

Clinical Benefits of **Astaxanthin**

- Revitalizes photoaged skin by quenching oxidative stress and inflammation in all skin layers
- Reduces the size of wrinkles and improves skin microtexture
- Lightens age spots by inhibiting overproduction and oxidation of melanin
- Restores smoothness and reduces fine lines and wrinkles by improving the moisture retention of the skin surface cells
- Reduces chronic itching and rebalances the immune response in individuals with atopic dermatitis



Reveal Your Skin's Natural Beauty with Astaxanthin

hen wrinkles or skin problems arise, most women reach for cosmetic products, like creams, gels, ointments, and makeup. Applying these products to the surface of the skin may temporarily conceal the problem, but their effect is superficial and doesn't tackle the underlying causes. The skin is an extremely complex organ, consisting of multiple layers that each have unique and important functions. For a product to truly improve the skin's health and beauty, it must provide protection and support to all layers of the skin.

Our skin is under constant attack from free radicals produced by UV rays, pollution, stress, and poor nutrition. The damage caused by free radicals is a major cause of skin aging and problems such as wrinkles and age spots. This free radical damage affects all layers of the skin, from the visible surface to the delicate deep layers where new skin is formed.

Natural algae astaxanthin is a powerful antioxidant with potent anti-inflammatory effects. Its unique molecular structure allows it to reside in the cell membrane and to protect the inside and outside of cells from free radical attack. Research shows that astaxanthin taken as an oral supplement is active in each of the skin's layer, provides protection from UV damage, shrinks wrinkles, and makes age spots smaller. Natural algae astaxanthin can help your reveal your skin's natural beauty from the inside out.



A series of experimental studies conducted in Japan, Germany, and Italy show that astaxanthin can:

- 1. Increase the vitality of fibroblasts (collagen-producing cells) and keratinocytes by quenching reactive oxygen species (ROS) in all skin layers
- 2. Combat premature skin sagging by preventing enzymes breaking down elastin and collagen in the dermis
- 3. Boost the efficacy of vitamin C and vitamin E as dermal repair agents by neutralizing free radicals on the cellular membrane





linical studies conducted in Japan and the USA revealed that supplementation of natural astaxanthin extracted from *Haematococcus pluvialis* microalgae (4-12 mg daily) can produce visible cosmetic benefits after 4 weeks of treatment. Clinical studies also suggest that combined oral and topical treatment can enhance the efficacy and penetration of astaxanthin in all layers of the skin. Clinical studies have shown what astaxanthin can do:

- 1. Reduce the width, length, and depth of dermal wrinkles by inhibiting the degeneration of elastic fibers and the collagen network
- 2. Reduce epidermal wrinkles and skin roughness by improving the hydration capacity of the skin surface layer
- 3. Lighten age spots by inhibiting overproduction and oxidation of melanin after UV exposure
- 4. Reduce itchiness and inflammation in individuals with atopic dermatitis by rebalancing the immune response and reducing DNA damage and levels of catecholamine, a hormone that accelerates the breakdown of skin cells
- 5. Enhance skin vitality by preserving the transportation of vital nutrients to skin cells, waste removal from tissues, and antioxidant activity

Natural Astaxanthin Provides Protection from Aging in All Skin Layers

Stratum Corneum

The stratum corneum is the outermost layer of the epidermis and consists of corneocytes, which absorb and retain moisture. The stratum corneum forms a parrier that protects the underlying tissue. Pollution and ozone can disrupt the functioning of the stratum corneum, resulting in chronic irritation, inflammation, dryness, oil imbalance, fine wrinkles,

How does astaxanthin work in this layer?

Astaxanthin fights skin dryness and skin roughness

Epidermis

The epidermis consists mainly of keratinocytes, but it also contains melanocytes, immune cells, and inflammatory cells. The epidermis protects the skin and provides resilience. UVB increases melanin production and the transfer of melanin-containing organelles to keratinocytes. This induces inflammatory responses, causing redness and pigmentation. UVA induces the oxidation of pre-existing melanin, which can lead to irreversible dark pigmentation.

How does astaxanthin work in this layer?

Astaxanthin quenches over-production and oxidation of melanin

How does astaxanthin work in this layer?

Astaxanthin fights lines and wrinkles, and boosts fibroblast and collagen integrity against UV-induced damage

3

Dermis

The dermis consists of water, elastin, and collagen fibers, and it provides resilience and strength to the skin. The dense capillary network of the dermis provides energy and nutrition to the upper layers of the skin and supports healing. UVA breaks down collagen-proteins and elastin fibers, which destabilizes fibroblasts, causing dermal scars, deep wrinkles, sagging, and loss of resilience.

