

# **Natural Astaxanthin for Skin Health and *“Beauty from Within”***

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# Introduction

Internationally famous singer Madonna eats salmon to get Natural Astaxanthin for her skin's health and appearance. Actress Gwyneth Paltrow and model Heidi Klum both take Natural Astaxanthin capsules for their internal beauty effect. The world's most famous dermatologist, best-selling author Nicholas Perricone, MD, writes about Astaxanthin for skin health in his books and used to talk about it on the Oprah Winfrey show. What do all of these people know that most people don't?

I'm sure you're probably thinking now: How is it possible that you can take a small capsule internally and it can improve your skin's appearance *from the inside out*? This seems incredible, particularly when we consider that for years, cosmetic marketers have aggressively promoted creams and lotions to improve skin health and appearance through topical application. The idea of an "Internal Beauty Pill" seems like something from an old Star Trek episode. (In fact, this was the subject of a Star Trek episode from almost fifty years ago.) Yet, as incredible as it may seem Astaxanthin has already been documented to serve as an "Internal Beauty Pill" in human clinical research:

- ★ Supplementation with 4mg per day of Natural Astaxanthin has been clinically validated to reduce wrinkles, improve skin elasticity and increase skin moisture levels in just six weeks in a landmark human clinical study on 49 middle-aged American women.

Astaxanthin is an extremely potent antioxidant as well as a safe & natural anti-inflammatory. When an Astaxanthin capsule is ingested, it has been documented to get throughout the entire body. Over the period of about one to two months of daily use, Astaxanthin concentrates in our blood, our muscles, in organs such as eyes, brains, hearts and livers, as well as in the body's largest single organ—the skin. As it concentrates in these organs, it protects them on a cellular level against damage to DNA and to the cells' mitochondria. The outcome for skin: Natural Astaxanthin protects skin cells against UV damage and aging, while at the same time it improves our skin's appearance by enhancing the cells' health status. Because of Astaxanthin's clinically validated health benefits for skin (as well as all the other organs mentioned above), it is perhaps the very best nutrient for anyone over the age of 40 to take on a daily basis. And even people under the age of 40 should consider Astaxanthin as a great preventive supplement to protect against the damaging effects of UV exposure to the skin and eyes (as well as all of its other preventative benefits for our bodies).

In order to fully understand Astaxanthin's benefits for our skin, we will look at a variety of human clinical studies on Astaxanthin alone as well as a few that were done in combination with other active ingredients. We will also cite relevant pre-clinical research in animals and test tubes that corroborate the human studies. Finally, we will examine Astaxanthin's cell-protective characteristics: We'll look at how it protects our DNA and the powerhouse of the cell, the mitochondria. And we'll devote an entire chapter to each of Astaxanthin's foundational blocks from which all of its health benefits including skin health emanate: Its exceptional antioxidant strength and its safe and natural anti-inflammatory abilities.

# Skin Health Benefits of Natural Astaxanthin

England's second most widely-read newspaper, the *Daily Mail*, reported back in 2011 that Gwyneth Paltrow and Heidi Klum were taking Natural Astaxanthin capsules to help their skin look healthy and beautiful as they got a little older. The article is titled "Extended life pill: 'Miracle supplement' promises to fight the signs of aging." The article says that Natural Astaxanthin:

- ✓ Fights wrinkles
- ✓ Improves skin elasticity
- ✓ Reduces visible signs of aging within four to six weeks of use
- ✓ Maintains a youthful appearance
- ✓ Reverses premature signs of aging
- ✓ Reduces the risk of skin cancer (Rawi, M., 2011)

A few years before this article in England's Daily Mail appeared, *Allure Magazine* ran an article called "Madonna's Fishy Fountain of Youth." This article cited best-selling author Nicholas Perricone, MD, a dermatologist who has written several books about health, some of which have landed on the New York Times' best-seller list. In fact, his book *The Perricone Promise: Look Younger, Live Longer in Three Easy Steps* with a three-page chapter about Astaxanthin even hit the #1 best-seller spot. Here we excerpt from the *Allure Magazine* article:

"Contrary to rumors that she's gone under the knife, Madonna's youthful appearance is due to something a lot fishier: Salmon. While only her personal chef knows for sure, to many in the anti-aging industry, it's obvious why she'd be stocking up on salmon, and why we should too: 'Wild salmon is an outstanding source of Natural Astaxanthin, a unique and multi-talented antioxidant,' says Nicholas Perricone, MD, author of *Ageless Face*, *Ageless Mind* and one of salmon's biggest cheerleaders. 'It's a superstar in the realm of anti-aging foods. Astaxanthin is shown to improve skin elasticity and reduce the appearance of fine lines,' he says. It also helps 'endurance and recovery following vigorous exercise'—key for Madonna who spends hours each day working out.

Now, before you dig in, make sure the salmon you're eating is wild, since only wild salmon is rich in Astaxanthin (Matlin, J. 2009)."

The basis for these stars and famous doctors using and recommending Natural Astaxanthin for improving skin health and appearance is not Hollywood hype, rumor or fiction; it's based on medical research studies that began back in the 1990's and remain ongoing today. The benefits of Natural Astaxanthin for skin are multi-fold based on a great variety of research. In fact, these benefits can be separated into three distinct categories:

- Internal Beauty Pill: First of all, as amazing as it may seem, the daily internal consumption of 4mg – 6mg of Natural Astaxanthin can improve the appearance and the quality of skin in four to six weeks.

- Skin Health Defender: Secondly, Astaxanthin has demonstrated that it not only can improve the appearance and quality of the skin, but it can also improve the health of the skin as well.
- UV Protectant: The last category is actually closely related to the first two: After Astaxanthin has had time to accumulate in the skin, it has demonstrated a protective effect against the ongoing ravages from ultraviolet light exposure.

# Internal Beauty Pill

One of the most amazing attributes that Astaxanthin has demonstrated is that it can improve the quality and appearance of the skin when taken internally. A landmark clinical trial done in the USA in 2006 reported that Natural Astaxanthin has several different benefits for skin quality and beauty. In this study, 49 middle aged women were divided into two homogenous groups based on several factors including their skin types, ages and measurement of skin parameters such as moisture levels. The subjects in the treatment group took 4mg of Natural Astaxanthin per day and the other group took a similar-looking placebo. The study was conducted over six weeks. Skin parameters were measured at the beginning of the study, in the middle after three weeks of supplementation, and finally at the end of the study after the sixth week. One of the most impressive factors in this study is how diligently the results were measured:

- ✓ Skin surface was photographed and results published within the study
- ✓ Fine lines and wrinkles were inspected by a dermatologist
- ✓ Skin elasticity was measured using Dermalab® (an instrument used for skin analysis)
- ✓ Skin moisture content was measured using Dermal Phase Meter 9003™ (a different skin analysis instrument)
- ✓ Skin elasticity and skin dryness were inspected by a dermatologist (in addition to the measurement methods above)
- ✓ Subjects answered a Yes or No Questionnaire at the end of the study which covered:
  - Fine lines and wrinkles
  - Elasticity
  - Roughness
  - Dryness
  - Moisture content

Regardless of how the effect of Astaxanthin supplementation was measured in all of the different tests above, the results were extremely positive. The instruments used to measure skin quality, the comparisons by a dermatologist, the before and after photos as well as the subjects' answers to questionnaires all indicated that Natural Astaxanthin supplementation had made these women's skin more beautiful:

- In the self-assessment (questionnaire), over 50% of the subjects taking Natural Astaxanthin rated improvements in all areas!
- Dermatologist assessment found improvements in all areas tested: Fine lines and wrinkles, elasticity and dryness.
- Dermatological clinical instruments recorded improvements in both parameters tested: Moisture content and elasticity.
- Before & after photos showed visible improvements in fine lines, wrinkles and elasticity.

