astaxanthin-induced alleviation of AFLD and may be a potential treatment for bacterial disorders induced by AFLD.

KEYWORDS:

Akkermansia; alcoholic fatty liver disease; astaxanthin; gut microbiota; inflammation

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[Free PMC Article](#)

Astaxanthin alleviated ethanol-induced liver injury by inhibition of oxidative stress and inflammatory responses via blocking of STAT3 activity.

[Han JH¹](#), [Ju JH¹](#), [Lee YS¹](#), [Park JH¹](#), [Yeo IJ¹](#), [Park MH¹](#), [Roh YS¹](#), [Han SB¹](#), [Hong JT²](#).

Author information

Abstract

Astaxanthin (AXT) is classified as a xanthophyll carotenoid compound which have broader functions including potent antioxidant, anti-inflammatory and neuroprotective properties. Considerable researches have demonstrated that AXT shows preventive and therapeutic properties against for Diabetes, Osteoarthritis and Rheumatoid Arthritis. However, the protective effect of AXT on liver disease has not yet been reported. In this study, we investigated effects of AXT on ethanol-induced liver injury in chronic plus binge alcohol feeding model. The hepatic steatosis and inflammation induced by ethanol administration were alleviated by AXT. Serum levels of aspartate transaminase and alanine transaminase were decreased in the livers of AXT administrated group. The ethanol-induced expression of cytochrome P450 2E1 (CYP2E1), pro-inflammatory proteins, cytokines, chemokines and reactive oxygen species (ROS) levels were also reduced in the livers of AXT administrated group. Moreover, ethanol-induced infiltration of neutrophils was decreased in the livers of AXT administrated group. Docking model and pull-down assay showed that AXT directly binds to the DNA binding site of STAT3. Moreover, AXT decreased STAT3 phosphorylation in the liver of AXT administration group. Therefore, these results suggest that AXT could prevent ethanol-induced hepatic injury via inhibition of oxidant and inflammatory responses via blocking of STAT3 activity.

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Free full text

Astaxanthin-Rich *Haematococcus pluvialis* Algal Hepatic Modulation in D-Galactose-Induced Aging in Rats: Role of Nrf2.

[El-Baz FK](#)¹, [Hussein RA](#)², [Abdel Jaleel GAR](#)³, [Saleh DO](#)³.

Author information

Abstract

Purpose: Aging is associated with hepatic morphological and physiological deterioration due to the accumulation of endogenous and exogenous free radicals and the resultant oxidative stress. The present study aims to investigate the effect of *Haematococcus pluvialis* microalgae on hepatic changes associated with D-galactose (D-Gal)-induced aging in rats. **Methods:** Aging was induced in rats by daily intraperitoneal injection of D-Gal (200 mg/kg/day) for eight consecutive weeks. D-Gal-injected rats were treated by astaxanthin (ATX)-rich *H. pluvialis* biomass, its carotenoid and polar fractions for two weeks. Twenty four hours after the last dose, blood samples were collected and the liver tissues were isolated for further biochemical and histopathological examinations. **Results:** D-Gal induced aging was associated with an elevation in serum liver function parameters, hepatic oxidative stress biomarkers viz., catalase (CAT), glutathione transferase (GST) and myeloperoxidase (MPO), as well as decreased expression of nuclear factor like-2 (Nrf2). Moreover, induction of aging exhibited an elevation of hepatic inflammatory cytokine; interleukin-6 (IL-6) and its modulator; nuclear factor Kappa B (NF-KB). However, treatment of D-Gal injected rats with ATX-rich *H. pluvialis* restored the serum liver function parameters as well as hepatic CAT, GST and MPO levels with an elevated expression of Nrf2. Treatment with ATX-rich *H. pluvialis* was also accompanied with a decrease in hepatic levels of NF-KB and IL-6. Histopathological examination emphasized all the previous results. Similarly, all trans-astaxanthin showed high affinity towards Nrf2 with -7.93 kcal/mol estimated free energy of binding as well as moderate affinities towards IL-6 and NF-KB through a docking study. **Conclusion:** ATX-rich *H. pluvialis* showed beneficial effects by ameliorating the hepatic changes associated with D-Gal induced aging in rats due to its modulatory role of the Nrf2/Keap pathway.

KEYWORDS:

Aging; Astaxanthin; D-galactose; *Haematococcus pluvialis*; Hepatic modulation

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Astaxanthin ameliorates experimental diabetes-induced renal oxidative stress and fibronectin by upregulating connexin43 in glomerular mesangial cells and diabetic mice.

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Author information

Abstract

Oxidative stress is the major cause of renal fibrosis in the progression of DN. Connexin43 (Cx43) exerts an anti-fibrosis effect on diabetic kidneys. The current study aimed to investigate whether astaxanthin (AST) could ameliorate the pathological progression of DN by upregulating Cx43 and activating the Nrf2/ARE signaling, which is a pivotal anti-oxidative stress system, to strengthen the cellular anti-oxidative capacity and diminish fibronectin (FN) accumulation in HG-induced glomerular mesangial cells (GMCs). Our hypothesis was verified in GMCs and the kidneys from db/db mice by western blot, immunofluorescence, immunohistochemistry, immunoprecipitation, dual luciferase reporter assay and reactive oxygen related detection kits. Results showed that AST simultaneously upregulated the Cx43 protein level and promoted the Nrf2/ARE signaling activity in the kidney of db/db mice and HG-treated GMCs. However, Cx43 depletion abrogated the Nrf2/ARE signaling activation induced by AST. AST reduced the interaction between c-Src and Nrf2 in the nuclei of GMCs cultured with HG, thereby enhancing the Nrf2 accumulation in the nuclei of GMCs. Our data suggested that AST promoted the Nrf2/ARE signaling by upregulating the Cx43 protein level to prevent renal fibrosis triggered by HG in GMCs and db/db mice. c-Src acted as a mediator in these processes.

KEYWORDS:

Astaxanthin; Connexin43; Diabetic nephropathy; Nrf2/ARE signaling; Renal fibrosis

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Protective effect of astaxanthin against contrast-induced acute kidney injury via SIRT1-p53 pathway in rats.

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Author information

Abstract

PURPOSE: The present study was designed to further investigate the protective effect of astaxanthin (AST) on contrast-induced acute kidney injury (CI-AKI) in rats and the relationship between SIRT1-p53 pathway and astaxanthin.

METHODS: 40 adult male Sprague Dawley (SD) rats were randomly divided into five groups (n = 8/group): control (CON), normal rats treated with AST (AST), CM-treated (CM), CM rats treated with isoform of nitric oxide synthase (iNOS) inhibitor (iNOS + CM), and CM rats treated with AST (AST + CM). Serum creatinine (Scr) and blood urea nitrogen (BUN) values were measured at 72 h following the procedure. Hematoxylin and eosin (H-E) staining was used to observe the pathologic changes of kidney. TUNEL staining was used to test apoptosis of kidney tubules. Oxidative stress, SIRT1 activity, nitric oxide (NO), and 3-nitrotyrosine (3-NT) content were individually measured with the commercial available kits.

RESULTS: Compared with the CON group, Scr and BUN levels significantly increased in the CM group ($P < 0.05$), and the values in two pre-treatment groups (iNOS + CM and AST + CM) had significantly decreased ($P < 0.05$). H-E and TUNEL staining had shown that renal tubular injury was severe in CM group. The renal injury score and apoptosis index in the two pre-treatment groups also decreased ($P < 0.05$). The present study showed that in CM group the levels of oxidative stress indicators significantly increased, and the activities of antioxidant stress indicators significantly decreased. These indicators in two pre-treatment groups significantly improved ($P < 0.05$). In the CM group the expression levels of SIRT1 significantly increased, and the ac-p53/p53 significantly increased ($P < 0.05$). Compared with the CM group, in AST + CM group the expression levels of SIRT1 increased, the expression levels of p53 and ac-p53/p53 decreased ($P < 0.05$). The levels of NO and 3-NT in CM group significantly increased ($P < 0.05$). Compared the CM group, the levels in the two pre-treatment groups significantly decreased ($P < 0.05$).

CONCLUSIONS: Astaxanthin has a protective effect on CI-AKI, the mechanism may be related to the SIRT1-p53 pathway. Astaxanthin can reduce the content of NO and 3-NT in renal tissue of CI-AKI, and alleviate the renal injury induced by contrast agents.

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[Methods Find Exp Clin Pharmacol](#). 2001 Mar;23(2):79-84.

Effect of astaxanthin on the hepatotoxicity, lipid peroxidation and antioxidative enzymes in the liver of CCl₄-treated rats.

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Astaxanthin is one of many carotenoids present in marine animals, vegetables and fruits. Since carotenoids are known to have antioxidant properties, we tested to determine if astaxanthin could have protective effects in the CCl₄-treated rat liver by activating the antioxidant system. Astaxanthin blocked the increase of glutamate-oxalacetate transaminase (GOT) and glutamate-pyruvate transaminase (GTP) activity and thiobarbituric acid reactive substances (TBARS) in response to carbon tetrachloride (CCl₄), while causing an increase in glutathione (GSH) levels and superoxide dismutase (SOD) activities in the CCl₄-treated rat liver. These results suggest that astaxanthin protects liver damage induced by CCl₄ by inhibiting lipid peroxidation and stimulating the cellular antioxidant system.

Publication Types:

- [Research Support, Non-U.S. Gov't](#)

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Protective effects of astaxanthin on ConA-induced autoimmune hepatitis by the JNK/p-JNK pathway-mediated inhibition of autophagy and apoptosis.

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[Author information](#)

Abstract

OBJECTIVE:

Astaxanthin, a potent antioxidant, exhibits a wide range of biological activities, including antioxidant, atherosclerosis and antitumor activities. However, its effect on concanavalin A (ConA)-induced autoimmune hepatitis remains unclear. The aim of this study was to investigate the protective effects of astaxanthin on ConA-induced hepatitis in mice, and to elucidate the mechanisms of regulation.

MATERIALS AND METHODS:

Autoimmune hepatitis was induced in Balb/C mice using ConA (25 mg/kg), and astaxanthin was orally administered daily at two doses (20 mg/kg and 40 mg/kg) for 14 days before ConA injection. Levels of serum liver enzymes and the histopathology of inflammatory cytokines and other marker proteins were determined at three time points (2, 8 and 24 h). Primary hepatocytes were pretreated with astaxanthin (80 μ M) in vitro 24 h before stimulation with TNF- α (10 ng/ml). The apoptosis rate and related protein expression were determined 24 h after the administration of TNF- α .

RESULTS:

Astaxanthin attenuated serum liver enzymes and pathological damage by reducing the release of inflammatory factors. It performed anti-apoptotic effects via the descending phosphorylation of Bcl-2 through the down-regulation of the JNK/p-JNK pathway.

CONCLUSION:

This research firstly expounded that astaxanthin reduced immune liver injury in ConA-induced autoimmune hepatitis. The mode of action appears to be downregulation of JNK/p-JNK-mediated apoptosis and autophagy.

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Astaxanthin prevents TGF β 1-induced pro-fibrogenic gene expression by inhibiting Smad3 activation in hepatic stellate cells.

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Author information

Abstract

BACKGROUND:

Non-alcoholic steatohepatitis (NASH) is a subset of non-alcoholic fatty liver disease, the most common chronic liver disease in the U.S. Fibrosis, a common feature of NASH, results from the dysregulation of fibrogenesis in hepatic stellate cells (HSCs). In this study, we investigated whether astaxanthin (ASTX), a xanthophyll carotenoid, can inhibit fibrogenic effects of transforming growth factor β 1 (TGF β 1), a key fibrogenic cytokine, in HSCs.

METHODS:

Reactive oxygen species (ROS) accumulation was measured in LX-2, an immortalized human HSC cell line. Quantitative realtime PCR, Western blot, immunocytochemical analysis, and in-cell Western blot were performed to determine mRNA and protein of fibrogenic genes, and the activation of Smad3 in TGF β 1-activated LX-2 cells and primary mouse HSCs.

RESULTS:

In LX-2 cells, ROS accumulation induced by tert-butyl hydrogen peroxide and TGF β 1 was abolished by ASTX. ASTX significantly decreased TGF β 1-induced α -smooth muscle actin (α -SMA) and procollagen type 1, alpha 1 (Col1A1) mRNA as well as α -SMA protein levels. Knockdown of Smad3 showed the significant role of Smad3 in the expression of α -SMA and Col1A1, but not TGF β 1, in LX-2 cells. ASTX attenuated TGF β 1-induced Smad3 phosphorylation and nuclear translocation with a concomitant inhibition of Smad3, Smad7, TGF β receptor I (T β RI), and T β RII expression. The inhibitory effect of ASTX on HSC activation was confirmed in primary mouse HSCs as evidenced by decreased mRNA and protein levels of α -SMA during activation.

CONCLUSION:

Taken together, ASTX exerted anti-fibrogenic effects by blocking TGF β 1-signaling, consequently inhibiting the activation of Smad3 pathway in HSCs.

GENERAL SIGNIFICANCE:

This study suggests that ASTX may be used as a preventive/therapeutic agent to prevent hepatic fibrosis.

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KEYWORDS:

Astaxanthin; Hepatic stellate cell; Liver fibrosis; Non-alcoholic steatohepatitis; Smad3; Transforming growth factor β 1

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ASTAXANTHIN PROTECTS AGAINST ACUTE KIDNEY INJURY IN RATS SUBJECTED TO FULL-THICKNESS BURNS.

Zhonghua Shao Shang Za Zhi. 2020 Nov 20;36(11):1050-1059.
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[Effect and mechanism of astaxanthin on acute kidney injury in rats with full-thickness burns]

[Article in Chinese]

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- DOI: [10.3760/cma.j.cn501120-20200526-00287](https://doi.org/10.3760/cma.j.cn501120-20200526-00287)

Abstract

in [English](#), [Chinese](#)

Objective: To explore the effect and mechanism of astaxanthin on acute kidney injury in rats with full-thickness burns. **Methods:** Forty-eight male Sprague Dawley rats of 8 to 10 weeks were divided into sham injury group, simple burn group, burn+ vehicle group, burn+ low-dose astaxanthin group, burn+ medium-dose astaxanthin group, and burn+ high-dose astaxanthin group according to the random number table, with 8 rats in each group. The back skin of rats in sham injury group were immersed in warm water of 20 °C for 15 s to simulate burn injury, and the back skin of rats in the other 5 groups were immersed in boiled water of 100 °C for 15 s to inflict full-thickness burn of 30% total body surface area. Fluid resuscitation was performed in rats in the 5 groups except of sham injury group immediately and 6 h after injury. At 30 min after injury, the rats in sham injury group and simple burn group were injected with 1 mL/kg normal saline via tail vein, rats in burn+ vehicle group were injected with 1 mL/kg astaxanthin solvent via tail vein, and rats in burn+ low-dose astaxanthin group, burn+ medium-dose astaxanthin group, and burn+ high-dose astaxanthin group were respectively injected with 5, 10, 20 mg/kg astaxanthin solution of 5, 10, 20 mg/mL via tail vein. The renal tissue was collected at post injury hour (PIH) 48, and hematoxylin eosin staining was used for histopathological observation and renal tubular injury score. At PIH 48, the

venous blood was collected for detecting serum creatinine level through blood biochemical analyzer, and blood urea nitrogen (BUN) level was detected by enzyme-linked immunosorbent assay. The renal tissue was collected to detect the mRNA expressions of myeloperoxidase (MPO), interleukin-1 β (IL-1 β), and IL-6 by real-time fluorescent quantitative reverse transcription polymerase chain reaction method, and the protein expressions of Toll like receptor 4 (TLR4), phosphorylated nuclear factor kappa B (p-NF- κ B) p65, and heme oxygenase 1 (HO-1) were detected by Western blotting. Besides, the expression of HO-1 in renal tissue was detected by immunofluorescence method. Data were statistically analyzed with Kruskal-Wallis *H* test, Dunn-Sidák correction, one-way analysis of variance, and Bonferroni method. **Results:** (1) At PIH 48, there were no inflammatory cell infiltrating and degeneration or necrosis of cells in renal tissue of rats in sham injury group, and the structure of renal tubules was intact. The renal tubules of burn rats in each group showed injury manifestation of separation between epithelial cell and basement membrane, and vacuole cells and lysate protein aggregation. The injury degree of renal tissue of rats in burn+ high-dose astaxanthin group was obviously decreased compared with that in simple burn group. (2) At PIH 48, compared with that of sham injury group, the renal tubular damage scores of rats in simple burn group, burn+ vehicle group, burn+ low-dose astaxanthin group, and burn+ medium-dose astaxanthin group were significantly increased ($P<0.05$ or $P<0.01$). Compared with those of simple burn group and burn+ vehicle group, the renal tubular damage scores of rats in burn+ medium-dose astaxanthin group and burn+ high-dose astaxanthin group were significantly decreased ($P<0.05$ or $P<0.01$). Compared with that of burn+ low-dose astaxanthin group, the renal tubular damage score of rats in burn+ high-dose astaxanthin group was significantly decreased ($P<0.01$). (3) At PIH 48, the level of serum creatinine of rats in sham injury group was (2.42 ± 0.06) mg/L, which was significantly lower than (6.11 ± 0.11), (6.48 ± 0.08), (5.79 ± 0.09), (4.03 ± 0.12) mg/L of simple burn group, burn+ vehicle group, burn+ low-dose astaxanthin group, and burn+ medium-dose astaxanthin group ($P<0.05$ or $P<0.01$). The level of BUN of rats was (21.9 ± 1.3) mmol/L in sham injury group, significantly lower than (32.1 ± 7.4) mmol/L of simple burn group and (30.2 ± 4.8) mmol/L of burn+ vehicle group ($P<0.05$ or $P<0.01$). At PIH 48, compared with those of simple burn group and burn+ vehicle group, the levels of serum creatinine and BUN of (16.0 ± 2.9) mmol/L in burn+ medium-dose astaxanthin group, serum creatinine of (3.02 ± 0.08) mg/L and BUN of (14.5 ± 2.9) mmol/L in burn+ high-dose astaxanthin group, and serum creatinine of (22.8 ± 5.5) mmol/L of rats in burn+ low-dose astaxanthin group were significantly decreased ($P<0.05$ or $P<0.01$). At PIH 48, compared with those of burn+ low-dose astaxanthin group, the levels of serum creatinine and BUN of burn+ high-dose astaxanthin group and serum creatinine of burn+ medium-dose group were obviously decreased ($P<0.05$ or $P<0.01$). (4) At PIH 48, compared with those of sham injury group, the mRNA expressions of MPO, IL-1 β , and IL-6 in renal tissue of rats in

simple burn group, burn+ vehicle group, burn+ low-dose astaxanthin group, and burn+ medium dose astaxanthin group, and the mRNA expressions of IL-1 β and IL-6 in renal tissue of rats in burn+ high-dose astaxanthin group were obviously increased ($P<0.01$). Compared with those of simple burn group and burn+ vehicle group, the mRNA expressions of MPO, IL-1 β , and IL-6 in renal tissue of rats were significantly decreased in burn+ low-dose astaxanthin group, burn+ medium-dose astaxanthin group, and burn+ high-dose astaxanthin group ($P<0.01$). Compared with those of burn+ low-dose astaxanthin group, the mRNA expressions of MPO, IL-1 β , and IL-6 in renal tissue of rats were significantly decreased in burn+ medium-dose astaxanthin group and burn+ high-dose astaxanthin group ($P<0.01$). The mRNA expressions of MPO, IL-1 β , and IL-6 in renal tissue of rats in burn+ high-dose astaxanthin group were significantly decreased compared with those of burn+ medium-dose astaxanthin group ($P<0.01$). (5) At PIH 48 h, compared with those of sham injury group, the protein expressions of TLR4 and p-NF- κ B p65 in renal tissue of rats in simple burn group, burn+ vehicle group, burn+ low-dose astaxanthin group, and burn+ high-dose astaxanthin group were obviously increased ($P<0.01$). Compared with those of simple burn group, the protein expressions of TLR4 and p-NF- κ B p65 in renal tissue of rats in burn+ low-dose astaxanthin group, burn+ medium dose astaxanthin group, and burn+ high-dose astaxanthin group were significantly decreased ($P<0.01$). (6) The results of Western blotting combined with immunofluorescence method showed that compared with that of sham injury group, the protein expression of HO-1 in renal tissue of rats in burn+ vehicle group, burn+ low-dose astaxanthin group, burn+ medium-dose astaxanthin group, and burn+ high-dose astaxanthin group were significantly increased at PIH 48 ($P<0.01$), and the protein expression of HO-1 in renal tissue of rats in burn+ medium-dose astaxanthin group and burn+ high-dose astaxanthin group was significantly increased compared with that of simple burn group ($P<0.01$). **Conclusions:** Astaxanthin can attenuate the structural damage and functional decline of renal tissue and regulate the release of injury-related inflammatory factors, thus to protect the rats from acute kidney injury after burn. The HO-1/TLR4/NF- κ B signaling pathway is the main regulatory mechanism of astaxanthin to achieve anti-inflammation-based renoprotection.

