

Medical Research Abstracts on Astaxanthin

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March, 2017

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Introduction

A wealth of research has been done on Astaxanthin showing far-ranging health benefits. 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; 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 and applications for athletes. The final chapter contains a vast amount of additional research in areas that currently consist exclusively of pre-clinical trials. However, it's important to note that within this final chapter, there are some areas that have a very impressive amount of research even though 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, while there are many of these studies, we feel that they 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 be at least a factor of 10X. 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 anti-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 many other health benefits emanate.

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 at universities and by private researchers around the world has increased quickly. The intense interest in undertaking new research on Astaxanthin is a direct result of the remarkable qualities of this fascinating molecule.

This document is distributed by BGG 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. Our farm produces the world's most highly concentrated algae biomass with over 6% Astaxanthin by volume (compared to other producers whose product generally ranges from 1.5% to 5%). BGG also provides white papers 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 or any other questions, please contact BGG by e-mail at support@bggworld.com or by telephone at our California office at 949.748.7348. (For a list of contact information for BGG's other 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 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 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 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 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 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](#), [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 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

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, [Gueguen 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 thermally dissociable 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

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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.

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](#)

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[PubMed - indexed for MEDLINE]

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

[PubMed - in process]

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 AR¹](#), [Sarada R²](#), [Shylaja MD³](#), [Ravishankar GA⁴](#).

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

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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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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 A](#)¹, [Kamoun Z](#)², [Ghliissi Z](#)³, [Makni M](#)², [Nasri M](#)⁴, [Sahnoun Z](#)³, [Nedjar-Arroume N](#)⁵, [Bougatef A](#)⁶.

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

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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 AP¹](#), [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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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

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PMCID: [PMC5018570](#)

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

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

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25732953

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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 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 (NO₂Na) (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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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

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[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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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 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 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 CS¹](#), [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-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

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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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]

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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 SE](#), [Jacob RF](#), [Mason RP](#).

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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 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.

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](#).

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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 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 lipid 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 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

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[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 LA¹](#), [Imaizumi T¹](#), [Suzuki T¹](#), [Tomita K¹](#), [Takashina M¹](#), [Hattori Y²](#).

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](#)

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 $O(2)(\cdot^-) / H(2)O(2)$ 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 ($LC_{50} = 11.67 \pm 0.42$ 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 CL](#)¹, [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 100µM 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 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 $E^{\text{degrees}} = 1.13$ and 1.10 V versus NHE corresponding to the uncharged puerarin and daidzein. For $\text{pH} > \text{pK}(\text{a}2)$, the apparent potentials of both puerarin and daidzein became constants and were $E^{\text{degrees}} = 0.69$ 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

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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-1β 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 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

Postgraduate Program - Health Sciences - CBS, Cruzeiro do Sul University, 03342000 Sao Paulo, SP, Brazil.

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 μ M) 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 μmol.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 μmol.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 μmol.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

University Lille Nord de France, UMR 8187 LOG CNRS/University Lille 1, Bât SN2, 59655 Villeneuve d'Ascq Cedex, France.

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/jcbrn.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]

Anti-Inflammatory Properties of Astaxanthin, Joint Health, Tendon Health and Muscle Health

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Studies Demonstrating Astaxanthin's Anti-Inflammatory Mechanism 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 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+/-4.10 microM, 28.76+/-1.48 microM, 9.79+/-1.50 microM and 8.09+/-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+/-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 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]

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PMC4488551

[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 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 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.

Supporting Pre-Clinical Trials

Astaxanthin prevents muscle atrophy by protecting membranes in rodent study.

Effect of Astaxanthin on Muscular Atrophy

Reference: Tateo Sugiura, Yoshiharu Iida, Hisashi Naito, Daijiro Ohmori, Katsumasa Goto, Toshitada Yoshioka. 2005 Japanese Journal of Physical Fitness and Sports Medicine. Vol. 54, No. 6, pg 466. December 2005. (Translated from Japanese)

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 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, Hiieebi 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 tubulin 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 M¹](#), [Matsuno T¹](#), [Asano K¹](#), [Mataga I¹](#).