This study found that, as an internal beauty pill, Natural Astaxanthin fights wrinkles, improves skin elasticity, increases skin moisture levels, reduces visible signs of UV-aging within four to six weeks of use and helps maintain a youthful appearance (Yamashita, 2006).

Additional human clinical studies in this same area of internal beauty have been performed. A group of researchers from Japan combined two separate human clinical trials into a single publication. They tested Natural Astaxanthin in men at 6mg per day in one of the studies, while in the other study they examined the effects of a combination internal/external Astaxanthin program in women. Both of these studies featured a variety of measurement criteria using dermatological instruments. At both the beginning and end of the supplementation period, the subjects' skin was tested after washing their faces and allowing the skin to settle after a fifteen minute seated resting period.

The study with male subjects was randomized, double-blind and placebo-controlled with 36 volunteers participating. The men in the treatment group took 6mg of Astaxanthin each day for six weeks. At the end of six weeks, several statistically significant results were noted:

- Reduced volume ratio of all wrinkles
- Reduced area ratio of all wrinkles
- Increased skin elasticity of crow's feet area
- Improved transepidermal water loss (this is the quantity of water that passes through the skin to the surrounding atmosphere)
- In addition, two parameters showed a tendency toward improvement:
  - Skin moisture levels of the cheeks at  $p=0.08$
  - Sebum oil of the cheeks at  $p=0.085$

The study with female subjects was an open-label study involving 30 healthy adult volunteers for eight weeks. Significant improvements were observed by combining 6mg per day oral supplementation and 2 ml (78.9  $\mu\text{M}$  solution) per day topical application of Natural Astaxanthin:

- Deepest point of the deepest wrinkle decreased
- Mean depth of the deepest wrinkle decreased
- Maximum width of the deepest wrinkle decreased
- Mean depth of all wrinkles decreased
- Skin elasticity of crow's feet area improved
- Visual age spots were reduced
- Visual rough skin improved
- Mean depth of skin texture decreased
- Total area of corneocyte (the outermost part of the epidermis) increased
- Additionally, in ten of the subjects who started with dry skin, a significant increase in skin moisture levels was found

It's interesting to note that both the internal study as well as the combination internal/topical study yielded a variety of statistically significant results. The women's study lasted two weeks longer than the men's study and took the "inside/outside" approach, yielding positive effects in a larger variety of beauty and skin health parameters. Because there were two major differences between the men's and the women's studies, we cannot be sure whether the additional two weeks led to more profound results or the topical application of Astaxanthin caused the greater variety of positive results. Most likely, both of these factors helped. (It's important to note that we've

seen above that Astaxanthin alone used internally results in visual skin improvement, and we'll see later in this paper that Astaxanthin used alone topically also leads to skin improvement.) The researchers' final verdict: "In conclusion, these results suggest that Astaxanthin derived from *Haematococcus pluvialis* can improve skin condition in all layers such as the corneocyte layer, epidermis, basal layer and dermis" (Tominaga, et al, 2012).

There are some excellent pre-clinical trials backing up these human studies:

- The first we'll look at was an in-vitro study of human skin cells. This study exposed the skin cells to UVA radiation and found that introducing Astaxanthin to the cells improved their viability. The researchers concluded: "We hypothesize that Astaxanthin would have a significant benefit on protecting against UVA-induced skin photo-aging such as sagging and wrinkles" (Suganuma, et al, 2010).
- An excellent study done this year again looked at the effects of ultraviolet radiation on human skin cells, this time examining both UVA and UVB and specifically how they manifest in wrinkling. Astaxanthin successfully inhibited damage from both UVA and UVB. This study elucidated the mechanism of action for Astaxanthin as an anti-wrinkling agent against UVB: It suppresses the secretion of "wrinkle-inducing cytokines interleukin-1a and granulocyte macrophage colony stimulating factor in UVB-exposed epidermal keratinocytes" (Nakajima, et al, 2016).
- In addition to helping prevent signs of photo-aging and wrinkling, Astaxanthin has shown potential against skin hyper-pigmentation. Hyper-pigmentation can be an unsightly problem as we age when it is irregular, as evidenced by a common occurrence associated with getting older: Age spots. In a model of skin pigmentation done in Japan, Astaxanthin was found to dose-dependently inhibit the stem cell factor-associated stimulation of pigmentation. In fact, at the highest dosage, Astaxanthin was found to almost completely inhibit this pigmentation (Nakajima, et al, 2012).
- A second study proclaimed Astaxanthin to be "a new candidate for a potent anti-pigmenting substance that avoids the risk of hypopigmentation" (Imokawa and Ishida, 2014). In other words, unlike other potent anti-pigmenting agents which may lead to loss of skin color, Astaxanthin can help prevent increased pigmentation of the skin without the risk of losing skin color.

# **The Synergistic Effect of Astaxanthin**

Four different human clinical trials have each shown that Astaxanthin can work in tandem with one or two other natural ingredients to improve the beauty of the skin from the inside out. The first was a placebo-controlled study done in Japan; it combined Natural Astaxanthin with an excellent natural derivative of Vitamin E called “tocotrienols.” Astaxanthin was used at 2mg per day and tocotrienols at 40mg per day; the capsules were given to women aged 38 - 42 with dry skin. This study was only conducted over four weeks, yet excellent results were found in the treatment group including a statistically significant increase in skin moisture levels, improved skin elasticity and a reduction in fine wrinkles and pimples (Yamashita, E., 2002).

Astaxanthin also worked in combination with collagen on 44 subjects who were fed 2mg per day of Astaxanthin and 3gm per day of collagen hydrolysate (or a placebo) over the course of 12 weeks. Several different parameters showed statistically significant improvements:

- Elasticity of facial skin
- Hydration of facial skin
- Appearance of new collagen fibers
- Inflammatory markers (Yoon, et al, 2014)

A product called “Estime” was developed in Switzerland as an internal beauty formula featuring 5mg of Natural Astaxanthin in each capsule along with omega-3 fatty acids, marine proteins, natural tocopherols and plant flavonoids. The treatment group in this study experienced continuous and significant improvement over the three-month course of the study. Before and after photos showed visible improvement to the skin’s appearance and reduction of fine wrinkles. Additionally, an increase in dermis density of up to 78% was found in the treatment group as well (Beguin, A., 2005).

Lastly, a study done in Canada on a product containing Astaxanthin along with omega-3 fatty acids and marine glycosaminoglycans showed benefits for both skin hydration and skin elasticity (Thibodeau, A., 2004).

The conclusions we can draw from the human clinical studies on Astaxanthin in combination with other ingredients would not in and of themselves substantiate Astaxanthin’s positive effects as an Internal Beauty Pill; however, the fact that Astaxanthin is the sole ingredient found in all four of these studies lends additional credence to its beauty-enhancing potential.

# Skin Health Defender

Skin cancer is one of the fastest growing diseases in the world today, ranking right at the top with age-related neurological disease and diabetes. In an extremely interesting study, Natural Astaxanthin has shown that it is more effective than Synthetic Astaxanthin in inhibiting skin cancer in rats. In fact, the natural forms tested were effective in reducing UV-induced tumor incidence by 96% and 88%, while the synthetic form only attained 66%. Other markers tested were also much more positive in the Natural Astaxanthin groups. The researchers hypothesized that “the better anti-cancer potency of Natural Astaxanthin could be due to increased bioavailability” (Rao, et al, 2013).