ASTAXANTHIN SHOWS POTENTIAL TO REDUCE LIVER FIBROSIS IN-VITRO.

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Astaxanthin inhibits the reduction of glycolysis during the activation of hepatic stellate cells

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- DOI: [10.1016/j.lfs.2020.117926](https://doi.org/10.1016/j.lfs.2020.117926)

Abstract

Aims: Hepatic stellate cells (HSCs) play an essential role in the development of liver fibrosis by producing extracellular matrix proteins, growth factors, and pro-inflammatory and pro-fibrogenic cytokines once activated. We previously demonstrated that astaxanthin (ASTX), a xanthophyll carotenoid, attenuates HSC activation. The objective of this study was to investigate whether there is a difference in glycolysis between quiescent and activated HSCs and the effect of ASTX on glycolysis during HSC activation.

Materials and Methods: Mouse primary HSCs were activated for 7 days in the presence or absence of 25 μ M of ASTX. Quiescent HSCs (qHSCs), 1 day after isolation, and activated HSCs (aHSCs) treated with/without ASTX were plated in a Seahorse XF24 cell culture microplate for Glycolysis Stress tests.

Key findings: aHSCs had significantly lower glycolysis, but higher glycolytic capacity, maximum capacity of glycolysis, and non-glycolytic acidification than qHSCs. Importantly, ASTX markedly increased glycolysis during HSC activation with a concomitant increase in lactate formation and secretion. Compared with qHSCs, aHSCs had significantly lower expression of glucose transporter 1, the major glucose transporter in HSCs, and its transcription factor hypoxia-inducible factor 1 α , which was markedly increased by ASTX in aHSCs.

Significance: Our data suggest that ASTX may prevent the activation of HSCs by altering glycolysis and the expression of genes involved in the pathways.

ASTAXANTHIN PROTECTS AGAINST EARLY ACUTE KIDNEY INJURY IN SEVERELY BURNED RATS.

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doi: 10.1038/s41598-021-86146-w.

Astaxanthin protects against early acute kidney injury in severely burned rats by inactivating the TLR4/MyD88/NF- κ B axis and upregulating heme oxygenase-1

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- PMID: [33758309](#) PMCID: [PMC7988001](#) DOI: [10.1038/s41598-021-86146-w](#) **Free PMC article**

Abstract

Early acute kidney injury (AKI) contributes to severe morbidity and mortality in critically burned patients. Renal inflammation plays a vital role in the progression of early AKI, acting as a therapeutic target. Astaxanthin (ATX) is a strong antioxidant widely distributed in marine organisms that exerts many biological effects in trauma and disease. ATX is also suggested to have anti-inflammatory activity. Hence, we attempted to explore the role of ATX in protecting against early postburn AKI via its anti-inflammatory effects and the related mechanisms. A severely burned model was established for histological and biochemical assessments based on adult male rats. We found that oxidative stress-induced tissue inflammation participated in the development of early AKI after burn injury and that the MyD88-dependent TLR4/NF- κ B pathway was activated to regulate renal inflammation. The TLR4 and NF- κ B inhibitors TAK242 and PDTC showed similar effects in attenuating burn-induced renal inflammation and early AKI. Upon ATX treatment, the release of inflammatory mediators in the kidneys was downregulated, while the TLR4/MyD88/NF- κ B axis was inhibited in a dose-related manner. TAK242 and PDTC could enhance the anti-inflammatory effect of high-dose ATX, whereas lipopolysaccharide (LPS) reversed its action. Furthermore, the expression of heme oxygenase (HO)-1 was upregulated by ATX in a dose-related manner. Collectively, the above data suggest that ATX protects against renal inflammation in a dose-related manner by regulating the TLR4/MyD88/NF- κ B axis and HO-1 and ultimately prevents early AKI following severe burns.

[Toxicol Ind Health](#). 2014 Mar;30(2):101-12. doi: 10.1177/0748233712452607. Epub 2012 Jul 9.

Hepatoprotective potential of astaxanthin against 2,3,7,8-tetrachlorodibenzo-p-dioxin in cultured rat hepatocytes.

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Author information

Abstract

The purpose of this study was to evaluate the effect of carotenoid astaxanthin (ASTA) on cultured primary rat hepatocytes treated with 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) on the cell viability (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide, MTT), lactate dehydrogenase (LDH) activity, 8-oxo-2-deoxyguanosine (8-OH-dG), total antioxidant capacity (TAC), and total oxidative stress (TOS) levels, and liver micronucleus rates. ASTA (2.5, 5, and 10 μ M) was added to cultures alone or simultaneously with TCDD (5 and 10 μ M) for 48 h. The results of MTT and LDH assays showed that both doses of TCDD caused significant decrease in cell viability. Also, TCDD significantly increased TOS and decreased TAC level in rat hepatocytes. On the basis of increasing doses, the dioxin caused significant increase in micronucleated hepatocytes) and 8-OH-dG level as compared to control culture. The presence of ASTA with TCDD minimized its effects on primary hepatocytes cultures and DNA damages.

KEYWORDS:

TCDD; astaxanthin; cell viability; cultured rat hepatocytes; genotoxicity; oxidative status

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Beneficial effect of astaxanthin on 2,3,7,8-tetrachlorodibenzo-p-dioxin-induced liver injury in rats.

[Turkez H¹](#), [Geyikoglu F](#), [Yousef MI](#).

Author information

Abstract

Exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) represents a potential health risk and hepatotoxicity. Astaxanthin (ASTA) exhibits antioxidant properties and can influence hepatotoxicity. Therefore, the present study was carried out for using ASTA against hepatotoxicity induced by TCDD in the liver of rats. Animals were treated intraperitoneally daily with TCDD (8 µg/kg body weight (b.w.)), ASTA (12.5 mg/kg b.w. and 25 mg/kg b.w.) and TCDD plus ASTA (12.5 and 25 mg/kg b.w.) for 21 days. TCDD significantly decreased the activities of antioxidant enzymes and resulted in serious pathological findings. Moreover, the rate of micronucleus (MN) in hepatocytes increased after treating with TCDD. The activities of enzymes, frequencies of MNs and liver histology in lower dosage group of ASTA remained unchanged compared with the control group. In rats treated with ASTA, at higher dosage alone, the MNs remained unchanged and the activities of antioxidant enzymes significantly increased. The presence of ASTA (except for lower dose) with TCDD alleviated its pathological effects in hepatic tissue. ASTA also prevented the suppression of antioxidant enzymes in the livers of animals exposed to TCDD and displayed a strong protective effect against MNs. Thus, the present findings might provide new insight into the development of therapeutic and preventive approaches of TCDD toxicity.

KEYWORDS:

TCDD; antioxidant enzymes; astaxanthin; histopathology; micronucleus assay; rat

PMID:

22312033

[PubMed - indexed for MEDLINE]

[Med Hypotheses](#). 2011 Oct;77(4):550-6. doi: 10.1016/j.mehy.2011.06.029. Epub 2011 Jul 20.

Full-spectrum antioxidant therapy featuring astaxanthin coupled with lipoprivic strategies and salsalate for management of non-alcoholic fatty liver disease.

[McCarty MF](#)¹.

Author information

Abstract

Owing to the worldwide epidemic of obesity, and the popularity of diets rich in sugar and saturated fat, nonalcoholic fatty liver disease (NAFLD) is increasingly common; it is usually associated with insulin resistance, and may be considered a component of the metabolic syndrome. The pathologies which can complicate hepatic steatosis--steatohepatitis, cirrhosis, and hepatic cancer--appear to result from an interaction of hepatic lipid overload and hepatic oxidative stress. It is therefore proposed that comprehensive regimens which effectively target each of these precipitating factors should achieve the best therapeutic benefit in NAFLD. Appropriate weight loss, and a diet low in saturated fat, glycemic index, and added sugars, should decrease hepatic lipid load. Measures which enhance adipocyte insulin sensitivity--such as pioglitazone, astaxanthin, and spirulina--may also be helpful in this regard, as may agents that boost hepatocyte capacity for fatty acid oxidation, such as metformin, carnitine, hydroxycitrate, long-chain omega-3 fats, and glycine. Astaxanthin and spirulina appear to have considerable potential for controlling the oxidative stress associated with NAFLD - the former because it may help to prevent the mitochondrial damage that renders mitochondria a key source of superoxide in this syndrome, the latter because it is exceptionally rich in phycocyanobilin, a phytochemical inhibitor of NADPH oxidase. Other antioxidants which show some promise in this syndrome include high-dose folate, lipoic acid, melatonin, N-acetylcysteine, vitamin E, and taurine. Finally, treatment with salsalate, an inhibitor of I κ B kinase-beta, has potential for blunting the adverse impact of hepatic steatosis on oxidative stress and inflammation.

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Astaxanthin lowers plasma TAG concentrations and increases hepatic antioxidant gene expression in diet-induced obesity mice.

[Yang Y¹](#), [Pham TX¹](#), [Wegner CJ¹](#), [Kim B¹](#), [Ku CS¹](#), [Park YK¹](#), [Lee JY¹](#).

Author information

Abstract

Non-alcoholic fatty liver disease (NAFLD) is significantly associated with hyperlipidaemia and oxidative stress. We have previously reported that astaxanthin (ASTX), a xanthophyll carotenoid, lowers plasma total cholesterol and TAG concentrations in apoE knockout mice. To investigate whether ASTX supplementation can prevent the development of NAFLD in obesity, male C57BL/6J mice (n 8 per group) were fed a high-fat diet (35%, w/w) supplemented with 0, 0.003, 0.01 or 0.03% of ASTX (w/w) for 12 weeks. The 0.03% ASTX-supplemented group, but not the other groups, exhibited a significant decrease in plasma TAG concentrations, suggesting that ASTX at a 0.03% supplementation dosage exerts a hypotriacylglycerolaemic effect. Although there was an increase in the mRNA expression of fatty acid synthase and diglyceride acyltransferase 2, the mRNA levels of acyl-CoA oxidase 1, a critical enzyme in peroxisomal fatty acid β -oxidation, exhibited an increase in the 0.03% ASTX-supplemented group. There was a decrease in plasma alanine transaminase (ALT) and aspartate transaminase (AST) concentrations in the 0.03% ASTX-supplemented group. There was a significant increase in the hepatic mRNA expression of nuclear factor erythroid 2-related factor 2 and its downstream genes, which are critical for endogenous antioxidant mechanism, in the 0.03% ASTX-supplemented group. Furthermore, there was a significant decrease in the mRNA abundance of IL-6 in the primary splenocytes isolated from the 0.03% ASTX-supplemented group upon lipopolysaccharide (LPS) stimulation when compared with that in the splenocytes isolated from the control group. In conclusion, ASTX supplementation lowered the plasma concentrations of TAG, ALT and AST, increased the hepatic expression of endogenous antioxidant genes, and rendered splenocytes less sensitive to LPS stimulation. Therefore, ASTX may prevent obesity-associated metabolic disturbances and inflammation.

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25328157

[PubMed - indexed for MEDLINE]

[Mediators Inflamm.](#) 2014;2014:954502. doi: 10.1155/2014/954502. Epub 2014 Apr 17.

Protective effect of astaxanthin on liver fibrosis through modulation of TGF- β 1 expression and autophagy.

[Shen M¹](#), [Chen K¹](#), [Lu J¹](#), [Cheng P¹](#), [Xu L¹](#), [Dai W¹](#), [Wang F¹](#), [He L¹](#), [Zhang Y¹](#), [Chengfen W¹](#), [Li J¹](#), [Yang J¹](#), [Zhu R¹](#), [Zhang H¹](#), [Zheng Y¹](#), [Zhou Y¹](#), [Guo C¹](#).

Author information

Abstract

Liver fibrosis is a common pathway leading to cirrhosis and a worldwide clinical issue. Astaxanthin is a red carotenoid pigment with antioxidant, anticancer, and anti-inflammatory properties. The aim of this study was to investigate the effect of astaxanthin on liver fibrosis and its potential protective mechanisms. Liver fibrosis was induced in a mouse model using CCL4 (intraperitoneal injection, three times a week for 8 weeks), and astaxanthin was administered everyday at three doses (20, 40, and 80 mg/kg). Pathological results indicated that astaxanthin significantly improved the pathological lesions of liver fibrosis. The levels of alanine aminotransferase aspartate aminotransferase and hydroxyproline were also significantly decreased by astaxanthin. The same results were confirmed in bile duct ligation, (BDL) model. In addition, astaxanthin inhibited hepatic stellate cells (HSCs) activation and formation of extracellular matrix (ECM) by decreasing the expression of NF- κ B and TGF- β 1 and maintaining the balance between MMP2 and TIMP1. In addition, astaxanthin reduced energy production in HSCs by downregulating the level of autophagy. These results were simultaneously confirmed in vivo and in vitro. In conclusion, our study showed that 80 mg/kg astaxanthin had a significant protective effect on liver fibrosis by suppressing multiple profibrogenic factors.

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24860243

[PubMed - indexed for MEDLINE]

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PMC4016904

[Free PMC Article](#)

[Cell Stress Chaperones](#). 2014 Mar;19(2):183-91. doi: 10.1007/s12192-013-0443-x. Epub 2013 Jul 14.

Astaxanthin reduces hepatic endoplasmic reticulum stress and nuclear factor- κ B-mediated inflammation in high fructose and high fat diet-fed mice.

[Bhuvaneshwari S¹](#), [Yogalakshmi B](#), [Sreeja S](#), [Anuradha CV](#).

Author information

Abstract

We recently showed that astaxanthin (ASX), a xanthophyll carotenoid, activates phosphatidylinositol 3-kinase pathway of insulin signaling and improves glucose metabolism in liver of high fructose-fat diet (HFFD)-fed mice. The aim of this study is to investigate whether ASX influences phosphorylation of c-Jun-N-terminal kinase 1 (JNK1), reactive oxygen species (ROS) production, endoplasmic reticulum (ER) stress, and inflammation in liver of HFFD-fed mice. Adult male *Mus musculus* mice were fed either with control diet or HFFD for 15 days. After this period, mice in each group were divided into two and administered ASX (2 mg/kg/day, p.o) in 0.3 ml olive oil or 0.3 ml olive oil alone for the next 45 days. At the end of 60 days, liver tissue was excised and examined for lipid accumulation (Oil red O staining), intracellular ROS production, ER stress, and inflammatory markers. Elevated ROS production, lipid accumulation, and increased hepatic expression of ER stress markers such as Ig-binding protein, PKR-like ER kinase, phosphorylated eukaryotic initiation factor 2 α , X-box binding protein 1, activating transcription factor 6, and the apoptotic marker caspase 12 were observed in the liver of the HFFD group. ASX significantly reversed these changes. This reduction was accompanied by reduced activation of JNK1 and I kappa B kinase β phosphorylation and nuclear factor-kappa B p65 nuclear translocation in ASX-treated HFFD mice. These findings suggest that alleviation of inflammation and ER stress by ASX could be a mechanism responsible for its beneficial effect in this model. ASX could be a promising treatment strategy for insulin resistant patients.

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23852435

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PMC3933623

[Free PMC Article](#)

[Xenobiotica](#). 1996 Sep;26(9):909-19.

beta-Apo-8'-carotenal, but not beta-carotene, is a strong inducer of liver cytochromes P450A1 and 1A2 in rat.

[Gradelet S](#), [Leclerc J](#), [Siess MH](#), [Astorg PO](#).

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1. The catalytic activities of several phase I and II xenobiotic-metabolizing enzymes and their immunochemical detection have been investigated in liver microsomes and cytosol of the male rat, which had been fed for 15 days with diets containing 300 mg/kg beta-carotene isomers (all-trans beta-carotene or beta-carotene from *Dunaliella salina* rich in 9-cis isomer or isomerized beta-carotene), or apocarotenoids as beta-apo-8'-carotenal, ethyl beta-apo-8'-carotenoate and citranaxanthin. 2. Beta-carotene, either all-trans or containing cis isomers, did not induce any significant change in the measured activities. By contrast, beta-apo-8'-carotenal increased the liver content of cytochrome P450, the activity of NADH- and NADPH-cytochrome c reductase, and strongly increased some cytochrome P450-dependent activities, particularly ethoxyresorufin O-deethylase (x158), methoxyresorufin O-demethylase (x22), pentoxy- and benzoxyresorufin O-dealkylases, but did not affect erythromycin N-demethylase nor nitrosodimethylamine N-demethylase activities. Phase II p-nitrophenol- and 4-hydroxy- biphenyl-uridine diphosphoglucuronosyl transferase activities were also increased by beta-apo-8'carotenal. Western blots of microsomal proteins clearly showed the induction of CYP1A1 and 1A2 by beta-apo-8'-carotenal. This induction profile resembles that produced by two other carotenoids: canthaxanthin and astaxanthin. Ethyl beta-apo-8'-carotenoate and citranaxanthin showed similar effects to beta-apo-8'-carotenal but of less intensity. 3. Three carotenoids: beta-apo-8'-carotenal, canthaxanthin and astaxanthin, are inducers of CYP1A1 and 1A2 in the rat. These carotenoids form a new class of inducers of CYP1A, structurally very different from the classical inducers as 3-methylcholanthrene, beta-naphthoflavone or dioxin.

Publication Types:

- [Research Support, Non-U.S. Gov't](#)

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Astaxanthin Pretreatment Attenuates Hepatic Ischemia Reperfusion-Induced Apoptosis and Autophagy via the ROS/MAPK Pathway in Mice.

[Li J](#)¹, [Wang F](#)², [Xia Y](#)³, [Dai W](#)⁴, [Chen K](#)⁵, [Li S](#)⁶, [Liu T](#)⁷, [Zheng Y](#)⁸, [Wang J](#)⁹, [Lu W](#)¹⁰, [Zhou Y](#)¹¹, [Yin Q](#)¹², [Lu J](#)¹, [Zhou Y](#)⁸, [Guo C](#)¹³.

Author information

Abstract

BACKGROUND:

Hepatic ischemia reperfusion (IR) is an important issue in complex liver resection and liver transplantation. The aim of the present study was to determine the protective effect of astaxanthin (ASX), an antioxidant, on hepatic IR injury via the reactive oxygen species/mitogen-activated protein kinase (ROS/MAPK) pathway.

METHODS:

Mice were randomized into a sham, IR, ASX or IR + ASX group. The mice received ASX at different doses (30 mg/kg or 60 mg/kg) for 14 days. Serum and tissue samples at 2 h, 8 h and 24 h after abdominal surgery were collected to assess alanine aminotransferase (ALT), aspartate aminotransferase (AST), inflammation factors, ROS, and key proteins in the MAPK family.

RESULTS:

ASX reduced the release of ROS and cytokines leading to inhibition of apoptosis and autophagy via down-regulation of the activated phosphorylation of related proteins in the MAPK family, such as P38 MAPK, JNK and ERK in this model of hepatic IR injury.

CONCLUSION:

Apoptosis and autophagy caused by hepatic IR injury were inhibited by ASX following a reduction in the release of ROS and inflammatory cytokines, and the relationship between the two may be associated with the inactivation of the MAPK family.

KEYWORDS:

astaxanthin; hepatic ischemia reperfusion; oxidative stress; reactive oxygen species

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PMCID:

PMC4483634

[Free PMC Article](#)

[J Am Geriatr Soc.](#) 2015 Jun;63(6):1271-3. doi: 10.1111/jgs.13505.

Astaxanthin Improves Nonalcoholic Fatty Liver Disease in Werner Syndrome with Diabetes Mellitus.

[Takemoto M](#)^{1,2}, [Yamaga M](#)^{1,2}, [Furuichi Y](#)³, [Yokote K](#)^{1,2}.

[Author information](#)

PMID:

26096415

[PubMed - indexed for MEDLINE]

[Toxicology](#). 2010 Jan 12;267(1-3):147-53. Epub 2009 Nov 10.

Effect of astaxanthin on hepatocellular injury following ischemia/reperfusion.