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 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 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] PMID:

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 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

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 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 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.

[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.

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 L¹](#), [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 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 S¹](#), [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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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 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-κB-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 YJ¹](#), [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]

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 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 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 µM MGO followed or not by the addition of the antioxidants astaxanthin (2 µM) and vitamin C (100 µM). 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-1β 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]

Free full text

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

[PubMed - indexed for MEDLINE]

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

[PubMed - 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 SF¹](#), [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 RG¹](#), [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](#).

Mera Pharmaceuticals Inc., 73-4460 Queen Kaahumanu Hwy, Suite 110, Kailua-Kona, Hawaii 96740, USA.

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.

PMID:

22214255

[PubMed - indexed for MEDLINE]

Free full text

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

Free PMC Article

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 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](#).

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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.

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.

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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 μM) 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 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 S](#)¹, [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 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.

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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.

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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](#).

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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 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.

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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

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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.

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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 µl) 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](#)

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.

Inaida Endowed Department of Anti-Aging Ophthalmology, Laboratory of Retinal Cell Biology, Center for Integrated Medical Research, Keio University School of Medicine, Tokyo, Japan.
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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 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 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](#) PMCID: [PMC5007682](#)

DOI: [10.1186/s12868-016-0295-2](#)

[PubMed - in process]

[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 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 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 (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

PMID:

25732953

[PubMed – as supplied by publisher]

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 CS¹](#), [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

PMID: [23906231](#) DOI: [10.1016/j.kjms.2012.12.002](#)

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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PMCID:

PMC4278222

[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 Q¹](#), [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 X¹](#), [Qi Z²](#), [Zhao L³](#), [Yu Z⁴](#).

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 astaxantin (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 N](#)¹, [Martin-Eauclaire MF](#)², [Laraba-Djebari F](#)³.

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 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-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

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24948541

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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

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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 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 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

[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'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.

[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 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](#).

Research Team for Molecular Biomarkers, Tokyo Metropolitan Institute of Gerontology, Tokyo, Japan.

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 the its potent antioxidative ability.

Publication Types:

PMID: 19014378 [PubMed – indexed for MEDLINE]

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](#).

Departamento de Bioquímica, Universidade Federal de Pernambuco, 50670-901 Recife, PE, Brazil.

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 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 (<or=middle treatment group) is really good for improving the memory.

PMID: 17721823 [PubMed - indexed for MEDLINE]

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 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 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 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 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 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 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 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 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

Department of Biomaterial Control, Dong-Eui University, Busan, 614-714, Korea; E-Mails: 12845@deu.ac.kr (J.-H.K.); bwkim@deu.ac.kr (B.-W.K.); wbchoi@deu.ac.kr (W.C.); jonghwanlee@deu.ac.kr (J.-H.L.).

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 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

[PubMed - indexed for MEDLINE]

PMCID:

PMC3967194

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.

PMID:

24522549

[PubMed - indexed for MEDLINE]

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 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](#).

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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 blood flow rate improves 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 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 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 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 M^J](#).

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](#).

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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 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 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.

[Lockwood SF](#), [Jackson HL](#), [Gross GJ](#).

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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.

[Lockwood SE](#), [Penn MS](#), [Hazen SL](#), [Bikádi Z](#), [Zsila F](#).

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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.

PMID: 16466747 [PubMed - indexed for MEDLINE]

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.

Gross GJ, Hazen SL, Lockwood SF.

Department of Pharmacology and Toxicology, Medical College of Wisconsin, Milwaukee, 53226, USA.

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.

PMID: 16444582 [PubMed - 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.

Department of Pharmacology and Toxicology, Medical College of Wisconsin, Milwaukee, WI, USA.

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.**

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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](#).

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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

Hyesun P. McNulty a,□, Jungsoo Byun a, Samuel F. Lockwood b,
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 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.

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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

PMID:

22798712

[PubMed]

PMCID:

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](#).

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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 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 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 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](#).

John A. Burns School of Medicine, University of Hawaii, Honolulu, Hawaii, USA.
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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.
slockwood@hibiotech.com

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 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 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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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 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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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.