In research that is extremely relevant to several aspects of our discussion in this paper, Astaxanthin showed anti-cancer potential in a mouse study which used UV radiation to induce carcinogenesis. This study tested two other carotenoids in addition to Astaxanthin. The results showed that, while both Astaxanthin and beta-carotene showed cancer preventative properties, lycopene had no effect (Black, 1998).

An excellent study was published earlier this year on atopic dermatitis, a common chronic inflammatory skin disease that is caused by several different factors such as allergic reactions to certain substances that come in contact with the skin or immunological abnormalities. Due to Astaxanthin’s known anti-inflammatory activity, researchers in Japan tested its effects in a mouse model of atopic dermatitis. After 26 days of supplementation, the mice in the treatment group had many significant results. In fact, all ten of these parameters decreased in the mice supplemented with Astaxanthin:

- Clinical skin severity score
- Spontaneous scratching
- Immunoglobulin E levels
- Number of eosinophils (a type of white blood cell) in the skin
- Total mast cells and degranulated mast cells in the skin
- Messenger RNA
- Protein levels of eotaxin
- Macrophage migration inhibitory factor
- Interleukins 4 and 5
- L-histidine decarboxylase

The variety of statistically significant results for this common skin disease in this mouse model is extremely promising. The researchers concluded: “These results suggest that Astaxanthin improves dermatitis and pruritus in atopic dermatitis via the regulation of the inflammatory effects and the expression of inflammatory cytokines (Yoshihisa, et al, 2016).

Collagen is a major component in human skin. It is the most common protein found throughout the human body, but it is consummately important to skin health. When we see unhealthy signs in people’s skin as they age such as wrinkles and age spots, this is a sign that collagen is

breaking down. In fact, age is not the only factor that can adversely affect collagen; excessive UV exposure and some diseases can also result in decreased collagen. Collagen helps maintain good skin elasticity and helps keep it wrinkle-free. Our bodies produce collagen naturally, so keeping collagen production going strong is a great way to keep your skin healthy and give it a youthful appearance.

In a very promising cell study, researchers examined a variety of antioxidants and chose Natural Astaxanthin as a viable example for repairing oxidative stress-induced skin damage. They used human skin cells as the subject matter, and then treated the cells with an oxidative substance. By introducing Astaxanthin into these oxidizing cells, the collagen concentrations increased. The addition of Astaxanthin led to an increase in the expression of certain proteins that promote cell proliferation and vascular endothelial growth factor. This study compared the effects of Natural Astaxanthin with doxycycline (a common antibiotic) and found that Astaxanthin is a better alternative for collagen production (Chou, et al, 2016).

Lastly, in an area of research that is related to most of the benefits we'll examine throughout this paper and which we'll describe in more detail later, Astaxanthin was shown to be effective against DNA damage in skin cells. In this particular study, benefits were found in three separate skin components. DNA damage is commonly considered a root cause of carcinogenesis. This led the researchers to theorize that Astaxanthin may be useful in preventing the formation of skin cancer (Lyons and O'Brien, 2002).

# UV Protector

A US patent for the use of Astaxanthin as an internal sunscreen was awarded in 2002 (US Patent #6,433,025, 2002). The company that holds this patent sponsored a clinical trial to test if Natural Astaxanthin can increase the amount of time it takes for UV light to cause sunburn. This trial dosed subjects at 4mg per day and the trial lasted for only two weeks. Yet, at the end of this very short supplementation period, subjects taking Astaxanthin showed a statistically significant increase in the amount of time it took to cause erythema (reddening of the skin or sunburn). This is extremely promising at this low dose and for such a short period of time; it would be extremely interesting to see what results a larger dose over a significantly longer trial period would yield (Lorenz, T, 2002; Capelli and Cysewski, 2014).

Pre-clinical research has also shown that Astaxanthin can effectively protect skin from the ravaging effects of UV exposure. There have been several studies on UV exposure and the end result of this exposure, photo-aging. An early study using hairless mice measured the effects of Astaxanthin as well as beta-carotene and retinol in preventing UV damage. Astaxanthin performed better than beta-carotene either by itself or in combination with retinol. In fact, it was extremely proficient at preventing photo-aging of the skin (Savoure, et al, 1995).

In addition, Astaxanthin was found to be effective in protecting skin cells from UV-induced oxidative stress. In fact, an early study demonstrated in-vitro that Astaxanthin is 100 times stronger than beta-carotene and, remarkably, 1000 times stronger than lutein in protecting cells against UVA light-induced oxidative stress (O'Connor and O'Brien, 1998).

Many other studies corroborate these early findings:

- In a study we cited in the “Internal Beauty Pill” section above, Astaxanthin showed excellent results in-vitro in human skin cells exposed to UVA. This led to the conclusion that Astaxanthin would have significant benefits on protecting against UVA-induced skin photo-aging such as sagging and wrinkles (Suganuma, et al, 2010).
- Another study cited above examined Astaxanthin’s effects on both UVA and UVB and found it successfully inhibited damage from both of these forms of radiation (Nakajima, et al, 2016).
- Astaxanthin was found to have superior photo-aging preventive properties when compared with other carotenoids such as beta-carotene and canthaxanthin in-vitro. “Astaxanthin exhibited a pronounced photoprotective effect and counteracted all of the above-mentioned UVA-induced alterations to a significant extent...The data indicate that the oxo-carotenoid Astaxanthin has a superior preventive effect toward photo-oxidative changes in cell culture” (Camera, et al, 2009).
- Astaxanthin successfully protected against UV-induced inflammation by decreasing inducible nitric oxide and the Cox-2 enzyme in-vitro. This helped in reducing cell death of skin cells (Yoshihisa, et al, 2014).

# **Topical Effects of Astaxanthin**

Based on several studies, it appears that Astaxanthin may work not only as an internal beauty pill, but also as a topical ingredient for skin health and beauty. While the main focus of our present discussion is the internal use of Natural Astaxanthin, we will briefly cite the research done on topical application as we feel it is relevant and closely tied to Astaxanthin's anti-inflammatory and antioxidant properties (which we'll discuss in detail below).

1. In a human clinical trial, Astaxanthin applied topically to skin showed a wrinkle-reducing effect (Taisuke, et al, 2001).
2. In exploration done at Japan's Kose Corporation, Astaxanthin was compared to other common cosmetic ingredients that are used to protect skin from sun damage. The researcher's conclusion was that Astaxanthin shows greater potential than the other ingredients against premature signs of aging (Arakane, K, 2002).
3. A study done on hairless mice which were irradiated with UVB to induce photoaging examined Astaxanthin's effects on wrinkle formation, skin elasticity, collagen fiber bundles and the level of MMP-1 (matrix metalloproteinase-1) activity. The results indicated that Astaxanthin exhibits superior protection against photoaging as a reactive oxygen species scavenger (Mizutani, et al, 2005).
4. Astaxanthin used topically in mice and in-vitro exhibited properties indicating that it may be effective in treating patients with allergic skin conditions (Kim, et al, 2015).
5. An Astaxanthin liposome product applied topically prevented UV-induced skin damage and inhibited melanin production (Hama, et al, 2012).
6. Finally, a very interesting study in mice showed that eye drops with Astaxanthin prevented UV damage to the eyes (Lennikov, et al, 2012).

# **Protection of our Cells by Astaxanthin**

The most obvious ways that Astaxanthin protects the cells in our bodies are through its antioxidant and anti-inflammatory activity. These are in-depth topics that we've reserved for the last chapters of this paper. And as we mentioned above, these two properties are at the very root of all the health benefits that Astaxanthin bestows on consumers. But there are also many studies on two very important components of our cells showing that Astaxanthin has a protective effect: These two components are DNA and the cells' powerhouse, the mitochondria.