[Curek GD](#), [Cort A](#), [Yucel G](#), [Demir N](#), [Ozturk S](#), [Elpek GO](#), [Savas B](#), [Aslan M](#).

Department of Biochemistry, Akdeniz University Medical School, Antalya 07070, Turkey.

Abstract

This study investigated the effect of astaxanthin (ASX; 3,3-dihydroxybeta, beta-carotene-4,4-dione), a water-dispersible synthetic carotenoid, on liver ischemia-reperfusion (IR) injury.

Astaxanthin (5 mg/kg/day) or olive oil was administered to rats via intragastric intubation for 14 consecutive days before the induction of hepatic IR. On the 15th day, blood vessels supplying the median and left lateral hepatic lobes were occluded with an arterial clamp for 60 min, followed by 60 min reperfusion. At the end of the experimental period, blood samples were obtained from the right ventricle to determine plasma alanine aminotransferase (ALT) and xanthine oxidase (XO) activities and animals were sacrificed to obtain samples of nonischemic and postischemic liver tissue. The effects of ASX on IR injury were evaluated by assessing hepatic ultrastructure via transmission electron microscopy and by histopathological scoring. Hepatic conversion of xanthine dehydrogenase (XDH) to XO, total GSH and protein carbonyl levels were also measured as markers of oxidative stress. Expression of NOS2 was determined by immunohistochemistry and Western blot analysis while nitrate/nitrite levels were measured via spectral analysis. Total histopathological scoring of cellular damage was significantly decreased in hepatic IR injury following ASX treatment. Electron microscopy of postischemic tissue demonstrated parenchymal cell damage, swelling of mitochondria, disarrangement of rough endoplasmatic reticulum which was also partially reduced by ASX treatment.

Astaxanthine treatment significantly decreased hepatic conversion of XDH to XO and tissue protein carbonyl levels following IR injury. The current results suggest that the mechanisms of action by which ASX reduces IR damage may include antioxidant protection against oxidative injury. 2009 Elsevier Ireland Ltd. All rights reserved.

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Effects of canthaxanthin, astaxanthin, lycopene and lutein on liver xenobiotic-metabolizing enzymes in the rat.

[Gradelet S](#), [Astorg P](#), [Leclerc J](#), [Chevalier J](#), [Vernevaut MF](#), [Siess MH](#).

Unité de Toxicologie Nutritionnelle, Institut National de la Recherche Agronomique, DIJON, France.

1. The catalytic activities of several phase I and II xenobiotic-metabolizing enzymes and the immunochemical detection of P4501A and 2B have been investigated in liver microsomes and cytosol of male rats fed for 15 days with diets containing canthaxanthin, astaxanthin, lycopene or lutein (as lutein esters) (300 mg/kg diet) and in rats fed increasing levels (10, 30, 100 and 300 ppm) of canthaxanthin or astaxanthin in the diet. 2. Canthaxanthin increased the liver content of P450, the activities of NADH- and NADPH-cytochrome c reductase, and produced a substantial increase of some P450-dependent activities, especially ethoxyresorufin O-deethylase (EROD) (x 139) and methoxyresorufin O-demethylase (MROD) (x 26). Canthaxanthin also increased pentoxy-(PROD) and benzoxyresorufin O-dealkylases (BROD), but did not affect. NADPH-cytochrome c reductase and erythromycin N-demethylase (ERDM) activities and decreased nitrosodimethylamine N-demethylase (NDMAD) activity. Phase II p-nitrophenol UDP-glucuronosyl transferase (4NP-UGT) and quinone reductase (QR) activities were also increased by canthaxanthin treatment. These enhancing effects on EROD, MROD and 4NP-UGT were clearly detectable at a dose as low as 10 ppm of canthaxanthin in the diet; the induction of QR was only observed in rats fed > or = 100 ppm. Astaxanthin induced the same pattern of enzymes activities as canthaxanthin, but to a lesser extent: its effects on phase I enzymes and 4NP-UGT were observed in rats fed > or = 100 ppm, and QR was not increased. Western blots of microsomal proteins clearly showed the induction of P4501A1 and 1A2 by canthaxanthin and astaxanthin. By contrast, lutein had no effect on the phase I and II xenobiotic-metabolizing enzymes activities measured. Lycopene only decreased NDMAD activity. 3. The two 4-oxocarotenoids canthaxanthin and astaxanthin are substantial inducers of liver P4501A1 and 1A2 in the rat, and coinduce 4NP-UGT and QR, just like polycyclic aromatic hydrocarbon, beta-naphtoflavone or dioxin (TCDD). However, these latter classical P4501A inducers also induce aldehyde dehydrogenase class 3 (ALDH3); this enzyme is not increased, or only marginally, by canthaxanthin and astaxanthin. These two oxocarotenoids form a new class of inducers of P4501A, are structurally very different from the classical inducers quoted above, which are ligands of the AH receptor.

Publication Types:

- [In Vitro](#)
- [Research Support, Non-U.S. Gov't](#)
PMID: 8851821 [PubMed - indexed for MEDLINE]

[Mar Drugs](#). 2015 Apr 13;13(4):2105-23. doi: 10.3390/md13042105.

Astaxanthin attenuates early acute kidney injury following severe burns in rats by ameliorating oxidative stress and mitochondrial-related apoptosis.

[Guo SX](#)¹, [Zhou HL](#)², [Huang CL](#)³, [You CG](#)⁴, [Fang Q](#)⁵, [Wu P](#)⁶, [Wang XG](#)⁷, [Han CM](#)⁸.

Author information

Abstract

Early acute kidney injury (AKI) is a devastating complication in critical burn patients, and it is associated with severe morbidity and mortality. The mechanism of AKI is multifactorial. Astaxanthin (ATX) is a natural compound that is widely distributed in marine organisms; it is a strong antioxidant and exhibits other biological effects that have been well studied in various traumatic injuries and diseases. Hence, we attempted to explore the potential protection of ATX against early post burn AKI and its possible mechanisms of action. The classic severe burn rat model was utilized for the histological and biochemical assessments of the therapeutic value and mechanisms of action of ATX. Upon ATX treatment, renal tubular injury and the levels of serum creatinine and neutrophil gelatinase-associated lipocalin were improved. Furthermore, relief of oxidative stress and tubular apoptosis in rat kidneys post burn was also observed. Additionally, ATX administration increased Akt and Bad phosphorylation and further down-regulated the expression of other downstream pro-apoptotic proteins (cytochrome c and caspase-3/9); these effects were reversed by the PI3K inhibitor LY294002. Moreover, the protective effect of ATX presents a dose-dependent enhancement. The data above suggested that ATX protects against early AKI following severe burns in rats, which was attributed to its ability to ameliorate oxidative stress and inhibit apoptosis by modulating the mitochondrial-apoptotic pathway, regarded as the Akt/Bad/Caspases signalling cascade.

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25871290

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PMCID:

PMC4413202

[Free PMC Article](#)

Protective effects of astaxanthin against ischemia/reperfusion induced renal injury in mice.

[Qiu X](#)^{1,2,3}, [Fu K](#)^{4,5}, [Zhao X](#)^{6,7}, [Zhang Y](#)⁸, [Yuan Y](#)⁹, [Zhang S](#)¹⁰, [Gu X](#)¹¹, [Guo H](#)¹².

[Author information](#)

Abstract

Astaxanthin (ATX) is a powerful antioxidant that occurs naturally in a wide variety of living organisms. Previous studies have shown that ATX has effects of eliminating oxygen free radicals and can protect organs from ischemia/reperfusion (IR) induced injury. The present study was designed to further investigate the protective effects of ATX on oxidative stress induced toxicity in tubular epithelial cells and on IR induced renal injury in mice. ATX, at a concentration of 250 nM, attenuated 100 μ M H₂O₂-induced viability decrease of tubular epithelial cells. In vivo, ATX preserved renal function 12 h or 24 h post IR. Pretreatment of ATX via oral gavage for 14 consecutive days prior to IR dramatically prevented IR induced histological damage 24 h post IR. Histological results showed that the pathohistological score, number of apoptotic cells, and the expression of α -smooth muscle actin were significantly decreased by pretreatment of ATX. In addition, oxidative stress and inflammation in kidney samples were significantly reduced by ATX 24 h post IR. Taken together, the current study suggests that pretreatment of ATX is effective in preserving renal function and histology via antioxidant activity.

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25623758

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[Free PMC Article](#)

Production and extraction of astaxanthin from *Phaffia rhodozyma* and its biological effect on alcohol-induced renal hypoxia in *Carassius auratus*.

[Alesci A¹](#), [Salvo A](#), [Lauriano ER](#), [Gervasi T](#), [Palombieri D](#), [Bruno M](#), [Pergolizzi S](#), [Cicero N](#).

Author information

Abstract

The effect of astaxanthin (3,3'-dihydroxy-s-carotene-4,4'-dione) on alcohol-induced morphological changes in *Carassius auratus*, as an experimental model, was determined. The yeast *Phaffia rhodozyma* was used as a source of astaxanthin. The animals were divided into three groups for 30 days: one group was treated with ethanol at a dose of 1.5% mixed in water, the second one with EtOH 1.5% and food enriched with astaxanthin from *P. rhodozyma*, and the third was a control group. After a sufficient experimental period, the samples were processed using light microscopy and evaluated by histomorphological and histochemical staining, and the data were supported by immunohistochemical analysis, using a wide range of antibodies, such as calbindin, vimentin and alpha-smooth muscle actin. The results show that the alcoholic damage in the kidney led to hypoxia. In contrast, the group fed with astaxanthin from *P. rhodozyma* showed a normal morphological picture, with better glomeruli organisation and the presence of the area of filtration. Furthermore, the immunohistochemistry has confirmed these results.

KEYWORDS:

Carassius auratus; *Phaffia rhodozyma*; astaxanthin; kidney

PMID:

25492637

[PubMed - in process]

Astaxanthin from shrimp by-products ameliorates nephropathy in diabetic rats.

[Sila A¹](#), [Ghlyssi Z](#), [Kamoun Z](#), [Makni M](#), [Nasri M](#), [Bougatef A](#), [Sahnoun Z](#).

Author information

Abstract

AIM:

This study investigated the hypoglycemic and antioxidant effects of shrimp astaxanthin on the kidney of alloxan-induced diabetic rats.

METHODS:

Animals were distributed into four groups of six rats each: a control group (C), a diabetic group (D), a diabetic group supplemented with Astaxanthin (D+As) dissolved in olive oil and a diabetic group supplemented with olive oil (D+OO). In vitro antidiabetic effect was tested in plasma and kidney tissue.

RESULTS:

The group D of rats showed significant ($P < 0.05$) increase of glycemia, creatinine, urea and uric acid levels compared to those of the control group (C). Moreover, plasma and kidney malondialdehyde (MDA) and protein carbonyl (PCO) levels for the rats of the group D were significantly increased compared to the control group. Contrariwise, antioxidant enzyme activities, such as catalase (EC 1.11.1.6), superoxide dismutase (EC 1.15.1.1) and non-enzymatic levels of reduced glutathione, were significantly ($P < 0.05$) decreased in the plasma and kidney of diabetic rats compared to the control ones.

The astaxanthin supplementation in rats diet improved the antioxidant enzyme activities and significantly decreased the MDA and PCO levels compared to diabetic rats. Indeed, no significant ($P \geq 0.05$) improvement was observed for the fourth group (D+OO) compared to the control group (C). Histological analysis of kidney showed glomerular hypertrophy and tubular dilatation for the diabetic rats. For D+As rats, these histopathological changes were less prominent.

CONCLUSIONS:

Our results suggest that shrimp astaxanthin may play an important role in reduction of oxidative damage and could prevent pathological changes in diabetic rats suggesting promising application of shrimp astaxanthin in diabetes treatment.

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24821271

[PubMed - indexed for MEDLINE]

Astaxanthin modulates osteopontin and transforming growth factor β 1 expression levels in a rat model of nephrolithiasis: a comparison with citrate administration.

[Alex M¹](#), [Sauganth Paul MV](#), [Abhilash M](#), [Mathews VV](#), [Anilkumar TV](#), [Nair RH](#).

Author information

Abstract

OBJECTIVES:

To evaluate the effect of astaxanthin on renal angiotensin-I converting enzyme (ACE) levels, osteopontin (OPN) and transforming growth factor β 1 (TGF- β 1) expressions and the extent of crystal deposition in experimentally induced calcium oxalate kidney stone disease in a male Wistar rat model. To compare the efficacy of astaxanthin treatment with a currently used treatment strategy (citrate administration) for kidney stones.

MATERIALS AND METHODS:

The expression of OPN was assessed by immunohistochemistry. One step reverse transcriptase polymerase chain reaction followed by densitometry was used to assess renal OPN and TGF- β 1 levels. Renal ACE levels were quantified by an enzyme-linked immunosorbent assay method. Crystal deposition in kidney was analysed by scanning electron microscopic (SEM)-energy-dispersive X-ray (EDX).

RESULTS:

The renal ACE levels and the expression of OPN and TGF- β 1 were upregulated in the nephrolithiasis-induced rats. Astaxanthin treatment reduced renal ACE levels and the expression OPN and TGF- β 1. SEM-EDX analysis showed that crystal deposition was reduced in the astaxanthin-treated nephrolithiatic group. Astaxanthin treatment was more effective than citrate administration in the regulation of renal ACE levels, OPN and TGF- β 1 expressions.

CONCLUSIONS:

Astaxanthin administration reduced renal calcium oxalate crystal deposition possibly by modulating the renal renin-angiotensin system (RAS), which reduced the expression of OPN and TGF- β 1 levels. Astaxanthin administration was more effective than citrate treatment in reducing crystal deposition and down-regulating the expression of OPN and TGF- β 1.

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KEYWORDS:

angiotensin converting enzyme; astaxanthin; nephrolithiasis; osteopontin

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Free full text

[Pharmacology](#). 2015;95(3-4):193-200. doi: 10.1159/000381314. Epub 2015 Apr 22.

Astaxanthin attenuates adriamycin-induced focal segmental glomerulosclerosis.

[Liu G¹](#), [Shi Y](#), [Peng X](#), [Liu H](#), [Peng Y](#), [He L](#).

Author information

Abstract

BACKGROUND/AIM:

Focal segmental glomerulosclerosis (FSGS) is a specific pattern of chronic renal injury with progressive glomerular scarring. The phenotypic alterations that contribute to FSGS include inflammatory response and oxidative stress. Astaxanthin (ATX) has a broad range of biological functions, particularly antioxidant and anti-inflammatory ones. This study was designed to evaluate the renoprotective effect of ATX treatment on Adriamycin-induced FSGS.

METHODS:

In Balb/c mice, Adriamycin nephropathy was induced by Adriamycin (10 mg/kg body weight, diluted in normal saline) via a tail vein on day 0. Then the mice were treated with ATX (50 mg/kg body weight) once daily by oral gavage, again starting on the day of Adriamycin injection and continued for 6 weeks. At 6 weeks, the mice were sacrificed; kidneys and blood samples were collected for further analysis.

RESULTS:

Animals that underwent intermittent exposure to ATX treatment exhibited significant improvements in renal functional parameters as well as in glomerular and interstitial fibrosis compared to those undergoing saline treatment in FSGS mouse models. ATX treatment exerted anti-inflammatory and antioxidant effects by promoting Nrf2 expression and suppressing renal nucleotide-binding oligomerization domain-like receptor protein 3 inflammasome activation.

CONCLUSION:

ATX might offer a ray of hope for ameliorating FSGS.

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Effect of astaxanthin on kidney function impairment and oxidative stress induced by mercuric chloride in rats.

[Augusti PR](#), [Conterato GM](#), [Somacal S](#), [Sobieski R](#), [Spohr PR](#), [Torres JV](#), [Charão MF](#), [Moro AM](#), [Rocha MP](#), [Garcia SC](#), [Emanuelli T](#).

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Reactive oxygen species are implicated as mediators of tissue damage in the acute renal failure induced by inorganic mercury. Astaxanthin (ASX), a carotenoid with potent antioxidant properties, exists naturally in various plants, algae, and seafoods. This paper evaluated the ability of ASX to prevent HgCl₂ nephrotoxicity. Rats were injected with HgCl₂ (0 or 5 mg/kg b.w., sc) 6h after ASX had been administered (0, 10, 25, or 50mg/kg, by gavage) and were killed 12h after HgCl₂ exposure. Although ASX prevented the increase of lipid and protein oxidation and attenuated histopathological changes caused by HgCl₂ in kidney, it did not prevent creatinine increase in plasma and delta-aminolevulinic acid dehydratase inhibition induced by HgCl₂. Glutathione peroxidase and catalase activities were enhanced, while superoxide dismutase activity was depressed in HgCl₂-treated rats when compared to control and these effects were prevented by ASX. Our results indicate that ASX could have a beneficial role against HgCl₂ toxicity by preventing lipid and protein oxidation, changes in the activity of antioxidant enzymes and histopathological changes.

Publication Types:

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Drug Des Devel Ther. 2020 Jun 9;14:2275-2285.
doi: 10.2147/DDDT.S230749. eCollection 2020.

Astaxanthin in Liver Health and Disease: A Potential Therapeutic Agent

[Jingjing Li](#)¹, [Chuanyong Guo](#)², [Jianye Wu](#)¹

- PMID: [32606597](#)
- PMCID: [PMC7293384](#)
- DOI: [10.2147/DDDT.S230749](#)

Free PMC article

Abstract

Astaxanthin is a carotenoid derived from oxygen-containing non-vitamin A sources and is mainly obtained from marine organisms. Studies have demonstrated that astaxanthin is a natural antioxidant product and it is widely used in the fields of medicine, health-care products and cosmetics. Studies have shown that astaxanthin has important preventive and therapeutic effects on liver fibrosis, non-alcoholic fatty liver, liver cancer, drug and ischemia-induced liver injury, and its mechanism is related to antioxidant and anti-inflammatory activities, and the regulation of multiple signaling pathways. In this review, we discuss the latest data on astaxanthin in the prevention and treatment of liver diseases. An understanding of the structure, source and mechanism of action of astaxanthin in the body would not only provide a theoretical basis for its clinical application but could also have important significance in screening and improving related compounds for the treatment of liver diseases.

Life Extension

ASTAXANTHIN'S MECHANISM FOR INCREASING LIFESPAN IN MODEL ORGANISM FOR MAMMALIAN LONGEVITY DEMONSTRATED.

Food Funct 2021 Aug 16. doi: 10.1039/d1fo01069g. Online ahead of print.

DAF-16 acts as the "hub" of astaxanthin's anti-aging mechanism to improve aging-related physiological functions in *Caenorhabditis elegans*

[Xiaojuan Liu](#)¹, [Han Liu](#)¹, [Zhiqing Chen](#)¹, [Jie Xiao](#)¹, [Yong Cao](#)¹

- PMID: 34397058 DOI: [10.1039/d1fo01069g](https://doi.org/10.1039/d1fo01069g) **Free article**

Abstract

Astaxanthin (AX) is a xanthophyll carotenoid that can effectively inhibit the production of peroxides and thereby protect the body from oxidative damage. In recent years, AX had been shown to have anti-aging properties, both in vivo and in vitro. However, the underlying mechanisms by which AX regulates senescence related proteins and signaling pathways remain unclear. Therefore, we used *Caenorhabditis elegans* (*C. elegans*) model binding proteomics to reveal AX anti-aging activity and its molecular mechanism. Our results suggest that AX promotes the health and lifespan of *C. elegans* by improving mobility, reducing the accumulation of age pigments, and increasing resistance to heat stress. In terms of the underlying mechanism, AX helps prolong the life of worms by regulating AGE-1 in the insulin signaling pathway, promoting the transport of DAF-16 into the nucleus and then up-regulating the expression level of DAF-16's downstream proteins (such as superoxide dismutase [Mn] 2 (SOD-3), heat shock proteins (HSPs), glutathione s-transferase (GST-4), etc.). Furthermore, AX may be a relevant response target for activation of dietary restriction pathways in vivo as a dietary restriction mimic. Meanwhile, proteomics data confirmed that there were 15 proteins enriched in the longevity regulation pathway. AX mainly regulates oxidative stress and

the aging process by modulating the insulin signaling pathway around DAF-16 as the "hub". In addition to the insulin signaling pathway, other pathways including dietary restriction, AMP-activated protein kinase (AMPK), and mammal target of rapamycin (mTOR) are also dependent on DAF-16. These findings expand and deepen our knowledge of the underlying mechanism by which AX extends the lifespan of *C. elegans*.

Supplemental Cellular Protection by a Carotenoid Extends Lifespan via Ins/IGF-1 Signaling in *Caenorhabditis elegans*.