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 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 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 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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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 PMCID: [PMC5029912](#)

DOI: [10.1371/journal.pone.0161580](#) PubMed - in process]

[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 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 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]

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 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.

PMID:

24823877

[PubMed - indexed for MEDLINE]

PMCID:

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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[10.1111/exd.12347](https://doi.org/10.1111/exd.12347)

[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 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.

PMID:

26044209

DOI:

[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 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 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 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 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 JP¹](#), [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 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](https://doi.org/10.3390/ijms15058293)

[PubMed - indexed for MEDLINE]

[Free PMC Article](#)

Athletic Performance, Strength, Endurance, Recovery 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 cholesterols 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

Curt L. Malmsten(a) and Åke Lignell(b)

(a) Raddningshalsan AB, Yxvagen 11, 840 13 Torpshammar, Sweden

(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 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-.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 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 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

PMID:

23192897

[PubMed - indexed for MEDLINE]

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±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 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 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

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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 sarcopenia [muscular atrophy due to aging] in rats.

Long term dietary antioxidant intakes attenuate sarcopenia

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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 protects liver cells and improves mitochondrial activity by proton transferring 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

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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 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 50 μ M 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 IC₅₀ of 39 μM. 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

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25215580

[PubMed - indexed for MEDLINE]

PMCID:

PMC4224554

Free PMC Article

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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PMID:

21764223

[PubMed - indexed for MEDLINE]

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 JP¹](#), [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

Immunity Abstracts

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 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

School of Food Science, Lewisburg, OH 45338, USA. boonchew@wsu.edu

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 $\mu\text{g}/\text{mL}$)- or concanavalin A (Con A, 10 $\mu\text{g}/\text{mL}$)-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

PMID: 26729100

[PubMed - in process]

PMCID: PMC4730289

Free PMC Article

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]Ijima, 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 H¹](#), [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 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 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 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

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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](#).

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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 Y¹](#), [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). [3 H]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 BP¹](#), [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.](#)

Hacettepe University, School of Medicine, Department of Microbiology and Clinical Microbiology, Ankara, Turkey. yakyon@tr.net

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 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.

[Chew BP](#), [Park JS](#).

Department of Animal Sciences, Washington State University, Pullman, WA 99164-6351, USA.
boonchew@wsu.edu

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.

Centro de Investigación en Alimentación y Desarrollo, A.C., P.O. Box 1735. Hermosillo, Sonora, 83000, México. higuera@cascabel.ciad.mx

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

Anti-Aging, DNA and Cellular Health

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 in US Patent Application.

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 396andomized396d to prevent the accumulation. In the present study, we conducted a 396andomized, 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 astaxanthinsupplementation 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 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/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 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 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

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

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 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 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 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](#), [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 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 shown to be 75X to 6000X stronger than other common natural antioxidants in singlet oxygen quenching activity.

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 thermally dissociable 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

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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 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](#).

Department of Ophthalmology and Visual Sciences, Hokkaido University Graduate School of Medicine, Sapporo, Japan. kohgami@med.hokudai.ac.jp

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 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+/-4.10 microM, 28.76+/-1.48 microM, 9.79+/-1.50 microM and 8.09+/-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+/-0.50 microM.

Publication Types:

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

PMID: 14758027 [PubMed - indexed for MEDLINE]

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](#).

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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 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 increases 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/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

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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

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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 with 6mg per day as the optimal dose.

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 is 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 derived from *Haematococcus pluvialis* 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 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]

Carotenoid Science Vol 10, p 91-5 (2006)

The Effects of a Dietary Supplement Containing Astaxanthin on Skin Condition

Eiji Yamashita, Life Science Division, Fuji Chemical Industry Co., Ltd., 55 Yokohoonji, 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 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.

2010 Japanese Society for Investigative Dermatology. Published by Elsevier Ireland Ltd. All rights reserved.

PMID:

20219323

[PubMed - indexed for MEDLINE]

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 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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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] PMCID: 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.

X

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 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 AM¹](#), [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 from irradiation.