**Prevention of DNA Damage.** DNA is the main constituent of chromosomes in all living organisms. It carries genetic information which makes us who we are. Damage to DNA has profound implications to our cells; in fact, when DNA is damaged, it can have grave effects up to and including development of a cancerous cell line (Moorhead, et al, 2005). For our present discussion on skin health it's very important to note that UV damage to DNA in our skin is a root cause of basal cell carcinoma, squamous cell carcinoma and melanoma, the three major types of skin cancer. A supplement that can help prevent DNA damage is certainly a powerful preventive medicine to keep our skin healthy and potentially protect against skin carcinogenesis.

For our discussion of how Natural Astaxanthin can prevent DNA damage, let's look at important research of two noted carotenoid researchers from Washington State University, Dr. Boon Chew and Dr. Jean Soon Park. They hold a patent on preventing DNA damage from oxidation through the use of Astaxanthin. As amazing as this may seem, the findings from their research show that supplementing with only 2mg of Natural Astaxanthin each day over four weeks can reduce DNA damage by approximately 40% (Chew and Park, 2006). This is really a phenomenal result—in only one month and at an incredibly low dosage level of only 2mg per day, Natural Astaxanthin can effectively prevent DNA damage by close to half.

In addition to their patent, Drs. Park and Chew published a randomized, double-blind, placebo-controlled human clinical trial in 2010 that outlines the effects of 2mg of Natural Astaxanthin supplementation on several parameters including oxidative stress, inflammation, immune response as well as DNA damage. This study concluded that “dietary Astaxanthin decreases a DNA damage biomarker and acute phase protein, and enhances immune response in young healthy females” (Park, et al, 2010).

While the research of Drs. Chew and Park is excellent and clearly demonstrates Astaxanthin's prevention of DNA damage, one wonders how much damage could be prevented over a longer period of time than just one month as Astaxanthin accumulates throughout the cells in our bodies. And it would be very interesting to see how Astaxanthin performs on DNA damage at a dosage level toward the 12mg per day upper end of the recommended range. We suspect that the effect would be much more pronounced than the 40% result that was found at 2mg per day for one month.

**Supporting Pre-Clinical DNA Research.** In addition to the human research done by Drs. Chew and Park, a flurry of pre-clinical studies has been performed related to DNA damage over the last ten years. The focus of many of these studies is in areas other than skin health; yet the common element in each is that Astaxanthin appears to have a protective effect on DNA:

- Astaxanthin enhances a DNA repair enzyme and is a novel candidate for cancer prevention (Kavitha, et al, 2013)
- Astaxanthin improves oxidative stress and DNA damage in rats (Tripathi and Jena 2010)
- Astaxanthin inhibits cytotoxic and genotoxic effects and restores DNA damage in mouse cells (Tripathi and Jena, 2008)
- Astaxanthin protects against DNA damage in human neuroblastoma cells (Santocono, et al, 2007)
- 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 (Dong, et al, 2013)
- Astaxanthin may protect against oxidative impairment and DNA damage (Zhao, et al, 2011)
- Astaxanthin shows a neuroprotective effect in rat retinal cells and aids against oxidative stress, glutamate stress and DNA damage (Yamagishi and Aihara, 2014)
- Astaxanthin modulates age-associated mitochondrial dysfunction in dogs which is attributed to alleviating oxidative damage to cellular DNA and protein (Park, et al, 2013)
- Astaxanthin reduces DNA damage in rat liver cells (Turkez, et al, 2014)
- Astaxanthin heightens the immune response and reduces DNA damage and inflammation in dogs (Chew, et al, 2011)
- Astaxanthin protects retinal cells against oxidative stress and reduces an indicator of DNA damage in mice (Nakajima, et al, 2008)
- Astaxanthin reduces DNA damage in UVA-irradiated cells (Santocono, et al, 2006)

**Astaxanthin's Effects on the Mitochondria:** Mitochondria are commonly known as the “powerhouse of the cell.” To put it simply, mitochondria are responsible for energy production in our cells. As with all other cells in our body, the health of skin cells is dependent on mitochondrial function.

“Looking at cellular metabolism at the mitochondrial level and how their improper function can have negative ramifications on skin health allows for a unique perspective on how skin changes throughout time (intrinsically) and when exposed to different conditions (extrinsically). Currently, the skincare industry is engaged in research to determine the best ways to harness mitochondrial functions for use in the fight against premature aging and skin cancer, and to provide clues on winning the ongoing quest for healthy, youthful skin...Due to the prominent role of mitochondrial function in both intrinsic and extrinsic aging, the skincare industry is actively looking into the many ways mitochondria might play a role in skin health and anti-aging specifically” (Veljkovic, I., 2013).

There is already a great deal of research on how Astaxanthin can protect and benefit the mitochondria. We'll briefly review some of the most relevant of these studies here:

- In perhaps the earliest study on Astaxanthin's effects on the mitochondria, Japanese researchers at Kochi Medical School found that Astaxanthin protects the mitochondria of rats better than a-tocopherol (Kurashige, et al, 1990).
- In a study done at Washington State University under the auspices of the famous carotenoid researcher Boon Chew, PhD, Astaxanthin prevented age-related mitochondrial dysfunction in dogs (Park, et al, 2013).
- Astaxanthin extended the lifespan of *C. elegans* (a model organism used in longevity studies) by protecting the mitochondria and the nucleus of the cells (Yazaki, et al, 2011).
- In a study done at University of Pittsburgh's School of Medicine, Astaxanthin protected against mitochondrial dysfunction and reactive oxygen species in a mouse model of Parkinson's disease and also in-vitro (Lee, et al, 2011).
- Astaxanthin can protect mitochondria that are subjected to oxidative stress. This study's abstract summarized the study very well:

“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 neurodegeneration and lifestyle-related diseases. Effective antioxidants thus offer great therapeutic promise...Astaxanthin at nanomolar concentrations was effective in maintaining mitochondria in a reduced state. Additionally, Astaxanthin improved the ability of mitochondria to remain in a reduced state under oxidative challenge. Taken together, these results suggest that Astaxanthin is effective in improving mitochondrial function through retaining mitochondria in a reduced state” (Wolf, et al, 2009).
- Astaxanthin was found capable of protecting the mitochondrial membrane and preventing DNA damage and cell-death in-vitro in a university study done in Taiwan (Chan, et al, 2009).
- Cells subjected to heat stress in-vitro were protected by Astaxanthin, which the researchers attributed to Astaxanthin's positive effect on the mitochondria (Kuroki, et al, 2013).

# **The World's Strongest & Highest Quality Natural Antioxidant**

Astaxanthin has been tested head-to-head in many experiments on antioxidant strength against several other carotenoids and antioxidants; it has consistently come out as the very strongest of all natural antioxidants in these tests regardless of the type of test. For example, whether examining free radical elimination or singlet oxygen quenching, Astaxanthin's power as an antioxidant comes out far beyond the capacity of other antioxidants. This is really amazing when you think about it, since many of the antioxidants Astaxanthin has been tested against are closely related molecules in the carotenoid family. Yet Astaxanthin usually comes out superior by at least a power of ten. And when comparing with vitamin antioxidants such as Vitamin C and Vitamin E, Astaxanthin has been shown to be as high as 550X to 6000X stronger!

Yet, as we'll examine below, it is not only that Astaxanthin is so much stronger than other antioxidants that makes it unique; Astaxanthin also has four remarkable qualitative properties that demonstrate its superiority over other antioxidants. When taking together both its quantitative and qualitative properties, it quickly becomes crystal clear that Astaxanthin is the best antioxidant we can take to supplement our diets and would provide anyone with a healthy dose of preventative antioxidant protection, which of course will should to great benefits for our skin.