[Yazaki K](#), [Yoshikoshi C](#), [Oshiro S](#), [Yanase S](#).

Source

Department of Health Science, Daito Bunka University School of Sports and Health Science, Iwadono 560, Higashi-matsuyama, Saitama 355-8501, Japan.

Abstract

Astaxanthin (AX), which is produced by some marine animals, is a type of carotenoid that has antioxidative properties. In this study, we initially examined the effects of AX on the aging of a model organism *C. elegans* that has the conserved intracellular pathways related to mammalian longevity. The continuous treatments with AX (0.1 to 1 mM) from both the prereproductive and young adult stages extended the mean lifespans by about 16-30% in the wild-type and long-lived mutant *age-1* of *C. elegans*. In contrast, the AX-dependent lifespan extension was not observed even in a *daf-16* null mutant. Especially, the expression of genes encoding superoxide dismutases and catalases increased in two weeks after hatching, and the DAF-16 protein was translocated to the nucleus in the AX-exposed wild type. These results suggest that AX protects the cell organelle mitochondria and nucleus of the nematode, resulting in a lifespan extension via an Ins/IGF-1 signaling pathway during normal aging, at least in part.

PMID: 22013497 [PubMed - in process]

PMCID: PMC3195502

Mechanism of Different Stereoisomeric Astaxanthin in Resistance to Oxidative Stress in *Caenorhabditis elegans*.

[Liu X¹](#), [Luo Q²](#), [Cao Y²](#), [Goulette T³](#), [Liu X³](#), [Xiao H⁴](#).

[Author information](#)

Abstract

As a potent antioxidant in human diet, astaxanthin (AST) may play important roles in alleviating oxidative stress-driven adverse physiological effects. This study examined the effects of different stereoisomers of AST in protecting *Caenorhabditis elegans* from chemically induced oxidative stress. Three stereoisomers of AST investigated herein included 3S,3'S (S) AST, 3R,3'R (R) AST, and a statistical mixture (S: meso: R = 1:2:1) (M) AST. Under paraquat-induced oxidative conditions, all three types of AST significantly enhanced survival rate of *C. elegans*. The accumulation levels of ROS in the worms were reduced by 40.12%, 30.05%, and 22.04% by S, R, and M AST, respectively ($P < 0.05$). Compared with R and M AST, S significantly enhanced the expression levels of SOD-3. The results of RNA-Seq analysis demonstrated that AST protected *C. elegans* from oxidative damage potentially by modulating genes involved in the insulin/insulin-like growth factor (IGF) signaling (IIS) pathway and the oxidoreductase system. It is noteworthy that different stereoisomers of AST showed different effects on the expression levels of various genes related with oxidative stress. This study revealed important information on the in vivo antioxidative effects of AST stereoisomers, which might provide useful information for better utilization of AST.

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KEYWORDS:

Caenorhabditis elegans; RNA-seq; astaxanthin; oxidative stress; stereoisomeric

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27527357

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[10.1111/1750-3841.13417](https://doi.org/10.1111/1750-3841.13417)

[PubMed - in process]

ASTAXANTHIN INCREASES LIFESPAN IN MODEL ORGANISM OF MAMMAL LONGEVITY.

Rejuvenation Res. 2021 Jun;24(3):198-205.

doi: 10.1089/rej.2020.2355. Epub 2020 Nov 30.

Autophagy Plays a Role in the Prolongation of the Life Span of *Caenorhabditis elegans* by Astaxanthin

[Min Fu](#)^{1,2}, [Xumei Zhang](#)^{1,2}, [Xuguang Zhang](#)³, [Liu Yang](#)^{1,2}, [Suhui Luo](#)^{1,2}, [Huan Liu](#)^{1,2}

- PMID: [33115330](#)
- DOI: [10.1089/rej.2020.2355](#)

Abstract

Astaxanthin (AST), a xanthophyll belonging to the family of carotenoids, is a potent antioxidant. The effect of AST on longevity and its physiological and molecular mechanism are still unclear. In this study, we proved that AST could prolong the life span of *Caenorhabditis elegans*. To uncover whether AST could delay aging by upregulating autophagy, we measured the expression of autophagy gene and the life span of autophagy gene *bec-1* mutant nematodes, and the results showed that the expression of autophagy gene was upregulated after AST intervention and the disruption of *bec-1* weakened the extension of the life span. To explore the molecular mechanism of AST-induced autophagy upregulation, we knocked out the *daf-16* or *hlh-30* (key genes of insulin/insulin growth factor-1 [IGF-1] signal pathway or target of rapamycin [TOR] signal pathway) by RNA interference, and the expression of autophagy gene *lgg-1* decreased. Collectively, our results strongly suggest that autophagy, which is both the insulin/IGF-1 signal pathway dependent and TOR signal pathway dependent, plays a role in the prolongation of the life span of *Caenorhabditis elegans* by AST.

ASTAXANTHIN'S MECHANISM OF ACTION IN EXTENDING THE LIFE OF A MODEL ORGANISM FOR MAMMALIAN LONGEVITY IS HYPOTHESIZED.

Rejuvenation Res. 2020 Nov 30.

doi: 10.1089/rej.2020.2355. Online ahead of print.

Autophagy Plays a Role in the Prolongation of the Life Span of *Caenorhabditis elegans* by Astaxanthin

[Min Fu](#)^{1,2}, [Xumei Zhang](#)^{1,2}, [Xuguang Zhang](#)³, [Liu Yang](#)^{1,2}, [Suhui Luo](#)^{1,2}, [Huan Liu](#)^{1,2}

- PMID: 33115330
- DOI: [10.1089/rej.2020.2355](https://doi.org/10.1089/rej.2020.2355)

Abstract

Astaxanthin (AST), a xanthophyll belonging to the family of carotenoids, is a potent antioxidant. The effect of AST on longevity and its physiological and molecular mechanism are still unclear. In this study, we proved that AST could prolong the life span of *Caenorhabditis elegans*. To uncover whether AST could delay aging by upregulating autophagy, we measured the expression of autophagy gene and the life span of autophagy gene *bec-1* mutant nematodes, and the results showed that the expression of autophagy gene was upregulated after AST intervention and the disruption of *bec-1* weakened the extension of the life span. To explore the molecular mechanism of AST-induced autophagy upregulation, we knocked out the *daf-16* or *hh-30* (key genes of insulin/insulin growth factor-1 [IGF-1] signal pathway or target of rapamycin [TOR] signal pathway) by RNA interference, and the expression of autophagy gene *lgg-1* decreased. Collectively, our results strongly suggest that autophagy, which is both the insulin/IGF-1 signal pathway dependent and TOR signal pathway dependent, plays a role in the prolongation of the life span of *Caenorhabditis elegans* by AST.

Protective effect of astaxanthin against multiple organ injury in a rat model of sepsis.

[Zhou L](#)¹, [Gao M](#)², [Xiao Z](#)³, [Zhang J](#)¹, [Li X](#)¹, [Wang A](#)⁴.

[Author information](#)

Abstract

BACKGROUND:

Astaxanthin, a xanthophyll carotenoid, holds exceptional promise as an antioxidant, anti-inflammatory, and anticancer agent. No evidence has been published whether it has protective effects on sepsis. The study aimed to investigate the potential effects of astaxanthin on sepsis and multiple organ dysfunctions.

MATERIALS AND METHODS:

Sepsis was induced by cecal ligation and puncture (CLP) in Sprague-Dawley rats. Animals subjected to CLP and sham-operated control rats were given vehicle or astaxanthin 100 mg/kg/d by oral gavage for 7 d before the operation. The rats were killed at the indicated time points, and the specimen was collected. Cytokines and multiorgan injury-associated enzymatic and oxidative stress indicators were investigated. Multiorgan tissues were assessed histologically, the peritoneal bacterial load and the 72-h survival was observed too.

RESULTS:

Sepsis resulted in a significant increase in serum tumor necrosis factor- α , interleukin-1 β , and interleukin-6 levels showing systemic inflammatory response; it also caused a remarkable decrease in the superoxide dismutase activity and a significant increase in the malondialdehyde content showing oxidative damage; sepsis caused a great increase in organ injury-associated indicators, including blood urea nitrogen, creatinine, lactate dehydrogenase, creatine kinase isoenzyme-MB isotype, alanine aminotransferase, and aspartate aminotransferase, which was confirmed by histologic examination. And there was a dramatical increase of colony-forming units in the peritoneal cavity in septic rats. Astaxanthin reversed these inflammatory and oxidant response, alleviated the organ injury, reduced the peritoneal bacterial load, and improved the survival of septic rats induced by CLP.

CONCLUSIONS:

Astaxanthin exerts impressively protective effects on CLP-induced multiple organ injury. It might be used as a potential treatment for clinical sepsis.

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KEYWORDS:

Astaxanthin; Cecal ligation and puncture; Multiple organ dysfunction syndrome; Sepsis

PMID:

25770740

[PubMed - indexed for MEDLINE]

[J Agric Food Chem](#). 2013 Aug 14;61(32):7800-4. doi: 10.1021/jf402224w. Epub 2013 Aug 6.

Antiaging effects of astaxanthin-rich alga *Haematococcus pluvialis* on fruit flies under oxidative stress.

[Huangfu J¹](#), [Liu J](#), [Sun Z](#), [Wang M](#), [Jiang Y](#), [Chen ZY](#), [Chen F](#).

Author information

Abstract

The microalga *Haematococcus pluvialis* (HP) is the best natural producer of astaxanthin (AX), which is a potent antioxidant with broad health benefits. The present study investigated the antiaging potential of HP biomass using the fruit fly *Drosophila melanogaster* as the animal model. The results showed that in wild-type flies the treatment of HP induced the early mortality at a concentration of 20 mg/mL, which was associated with the decreased enzymatic activities of CuZn-superoxide dismutase (SOD1) and Mn-superoxide dismutase (SOD2) as well as the down-regulation of SOD1, SOD2, and catalase (CAT) at the transcriptional level. In SOD(n108) mutant flies, the supplementation of HP (10 or 20 mg/mL) significantly extended their lifespan and ameliorated the age-related decline in locomotor function. Further studies suggested that HP may play a role as a complement to the defective endogenous antioxidant system to exert such lifespan elongation effects. These results, taken together, strongly support the antiaging properties of HP and its therapeutic rather than preventive potential against aging-related diseases.

PMID:

23879808

[PubMed - indexed for MEDLINE]

ASTAXANTHIN INCREASES LONGEVITY IN YEAST.

FEMS Yeast Res. 2019 Jan 1;19(1).

doi: 10.1093/femsyr/foy113.

Astaxanthin enhances the longevity of *Saccharomyces cerevisiae* by decreasing oxidative stress and apoptosis

[Sudharshan Sij](#)[‡], [Bhavana Veerabhadrapa](#)[‡], [Subasri Subramaniyan](#)[‡], [Madhu Dyavaiah](#)[‡]

- PMID: [30312390](#)
- DOI: [10.1093/femsyr/foy113](#)

Abstract

The budding yeast, *Saccharomyces cerevisiae*, is an efficient model for studying oxidative stress, programmed cell death and aging. The present study was carried out to investigate antioxidant, the anti-apoptotic and anti-aging activity of a natural compound, astaxanthin, in *S. cerevisiae* model. The survivability of yeast antioxidant-deficient strains (*sod1Δ*, *sod2Δ*, *cta1Δ*, *ctt1Δ* and *tsa1Δ*) increased by 20%-40% when cells were pre-treated with astaxanthin, compared to hydrogen peroxide alone, as demonstrated in spot and colony forming unit assays. Reduced reactive oxygen species (ROS) levels, increased glutathione, decreased lipid peroxidation and induced superoxide dismutase activity in astaxanthin-treated cells indicate that astaxanthin protected the cells from oxidative-stress-induced cell death. In addition, astaxanthin protected anti-apoptotic-deficient strains (*pep4Δ* and *fis1Δ*) against acetic acid and hydrogen peroxide-induced cell death that suggests anti-apoptotic property of astaxanthin, and it was further confirmed by acridine orange/ethidium bromide, annexin V and 4',6-diamidino-2-phenylindole staining. The yeast chronological lifespan assay results showed that astaxanthin extends the lifespan of antioxidant-deficient strains by scavenging ROS, and anti-apoptotic-deficient mutants by protecting from apoptotic cell death compared to their respective untreated cells and wild type. Our results suggest that astaxanthin enhances the longevity of yeast *S. cerevisiae* by reducing oxidative stress and apoptosis.

Dietary supplementation of *Haematococcus pluvialis* improved the immune capacity and low salinity tolerance ability of post-larval white shrimp, *Litopenaeus vannamei*.

[Xie S](#)¹, [Fang W](#)¹, [Wei D](#)¹, [Liu Y](#)¹, [Yin P](#)¹, [Niu J](#)¹, [Tian L](#)².

Author information

Abstract

A 25-days experiment was conducted to evaluate the effect of dietary *Haematococcus pluvialis* on growth, survival, immune response and stress tolerance ability of post-larval *Litopenaeus vannamei*. Post-larval white shrimp (mean initial weight 2.1 mg) were fed five isoenergetic and isonitrogenous diets containing grade levels of *Haematococcus pluvialis* (0, 1.7, 3.3, 6.7 and 13.3 g kg⁻¹ diet, respectively). Results indicated that 3.3 g *Haematococcus pluvialis* kg⁻¹ diet increased the survival rate of post-larval white shrimp. Specific growth rate (SGR) and weight gain (WG) showed no difference among each groups. After the acute salinity stress (salinity decreased rapidly from 28‰ to 5‰), survival of shrimp fed 6.7 g *Haematococcus pluvialis* kg⁻¹ diet significant higher than the control ($P < 0.05$), and the total antioxidant capacity (T-AOC) was increased with the increasing dietary *Haematococcus pluvialis* levels. The malonaldehyde (MDA) contents in whole body decreased with the increasing dietary *Haematococcus pluvialis* levels before and after the salinity stress. Before the salinity stress, relative mRNA levels of Caspase 3, Rho and Janus kinase (JAK) decreased in shrimp fed diets contain *Haematococcus pluvialis*. After the salinity stress, relative mRNA levels of anti-oxidative related genes and immune related genes decreased with the dietary *Haematococcus pluvialis* level increased to 3.3 g kg⁻¹. Based on the effect of *Haematococcus pluvialis* on survival, salinity stress tolerance ability and the immune response of post-larval *L. vannamei*, the optimal level of *Haematococcus pluvialis* was 3.3-6.7 g kg⁻¹ diet (100-200 mg astaxanthin kg⁻¹ diet).

KEYWORDS:

Haematococcus pluvialis; Immune capacity; NF-κB pathway; Post-larval; Salinity stress

PMID: 29933110

DOI: [10.1016/j.fsi.2018.06.039](https://doi.org/10.1016/j.fsi.2018.06.039)

Antioxidant Protection by Astaxanthin in the Citrus Red Mite (Acari: Tetranychidae).

[Atarashi M](#)¹, [Manabe Y](#)², [Kishimoto H](#)³, [Sugawara T](#)², [Osakabe M](#)¹.

Author information

Abstract

Solar ultraviolet-B (UVB) radiation and radiant heat have lethal effects on plant-dwelling mites, including spider mites, and their natural enemies, such as phytoseiid mites, leading them to reside on lower leaf surfaces. Panonychus spider mites are outcompeted by Tetranychus spider mites and thus exploit upper leaf surfaces, where they are exposed to both UVB radiation and radiant heat. Panonychus spider mites are thought to produce astaxanthin constitutionally. In this study, we compared carotenoid components, antioxidant capacity, lipid peroxidation, survival, and egg production in wild-type (WTS) and albino-type strains (ATS) of *Panonychus citri* (McGregor). Four carotenoids (neoxanthin, violaxanthin, lutein, and carotene) and their isomers and esters were identified in both strains, but astaxanthin and its esters were present only in WTS. The singlet oxygen scavenging capacity of lipid-soluble ingredients was greater in WTS than in ATS, whereas the oxygen radical absorbance capacities of hydrophilic ingredients were equivalent between them. Lipid peroxide accumulation was clearly higher in ATS than in WTS under both UVB irradiation (25 °C) and high temperature (35 °C) conditions. The findings are consistent with an antioxidant protective function of astaxanthin in this mite. Survival periods at 38 °C were longer in WTS than in ATS, although no difference was shown at 35 °C or under UVB irradiation.

Therefore, astaxanthin accumulation was shown to be a major mechanism for survival under radiant heat, although other mechanisms, such as photoreactivation, might play a major role in survival under UVB radiation.

KEYWORDS:

Carotenoid; Lipid peroxidation; Oxygen Radical Absorbance Capacity; Singlet Oxygen Scavenging Capacity; Tetranychidae

PMID: 28981670

DOI: [10.1093/ee/nvx121](#)

[Indexed for MEDLINE]

Pancreatic Health

ASTAXANTHIN DECREASES INFLAMMATORY MARKER IN PANCREATIC CELL MODEL AND MAY PREVENT OR DELAY OBESITY-RELATED PANCREATITIS.

Mediators Inflamm 2021 Jul 24;2021:5587297. doi: 10.1155/2021/5587297. eCollection 2021.

Astaxanthin Inhibits Interleukin-6 Expression in Cerulein/Resistin-Stimulated Pancreatic Acinar Cells

[Min Seung Kwak](#)¹, [Joo Weon Lim](#)¹, [Hyeyoung Kim](#)¹

- PMID: 34349610 PMCID: [PMC8328718](#) DOI: [10.1155/2021/5587297](#)

Free PMC article

Abstract

Acute pancreatitis is a common clinical condition with increasing the proinflammatory mediators, including interleukin-6 (IL-6). Obesity is a negative prognostic factor in acute pancreatitis. Obese patients with acute pancreatitis have a higher systemic inflammatory response rate. Levels of serum resistin, an adipocytokine secreted by fat tissues, increase with obesity. Cerulein, a cholecystokinin analog, induces calcium (Ca²⁺) overload, oxidative stress, and IL-6 expression in pancreatic acinar cells, which are hallmarks of acute pancreatitis. A recent study showed that resistin aggravates the expression of inflammatory cytokines in cerulein-stimulated pancreatic acinar cells. We aimed to investigate whether resistin amplifies cerulein-induced IL-6 expression and whether astaxanthin (ASX), an antioxidant carotenoid with anti-inflammatory properties, inhibits cerulein/resistin-induced IL-6 expression in pancreatic acinar AR42J cells. We found that resistin enhanced intracellular Ca²⁺ levels, NADPH oxidase activity, intracellular reactive oxygen species (ROS) production, NF-κB activity, and IL-6 expression in cerulein-stimulated AR42J cells, which were inhibited by ASX in a dose-dependent manner. The calcium chelator BAPTA-AM inhibited cerulein/resistin-induced NADPH oxidase activation and ROS production. Antioxidant N-acetyl cysteine (NAC) and ML171, a

specific NADPH oxidase 1 inhibitor, suppressed cerulein/resistin-induced ROS production, NF- κ B activation, and IL-6 expression. In conclusion, ASX inhibits IL-6 expression, by reducing Ca²⁺ overload, NADPH oxidase-mediated ROS production, and NF- κ B activity in cerulein/resistin-stimulated pancreatic acinar cells. Consumption of ASX-rich foods could be beneficial for preventing or delaying the incidence of obesity-associated acute pancreatitis.

Astaxanthin ameliorates cerulein-induced acute pancreatitis in mice.

[Zhang H¹](#), [Yang W²](#), [Li Y³](#), [Hu L⁴](#), [Dai Y⁵](#), [Chen J⁶](#), [Xu S⁷](#), [Xu X⁸](#), [Jiang H⁹](#).

Author information

Abstract

BACKGROUND: A various of pharmacological effects of astaxanthin has been confirmed. However, the mechanism underlying protective effect of astaxanthin on acute pancreatitis (AP) induced by cerulein still unclear. The present study is to investigate the mechanism underlying the effect of astaxanthin on autophagy and apoptosis via the JAK/STAT3 pathway.

METHODS: Intraperitoneal injection of cerulein at hourly intervals followed by lipopolysaccharide injection were used in Balb/C mice. Vehicle or astaxanthin, which intraperitoneal injected in two doses (20 mg/kg and 40 mg/kg), were injected in mice 1 h before the first cerulein injection. At 3 h after the last injection, when the pathological changes were most severe, pancreatic tissue was analyzed by pathologically scored and hematoxylin and eosin (H&E) staining. The severity of AP was assessed by histological grading, proinflammatory cytokine levels, biochemistry, myeloperoxidase (MPO) activity, and analysis of JAK/STAT3 activity.