[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 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 M¹](#), [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

[PubMed - indexed for MEDLINE]

Fertility and Sperm Improvement

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.

X

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 (Proxead). 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 improved 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 M¹](#), [Vahidinia A²](#), [Mehdinejadi S³](#), [Shokri S⁴](#), [Alizadeh Z¹](#).

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 improved testes weight, sperm count, sperm head morphology, sperm comet assay, restored sperm DNA damage and protected 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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[10.1016/j.tox.2008.03.015](https://doi.org/10.1016/j.tox.2008.03.015)

[PubMed - 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

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 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.

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[PMC4377989](#)

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[PubMed - 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*).

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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

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[PubMed - indexed for MEDLINE]

Astaxanthin in combination with Vitamins A & E improved 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 M¹](#), [Salehi I²](#), [Alizadeh Z¹](#), [Vahabian M³](#), [Roushandeh AM⁴](#).

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 in combination with Vitamins C & E improved 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)

Additional Areas of ***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 and diabetes, 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 trials in rodents related to cancer prevention and tumor reduction with over forty studies already published is extremely promising.

We hope to see human trials in these areas 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

[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

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26184238

[PubMed - in process]

PMCID:

PMC4515619

[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

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26147624

[PubMed - as supplied by publisher]

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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25296162

[PubMed - indexed for MEDLINE]

PMCID:

PMC4189964

Free PMC Article

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 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]

Effects of astaxanthin supplementation on chemically induced tumorigenesis in Wistar rats.

[Gal AF¹](#), [Andrei S](#), [Cernea C](#), [Talescu 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

[PubMed - indexed for MEDLINE]

PMCID:

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.

PMID:

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.

PMID:

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-κB 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

[PubMed - in process]

PMCID:

PMC4626679

[Free PMC Article](#)

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}

PMID:

26470770

[PubMed - as supplied by publisher]

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](#).

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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.

PMID: 19423215 [PubMed - as supplied by publisher]

[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.

PMID: 16716595 [PubMed - indexed for MEDLINE]

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.

PMID: 15888493 [PubMed - indexed for MEDLINE]

[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.

PMID: 12173414 [PubMed - indexed for MEDLINE]

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.

[Tanaka T](#), [Kawamori T](#), [Ohnishi M](#), [Makita H](#), [Mori H](#), [Satoh K](#), [Hara A](#).

First Department of Pathology, Gifu University School of Medicine, Japan.

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]

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:

PMID: 7664280 [PubMed - indexed for MEDLINE]

Marine Carotenoids: Bioactivities and Potential Benefits to Human Health.

[Chuyen VH](#)^{1,2}, [Eun JB](#)¹.

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](#).

First Department of Pathology, Gifu University School of Medicine, Japan.

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](#), [Dav 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:

PMID: 8180322 [PubMed - indexed for MEDLINE]

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±1 g) 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.

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.

[Nagendraprabhu P](#), [Sudhandiran G](#).

Department of Biochemistry, University of Madras, Guindy campus, Chennai, 600 025, 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-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]

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 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 IC₅₀ of 39 μM. 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]

Diabetes

[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

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25569034

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[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.

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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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[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.

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23715867

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

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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]

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Astaxanthin ameliorates features of metabolic syndrome in SHR/NDmcr-cp.

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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 from shrimp by-products ameliorates nephropathy in diabetic rats.

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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

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Astaxanthin improves cognitive deficits from oxidative stress, nitric oxide synthase and inflammation through upregulation of PI3K/Akt in diabetes rat.

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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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PMC4525820

[Free PMC Article](#)

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

[PubMed - in process]

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.

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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.

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[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:

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Prevention of diabetic nephropathy by treatment with astaxanthin in diabetic db/db mice.

[Naito Y](#), [Uchiyama K](#), [Aoi W](#), [Hasegawa G](#), [Nakamura N](#), [Yoshida N](#), [Maoka T](#), [Takahashi J](#), [Yoshikawa T](#).

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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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First Department of Medicine, Kyoto Prefectural University of Medicine, Kyoto, Japan.