**Quantitative Differences Between Astaxanthin and Other Antioxidants:** As far back as the 1940's, scientists had discovered the antioxidant abilities of carotenoids and had isolated Astaxanthin as being extremely potent. Research in France in 1946 found that Astaxanthin and beta-carotene were both powerful antioxidants, with Astaxanthin being the stronger of the two (Herisset, A., 1946).

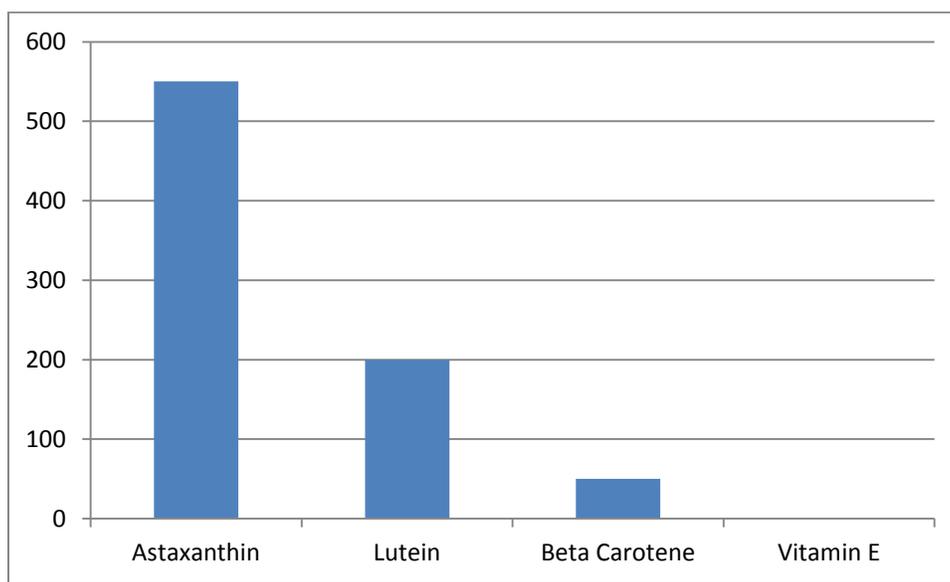
By the 1990's, Astaxanthin's powerful antioxidant activity was becoming widely accepted. A paper published in Japan in 1991 set the platform for the flurry of research that would follow:

“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 beta-carotene, and 100 times greater than a-tocopherol. Astaxanthin also has shown 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’” (Miki, et al, 1991).

Dr. Miki must have been extremely impressed to call Astaxanthin a “Super Vitamin E.” During that period in the early 1990's, Vitamin E was considered by many to be the most beneficial

nutrient for both topical application and internal consumption. However, in finding that Astaxanthin was 10 times stronger as an antioxidant than its carotenoid cousins and 100 times stronger than Vitamin E, he must have felt that it deserved such a venerable title.

Many other experiments have been done since Dr. Miki's, all with the same results—Astaxanthin remains the most powerful natural antioxidant found to date. The volume of studies is far too great to review in their totality in a paper of this scope, so we will look at a few of the most important studies which will enable our Readers to get a general idea of Astaxanthin's superior antioxidant strength. The first study we'll examine was also done in the 1990's and also in Japan. This study focused on singlet oxygen quenching. It pitted Astaxanthin against several other antioxidants including carotenoids such as lutein and beta-carotene, and it also tested Astaxanthin against Vitamin E. The results were heavily favored toward Astaxanthin; lutein got within the same realm as Astaxanthin in this particular test, but beta-carotene and particularly Vitamin E were far weaker than Astaxanthin.



Singlet Oxygen Elimination (Shimidzu, Goto, Miki, 1996)

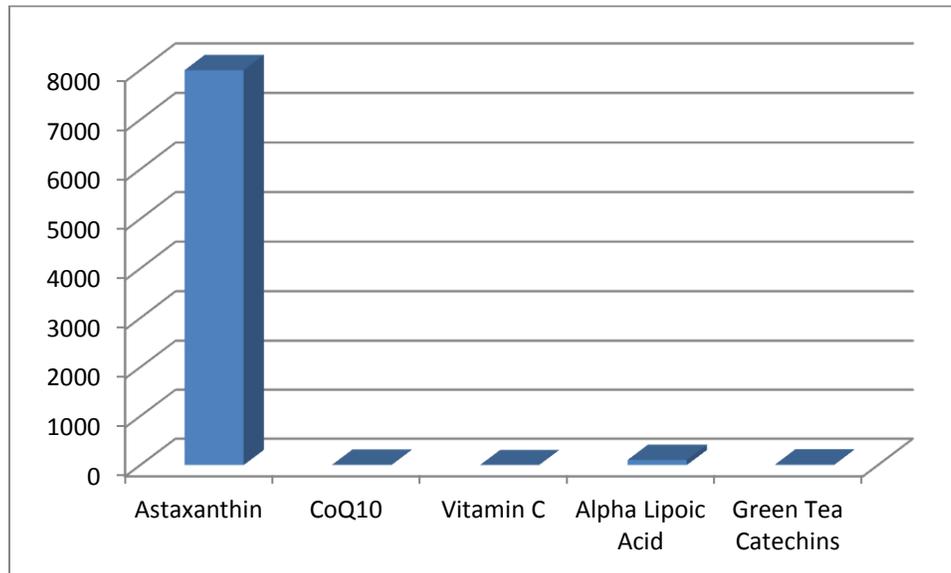
In singlet oxygen elimination, results of this study found Astaxanthin to be:

- 550 times stronger than Vitamin E
- 11 times stronger than beta-carotene
- 2.75 times stronger than lutein (Shimidzu, et al, 1996)

One of the authors of this study was Dr. Miki, the original researcher who did the oft-times quoted study from 1991 showing Astaxanthin to be phenomenally stronger than other antioxidants and calling it a “Super Vitamin E.” As a great fan of Astaxanthin, Dr. Miki participated in another study of Astaxanthin's strength against singlet oxygen many years later in 2007. This time they pitted Astaxanthin against a completely different set of antioxidants. The antioxidants evaluated in this study were Coenzyme Q10, green tea catechins, alpha lipoic acid

and Vitamin C. The main difference between this study and Dr. Miki's earlier work is that the results were even more slanted in Astaxanthin's favor.

Many people consider CoQ10 an excellent antioxidant. And among vitamins, Vitamin C is also fairly highly regarded as an antioxidant. Yet when tested against Astaxanthin for their ability to eliminate singlet oxygen, Astaxanthin wasn't just superior—it was incredibly more potent.