RESULTS: Astaxanthin administration markedly reduced serum digestive enzyme activities, pancreatic histological scores, proinflammatory cytokine levels (tumor necrosis factor- α (TNF- α), Interleukin-1 β (IL-1 β), and Interleukin-6 (IL-6)), MPO and JAK/STAT3 activity.

CONCLUSION: Collectively, these results indicate that astaxanthin inhibits pancreatic injury in AP by targeting JAK/STAT3-mediated apoptosis and autophagy.

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KEYWORDS: Acute pancreatitis; Apoptosis; Astaxanthin; Autophagy; JAK/STAT3 pathway

PMID: 29328945

DOI: [10.1016/j.intimp.2018.01.011](#)

[Indexed for MEDLINE]

ASTAXANTHIN REDUCES OXIDATIVE DAMAGE IN A RAT MODEL OF ACUTE PANCREATITIS.

_Turk J Gastroenterol. 2020 Oct;31(10):706-712.

doi: 10.5152/tjg.2020.19520.

Astaxanthin alleviates oxidative damage in acute pancreatitis via direct antioxidant mechanisms

[Dilek Özbeyli](#)¹, [Esra Bihter Gürler](#)², [Hülya Buzcu](#)³, [Özlem Tuğçe Çilingir-Kaya](#)⁴, [Muhammet Emin Cam](#)⁵, [Meral Yüksel](#)⁶

PMID: 33169708 PMCID: [PMC7659906](#) DOI: [10.5152/tjg.2020.19520](#) **Free PMC article**

Abstract

Background/Aims: Astaxanthin (ATX) is a naturally occurring carotenoid and a potent antioxidant. Various anti-inflammatory effects of ATX have been examined. We aimed to investigate the protective effect of ATX and its mechanism in a cerulein-induced acute pancreatitis rat model.

Materials and Methods: The rats were randomized into 2 main groups as control (C) and acute pancreatitis group (AP). AP group was subsequently divided into subgroups as AP+vehicle (AP), AP+ATX, and ATX+peroxisome proliferator-activated receptor- α antagonist GW6471 (ATX+GW) groups. To induce AP, the rats were administered cerulein (50 μ g/kg, intraperitoneally [ip]) at 1 hour intervals, whereas the C group received saline. The AP group was treated with vehicle olive oil, ATX 40 mg/kg/orally, or GW6471 and ATX (GW1 mg/kg/ip; ATX; 40 mg/kg/peroral). Treatments were administered after the 1st cerulein injection. At the 7th hour after the final injection, the rats were killed and the pancreatic tissue was used for the determination of malondialdehyde (MDA), glutathione (GSH), and myeloperoxidase (MPO) activities and luminol-lucigenin chemiluminescence levels. Serum amylase, lipase, and histopathological analyses were performed.

Results: Elevated serum lipase and amylase levels in the vehicle-treated AP group ($p < 0.01$) decreased in the ATX and ATX+GW groups ($p < 0.05$). In the AP groups, GSH was reduced and MDA, MPO, luminol, and lucigenin levels were increased ($p < 0.05-0.001$). ATX reversed these changes ($p < 0.05-0.001$). The vehicle-treated group revealed significant severe cytoplasmic degeneration and vacuolization, whereas ATX ameliorated these destructions. GW6471 did not abolish the positive effects of ATX biochemically or histologically.

Conclusion: ATX has a potent protective effect on AP via its radical scavenging and antioxidant properties. Therefore, we believe that ATX may have therapeutic potential.

Astaxanthin inhibits gemcitabine-resistant human pancreatic cancer progression through EMT inhibition and gemcitabine resensitization.

[Yan T](#)¹, [Li HY](#)¹, [Wu JS](#)¹, [Niu Q](#)¹, [Duan WH](#)¹, [Han QZ](#)², [Ji WM](#)¹, [Zhang T](#)¹, [Lv W](#)¹.

Author information

Abstract

Pancreatic cancer rapidly acquires resistance to chemotherapy resulting in its being difficult to treat. Gemcitabine is the current clinical chemotherapy strategy; however, owing to gemcitabine resistance, it is only able to prolong the life of patients with pancreatic cancer for a limited number of months. Understanding the underlying molecular mechanisms of gemcitabine resistance and selecting a suitable combination of agents for the treatment of pancreatic cancer is required. Astaxanthin (ASX) is able to resensitize gemcitabine-resistant human pancreatic cancer cells (GR-HPCCs) to gemcitabine. ASX was identified to upregulate human equilibrative nucleoside transporter 1 (hENT1) and downregulate ribonucleoside diphosphate reductase (RRM) 1 and 2 to enhance gemcitabine-induced cell death in GR-HPCCs treated with gemcitabine, and also downregulates TWIST1 and ZEB1 to inhibit the gemcitabine-induced epithelial-mesenchymal transition (EMT) phenotype in GR-HPCCs and to mediate hENT1, RRM1 and RRM2. Furthermore, ASX acts through the hypoxia-inducible factor 1 α /signal transducer and activator of transcription 3 signaling pathway to mediate TWIST1, ZEB1, hENT1, RRM1 and RRM2, regulating the gemcitabine-induced EMT phenotype and gemcitabine-induced cell death. Co-treatment with ASX and gemcitabine in a tumor xenograft model induced by GR-HPCCs supported the *in vitro* results. The results of the present study provide a novel therapeutic strategy for the treatment of gemcitabine-resistant pancreatic cancer.

KEYWORDS:

astaxanthin; epithelial-mesenchymal transition; gemcitabine; gemcitabine-resistance human pancreatic cancer cells

PMID: 29098031

PMCID: [PMC5652142](#)

DOI: [10.3892/ol.2017.6836](#)

[Free PMC Article](#)

Body Fat Reduction and Weight Loss

Astaxanthin reduces body fat percentage versus placebo in individuals doing moderate exercise over six weeks in placebo-controlled human clinical trial.

Fukamauchi M. Food Style 21. 2007;11:1-4. ?15

Astaxanthin increases fat utilisation during exercise

A randomised, double-blind study on humans has confirmed that natural astaxanthin increases fat utilisation during exercise.¹⁵ In the study, 32 individuals were supplemented with 2 x 6mg of astaxanthin per day, or placebo, for six weeks. The participants were instructed to undertake 40 minutes of continuous exercise three times per week during the 6-week period. After six weeks, the astaxanthin group had a significant reduction in body fat percentage, whereas there was no difference in the placebo group. These results indicate that astaxanthin increases muscle endurance and reduces lactic acid during intensive training by promoting the use of fat compared with glycogen stores.

ASTAXANTHIN INCREASES LIPID EXCRETION AND IMPROVES ENERGY METABOLISM TO REDUCE OBESITY IN MICE FED A HIGH-FAT DIET.

J Agric Food Chem. 2021 Apr 28;69(16):4745-4754.

doi: 10.1021/acs.jafc.1c01117. Epub 2021 Apr 13.

Molecular Mechanisms of the Anti-obesity Properties of *Agardhiella subulata* in Mice Fed a High-Fat Diet

[Yu-Hsuan Hsiao](#)¹, [Yu-Hsin Wang](#)¹, [Wei-Sheng Lin](#)¹, [Yung-Chen Cheng](#)², [Kalyanam Nagabhushanam](#)³, [Chi-Tang Ho](#)⁴, [Min-Hsiung Pan](#)^{1,5,6}

- PMID: 33848157 DOI: [10.1021/acs.jafc.1c01117](https://doi.org/10.1021/acs.jafc.1c01117)

Abstract

The overweight and obese population has skyrocketed, resulting in a high incidence of metabolic disorders. *Agardhiella subulata* (AS) contains a variety of beneficial components, such as sulfur-containing polysaccharides (dietary fiber) and astaxanthin, which is considered to have anti-obesity potential. In this study, we investigated the effects and possible mechanisms of dietary AS on high-fat diet (HFD)-induced obesity in mice. AS supplementation significantly reduced HFD-induced weight gain (19%) and the visceral adiposity index (4.1%). In addition, the level of total cholesterol, triglyceride, and low-density lipoprotein was significantly decreased; adiponectin was significantly increased in serum and fecal triglyceride excretion was significantly higher in mice fed AS compared with mice on an HFD. Preadipocyte factor 1 and Sry-box transcription factor 9 that were significantly higher than the levels found for the HFD group lead to reduced adipogenesis. Moreover, accompanying the lipolysis and fatty acid β -oxidation that occur in the AS group, the concentration of non-esterified fatty acids was lowered to 0.4 ± 0.1 mEq/L. In addition, peroxisome proliferator-activated receptor γ and phosphorylation acetyl-CoA carboxylase increased 1.5- and 1-fold, thus increasing the expression of adiponectin and the activation of AMPK and ultimately resulting in lower blood glucose levels. The results of this study suggest that AS supplementation increases lipid excretion and improves energy metabolism to prevent obesity in mice fed a HFD.

Astaxanthin reduces blood pressure, improves glucose metabolism and reduces visceral body fat mass in placebo-controlled randomized study on patients with Type-2 diabetes.

[Asia Pac J Clin Nutr](#). 2018;27(2):341-346. doi: 10.6133/apjcn.052017.11.

Astaxanthin improves glucose metabolism and reduces blood pressure in patients with type 2 diabetes mellitus.

[Mashhadi NS](#)¹, [Zakerkish M](#)², [Mohammadiasl J](#)³, [Zarei M](#)⁴, [Mohammadshahi M](#)⁵, [Haghighizadeh MH](#)⁶.

Author information

Abstract

BACKGROUND AND OBJECTIVES:

This randomized, placebo-controlled trial was performed for 8 weeks to investigate the potential effects of astaxanthin (AST) supplementation on the adiponectin concentration, lipid peroxidation, glycemic control, insulin sensitivity, and anthropometric indices in participants with type 2 diabetes mellitus.

METHODS AND STUDY DESIGN:

We enrolled 44 participants with type 2 diabetes who met our inclusion criteria. Eight milligrams of AST supplementation or a placebo were randomly administered once daily for 8 weeks to these participants.

RESULTS:

The 8-week administration of AST supplementation increased the serum adiponectin concentration and reduced visceral body fat mass ($p < 0.01$), serum triglyceride and very-low-density lipoprotein cholesterol concentrations, and systolic blood pressure ($p < 0.05$). Furthermore, AST significantly reduced the fructosamine concentration ($p < 0.05$) and marginally reduced the plasma glucose concentration ($p = 0.057$).

CONCLUSIONS:

We demonstrated that because participants with type 2 diabetes often have hypertriglycemia and uncontrolled glucose metabolism; our findings of dual beneficial effects are clinically valuable. Our results may provide a novel complementary treatment with potential impacts on diabetic complications without adverse effects.

PMID: 29384321 DOI: [10.6133/apjcn.052017.11](#) **Free full text**

ASTAXANTHIN SUPPRESSES LIPID ACCUMULATION IN VITRO AND MAY HAVE POTENTIAL AS AN ANTI-OBESITY INGREDIENT.

Molecules. 2020 Aug 7;25(16):3598.
doi: 10.3390/molecules25163598.

Effect of Astaxanthin on the Inhibition of Lipid Accumulation in 3T3-L1 Adipocytes via Modulation of Lipogenesis and Fatty Acid Transport Pathways

[Mei-Chih Tsai](#)¹, [Shih-Chien Huang](#)¹, [Wei-Tang Chang](#)², [Shiuan-Chih Chen](#)^{3,4}, [Chin-Lin Hsu](#)^{1,5}

PMID: [32784687](#) PMCID: [PMC7466122](#) DOI: [10.3390/molecules25163598](#) [Free PMC article](#)

Abstract

Obesity is defined as a condition of excessive fat tissue accumulation. It was the major factor most closely associated with lifestyle-related diseases. In the present study, we investigated the effect of astaxanthin on the inhibition of lipid accumulation in 3T3-L1 adipocytes. 3T3-L1 adipocytes were treated with 0-25 µg/mL of astaxanthin for 0-48 h. The result indicated that astaxanthin significantly decreased the oil Red O stained material (OROSM), intracellular triglyceride accumulation, and glycerol 3-phosphate dehydrogenase (GPDH) activity in 3T3-L1 adipocytes ($p < 0.05$). At the molecular level, astaxanthin significantly down-regulated the mRNA expression of *peroxisome proliferator-activated receptor-γ* (PPAR γ) in 3T3-L1 adipocytes ($p < 0.05$). Moreover, target genes of PPAR γ on the inhibition of lipogenesis, such as *Acetyl-CoA carboxylase* (ACC), *fatty acid synthase* (FAS), *fatty acid binding protein* (aP2), *cluster of differentiation 36* (CD36), and *lipoprotein lipase* (LPL) in 3T3-L1 adipocytes were significantly down-regulated at a time-dependent manner ($p < 0.05$). These results suggested that astaxanthin efficiently suppressed lipid accumulation in 3T3-L1 adipocytes and its action is associated with the down-regulation of lipogenesis-related genes and the triglyceride accumulation in 3T3-L1 adipocytes. Therefore, astaxanthin can be developed as a potential nutraceutical ingredient for the prevention of obesity in a niche market.

[Biosci Biotechnol Biochem.](#) 2007 Apr;71(4):893-9. Epub 2007 Apr 7

Effects of astaxanthin in obese mice fed a high-fat diet.

[Ikeuchi M](#), [Koyama T](#), [Takahashi J](#), [Yazawa K](#).

Laboratory of Nertraceuticals and Functional Foods Science, Graduate School of Marine Science and Technology, Tokyo University of Marine Science and Technology, Tokyo, Japan.

Astaxanthin is a natural antioxidant carotenoid that occurs in a wide variety of living organisms. We investigated the effects of astaxanthin supplementation in obese mice fed a high-fat diet. Astaxanthin inhibited the increases in body weight and weight of adipose tissue that result from feeding a high-fat diet. In addition, astaxanthin reduced liver weight, liver triglyceride, plasma triglyceride, and total cholesterol. These results suggest that astaxanthin might be of value in reducing the likelihood of obesity and metabolic syndrome in affluent societies.

PMID: 17420580 [PubMed - indexed for MEDLINE]

[Food Funct.](#) 2012 Feb;3(2):120-6. doi: 10.1039/c1fo10161g. Epub 2011 Nov 17.

An intervention study in obese mice with astaxanthin, a marine carotenoid--effects on insulin signaling and pro-inflammatory cytokines.

[Arunkumar E¹](#), [Bhuvanewari S](#), [Anuradha CV](#).

Author information

Abstract

Astaxanthin (ASX), a xanthophyll carotenoid from the marine algae *Hematococcus pluvialis*, has anti-obesity and insulin-sensitivity effects. The specific molecular mechanisms of its actions are not yet established. The present study was designed to investigate the mechanisms underlying the insulin sensitivity effects of ASX in a non-genetic insulin resistant animal model. A group of male Swiss albino mice was divided into two and fed either a starch-based control diet or a high fat-high fructose diet (HFFD). Fifteen days later, mice in each dietary group were divided into two and were treated with either ASX (6 mg kg⁻¹) per day) in olive oil or olive oil alone. At the end of 60 days, glucose, insulin and pro-inflammatory cytokines in plasma, lipids and oxidative stress markers in skeletal muscle and adipose tissue were assessed. Further, post-receptor insulin signaling events in skeletal muscle were analyzed. Increased body weight, hyperglycemia, hyperinsulinemia and increased plasma levels of tumor necrosis factor- α and interleukin-6 observed in HFFD-fed mice were significantly improved by ASX addition. ASX treatment also reduced lipid levels and oxidative stress in skeletal muscle and adipose tissue. ASX improved insulin signaling by enhancing the autophosphorylation of insulin receptor- β (IR- β), IRS-1 associated PI3-kinase step, phospho-Akt/Akt ratio and GLUT-4 translocation in skeletal muscle. This study demonstrates for the first time that chronic ASX administration improves insulin sensitivity by activating the post-receptor insulin signaling and by reducing oxidative stress, lipid accumulation and proinflammatory cytokines in obese mice.

PMID:

22089895

[PubMed - indexed for MEDLINE]

Gum Disease

[J Periodontol Res.](#) 2018 Feb;53(1):131-138. doi: 10.1111/jre.12497. Epub 2017 Oct 17.

Investigation of the effect of astaxanthin on alveolar bone loss in experimental periodontitis.

[Balci Yuce H¹](#), [Lektemur Alpan A²](#), [Gevrek F³](#), [Toker H⁴](#).

Author information

Abstract

BACKGROUND AND OBJECTIVE: Astaxanthin is a keto-carotenoid that has a strong antioxidant effect. The purpose of this study was to evaluate the effects of astaxanthin on alveolar bone loss and histopathological changes in ligature-induced periodontitis in rats.

MATERIAL AND METHODS: Wistar rats were divided into four experimental groups: non-ligated (C, n = 6); ligature only (L, n = 6); ligature and astaxanthin (1 mg/kg/day astaxanthin, AS1 group, n = 8); ligature and astaxanthin (5 mg/kg/day astaxanthin, AS5 group, n = 8). Silk ligatures were placed at the gingival margin of lower first molars of the mandibular quadrant. The study duration was 11 days and the animals were killed at the end of this period. Changes in alveolar bone levels were clinically measured and tissues were immunohistochemically examined, osteocalcin, bone morphogenic protein-2, inducible nitric oxide synthase, Bax and bcl-2 levels in alveolar bone and tartrate-resistant acid phosphatase-positive osteoclast cells, osteoblast and inflammatory cell counts were determined.

RESULTS: Alveolar bone loss was highest in the L group and the differences among the L, AS1 and AS5 groups were also significant ($P < .05$). Both doses of astaxanthin decreased tartrate-resistant acid phosphatase-positive osteoclast cell and increased osteoblast cell counts ($P < .05$). The inflammation in the L group was also higher than those of the C and AS1 groups were ($P < .05$) indicating the anti-inflammatory effect of astaxanthin. Although inducible nitric oxide synthase, osteocalcin, bone morphogenic protein-2 and bax staining percentages were all highest in the AS5 group and bcl-2 staining percentage was highest in the AS1 group, values were close to each other ($P > .05$).

CONCLUSION: Within the limits of this study, it can be suggested that astaxanthin administration may reduce alveolar bone loss by increasing osteoblastic activity and decrease osteoclastic activity in experimental periodontitis model.

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KEYWORDS: antioxidants; astaxanthin; experimental periodontitis; inducible nitric oxide synthase; tartrate-resistant acid phosphatase

PMID: 29044575 DOI: [10.1111/jre.12497](#) [Indexed for MEDLINE]

Sickle Cell Disease

Astaxanthin affects various markers in patients with sickle cell disease in human trial.

Free Radicals and Antioxidants (2013). <http://dx.doi.org/10.1016/j.fra.2013.10.1003>

Supplementation of patients with sickle cell disease with astaxanthin increases plasma- and erythrocyte-astaxanthin and may improve the hemolytic component of the disease

Begoña Ruiz-Núñez^aStéphanie A.De Rooij^aPieter J.Offringa^bGert E.Schuitemaker^cTomTeerlink^dHose S.M.Booi^eJanneke D.A.Dijck-Brouwer^aFrits A.J.Muskiet^a

<https://doi.org/10.1016/j.fra.2013.10.003>Get rights and content

Aim & background: [Sickle cell disease](#) (SCD) is characterized by hemolytic and vaso-occlusive components. [Astaxanthin](#) is a [carotenoid](#) of marine origin, without [pro-oxidant](#) properties.

Methods: In this open label pilot study, we investigated whether orally administered astaxanthin incorporates into erythrocytes (RBC) of SCD patients and studied the effect on hematological and clinical chemical parameters. Ten SCD patients (6–52 years) in Sint Maarten received 8–12 mg astaxanthin during 3 months.

Results: Baseline plasma- (33 nmol/L) and RBC- (11 nmol/L packed RBC) astaxanthin increased to 225, 174, 167 nmol/L (plasma) and 149, 100, 71 nmol/L packed RBC at 1–3 months, respectively. [Reticulocytes](#) decreased from baseline and 2 months (9.5 and 8.8%) to 3 months (5.6%), [MCV](#) from 2 to 3 months (88–86 fL), [MCH](#) from baseline to 3 months (30–28 pg) and [RDW](#) from baseline and 2 months (19.2 and 19.0%) to 3 months (16.7%). Plasma [arginine](#) decreased from 2 to 3 months (46.6–39.4 μmol/L). [Asymmetric dimethylarginine](#) (ADMA) did not change. Reticulocytes at baseline correlated with relative changes in reticulocytes from baseline to 3 months. Relative changes in reticulocytes correlated with relative changes in RBC, [RDW](#), [LDH](#), [ALAT](#), but not [hematocrit](#), within the same period.