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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Jiro Takahashi², Toshikazu Yoshikawa¹

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 – 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.

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[Author information](#)

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[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.

PMID: 20513374 [PubMed - indexed for MEDLINE]

[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.

[Leite MF](#), [de Lima A](#), [Massuyama MM](#), [Otton R](#).

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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 ($\text{O}_2^{\cdot-}$), 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, $\text{O}_2^{\cdot-}$, 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]

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

Department of Cardiology, Union Hospital, Fujian Medical University, and Fujian Institute of Coronary Artery Disease, Fuzhou, PR China.

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-i (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.

PMID: 21650083 [PubMed - indexed for MEDLINE]

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.

PMID: 21326955 [PubMed - indexed for MEDLINE]

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

Postgraduate Program, Human Movement Sciences Institute of Physical Activity and Sport Sciences, Cruzeiro do Sul University, São Paulo, SP, Brazil, 01506-000.

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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PMID: 21055504 [PubMed - indexed for MEDLINE]

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

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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]

Ulcers and Gastrointestinal Health

[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]

[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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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 Q¹](#), [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](#).

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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](#).

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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:

PMID: 18467083 [PubMed - indexed for MEDLINE]

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.

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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]

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.

Publication Types:

PMID: 12199857 [PubMed - indexed for MEDLINE]

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.

PMID: 10952594 [PubMed - indexed for MEDLINE]

PMCID: PMC90084

[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.

Wang X, Willen R, Wadstrom T.

Department of Infectious Diseases and Medical Microbiology, University of Lund, Sweden.

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

School of Veterinary Medicine, Rakuno Gakuen University, Hokkaido, Japan. y-yasui@rakuno.ac.jp

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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Asthma

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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

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[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.

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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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Free full text

[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](#)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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Hepatoprotective and Renal Protective

[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 µM) 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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PMC4356569 [Free PMC Article](#)

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

[PubMed - in process]

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PMC4658633

[Free PMC Article](#)

[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.

[Kang JO](#), [Kim SJ](#), [Kim H](#).

Department of Food and Nutrition, College of Human Ecology, Seoul National University, Korea.

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.

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.

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Free PMC Article

Astaxanthin prevents TGF β 1-induced pro-fibrogenic gene expression by inhibiting Smad3 activation in hepatic stellate cells.

[Yang Y¹](#), [Kim B¹](#), [Park YK¹](#), [Koo SI¹](#), [Lee JY²](#).

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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[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

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22778115

[PubMed - indexed for MEDLINE]

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.

PMID:

25328157

[PubMed - indexed for MEDLINE]

Protective effect of astaxanthin on liver fibrosis through modulation of TGF- β 1 expression and autophagy.

[Shen M](#)¹, [Chen K](#)¹, [Lu J](#)¹, [Cheng P](#)¹, [Xu L](#)¹, [Dai W](#)¹, [Wang F](#)¹, [He L](#)¹, [Zhang Y](#)¹, [Chengfen W](#)¹, [Li J](#)¹, [Yang J](#)¹, [Zhu R](#)¹, [Zhang H](#)¹, [Zheng Y](#)¹, [Zhou Y](#)¹, [Guo C](#)¹.

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]

PMCID:

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.

PMID:

23852435

[PubMed - indexed for MEDLINE]

PMCID:

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 P4501A1 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](#)

PMID: 8893038 [PubMed - indexed for MEDLINE]

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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26023842

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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](#).

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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.

PMID: 19900500 [PubMed - indexed for MEDLINE]

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-naphthoflavone 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

[PubMed - in process]

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

[PubMed - in process]

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PMC4323259

[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](#), [Ghliissi 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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24712822

[PubMed - indexed for MEDLINE]

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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PMID:

25924598

[PubMed - in process]

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]

Life Extension

[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

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

[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]

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](#).

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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]

Weight Loss

[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.

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.

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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.

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22089895

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General Health

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Astaxanthin, a Carotenoid with Potential in Human Health and Nutrition

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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.

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.

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](#).

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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.

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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.

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.

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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](#)

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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]