Singlet Oxygen Quenching (Nishida, Yamashita, Miki, 2007)

As you can see from the chart above, none of the other antioxidants were even remotely close to Astaxanthin's capacity to eliminate harmful singlet oxygen. The closest of the four was alpha lipoic acid, yet Astaxanthin was still 75 times more potent. Results showed that, in singlet oxygen quenching, Astaxanthin is:

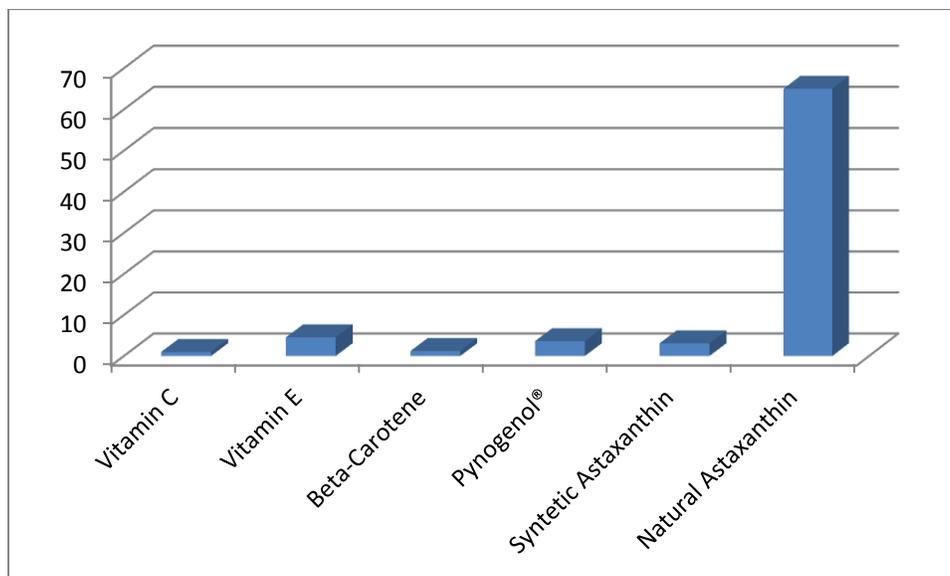
- 8000 times more potent than Vitamin C
- 800 times more potent than CoQ10
- 550 times more potent than Green Tea Catechins
- 75 times more potent than Alpha Lipoic Acid (Nishida, et al, 2007)

The last comparative antioxidant study we'll review was done at Creighton University by a leading antioxidant and nutritional supplement researcher, Debasis Bagchi, PhD. Professor Bagchi is very well respected in his field with almost 300 publications including several books and hundreds of peer-reviewed studies. Incredibly, Dr. Bagchi's work has been cited by his colleagues over 12,000 times.

When comparing antioxidants, it is very important to analyze them head-to-head and to test them in different experiments. A single test of, for example, Astaxanthin versus Vitamin E as a singlet oxygen eliminator is not a comprehensive view of the two different molecules' antioxidant capacity. Singlet oxygen molecules are without a doubt extremely harmful to our cells over

time, but they are just one of many different types of oxidants that wreak havoc in our bodies. The research in the 1990's focused primarily on Astaxanthin as a singlet oxygen eliminator, so Dr. Bagchi decided to look at Astaxanthin from a different angle: He tested Astaxanthin head-to-head against other well-known antioxidants by measuring their ability to eliminate free radicals in a very well designed experiment.

While this research was originally done in 2001, Dr. Bagchi and his co-author Dr. Gerald Cysewski had great foresight and decided to test both Natural Astaxanthin and Synthetic Astaxanthin in this study even though Synthetic Astaxanthin was not available at the time as a human nutritional supplement. He pitted the natural and synthetic versions of Astaxanthin against Vitamin E, Vitamin C, beta-carotene, and he also included the trademarked supplement Pycnogenol® in the mix as it was claiming to be an extremely powerful antioxidant in its marketing literature. Although this was a completely different way to measure antioxidant strength from the earlier Miki studies, and this set of antioxidants included two completely new molecules—Synthetic Astaxanthin and Pycnogenol®—Natural Astaxanthin again came out the undisputed champion with antioxidant strength ranging from 14X greater than Vitamin E to 65X greater than Vitamin C.



Free Radical Elimination (Capelli, Bagchi, Cysewski, 2013)

Natural Astaxanthin was again far more potent than all other antioxidants. The results showed that, in free radical quenching, Natural Astaxanthin is:

- 14X stronger than Vitamin E
- 18X stronger than Pycnogenol®
- 21X stronger than Synthetic Astaxanthin
- 54X stronger than Beta-Carotene
- 65X stronger than Vitamin C (Capelli, et al, 2013)

This university-based research led by one of the world's leading experts in the field did three very important things:

- ✓ It proved the consistency of Astaxanthin's superior antioxidant strength regardless of how it is analyzed.
- ✓ It quantitatively proved that Astaxanthin is much more potent than other antioxidants that were claiming to be extremely powerful at that time such as Pycnogenol®.
- ✓ It showed how incredibly different *Natural* Astaxanthin is from *Synthetic* Astaxanthin. (For a more detailed discussion of the differences between Natural and Synthetic Astaxanthin, please see Page 27.)

We see by the relationship between Astaxanthin and Vitamin E in the studies cited above how important it is to use more than one method of measuring antioxidant strength. In the singlet oxygen experiments in the 1990's, Astaxanthin was proven to be 550X stronger than Vitamin E. Yet, when Dr. Bagchi tested the two as free radical scavengers in 2001, Astaxanthin was shown to be 14X stronger. While 14X is still quite impressive, it is a far cry from 550X. So the question comes up as to which number is accurate. The answer is that both of these numbers are accurate, and Astaxanthin is 14 times better than Vitamin E in eliminating free radicals and 550 times better than Vitamin E in specifically eliminating singlet oxygen. It would be impossible to accurately give an exact number when comparing the two in "antioxidant strength," but if we had to, Dr. Miki's original estimate of 100X back in 1991 would probably be just about right. Which may be why Dr. Miki simplified things and started calling Astaxanthin a "Super Vitamin E."

**Qualitative Differences Between Astaxanthin and Other Antioxidants:** Astaxanthin is not only an incredibly powerful antioxidant, it is also a unique antioxidant in terms of how it works in our bodies. There are four distinct ways we can see these qualitative properties. While each of these independently would be a critical differentiator from other antioxidants in terms of health value and efficacy, the four of these taken together form a critical mass of evidence of Astaxanthin's superior qualitative antioxidant properties. Each of these on its own is very impressive, and while hard to pick the most important or least, below we list these qualitative differences in the order of their relative importance in our opinion:

1. **Spans the cell membrane to protect the entire cell:** A general rule of antioxidants is: "Lipid soluble antioxidants protect the lipid (oil) soluble part of our cells, and water soluble antioxidants protect the water soluble part of our cells." So when we ingest Vitamin C which is water soluble, its antioxidant properties are useful in one part of our cells, and when we ingest Vitamin E which is oil soluble, its antioxidant properties are useful in the remaining part of our cells. The unique shape of the Astaxanthin molecule allows it to span the cell membrane and have one end of the molecule in the lipid soluble part of the cell and the other end of the molecule in the water soluble part of the cell. This gives Astaxanthin the distinctive characteristic of being able to protect the entire cell. And Astaxanthin has been found capable of travelling throughout the entire body, into the bloodstream, muscle tissue, skin, as well as various critical organs (Capelli and Cysewski, 2014). This double feature of being able to get throughout the body and being

able to protect the entire cell makes Astaxanthin a super-effective antioxidant and anti-inflammatory for humans.

- 2. Never a Pro-Oxidant:** A lot of very good antioxidants can, under certain conditions, turn into oxidants and start harming our cells. This is what happened in the famous “Finnish Smokers Study” on beta-carotene published in the prestigious “New England Journal of Medicine” in 1994. This study tested consumption of synthetic beta-carotene, which (like Synthetic Astaxanthin) is completely different from the natural form. Heavy smokers (who were smoking on average three packs of cigarettes each day) were supplemented with synthetic beta-carotene and found after time to have a slightly higher incidence of cancer. This was amazing to all involved since dozens of epidemiological studies as well as pre-clinical research showed that beta-carotene has cancer-preventative properties (Moorhead, et al, 2005). What was happening was that the beta-carotene was turning into a pro-oxidant in the smokers’ bodies because smoking depleted their Vitamin C levels. In the absence of Vitamin C, the beta-carotene molecules had no supporting antioxidants to pass off the supercharged free radicals caused by smoking, so they “changed teams” and became oxidants. This caused additional cellular damage, which in turn increased the incidence of cancer (Heinonen and Albanes, 1994). “Without Vitamin C, beta-carotene can catch the destructive energy of a free radical and itself become a damaging molecule. In this situation, beta-carotene has entered a ‘pro-oxidant’ state. If Vitamin C is available this pro-oxidant state will quickly be converted back to an antioxidant state without damage to cells” (Malila, et al, 2006; Capelli and Cysewski, 2014).