Conclusion: Astaxanthin incorporates into SCD RBC and may favorably affect the hemolytic component. A larger randomized controlled trial is indicated, using similar or [higher dose](#), preferably during more than 3 months, concomitant with (other) [low dose antioxidants](#) (vitamin E, [beta-carotene](#), [vitamin C](#), folic acid), minerals (zinc, if necessary, selenium), arginine, [fish oil](#) and [vitamin D](#).

Vocal Health

Astaxanthin reduces inflammation and injury to vocal fold in human volunteers after 60 minutes vocal loading in human clinical trial.

[J Voice](#). 2017 May;31(3):352-358. doi: 10.1016/j.jvoice.2016.06.017. Epub 2016 Oct 26.

Protective Effect of Astaxanthin on Vocal Fold Injury and Inflammation Due to Vocal Loading: A Clinical Trial.

[Kaneko M](#)¹, [Kishimoto Y](#)¹, [Suzuki R](#)¹, [Kawai Y](#)¹, [Tateya I](#)¹, [Hirano S](#)².

Author information

Abstract

OBJECTIVES: Professional voice users, such as singers and teachers, are at greater risk of developing vocal fold injury from excessive use of voice; thus, protection of the vocal fold is essential. One of the most important factors that aggravates injury is the production of reactive oxygen species at the wound site. The purpose of the current study was to assess the effect of astaxanthin, a strong antioxidant, on the protection of the vocal fold from injury and inflammation due to vocal loading.

STUDY DESIGN: This study is an institutional review board-approved human clinical trial.

METHODS: Ten male subjects underwent a 60-minute vocal loading session and received vocal assessments prior to, immediately after, and 30 minutes postvocal loading (AST(-) status). All subjects were then prescribed 24 mg/day of astaxanthin for 28 days, after which they received the same vocal task and assessments (AST(+) status). Phonatory parameters were compared between both groups.

RESULTS: Aerodynamic assessment, acoustic analysis, and GRBAS scale (grade, roughness, breathiness, asthenia, and strain) were significantly worse in the AST(-) status immediately after vocal loading, but improved by 30 minutes after loading. In contrast, none of the phonatory parameters in the AST(+) status were statistically worse, even when measured immediately after vocal loading. No allergic responses or adverse effects were observed after administration of astaxanthin.

CONCLUSIONS: The current results suggest that astaxanthin can protect the vocal fold from injury and inflammation caused by vocal loading possibly through the regulation of oxidative stress.

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KEYWORDS: Astaxanthin; Clinical trial; Reactive oxygen species; Vocal fold; Vocal loading

PMID: 27481232 DOI: [10.1016/j.jvoice.2016.06.017](#) [Indexed for MEDLINE]

Bone Health

ASTAXANTHIN REDUCES BONE LOSS IN RATS SUBJECTED TO INDUCED OSTEOPOROSIS.

Biomed Pharmacother. 2019 Aug;116:109017.
doi: 10.1016/j.biopha.2019.109017. Epub 2019 May 31.

Heamatococcus pluvialis ameliorates bone loss in experimentally-induced osteoporosis in rats via the regulation of OPG/RANKL pathway

[Farouk K El-Baz](#)¹, [Dalia O Saleh](#)², [Gehad A Abdel Jaleel](#)³, [Rehab A Hussein](#)⁴, [Azza Hassan](#)⁵

- PMID: 31158803
- DOI: [10.1016/j.biopha.2019.109017](https://doi.org/10.1016/j.biopha.2019.109017)

Free article

Abstract

Backgrounds: Osteoporosis prevailing in elderly involves a marked increase in bone resorption showing an initial fall in bone mineral density leading to a significant reduction in bone formation.

Aim: The present study aimed to investigate the effect of Heamatococcus pluvialis microalgae on osteoporosis in D-galactose-treated rats. The underlying mechanism was tracked targeting the osteoprotegerin (OPG)/ nuclear factor- κ B ligand (RANKL) pathway using micro-computed tomography scanning.

Methods: Osteoporosis was induced in rats by intraperitoneal injection of D-galactose (200 mg/kg/day) for eight consecutive weeks. Osteoporotic rats were orally treated with H. pluvialis biomass (BHP; 450 mg/kg), its polar (PHP; 30 mg/kg) and carotenoid (CHP;

30 mg/kg) fractions for the last 2 weeks of D-Gal injection. Twenty four hours after the last dose of the treatments, tibia bones of the rats were scanned using micro-computed tomography scanning for bone mineral density (BMD), bone volume fraction (BV/TV), trabecular thickness/separation/number (Tb.Th, Tb.Sp, Tb.N) evaluation, blood samples were withdrawn and sera were used for biochemical assessment. Moreover, femur bones were examined histopathologically using several stains.

Results: Induction of osteoporosis was associated with a marked reduction in BMD, BV/TV, Tb.Th, Tb.Sp, Tb.N and in serum levels of phosphorus and catalase. On the other hand, a significant elevation in serum levels of calcium, bone alkaline phosphatase (BALP) and interleukin-6 was observed. Moreover, up-regulation of OPG was detected in osteoporotic rats. Oral treatment with BHP, and PHP incremented tibia BMD and serum phosphorus level along with the decrease in serum levels of calcium, BALP, interleukin-6, OPG and RANKL. However, treatment with CHP almost restored all the fore mentioned parameters to normal values. Furthermore, the histopathological evaluation emphasized the biochemical outcomes.

Conclusion: H. pluvialis fractions rich in astaxanthin ameliorated bone loss in experimentally-induced osteoporosis in rats probably through the down-regulation of serum OPG in concurrence with up-regulation of serum RANKL.

ASTAXANTHIN FOUND TO HAVE BONE-FORMATIVE PROPERTIES IN MOUSE MODEL OF OSTEOPOROSIS.

Biochem Biophys Res Commun. 2020 Jun 18;527(1):270-275.
doi: 10.1016/j.bbrc.2020.04.013. Epub 2020 May 4.

Astaxanthin improves osteopenia caused by aldehyde-stress resulting from Aldh2 mutation due to impaired osteoblastogenesis

[Hiroko Hoshi](#)¹, [Fuka Monoe](#)², [Ikuroh Ohsawa](#)³, [Shigeo Ohta](#)⁴, [Takeshi Miyamoto](#)⁵

Affiliations expand

- PMID: [32446379](#)
- DOI: [10.1016/j.bbrc.2020.04.013](#)

Abstract

Aldehyde dehydrogenase 2 (ALDH2) plays major roles in aldehyde detoxification and in the catalysis of amino acids. ALDH2*2, a dominant-negative transgenic expressing aldehyde dehydrogenase 2 (ALDH2) protein, is produced by a single nucleotide polymorphism (rs671) and is involved in the development of osteoporosis and hip fracture with aging. In a previous study, transgenic mice expressing Aldh2*2(Aldh2*2 Tg) osteoblastic cells or acetaldehyde -treated MC3T3-E1 showed impaired osteoblastogenesis and caused osteoporosis [1]. In this study, we demonstrated the effects of astaxanthin for differentiation to osteoblasts of MC3T3-E1 by the addition of acetaldehyde and Aldh2*2 Tg mesenchymal stem cells in bone marrow. Astaxanthin restores the inhibited osteoblastogenesis by acetaldehyde in MC 3T3-E1 and in bone marrow mesenchymal stem cells of Aldh2*2 Tg mice. Additionally, astaxanthin administration improved femur bone density in Aldh2*2 Tg mice. Furthermore, astaxanthin improved cell survival and mitochondrial function in acetaldehyde-treated MC 3T3-E1 cells. Our results suggested that astaxanthin had restorative effects on osteoblast formation and provide new insight into the regulation of osteoporosis and suggest a novel strategy to promote bone formation in osteopenic diseases caused by impaired acetaldehyde metabolism.

Mol Med Rep. 2020 Sep;22(3):1695-1701.

doi: 10.3892/mmr.2020.11284. Epub 2020 Jun 26.

A potential role for astaxanthin in the treatment of bone diseases (Review)

[Maria Teresa Valenti](#)¹, [Massimiliano Perduca](#)², [Maria Grazia Romanelli](#)³, [Monica Mottes](#)³, [Luca Dalle Carbonare](#)¹

- PMID: **32705183**
- DOI: [10.3892/mmr.2020.11284](https://doi.org/10.3892/mmr.2020.11284)

Abstract

Alterations in molecular signaling impair cellular functions and induce degenerative diseases. Among the factors affecting intracellular signaling pathways, oxidative stress serves an important role. Astaxanthin (3,3'-dihydroxy- β , β -carotene-4,4'-dione), a pigment found in aquatic organisms, belongs to the xanthophylls family. Astaxanthin exerts a strong antioxidant activity and is widely used in food, cosmetic and pharmaceutical industries. Oxidative stress damages bone homeostasis by producing reactive oxygen species and increasing the production of pro-resorption cytokines, such as interleukin (IL)-1, tumor necrosis factor- α and IL-6. Therefore, antioxidant molecules can counteract the negative effects of oxidative stress on bone. Accordingly, previous studies have demonstrated that supplementation of astaxanthin in bone contributes to the restoration of bone homeostasis. The present review summarizes the negative effects of oxidative stress in bone and explores the role of astaxanthin in counteracting skeletal injuries consequent to oxidative stress.

Ear Health

ASTAXANTHIN INVESTIGATED AS A THERAPEUTIC AGENT IN THE TREATMENT OF HEARING LOSS DUE TO CANCER DRUG TOXICITY—POSITIVE RESULTS FOUND IN FISH, GUINEA PIGS AND IN-VITRO.

J Nanobiotechnology. 2020 Mar 19;18(1):53.

doi: 10.1186/s12951-020-00600-x.

Astaxanthin-loaded polymer-lipid hybrid nanoparticles (ATX-LPN): assessment of potential otoprotective effects

[Jiayi Gu](#)^{1,2,3}, [Yuming Chen](#)^{1,2,3}, [Ling Tong](#)^{1,2,3}, [Xueling Wang](#)^{4,5,6}, [Dehong Yu](#)^{7,8,9}, [Hao Wu](#)^{10,11,12}

- PMID: **32192504**
- PMCID: [PMC7081530](#)
- DOI: [10.1186/s12951-020-00600-x](#)

Free PMC article

Erratum in

- [Correction to: Astaxanthin-loaded polymer-lipid hybrid nanoparticles \(ATX-LPN\): assessment of potential otoprotective effects.](#)

Gu J, Chen Y, Tong L, Wang X, Yu D, Wu H.J Nanobiotechnology. 2020 May

19;18(1):78. doi: 10.1186/s12951-020-00627-0.PMID: 32429998 **Free PMC article.**

Abstract

Background: Ototoxicity is one of the major side effects of platinum-based chemotherapy, especially cisplatin therapy. To date, no FDA approved agents to alleviate or prevent this ototoxicity are available. However, ototoxicity is generally believed to be produced by excessive generation of reactive oxygen species (ROS) in the inner ear, thus leading to the development of various antioxidants, which act as otoprotective agents. Astaxanthin (ATX) is an interesting candidate in the development of new therapies for

preventing and treating oxidative stress-related pathologies, owing to its unique antioxidant capacity.

Methods and Results: In this study, we aimed to evaluate the potential antioxidant properties of ATX in the inner ear by using the HEI-OC1 cell line, zebrafish, and guinea pigs. Because ATX has poor solubility and cannot pass through round window membranes (RWM), we established lipid-polymer hybrid nanoparticles (LPN) for loading ATX. The LPN enabled ATX to penetrate RWM and maintain concentrations in the perilymph in the inner ear for 24 h after a single injection. ATX-LPN were found to have favorable biocompatibility and to strongly affect cisplatin-induced generation of ROS, on the basis of DCFHDA staining in HEI-OC1 cells. JC-1 and MitoTracker Green staining suggested that ATX-LPN successfully reversed the decrease in mitochondrial membrane potential induced by cisplatin *in vitro* and rescued cells from early stages of apoptosis, as demonstrated by FACS stained with Annexin V-FITC/PI. Moreover, ATX-LPN successfully attenuated OHC losses in cultured organ of Corti and animal models (zebrafish and guinea pigs) *in vivo*. In investigating the protective mechanism of ATX-LPN, we found that ATX-LPN decreased the expression of pro-apoptotic proteins (caspase 3/9 and cytochrome-c) and increased expression of the anti-apoptotic protein Bcl-2. In addition, the activation of JNK induced by CDDP was up-regulated and then decreased after the administration of ATX-LPN, while P38 stayed unchanged.

Conclusions: To best of our knowledge, this is first study concluded that ATX-LPN as a new therapeutic agent for the prevention of cisplatin-induced ototoxicity.

ASTAXANTHIN PREVENTS HEARING LOSS IN RATS.

Ear Nose Throat J. 2019 Sep 26;145561319866826.

doi: 10.1177/0145561319866826. Online ahead of print.

Investigation of Astaxanthin Effect on Cisplatin Ototoxicity in Rats by Using Otoacoustic Emission, Total Antioxidant Capacity, and Histopathological Methods

[M Emrah Kinal](#)¹, [Arzu Tatlıpınar](#)¹, [Selami Uzun](#)¹, [Serhan Keskin](#)¹, [Emrah Tekdemir](#)¹, [Dilek Özbeyli](#)², [Dilek Akakin](#)³

PMID: 31558064 DOI: [10.1177/0145561319866826](https://doi.org/10.1177/0145561319866826) [Free article](#)

Abstract

Background: Cisplatin-induced ototoxicity is related to oxidative stress. Astaxanthin is one of the most powerful antioxidants in nature.

Aims/Objectives: To investigate the protective effect of astaxanthin on cisplatin-induced ototoxicity.

Materials and Methods: Thirty-five Sprague Dawley female rats were divided into 5 groups: control, cisplatin, and cisplatin with 10, 20, and 40 mg/kg astaxanthin groups. Cisplatin group received a single intraperitoneal injection of 14 mg/kg cisplatin. While saline was administered in the control group, in the other 3 groups, 10, 20, and 40 mg/kg daily doses of astaxanthin were administered through orogastric cannula before administration of cisplatin. Baseline and 10th day otoacoustic emission tests were administered. An intracardiac blood sample was taken to measure total antioxidant capacity (TAC), and the cochleas of the animals were investigated histopathologically.

Results: Hearing level of astaxanthin 40 mg/kg + cisplatin group was higher at 24 kHz and 32 kHz frequencies compared to the cisplatin group. The TAC value of the cisplatin group was lower than both the control and astaxanthin + cisplatin groups ($P < .05$). On histopathological examination, the other groups were deformed compared to the control group, but no statistically significant difference was observed between the astaxanthin + cisplatin and cisplatin groups.

Conclusions and Significance: Astaxanthin showed protective effect at high frequencies when it was administered at high dose. Thus, astaxanthin may have protective effect against cisplatin-induced ototoxicity.

ASTAXANTHIN REVIEWED FOR PREVENTION OF HEARING LOSS DUE TO A CANCER TREATMENT DRUG.

Drug Des Devel Ther. 2019 Dec 18;13:4291-4303.

doi: 10.2147/DDDT.S212313. eCollection 2019.

The Role of the Reactive Oxygen Species Scavenger Agent, Astaxanthin, in the Protection of Cisplatin-Treated Patients Against Hearing Loss

[Benyu Nan](#)^{1,2}, [Xi Gu](#)³, [Xinsheng Huang](#)²

- PMID: **31908415**
- PMCID: [PMC6927222](#)
- DOI: [10.2147/DDDT.S212313](#)

Free PMC article

Abstract

Emerging evidence of significant hearing loss occurring shortly after cisplatin administration in cancer patients has stimulated research into the causes and treatment of this side effect. Although the aetiology of cisplatin-induced hearing loss (CIHL) remains unknown, an increasing body of research suggests that it is associated with excessive generation of intracellular reactive oxygen species (ROS) in the cochlea. Astaxanthin, a xanthophyll carotenoid, has powerful anti-oxidant, anti-inflammatory, and anti-apoptotic properties based on its unique cell membrane function, diverse biological activities, and ability to permeate the blood-brain barrier. In this review, we summarize the role of ROS in CIHL and the effect of astaxanthin on inhibiting ROS production. We focus on investigating the mechanism of action of astaxanthin in suppressing excessive production of ROS.

ASTAXANTHIN PROTECTS EARS RESULTING IN IMPROVED HEARING AT HIGH FREQUENCY LEVELS IN RAT MODEL OF OTOTOXICITY.

Ear Nose Throat J. 2021 May;100(4):NP198-NP205.

doi: 10.1177/0145561319866826. Epub 2019 Sep 26.

Investigation of Astaxanthin Effect on Cisplatin Ototoxicity in Rats by Using Otoacoustic Emission, Total Antioxidant Capacity, and Histopathological Methods

[M Emrah Kinal¹](#), [Arzu Tatlıpınar¹](#), [Selami Uzun¹](#), [Serhan Keskin¹](#), [Emrah Tekdemir¹](#), [Dilek Özbeyli²](#), [Dilek Akakin³](#)

- PMID: 31558064 DOI: [10.1177/0145561319866826](https://doi.org/10.1177/0145561319866826) **Free article**

Abstract

Background: Cisplatin-induced ototoxicity is related to oxidative stress. Astaxanthin is one of the most powerful antioxidants in nature.

Aims/objectives: To investigate the protective effect of astaxanthin on cisplatin-induced ototoxicity.

Materials and methods: Thirty-five Sprague Dawley female rats were divided into 5 groups: control, cisplatin, and cisplatin with 10, 20, and 40 mg/kg astaxanthin groups. Cisplatin group received a single intraperitoneal injection of 14 mg/kg cisplatin. While saline was administered in the control group, in the other 3 groups, 10, 20, and 40 mg/kg daily doses of astaxanthin were administered through orogastric cannula before administration of cisplatin. Baseline and 10th day otoacoustic emission tests were administered. An intracardiac blood sample was taken to measure total antioxidant capacity (TAC), and the cochleas of the animals were investigated histopathologically.

Results: Hearing level of astaxanthin 40 mg/kg + cisplatin group was higher at 24 kHz and 32 kHz frequencies compared to the cisplatin group. The TAC value of the cisplatin group was lower than both the control and astaxanthin + cisplatin groups ($P < .05$). On

histopathological examination, the other groups were deformed compared to the control group, but no statistically significant difference was observed between the astaxanthin + cisplatin and cisplatin groups.

Conclusions and significance: Astaxanthin showed protective effect at high frequencies when it was administered at high dose. Thus, astaxanthin may have protective effect against cisplatin-induced ototoxicity.

General Health

J. Nat. Prod. **2006**, *69*, 443-449

Astaxanthin, a Carotenoid with Potential in Human Health and Nutrition

Ghazi Hussein,^{*,†,‡} Ushio Sankawa,[†] Hirozo Goto,[§] Kinzo Matsumoto,[‡] and Hiroshi Watanabe[‡]

Astaxanthin (1), a red-orange carotenoid pigment, is a powerful biological antioxidant that occurs naturally in a wide variety of living organisms. The potent antioxidant property of 1 has been implicated in its various biological activities demonstrated in both experimental animals and clinical studies. Compound 1 has considerable potential and promising applications in human health and nutrition. In this review, the recent scientific literature (from 2002 to 2005) is covered on the most significant activities of 1, including its antioxidative and anti-inflammatory properties, its effects on cancer, diabetes, the immune system, and ocular health, and other related aspects. We also discuss the green microalga *Haematococcus pluVialis*, the richest source of natural 1, and its utilization in the promotion of human health, including the antihypertensive and neuroprotective potentials of 1, emphasizing our experimental data on the effects of dietary astaxanthin on blood pressure, stroke, and vascular dementia in animal models, is described.

Astaxanthin: A Review of its Chemistry and Applications

HIGUERA-CIAPARA, L. FE´LIX-VALENZUELA, and F. M. GOYCOOLEA

Astaxanthin is a carotenoid widely used in salmonid and crustacean aquaculture to provide the pink color characteristic of that species. This application has been well documented for over two decades and is currently the major market driver for the pigment. Additionally, astaxanthin also plays a key role as an intermediary in reproductive processes. Synthetic astaxanthin dominates the world market but recent interest in natural sources of the pigment has increased substantially. Common sources of natural astaxanthin are the green algae *Haematococcus pluvialis*, the red yeast, *Phaffia rhodozyma*, as well as crustacean byproducts. Astaxanthin possesses an unusual antioxidant activity which has caused a surge in the nutraceutical market for the encapsulated product. Also, health benefits such as cardiovascular disease prevention, immune system boosting, bioactivity against *Helicobacter pylori*, and cataract prevention, have been associated with astaxanthin consumption. Research on the health benefits of astaxanthin is very recent and has mostly been performed in vitro or at the pre-clinical level with humans. This paper reviews the current available evidence regarding astaxanthin chemistry and its potential beneficial effects in humans.

ASTAXANTHIN REVIEWED FOR ITS POTENTIAL TO HELP WITH LIVESTOCK HEALTH AND PRODUCTION.

Res Vet Sci 2021 Sep;138:69-78. doi: 10.1016/j.rvsc.2021.05.023. Epub 2021 Jun 6.

Beneficial effects and health benefits of Astaxanthin molecules on animal production: A review

[Sayed Haidar Abbas Raza¹](#), [Syeda Rida Zahra Naqvi²](#), [Sameh A Abdelnour³](#), [Nicola Schreurs⁴](#), [Zuhair M Mohammedsaleh⁵](#), [Imran Khan⁶](#), [Abdullah F Shater⁵](#), [Mohamed E Abd El-Hack⁷](#), [Asmaa F Khafaga⁸](#), [Guobo Quan⁹](#), [Rajwali Khan¹⁰](#), [Sihu Wang¹¹](#), [Gong Cheng¹²](#), [Linsen Zan¹³](#)

- PMID: 34111716 DOI: [10.1016/j.rvsc.2021.05.023](https://doi.org/10.1016/j.rvsc.2021.05.023)

Abstract

Astaxanthin (AST) is a red pigment of carotenoid and is considered a high-quality keto-carotenoid pigment with food, livestock, cosmetic, therapeutic and nutraceutical proposes. Astaxanthin exists naturally in fish, crustacean, algae, and birds that naturally exists, principally as fatty acid esters. Many investigations have exhibited the beneficial impacts of astaxanthin when utilized as a pharmaceutical agent in animal nutrition. Astaxanthin has a variety of considerable biological actions, such as being antihypertensive, an antioxidant, anti-obesity properties, and anti-carcinogenic. Astaxanthin has recently acquired popularity as a powerful immunomodulator to maintain the health status and well-being of both animals and humans. The use of astaxanthin is broadly utilized in medical sciences and the nutrition of aquatic species; however, it presently has limited applications in broader animal nutrition. Understanding astaxanthin's structure, source, and mode of action in the body provides a conceptual base for its clinical application and could enhance the screening of compounds associated with the treatment of many diseases. This review article aims to clarify the important aspects of astaxanthin such as its synthesis, bioavailability, and therapeutics actions, with special interest in practical applications. Awareness of this benefits and production is expected to aid the livestock industry to develop nutritional strategies that ensure the protection of animal health.

Haematococcus astaxanthin: applications for human health and nutrition

Martin Guerin, Mark E, Huntley and Miguel Olaizola

The carotenoid pigment astaxanthin has important applications in the nutraceutical, cosmetics, food and feed industries. *Haematococcus pluvialis* is the richest source of natural astaxanthin and is now cultivated at industrial scale. Astaxanthin is a strong coloring agent and a potent antioxidant - its strong antioxidant activity points to its potential to target several health conditions. This article covers the antioxidant, UV-light protection, anti-inflammatory and other properties of astaxanthin and its possible role in many human health problems. The research reviewed supports the assumption that protecting body tissues from oxidative damage with daily ingestion of natural astaxanthin might be a practical and beneficial strategy in health management.

ASTAXANTHIN
Continuing Education Module

by Timothy J. Maher, Ph.D.

Goal:

The goal of this module is to introduce the reader to the carotenoid astaxanthin and examine its antioxidant actions especially as it relates to potential therapeutic approaches in addressing cardiovascular disease, neurodegenerative disease, cancer, immune function status and visual health.

Objectives:

Following successful completion of this module, the participant will be able to:

- describe the unique antioxidant features of the carotenoid astaxanthin;
- list the sources in nature and the functions of astaxanthin in animals that produce and consume astaxanthin;
- explain findings of recent research that describe the effects of astaxanthin in cardiovascular disease, neurodegenerative disease, visual health, cancer and immune system function;
- describe the pharmacokinetics of astaxanthin and list its potential side effects.

[Recenti Prog Med.](#) 2010 Apr;101(4):145-56.

[Omega-3 fatty acids and astaxanthin in health and disease. Recent knowledges]

[Article in Italian]

[Testino G](#), [Ancarani O](#), [Sumberaz A](#).

Dipartimento Medicina Specialistica, Azienda Ospedaliera-Universitaria Ospedale San Martino, Genova. testinogia@tiscalinet.it

Erratum in:

- [Recenti Prog Med.](#) 2010 May;101(5):180.

Abstract

At present, medicine is aimed to the treatment of lesions. Instead, it would be right to develop the maintenance of normal health. A number of authorities have recently recommended increases in intake of omega-3 fatty acids and astaxanthin for the health of general population. Omega-3 are necessary to provide the optimal function of cellular membrane in health and in disease states. It is well known how at least two servings of fish a week, or dietary supplementation of fatty acids omega-3, should be taken to obtain the health benefits of this essential nutrient. Astaxanthin is a powerful biological antioxidant. This property has been implicated in its various biological activities demonstrated in both experimental animals and clinical studies. For the recent evidence of the contemporary presence of omega-3 and astaxanthin in oil of Wild Pacific Salmon Sockeye, a review has been effected for the evaluation of a possible role of such association for the health promotion.

PMID: 20540399 [PubMed - indexed for MEDLINE]

Haematococcus astaxanthin: health and nutritional applications

Martin Guerin, Mark E. Huntley, Miguel Olaizola
Mera Pharmaceuticals, Inc.

This review was presented at the 1st Congress of the International Society for Applied Phycology/9th International Conference on Applied Phycology May 26-30, 2002, Almeria, Spain

Abstract

Astaxanthin, a carotenoid pigment, has important applications in the nutraceutical, cosmetics, food and feed industries. *Haematococcus pluvialis* is the richest source of natural astaxanthin and is now cultivated at industrial scale. Astaxanthin is a strong coloring agent and a potent antioxidant. Astaxanthin's strong antioxidant activity points to its potential to target a number of health conditions. Here we review the scientific literature on antioxidant, UV-light protection, and anti-inflammatory properties of astaxanthin, and its possible role in cellular health, cancer, immunology, liver function, heart health, eye health, central nervous system health, and other human health concerns. We also report results of a survey among users of a commercially available astaxanthin product (AstaFactor[®]). A detailed health questionnaire was mailed to 758 users of AstaFactor[®] of which 247 responses were returned. The respondents' age ranged from 20 to 87 years old. The reported effects of AstaFactor[®] supplementation conform to expectations of astaxanthin activity in chemical and animal models. Eighty eight percent of respondents reporting that they suffer from sore muscles or joints, observed a reduction in soreness or pain. Similarly, over 80% of those reporting back pain and symptoms from osteoarthritis or rheumatoid arthritis reported an improvement from astaxanthin supplementation. Astaxanthin supplementation was also reported to improve symptoms of asthma and enlarged prostate. All of these conditions have an inflammation component which is closely tied to oxidative damage. These results support the assumption that protecting body tissues from oxidative damage with daily ingestion of natural astaxanthin may be a practical and beneficial strategy in health management.

Mar Drugs. 2019 Sep 23;17(10):546.

doi: 10.3390/md17100546.

Astaxanthin Modulation of Signaling Pathways That Regulate Autophagy

[Suhn Hyung Kim](#)¹, [Hyeyoung Kim](#)²

- PMID: [31547619](#)
- PMCID: [PMC6836186](#)
- DOI: [10.3390/md17100546](#)

Free PMC article

Abstract

Autophagy is a lysosomal pathway that degrades and recycles unused or dysfunctional cell components as well as toxic cytosolic materials. Basal autophagy favors cell survival. However, the aberrant regulation of autophagy can promote pathological conditions. The autophagy pathway is regulated by several cell-stress and cell-survival signaling pathways that can be targeted for the purpose of disease control. In experimental models of disease, the carotenoid astaxanthin has been shown to modulate autophagy by regulating signaling pathways, including the AMP-activated protein kinase (AMPK), cellular homolog of murine thymoma virus akt8 oncogene (Akt), and mitogen-activated protein kinase (MAPK), such as c-Jun N-terminal kinase (JNK) and p38. Astaxanthin is a promising therapeutic agent for the treatment of a wide variety of diseases by regulating autophagy.

"Therapeutic uses of natural astaxanthin: An evidence-based review focused on human clinical trials"

[Andrea Donoso](#)¹, [Javiera González-Durán](#)², [Andrés Agurto Muñoz](#)¹, [Pablo A González](#)³, [Cristian Agurto-Muñoz](#)⁴

- PMID: **33549728**
- DOI: [10.1016/j.phrs.2021.105479](https://doi.org/10.1016/j.phrs.2021.105479)

Abstract

Astaxanthin is a natural C40 carotenoid with numerous reported biological functions, most of them associated with its antioxidant and anti-inflammatory activity, standing out from other antioxidants as it has shown the highest oxygen radical absorbance capacity (ORAC), 100-500 times higher than α -tocopherol and a 10 times higher free radical inhibitory activity than related antioxidants (α -tocopherol, α -carotene, β -carotene, lutein and lycopene). In vitro and in vivo studies have associated astaxanthin's unique molecular features with several health benefits, including neuroprotective, cardioprotective and antitumoral properties, suggesting its therapeutic potential for the prevention or co-treatment of dementia, Alzheimer, Parkinson, cardiovascular diseases and cancer. Benefits on skin and eye health promotion have also been reported, highlighting its potential for the prevention of skin photo-aging and the treatment of eye diseases like glaucoma, cataracts and uveitis. In this review, we summarize and discuss the currently available evidence on astaxanthin benefits, with a particular focus on human clinical trials, including a brief description of the potential mechanisms of action responsible for its biological activities.

Bioavailability of Astaxanthin

[Eur J Pharm Sci](#). 2003 Jul;19(4):299-304.

Oral bioavailability of the antioxidant astaxanthin in humans is enhanced by incorporation of lipid based formulations.

[Mercke Odeberg J](#), [Lignell A](#), [Pettersson A](#), [Höglund P](#).

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Astaxanthin is a carotenoid with antioxidant properties, synthesised by plants and algae, and distributed in marine seafood. Astaxanthin is also available as a food supplement, but, like other carotenoids, is a very lipophilic compound and has low oral bioavailability. However, bioavailability can be enhanced in the presence of fat. There is not much information in the literature about the pharmacokinetics of oral astaxanthin in humans. In this open parallel study, healthy male volunteers received a single dose of 40 mg astaxanthin, as lipid based formulations or as a commercially available food supplement, followed by blood sampling for further analysis of plasma concentrations. Pharmacokinetic parameters were calculated to evaluate the extent and rate of absorption from each formulation. The elimination half-life was 15.9±5.3 h (n=32), and showed a mono-phasic curve. Three lipid based formulations: long-chain triglyceride (palm oil) and polysorbate 80 (formulation A), glycerol mono- and dioleate and polysorbate 80 (formulation B), and glycerol mono- and dioleate, polysorbate 80 and sorbitan monooleate (formulation C), all showed enhanced bioavailability, ranging from 1.7 to 3.7 times that of the reference formulation. The highest bioavailability was observed with formulation B, containing a high content of the hydrophilic synthetic surfactant polysorbate 80.

Publication Types:

- [Comparative Study](#)

PMID: 12885395 [PubMed - indexed for MEDLINE]

On bioavailability and deposition of bent Z-isomers of astaxanthin

Marianne Østerlie, Bjørn Bjerkeng* and Synnøve Liaaen-Jensen

Experiments have been performed in which rainbow trout (*Oncorhynchus mykiss*) were fed diets containing a mixture of the all-E, 9Z, and 13Z geometrical isomers of astaxanthin or three male middle-aged human subjects were administered a single dose containing a similar astaxanthin isomer mixture. In rainbow trout, selective accumulation of all-E-astaxanthin was observed in tissues and blood plasma, and of 13Z-astaxanthin in the liver. In human blood plasma, 13Z-astaxanthin appeared to accumulate, and the distribution of the astaxanthin E/Z isomers remained constant in the mixed chylomicron and very low density (VLDL), and low density (LDL) and high density (HDL) lipoprotein fractions. In conclusion, more attention than assumed in the past must be paid to the E/Z configuration of xanthophylls when bioavailability and functional aspects are concerned in different species.

Plasma appearance and distribution of astaxanthin E/Z and R/S isomers in plasma lipoproteins of men after single dose administration of astaxanthin.

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Appearance, pharmacokinetics, and distribution of astaxanthin E/Z and R/S isomers in plasma and lipoprotein fractions were studied in 3 middle-aged male volunteers (37-43 years) after ingestion of a single meal containing a 100 mg dose of astaxanthin. The astaxanthin source consisted of 74% all-E-, 9% 9Z-, 17% 13Z-astaxanthin (3R,3'R-, 3R,3'S; meso-, and 3S,3'S-astaxanthin in a 1:2:1 ratio). The plasma astaxanthin concentration--time curves were measured during 72 hr. Maximum levels of astaxanthin (1.3 +/- 0.1 mg/L) were reached 6.7 +/- 1.2 hr after administration, and the plasma astaxanthin elimination half-life was 21 +/- 11 hr. 13Z-Astaxanthin accumulated selectively, whereas the 3 and 3'R/S astaxanthin distribution was similar to that of the experimental meal. Astaxanthin was present mainly in very low-density lipoproteins containing chylomicrons (VLDL/CM; 36-64% of total astaxanthin), whereas low-density lipoprotein (LDL) and high-density lipoprotein (HDL) contained 29% and 24% of total astaxanthin, respectively. The astaxanthin isomer distribution in plasma, VLDL/CM, LDL, and HDL was not affected by time. The results indicate that a selective process increases the relative proportion of astaxanthin Z-isomers compared to the all-E-astaxanthin during blood uptake and that astaxanthin E/Z isomers have similar pharmacokinetics.

PMID: 11120445 [PubMed]

Kinetics of plasma and erythrocyte-astaxanthin in healthy subjects following a single and maintenance oral dose

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¹Department of Laboratory Medicine, University of Groningen, University Medical Centre Groningen,

Groningen, ²Ortho Institute, Gendringen, The Netherlands

ABSTRACT

Aim and Background: Astaxanthin is a unique carotenoid of predominantly marine origin providing the pink-red color to certain microalgae and accumulating in various animals higher in the food chain. It is an antioxidant without pro-oxidant properties or known side-effects following oral intake.

Materials and Methods: We investigated astaxanthin kinetics in plasma and erythrocytes (red

blood cells [RBC]) of four healthy adults after a single oral 40 mg dose. Plasma- and RBC-astaxanthin were measured during 72 h. Subsequently, an 8 mg/day dose was given during 17 days. Plasma- and RBC-astaxanthin were measured each morning.

Results: Plasma-astaxanthin reached a peak (from 79 to 315 nmol/L) after 8 h and then declined (half-life, 18 h). Within 72 h, plasma-astaxanthin had returned to baseline. RBC-astaxanthin reached a peak (from 63 to 137 nmol/L packed cells) at 12 h and subsequently disappeared (half-life, 28 h). During the daily dose, plasma-astaxanthin increased until day 10 (187 nmol/L) and then decreased to a steady concentration similar to that reached after 2 days. RBC-astaxanthin appeared to be highly variable (group median concentration, 86 nmol/L packed cells).

Conclusion: We found high intra- and inter-individual variations, especially in RBC, possibly due to non-standardized time difference between astaxanthin intake and sampling, fluctuating background intake from the diet, variable bioavailability, large distribution volume, degradation or others. Oral astaxanthin is rapidly absorbed and incorporated into RBC. The subsequent rapid decline suggests that, for a higher-than-baseline status, astaxanthin should be taken daily, at least in an early phase when total body equilibrium, if any, has not been reached yet.

Key words: Absorption, antioxidant, carotenoid, half-life, humans, status

Astaxanthin Topical Skin Health Research

Astaxanthin applied topically shows anti-aging potential for skin.

[J Cosmet Dermatol](#). 2018 May 10. doi: 10.1111/jocd.12665. [Epub ahead of print]

Antioxidant properties evaluation of topical astaxanthin formulations as anti-aging products.

[Eren B¹](#), [Tuncay Tanrıverdi S¹](#), [Aydın Köse F²](#), [Özer Ö¹](#).

Author information

Abstract

BACKGROUND: The reactive oxygen species lead to skin aging via oxidative damage that are induced by UV radiation. Therefore, topical formulations which have antioxidant effect could reduce aging level. Astaxanthin is an antioxidant substance.

AIMS: The aim of this study was to investigate antioxidant activity and cytotoxicity potential of the astaxanthin-loaded gel formulations.

METHODS: Astaxanthin-loaded oleoresin and algae extract were used as natural active materials. The lipogel and hydrogel of these natural materials were prepared as anti-aging formulations. The formulations were characterized via parameters such as, pH, rheological analysis, mechanical properties, and stability. And also in vitro release experiments of the formulations were carried out. The antioxidant activity and cytotoxicity test were performed.

RESULTS: The results of characterization studies confirmed the formulations suitable for topical application. After 24 hours, 99 µg, 88.3 µg, 403 µg, and 234.8 µg of astaxanthin released through oleoresin lipogel, oleoresin hydrogel, algae extract lipogel, and algae extract hydrogel, respectively. It was found by the cytotoxicity tests that astaxanthin is more proliferative in lipogel formulations compared to hydrogel formulations. And finally, the highest antioxidant activity was found in the algae extract hydrogel and algae extract lipogel formulation, respectively (P < .05).

CONCLUSIONS: Topical formulations of astaxanthin-loaded oleoresin and algae extract were prepared successfully. At the same time, according to antioxidant activity and release studies, algae extract loaded could be suggested as topical anti-aging formulations.

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KEYWORDS: algae extract; anti-aging; antioxidant; astaxanthin; cell culture; gel systems

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Astaxanthin is a superior carotenoid to prevent photo-aging in topical applications.

Journal of Japanese Cosmetic Science Society VOL.29;NO.1;PAGE.9-19(2005)

[Preventive Effects of Carotenoids on Photoaging and Its Application for Cosmetics](#)

[MIZUTANI YUKI](#); [SAKATA OSAMU](#); [HOSHINO TAKU](#); [HONDA YOSHIKO](#);
[YAMASHITA MIKA](#); [ARAKANE KUMI](#); [SUZUKI TADASHI](#)

Carotenoids are functional materials and more than 650 kinds of carotenoids are isolated from nature. They have been applied for foods, but most of these carotenoids have not been studied in terms of their effects on skin functions, and because of their instability under light exposure they were hardly used in the cosmetics field until now. Using hairless mice irradiated with UVB to produce photoaged skin, we investigated the inhibitory effect of astaxanthin on wrinkle formation, decrease of skin elasticity, ultrastructural change of dermal collagen fiber bundles and elastic fibers and the level of matrix metalloproteinase-1 (MMP-1) activity. These results indicated that the astaxanthin had the superior protection effect on photoaging as a ROS scavenger. It is well known that carotenoids are easy to decompose during storage by UV light and oxygen. We found that the incorporation of dl- α -tocopherol and α -glucosyl rutin was able to maintain long-term stability of astaxanthin in preparation. This research demonstrated the superior anti-aging effects by carotenoids and this is the first time for carotenoids to be practically applicable to cosmetic formulation.

Astaxanthin applied topically prevents UV-induced skin damage.

[J Pharm Sci](#). 2012 Aug;101(8):2909-16. doi: 10.1002/jps.23216. Epub 2012 May 24.

Protective effects of topical application of a poorly soluble antioxidant astaxanthin liposomal formulation on ultraviolet-induced skin damage.

[Hama S¹](#), [Takahashi K](#), [Inai Y](#), [Shiota K](#), [Sakamoto R](#), [Yamada A](#), [Tsuchiya H](#), [Kanamura K](#), [Yamashita E](#), [Kogure K](#).