Many other excellent antioxidants besides beta-carotene can become pro-oxidants under certain conditions. For example, well-known vitamin antioxidants such as Vitamins C & E, zinc, and even carotenoid antioxidants such as lycopene and zeaxanthin can all become pro-oxidants (Martin, et al, 1999). Fortunately, Astaxanthin can never become a pro-oxidant and cause damage to our cells (Beutner, et al, 2000).

- 3. Crosses the blood-brain barrier and blood-retinal barrier:** A lot of very good antioxidants cannot help protect our eyes and brains. Even carotenoid antioxidants that are closely related to Astaxanthin such as beta-carotene and lycopene cannot get through these barriers that are present to protect our most vital organs from foreign matter and contaminants. Since our brains are the control center for everything we think and do, an antioxidant that cannot protect the brain seems to be of little value to us. Fortunately, Astaxanthin can get through the blood-brain barrier to protect our brains. When it reaches our brains, it can then travel through the blood-retinal barrier to help protect our eyes. Some of the earliest research on Astaxanthin back in the 1940’s and 1950’s showed Astaxanthin’s ability to get into the brains and eyes of rats (Grangaud, 1951; Massonet, 1958); meanwhile, many human clinical studies have been completed over the last several years to confirm Astaxanthin’s diverse health benefits for the eyes and brain. And once present in the eyes and brain, it is not only Astaxanthin’s antioxidant activity that is working prophylactically, but also its broad spectrum anti-inflammatory properties are providing additional protection to these vital organs. This one-two punch against

oxidation and inflammation is exactly what brains and eyes need to stay healthy and function well.

4. **Bonds with muscle tissue:** As we mentioned above, Astaxanthin can get throughout the entire body and into all the critical organs. It can also bond with muscle tissue to protect muscles from increased levels of oxidation and inflammation and keep the muscles functioning smoothly.

If Astaxanthin only had one distinct advantage over other antioxidants, it would be unjustified to call it the “Highest Quality Natural Antioxidant;” however, with four important, documented advantages over more commonplace antioxidants, we feel it’s perfectly warranted and that Astaxanthin has earned this title. Coupled with its broad spectrum anti-inflammatory properties, it becomes clear that Astaxanthin is unquestionably the most useful antioxidant to consume as a dietary supplement and is highly recommended for everyone over the age of 40 as a preventative anti-aging supplement.

## **A Safe & Natural, Broad-Spectrum Anti-Inflammatory**

It is difficult to say whether Astaxanthin's anti-inflammatory properties or its antioxidant power is more important with regards to skin health; both create benefits that promote skin health and can help improve the skin's beauty and quality. Fortunately Astaxanthin is quite capable in both respects—as an antioxidant as well as an anti-inflammatory—which leads to a variety of distinct advantages for anyone approaching middle age or beyond.

Astaxanthin works as an anti-inflammatory through multiple pathways. The various mechanisms of action for Astaxanthin as an anti-inflammatory have been demonstrated in several studies (Lee, et al, 2003; Ohgami, et al, 2003; Choi, et al, 2008; Kishimoto, et al, 2010). This research has consistently shown that Astaxanthin works on a variety of different causes of inflammation. In fact, there is evidence that it works on six different inflammatory markers, but that it works in a gentle, broad-spectrum manner. This is in distinct contrast to anti-inflammatory drugs such as Celebrex® and Vioxx® as well as over-the-counter anti-inflammatories such as Non-Steroidal Anti-Inflammatory Drugs (NSAIDs including Tylenol®, Motrin®, Alleve®, etc.) and aspirin, all of which target a single inflammatory marker, but in an intense manner. Inflammatory markers gently reduced by Astaxanthin include:

- Prostaglandin E-2
- Interleukin 1b
- Interleukin 6
- Tumor Necrosis Factor-A
- Nitric Oxide
- Cox 1 & 2 enzymes (Lee, et al, 2003; Ohgami, et al, 2003; Choi, et al, 2008; Kishimoto, et al, 2010)

Natural Astaxanthin has never been reported to have any side effect or contraindication in hundreds of medical research studies as well as over 15 years of commercial consumer use. There are countless safety studies such as acute toxicity and chronic toxicity studies showing that Natural Astaxanthin is completely safe with absolutely no adverse side effects or contraindications (Capelli and Cysewski, 2014). Meanwhile, prescription anti-inflammatory drugs as well as over-the-counter anti-inflammatories all have serious side effects. Over-the-counter anti-inflammatory NSAIDs such as Tylenol, Motrin and Alleve can all cause serious liver problems, while aspirin can harm the stomach lining and cause ulcers. The prescription drugs such as Vioxx and Celebrex are even more dangerous; Vioxx was taken off the market several years ago after causing an increase in heart disease and premature death in many consumers, while Celebrex remains on the market albeit with extensive warnings about its potential for adverse cardiovascular events.

Natural Astaxanthin is completely different from these drugs. It takes significantly longer to work, but it has no side effects. The prescription and over-the-counter drugs can work the same day to combat pain, while Astaxanthin usually takes at least two and up to six or eight weeks to show effects; but once it starts working, users report that Natural Astaxanthin has the same

positive effects on painful inflammatory conditions as the anti-inflammatory drugs, but without any side effects.

In addition to several human clinical trials, two consumer surveys have validated Natural Astaxanthin's ability to combat painful inflammatory conditions. In fact, one of these consumer surveys asked users to compare Natural Astaxanthin's anti-inflammatory effects to prescription and OTC anti-inflammatories and found that Natural Astaxanthin has similar results to those non-natural drugs:

- A survey of people with joint, muscle or tendon pain found that:
  - 84% had positive results from using Natural Astaxanthin
  - 83% experienced less pain
  - 60% had increased mobility
  - When asked how Natural Astaxanthin's effects compared to other anti-inflammatories found in the drug store:
    - 75% said that Natural Astaxanthin works the same or better than over-the-counter pain medications such as aspirin, Tylenol, Alleve or Motrin
    - 64% said that Natural Astaxanthin works the same or better than prescription anti-inflammatories such as Celebrex or Vioxx (Capelli, et al, 2008).
- In a consumer survey of 247 Natural Astaxanthin users, “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” (Guerin, et al, 2002).

To summarize, it appears from these consumer surveys that Natural Astaxanthin works about as well as prescription and OTC anti-inflammatories. It does, however, take considerably longer to work. But the critical distinction is that Natural Astaxanthin has never been reported to have any side effects or contraindications—it is completely safe and natural—while OTC pain pills and prescription anti-inflammatories all have serious side effects under certain conditions, some that can end up killing you (Capelli and Cysewski, 2014). So the crucial decision is left up to the consumer: Do you want fast results that may end up seriously hurting you, or would you rather wait about a month for the same results and be safe and healthy?

**Astaxanthin's Anti-Inflammatory Mechanisms of Action:** Back in 2003, scientists working concurrently but independently in Japan and Korea were honing in on Astaxanthin's broad-spectrum mechanisms of action for combatting inflammation. Although they were not corresponding or sharing information, and even though they used very different paths to get there, both groups of researchers arrived at similar conclusions. This was the start, but other studies since then have further substantiated the early findings. Below is a summary of some of the most significant research in this area:

1. First Study Proving Mechanism of Action: Researchers at Japan's Hokkaido Graduate School of Medicine were the first to prove Astaxanthin's multiple mechanisms for controlling inflammation. They did their research in test tubes and also in rats, focusing on the rats' eyes. They found that Astaxanthin reduced three key causes of inflammation: Nitric oxide (NO), tumor necrosis factor alpha (TNF-a) and prostaglandin E-2 (PGE-2) (Ohgami, et al, 2003).
2. Second Mechanism of Action Study: Later the same year, Korean researchers working independently found similar results to the Ohgami study in vitro and ex-vivo. In harmony with the Ohgami results, they found that Astaxanthin suppresses the inflammatory mediators nitric oxide, prostaglandin E-2 and tumor necrosis factor alpha. But they also demonstrated Astaxanthin's positive effects on three other inflammatory markers: Interleukin 1B (IL-1b), COX-2 enzyme and nuclear factor kappa-B (Lee, et al 2003).
3. Further Validation: Several years later, scientists from Korea University further validated the earlier results finding broad-spectrum anti-inflammatory activity (Choi, et al, 2008).
4. "Remarkable" Results: Japanese researchers referred to Astaxanthin's anti-inflammatory activity as "remarkable" and found a statistically significant reduction in the six different inflammatory markers tested (Kishimoto, et al, 2010).
5. Inhibition of Mast Cells: Mast cells are the key initiators of inflammation. Research at Kyoto University showed an inhibitory effect of Astaxanthin in rats' mast cells (Sakai, et al, 2009).
6. In the most recent study in this area, Astaxanthin was found to be effective at protecting against UV-induced inflammation in a broad-spectrum manner. In fact, cell death that is frequently caused by UV exposure was significantly decreased in the Astaxanthin-treated cells (Yoshihisa, et al, 2014).

# Differences Between *Natural* Astaxanthin and *Synthetic*

It is extremely important to understand the vast differences between Natural and Synthetic Astaxanthin since this distant synthetically-produced cousin of Natural Astaxanthin is now being falsely promoted in the supplement industry as “Nature Identical.” Synthetic Astaxanthin has been used for many years in the animal feed industry, primarily to pigment the flesh of farm-raised salmon. While a full review of the vast differences between these two molecules would be too comprehensive for this paper, it is important that our Readers understand that these are two completely distinct molecules. In fact, other than sharing the same chemical formula, they are almost exact opposites in all other respects.

A critical finding of a landmark series of head-to-head antioxidant experiments is the clear superiority of Natural Astaxanthin to Synthetic Astaxanthin in antioxidant strength. In both university research at Creighton University under the auspices of acclaimed antioxidant researcher Debasis Bagchi, PhD as well as in independent laboratory testing at Brunswick Laboratories, Natural Astaxanthin extracted from microalgae was found to be a minimum of 20X stronger in antioxidant strength than Synthetic Astaxanthin produced from petrochemicals (Capelli, et al, 2013).

Briefly, the primary differences between Natural and Synthetic Astaxanthin are:

- **Shape:** The Natural Astaxanthin molecule’s stereochemistry is unique (it is shaped differently than the Synthetic Astaxanthin molecule).
- **Esterification:** Natural Astaxanthin is 95% esterified (it has a fatty acid molecule attached to either one or both ends of the molecule). Synthetic Astaxanthin is exclusively “free” Astaxanthin and does not have fatty acid molecules attached to it.
- **Synergy:** Natural Astaxanthin from *Haematococcus pluvialis* microalgae comes complexed in nature with supporting carotenoids. There are consistently small amounts of other antioxidant carotenoids such as lutein, beta-carotene and canthaxanthin ranging from 3% - 15% of the total carotenoid fraction which may provide a synergistic effect when ingested. Synthetic Astaxanthin does not contain supporting carotenoids.
- **Source:** Synthetic Astaxanthin is synthesized from petrochemicals in an elaborate process. Natural Astaxanthin is extracted from natural *Haematococcus pluvialis* microalgae.
- **Safety:** Natural Astaxanthin has an extensive portfolio of human safety studies and a history of over 15 years of safe use as a commercially-sold nutritional supplement. Synthetic Astaxanthin has never been directly tested in humans for safety. (This is an overriding concern due to serious safety issues with related synthetic carotenoids beta-carotene and canthaxanthin.)
- **Efficacy:** Amazingly and perhaps most importantly, Synthetic Astaxanthin has never been shown to have any health benefit in human clinical research. It is completely untested and may turn out to not have any health benefit at all (which leads to the logical

question as to why the company that released it to the human nutritional supplement market made this groundless decision). Meanwhile, Natural Astaxanthin has been shown to have diverse health benefits in approximately 100 different positive human clinical trials.

- **Antioxidant Strength:** To expand on what we mentioned above, Natural Astaxanthin is 20X stronger than Synthetic Astaxanthin as an antioxidant in scavenging free radicals. In another antioxidant head-to-head comparison, it was shown that Natural Astaxanthin is over 50X stronger than Synthetic Astaxanthin in singlet oxygen quenching.
- **Dosage:** In the event that Synthetic Astaxanthin is ultimately proven safe for long-range human consumption, dosages would logically be a minimum of 20 times greater than corresponding dosages of Natural Astaxanthin due to its vastly inferior antioxidant profile. This high dosage requirement would most likely put Synthetic Astaxanthin out of reach economically for most consumers (Capelli, et al, 2013).

With this brief analysis of these distant Astaxanthin cousins, we quickly see that Synthetic Astaxanthin is far inferior to Natural Astaxanthin. It is comparatively very weak as an antioxidant, and even more frighteningly, it has never been tested for safety or for health benefits in humans. Regardless of how Synthetic Astaxanthin is marketed, it is clear that it is absolutely not “Nature Identical.”

# Conclusion

The body of evidence for Natural Astaxanthin's benefits for skin health is quickly attaining critical mass. Research related to Astaxanthin as an Internal Beauty Pill; as a Skin Health Defender; and as a UV Protector all point us toward this conclusion. As the best example, the landmark human clinical trial on Astaxanthin's benefits for beauty improvement clearly indicates this: Taking 4mg per day of Natural Astaxanthin for six weeks made women's skin more beautiful from the inside out in a variety of ways.

How does Astaxanthin accomplish these feats? It has been documented to concentrate throughout our bodies over two to six weeks of steady supplementation, including reaching the skin. On a cellular level, Astaxanthin can protect our skin's cells extremely efficiently and from many different pathways. For one, it is very well documented as the world's strongest natural antioxidant. Yet it is not only Astaxanthin's supreme antioxidant power that makes it so effective, but also its four distinct qualitative properties which clearly separate it from other antioxidants as well.

In addition to its effectiveness in quenching singlet oxygen and other free radicals, Natural Astaxanthin is also a very safe and very effective anti-inflammatory that also uses multiple pathways to combat inflammation in our bodies and skin. It works more slowly than anti-inflammatory drugs; but fortunately it has never been shown to have any dangerous side effects or contraindications that the fast-working drugs all have.

And finally in our discussion of Astaxanthin on a cellular level, a great deal of research has been done showing benefits of Astaxanthin specific to key parts of our cells. It can prevent damage to DNA and protect the mitochondria, which are two additional valuable characteristics of this fascinating molecule in its quest to maintain skin cells functioning well and staying healthy.

Based on clinical studies, pre-clinical trials and a wealth of research showing how Astaxanthin protects cells in our bodies, we strongly recommend that anyone concerned with protecting their skin and improving its quality and appearance from the inside out should supplement with 4mg to 6mg of Natural Astaxanthin on a daily basis.

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