Author information

Abstract

Astaxanthin (Asx) would be expected to prevent ultraviolet (UV)-induced skin damage, as it is regarded as a potent antioxidative carotenoid in biological membranes. However, it is difficult to administer Asx topically to skin because of its poor water solubility. In this study, we attempted to solve this problem by preparing liposomes containing Asx (Asx-lipo), which were dispersible in the water phase, and therefore, suitable for topical application to the skin. Asx-lipo was shown to have potent scavenging ability against chemiluminescence-dependent singlet oxygen production in the water phase. When Asx-lipo was applied to skin before UV exposure, UV-induced skin thickening was prevented. Interestingly, collagen reduction induced by UV exposure was also prevented by preadministration of Asx-lipo. In addition, topical administration of Asx-lipo containing cationic lipid inhibited melanin production in skin exposed to UV. Consequently, we succeeded in preventing UV-induced skin damage using a topical application of a liposomal formulation containing Asx.

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PMID:

22628205

[PubMed - indexed for MEDLINE]

Astaxanthin applied topically shows wrinkle-reducing effect.

Fragr J VOL.29;NO.12;PAGE.98-103(2001)

[Effects of astaxanthin from Haematococcus pluvialis on human skin. Patch testing Skin repeated application test Effect on wrinkle reduction.](#)

[SEKI TAISUKE; SUEKI HIROHIKO; KONO HIROMI; SUGANUMA KAORU; YAMASHITA EIJI](#)

Astaxanthin is a natural color carotenoid found in salmon, salmon eggs, krill, and crab. Therefore, astaxanthin has been contained in the human diet for a long time. Astaxanthin from krill has been used for cosmetics to suppress post-UVB hyperpigmentation in human skin and food color additives. Recently, astaxanthin from Haematococcus pluvialis is available using new fermentation technology of H. pluvialis and it is used for dietary supplements, food color additives and cosmetics. Effects of astaxanthin from Haematococcus pluvialis on human subjects were tested. No serious adverse effects were observed by patch testing and sequencing applied test on human skin. In a pilot study, the skin repeated application test of cream containing astaxanthin on human skin showed the visual wrinkle reduction. The present paper described about patch testing, skin repeated application test, and a pilot study evaluating the wrinkle reduction effect on human skin.

Astaxanthin topical liposome protects against photo-aging in mice skin.

[Sichuan Da Xue Xue Bao Yi Xue Ban](#). 2018 Sep;49(5):712-715.

[The Preliminary Study on Anti-photodamaged Effect of Astaxanthin Liposomes in Mice Skin].

[Article in Chinese]

[Li FM](#)¹, [Liu Y](#)², [Liao JF](#)¹, [Duan XL](#)¹.

Author information

Abstract

OBJECTIVE: To study the protective effects of astaxanthin liposome (Asx-lipo) on photodamage by UVB in mice skin.

METHODS: 40 C57BL/6J mice were randomly divided into four groups: The blank group (no irradiation, no drug use), model group (UVB light injury group, no drug use), control group (irradiation + astaxanthin), experimental group (irradiation + astaxanthin liposome), each group with 10 mice. Each group was given the corresponding light (the radiation intensity was 2 mW·cm², the time of irradiation was 60 s, 1 times a day for the first 5 days, and 1 times every other day for the next 9 days, 10 times in a total of 2 weeks.) and drug intervention (topically treated with 4 mL 0.2‰ astaxanthin or 4 mL 0.2‰ Asx-lipo 10 min before the irradiation) for two weeks. After that, samples were examined by the following indicators: the histological changes of skin, Ki-67, 8-hydroxy-2'-deoxyguanosine(8-OHdG), superoxide dismutase(SOD) activities and serum matrix metalloproteinase-13 (MMP-13).

RESULTS: HE staining the model group and the control group showed that the dermis became thin, the dermal collagen fibers were long and thin, and the arrangement was loose and disordered. Compared with the blank group, the expression of Ki-67, MMP-13 and 8-OHdG increased and SOD activity decreased, and the differences were statistically significant ($P<0.05$). Compared with the model group, the pathological changes of skin tissues in the experimental group were significantly improved, with decreased expressions of Ki-67, MMP-13 and 8-OHdG and increased SOD activity, and the differences were statistically significant ($P<0.05$).

CONCLUSION: The photodamage of mice skin can be improved by topical Asx-lipo. The mechanism may be related to the strong antioxidation of Asx-lipo.

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KEYWORDS: Astaxanthin liposome ; MMP-13 ; Photodamage ; SOD

PMID: 30378331

Astaxanthin used topically in mice and in-vitro exhibits properties indicating that it may be effective in treating patients with allergic skin conditions.

[Mol Med Rep](#). 2015 Sep;12(3):3632-8. doi: 10.3892/mmr.2015.3892. Epub 2015 Jun 4.

Effects of astaxanthin on dinitrofluorobenzene-induced contact dermatitis in mice.

[Kim H¹](#), [Ahn YT²](#), [Lee GS³](#), [Cho SI¹](#), [Kim JM⁴](#), [Lee C⁵](#), [Lim BK⁶](#), [Ju SA⁷](#), [An WG¹](#).

Author information

Abstract

Astaxanthin (AST) is known to exhibit antioxidative and antitumor properties, therefore, the present study investigated its other potential medical applications. AST was observed to exhibit anti-allergic and anti-inflammatory effects in a dinitrofluorobenzene (DNFB)-induced contact dermatitis (CD) mouse model and RBL-2H3 cell lines. The topical application of AST effectively inhibited the enlargement of ear thickness and increase in weight, which occurred following repeated application of DNFB. Furthermore, topical application of different concentrations of AST inhibited inflammatory hyperplasia, edema, spongiosis, and the infiltration of mononuclear cells and mast cells in the ear tissue. In addition, the levels of TNF- α and IFN- γ produced were decreased by application of AST in vivo, and treatment of RBL-2H3 cells with AST inhibited the release of histamine and β -hexosaminidase in vitro. Taken together, these data suggested that AST may be used to treat patients with allergic skin diseases through a mechanism, which may be associated with that involved in anti-inflammatory or anti-allergic activities.

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[PubMed - indexed for MEDLINE]

Astaxanthin applied topically shows promise against allergic skin diseases.

[Mol Med Rep](#). 2015 Jun 4. doi: 10.3892/mmr.2015.3892. [Epub ahead of print]

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26044209

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Astaxanthin applied topically exerts anti-inflammatory activity in eczema model in rodents and in-vitro.

[Exp Dermatol.](#) 2018 Apr;27(4):378-385. doi: 10.1111/exd.13437.

Anti-inflammatory effect of astaxanthin in phthalic anhydride-induced atopic dermatitis animal model.

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Author information

Abstract

In this study, we investigated anti-dermatitic effects of astaxanthin (AST) in phthalic anhydride (PA)-induced atopic dermatitis (AD) animal model as well as in vitro model. AD-like lesion was induced by the topical application of 5% PA to the dorsal skin or ear of Hos:HR-1 mouse. After AD induction, 100 μ L of 1 mg/mL and 2 mg/mL of AST (10 μ g or 20 μ g/cm²) was spread on the dorsum of ear or back skin three times a week for four weeks. We evaluated dermatitis severity, histopathological changes and changes in protein expression by Western blotting for inducible nitric oxide synthase (iNOS), cyclooxygenase-2 (COX-2) and nuclear factor- κ B (NF- κ B) activity. We also measured tumor necrosis factor- α (TNF- α), interleukin-1 β (IL-1 β), interleukin-6 (IL-6) and immunoglobulin E (IgE) concentration in the blood of AD mice by enzyme-linked immunosorbent assay (ELISA). AST treatment attenuated the development of PA-induced AD. Histological analysis showed that AST inhibited hyperkeratosis, mast cells and infiltration of inflammatory cells. AST treatment inhibited expression of iNOS and COX-2, and NF- κ B activity as well as release of TNF- α , IL-1 β , IL-6 and IgE. In addition, AST (5, 10 and 20 μ M) potently inhibited lipopolysaccharide (LPS) (1 μ g/mL)-induced nitric oxide (NO) production, expression of iNOS and COX-2 and NF- κ B DNA binding activities in RAW 264.7 macrophage cells. Our data demonstrated that AST could be a promising agent for AD by inhibition of NF- κ B signalling.

KEYWORDS:

IgE; NF- κ B; astaxanthin; atopic dermatitis; cytokine; skin inflammation

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DOI: [10.1111/exd.13437](https://doi.org/10.1111/exd.13437)

Astaxanthin applied topically shows wound-healing effects in mice.

[Clin Cosmet Investig Dermatol](#). 2017 Jul 13;10:259-265. doi: 10.2147/CCID.S142795. eCollection 2017.

Effect of astaxanthin on cutaneous wound healing.

[Meephansan J¹](#), [Rungjang A¹](#), [Yingmema W²](#), [Deenonpoe R³](#), [Ponnikorn S³](#).

Author information

Abstract

Wound healing consists of a complex series of convoluted processes which involve renewal of the skin after injury. ROS are involved in all phases of wound healing. A balance between oxidative and antioxidative forces is necessary for a favorable healing outcome. Astaxanthin, a member of the xanthophyll group, is considered a powerful antioxidant. In this study, we investigated the effect of topical astaxanthin on cutaneous wound healing. Full-thickness dermal wounds were created in 36 healthy female mice, which were divided into a control group and a group receiving 78.9 μ M topical astaxanthin treatment twice daily for 15 days. Astaxanthin-treated wounds showed noticeable contraction by day 3 of treatment and complete wound closure by day 9, whereas the wounds of control mice revealed only partial epithelialization and still carried scabs. Wound healing biological markers including Col1A1 and bFGF were significantly increased in the astaxanthin-treated group since day 1. Interestingly, the oxidative stress marker iNOS showed a significantly lower expression in the study. The results indicate that astaxanthin is an effective compound for accelerating wound healing.

KEYWORDS:

antioxidant; astaxanthin; reactive oxygen species; wound healing

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[Free PMC Article](#)

Astaxanthin taken internally and topically improves the beauty of the skin in human clinical trial.

[Acta Biochim Pol.](#) 2012;59(1):43-7. Epub 2012 Mar 17.

Cosmetic benefits of astaxanthin on humans subjects.

[Tominaga K¹](#), [Hongo N](#), [Karato M](#), [Yamashita E](#).

Author information

Abstract

Two human clinical studies were performed. One was an open-label non-controlled study involving 30 healthy female subjects for 8 weeks. Significant improvements were observed by combining 6 mg per day oral supplementation and 2 ml (78.9 µM solution) per day topical application of astaxanthin. Astaxanthin derived from the microalgae, *Haematococcus pluvialis* showed improvements in skin wrinkle (crow's feet at week-8), age spot size (cheek at week-8), elasticity (crow's feet at week-8), skin texture (cheek at week-4), moisture content of corneocyte layer (cheek in 10 dryskin subjects at week-8) and corneocyte condition (cheek at week-8). It may suggest that astaxanthin derived from *H. pluvialis* can improve skin condition in all layers such as corneocyte layer, epidermis, basal layer and dermis by combining oral supplementation and topical treatment. Another was a randomized double-blind placebo controlled study involving 36 healthy male subjects for 6 weeks. Crow's feet wrinkle and elasticity; and transepidermal water loss (TEWL) were improved after 6 mg of astaxanthin (the same as former study) daily supplementation. Moisture content and sebum oil level at the cheek zone showed strong tendencies for improvement. These results suggest that astaxanthin derived from *Haematococcus pluvialis* may improve the skin condition in not only in women but also in men.

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Astaxanthin applied topically shows better photoprotective effect against premature signs of aging than other commonly used cosmetic ingredients.

Photoprotective Effect of Astaxanthin Applied to the Skin

Arakane, K. 2002. KOSE Corporation

Reactive oxygen species generated by exposing the skin to sunlight are responsible for sunburn, lipid peroxidation and degenerative changes in dermal connective tissues. This causes premature aging of the skin.

A researcher from a Japanese company called KOSE Corporation compared astaxanthin to other commonly used ingredients in cosmetics that are thought to protect the skin from the damaging effects of sunlight. He found that astaxanthin potentially offers greater antioxidant protection against premature signs of aging.

Astaxanthin in eye drops prevents UV damage in mice.

[Mol Vis.](#) 2012;18:455-64. Epub 2012 Feb 14.

Amelioration of ultraviolet-induced photokeratitis in mice treated with astaxanthin eye drops.

[Lennikov A¹](#), [Kitaichi N](#), [Fukase R](#), [Murata M](#), [Noda K](#), [Ando R](#), [Ohguchi T](#), [Kawakita T](#), [Ohno S](#), [Ishida S](#).

Author information

Abstract

PURPOSE:

Ultraviolet (UV) acts as low-dose ionizing radiation. Acute UVB exposure causes photokeratitis and induces apoptosis in corneal cells. Astaxanthin (AST) is a carotenoid, present in seafood, that has potential clinical applications due to its high antioxidant activity. In the present study, we examined whether topical administration of AST has preventive and therapeutic effects on UV-photokeratitis in mice.

METHODS:

C57BL/6 mice were administered with AST diluted in polyethylene glycol (PEG) in instillation form (15 μ l) to the right eye. Left eyes were given vehicle alone as controls. Immediately after the instillation, the mice, under anesthesia, were irradiated with UVB at a dose of 400 mJ/cm². Eyeballs were collected 24 h after irradiation and stained with H&E and TUNEL. In an in vitro study, mouse corneal epithelial (TKE2) cells were cultured with AST before UV exposure to quantify the UV-derived cytotoxicity.

RESULTS:

UVB exposure induced cell death and thinning of the corneal epithelium. However, the epithelium was morphologically well preserved after irradiation in AST-treated corneas. Irradiated corneal epithelium was significantly thicker in eyes treated with AST eye drops, compared to those treated with vehicles ($p < 0.01$), in a dose-dependent manner. Significantly fewer apoptotic cells were observed in AST-treated eyes than controls after irradiation ($p < 0.01$). AST also reduced oxidative stress in irradiated corneas. The in vitro study showed less cytotoxicity of TKE2 cells in AST-treated cultures after UVB-irradiation ($p < 0.01$). The cytoprotective effect increased with the dose of AST.

CONCLUSIONS:

Topical AST administration may be a candidate treatment to limit the damages by UV irradiation with wide clinical applications.

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Carotenoid Science Vol 10, p 91-5 (2006)

The Effects of a Dietary Supplement Containing Astaxanthin on Skin Condition

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The cosmetic effects on human skin by 4mg per day astaxanthin supplementation were demonstrated in a single blind placebo controlled study using forty-nine US healthy middle-aged women. There were significant improvements in fine lines/wrinkles and elasticity by dermatologist's assessment and in the moisture content by instrumental assessment at week 6 compared to base-line initial values.

Astaxanthin, widely and naturally distributed in marine organisms, including Crustacea such as shrimps and crabs and such fish as salmon and sea bream exhibits a strong anti-oxidative effect, and its action is reported to 1,000 times stronger than alpha-tocopherol and approximately 40 times stronger than beta-carotene. It has also been reported that astaxanthin doesn't have any pro-oxidative nature like beta-carotene and lycopene and its potent anti-oxidant property is exhibited at the cell membrane. Although used only as a coloring in the past (either as a food additive or a dye-up agent for cultured fish), astaxanthin has become one of the major materials eagerly anticipated by industries for dietary supplements and personal care products.

Furthermore its other various important benefits to date have suggested for human health such as anti-inflammation, LDL cholesterol oxidation suppression, immunomodulation, anti-stress, limiting diabetic nephropathy, improved semen quality, attenuating eye fatigue, sport performance and endurance, limiting exercised induced muscle damage and improving hypertension.

In terms of dermatological actions, suppression of hyper-pigmentation, inhibitions of melanin synthesis and photo-aging have been reported. We have also reported visual wrinkled reduction by topical astaxanthin. However, only one study for internal use about cosmetic benefit of a dietary supplement including astaxanthin and tocotrienol on human skin has been reported.

Here we report the effects of a dietary supplement containing astaxanthin on skin condition performed in the United States of America.

Astaxanthin as a cosmetic ingredient.

Carotenoid Science, Vol. 5, p21-4 April 2002 Toyama, Japan

Superior Skin Protection via Astaxanthin

Kumi Arakane

It has been believed for a long time that the skin exists only for the purpose of merely protecting our body by physically shielding it from outside factors. But in recent years, along with the radical progress in the field of dermatological science studies, it is known that the skin does actually indicate various responses and accept acute and chronic damages under UV irradiation. According to the enthusiastic studies to clarify the mechanism leading to the skin damages, nowadays the reactive oxygen species generated by UV irradiation is considered to be an important factor mediating photo-induced skin damages. Accumulation skin damages by reactive oxygen species such' as lipid peroxidation, sunburn and degenerative changes in dermal connective tissues induce the skin aging. To protect skin from reactive oxygen species, many cosmetics contain nowadays both naturally occurring molecules and synthetic compounds as antioxidant. However, B-carotene was the only carotenoid for cosmetics among more than 600 carotenoids which had been isolated from nature, until astaxanthin from Antarctic krill was approved for cosmetics in 1997. In this paper, I would like to show the possibility of astaxanthin as a cosmetic ingredient and the useful formula for maintaining the stability of astaxanthin in the preparation.

Astaxanthin combined with two other ingredients and used both internally and topically shows improvements in skin quality in human clinical trial.

(Excerpt from Nutrition Business Journal, December 2004)

Beauty clinical: Astaxanthin with Omega 3 and Marine Glycosaminoglycans

Alain Thibodeau, Director of Scientific Affairs for Atrium Biotechnologies Inc. in Quebec, Canada published results of a blinded parallel group clinical trial on topical and supplemental forms of a product they call MRT2 (Matrix Rejuvenation Technology 2). The trial was done using both a topical product containing marine glycosaminoglycans and a supplement containing marine glycosaminoglycans, astaxanthin and omega-3 fatty acids. The trial involved 100 subjects.

Significant improvements were measured in skin hydration and elasticity. Skin appearance (including skin tone, fine lines and sallowness) also showed benefits, with the strongest improvements made in subjects using both the supplement and the topical products.

“We can demonstrate a synergistic activity between the topical product and the dietary supplement...The topical product works. The supplement works as well, but you get much better results from using both” said Thibodeau.

Astaxanthin's reviewed as a topical wrinkle reducer and as a beauty from within supplement.

Fragr J VOL.34;NO.3;PAGE.21-27(2006)

[Biological activities of astaxanthin and its cosmeceutical application.](#)
[YAMASHITA EIJI](#)

The present review covers cosmeceutical benefits of astaxanthin that is one of the most abundant carotenoids in nature, particularly in marine based life. The anti-oxidant properties of astaxanthin without any pro-oxidative nature working at cell membrane and cosmeceutical effects such as anti-hyperpigmentation, anti-photoaging, melanin inhibition and visual wrinkle reduction by topical or internal use and one of the action mechanisms of astaxanthin on NF-kB dependent inflammation are introduced. And current and future cosmeceutical applications of astaxanthin particularly from a green microalgae *Haematococcus pluvialis* that is the most ideal source in the earth are discussed describing actual examples of astaxanthin containing skin care products in Japanese market.

Astaxanthin reviewed as an anti-pigmenting agent.

[Int J Mol Sci](#). 2014 May 12;15(5):8293-315. doi: 10.3390/ijms15058293.

Inhibitors of intracellular signaling pathways that lead to stimulated epidermal pigmentation: perspective of anti-pigmenting agents.

[Imokawa G](#)¹, [Ishida K](#)².

Author information

Abstract

Few anti-pigmenting agents have been designed and developed according to their known hyperpigmentation mechanisms and corresponding intracellular signaling cascades. Most anti-pigmenting agents developed so far are mechanistically involved in the interruption of constitutional melanogenic mechanisms by which skin color is maintained at a normal and unstimulated level. Thus, owing to the difficulty of confining topical application to a specific hyperpigmented skin area, potent anti-pigmenting agents capable of attenuating the natural unstimulated pigmentation process have the risk of leading to hypopigmentation. Since intracellular signaling pathways within melanocytes do not function substantially in maintaining normal skin color and are activated only by environmental stimuli such as UV radiation, specifically down-regulating the activation of melanogenesis to the constitutive level would be an appropriate strategy to develop new potent anti-pigmenting agents with a low risk of hypopigmentation. In this article, we review the hyperpigmentation mechanisms and intracellular signaling pathways that lead to the stimulation of melanogenesis. We also discuss a screening and evaluation system to select candidates for new anti-melanogenic substances by focusing on inhibitors of endothelin-1 or stem cell factor-triggered intracellular signaling cascades. From this viewpoint, we show that extracts of the herbs *Withania somnifera* and *Melia toosendan* and the natural chemicals Withaferin A and Astaxanthin are new candidates for potent anti-pigmenting substances that avoid the risk of hypopigmentation.

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