How does astaxanthin work in this layer?

Astaxanthin improves the supply of nutrients to skin tissues

Hypodermis

The hypodermis is the innermost and thickest layer of the skin and contains adipocytes and the vessels that provide nutrients to the dermis. Unhealthy diet, Smoking, Alcohol, Stress, and Medication: generate ROS, which reduce the antioxidant capacity of the cells in the hypodermis, increasing oxidative stress, lipid peroxidation, and the consequent deterioration of capillary integrity. This causes a decline in the supply of nutrients and oxygen, and prevents waste removal.



STRATUM CORNEUM

Astaxanthin Fights Skin Dryness and Skin Roughness

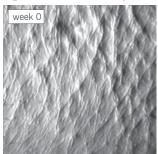
Toxic substances in the environment generate free radicals, which reduce the moisture retention of corneocytes and degrade sebum in the uppermost layer of the skin, known as the stratum corneum. Persistent oxidative stress causes chronic irritation, inflammation, and dryness of the skin surface¹.

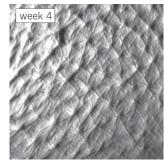
Clinical studies have shown that astaxanthin treatment improves visual skin roughness and oil imbalance in the stratum corneum². In a study involving 30 healthy women, topical astaxanthin serum and astaxanthin supplementation (6 mg daily) for 8 weeks, reduced transepidermal water loss (TEWL) and also improved the size of the corneocytes, thus increasing the moisture retention of the skin surface cells and leading to the improvement of skin roughness (Figure 1)². In another randomized double-blind study, 36 men were given either astaxanthin (6 mg daily) or a placebo for 6 weeks indicated that the sebum oil and TEWL in the astaxanthin group were decreased significantly². It is considered that the reduction of TEWL leaded to improve the sebum imbalance.

In another study, a serum containing either astaxanthin or a placebo was applied to skin roughened by tape stripping. Topical treatment with astaxanthin for 4 weeks promoted the development of the cornified envelope (CE), which is the primary skin barrier³.

In the astaxanthin-treated group, the CE matured as keratinocytes moved to the upper layer of the skin while they differentiated. However, in the placebo group the skin remained unhealthy because the CE remained immature, resulting in a rougher, more disordered skin layer.

Figure 1. Astaxanthin improved roughness of cheek skin²





Female participants (n=30, 20-55 years old) received 6 mg of astaxanthin supplement and applied astaxanthin topical product for 8 weeks. Skin topography of the participant's cheek was evaluated with replica by image analysis at the beginning, after 4 weeks and after 8 weeks of the clinical study. Photographs are the improvement example at week 4.



Clinical studies show that astaxanthin treatment improves the roughness, dryness, and sebum balance of the outermost layer of the skin. Objective parameters demonstrated that astaxanthin treatment reduces transepidermal water loss and increases the size of corneocytes, boosting the moisture retention and barrier strength of the skin surface.

Other clinical studies indicate that astaxanthin promotes skin smoothness through the healthy maturation of the cornified envelope, which forms the main protective barrier for the skin.

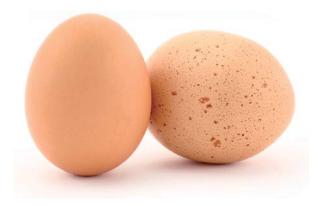
Astaxanthin reduces chronic itchiness and the rebalances immune response in patients with atopic dermatitis.



EPIDERMIS

Astaxanthin Quenches Over-Production and Oxidation of Melanin

Twenty minutes of sun exposure every day during summer is usually enough to cause DNA damage and the secretion of various inflammatory mediators in the epidermis. Persistent exposure to both UVB and UVA can lead to the overproduction and oxidation of melanin, which causes age-related pigmented spots or dark stains on the skin⁴. Furthermore, UVB-induced inflammatory mediators from epidermal cells disrupt fibroblast activity in the dermis, and promote the release of scissor-like collagen-digesting enzymes. Therefore, UVB also causes the degradation of dermal collagen and contributes to the formation of wrinkles⁵.



A pilot study conducted in Japan investigated the topical effects of astaxanthin on melanin-inhibition in participants exposed to UVB radiation. The participants were healthy men with skin type III, which tans, burns, and develops sunspots easily. Topical astaxanthin increased the speed at which inflammatory erythema caused by a single dose of the minimal erythema dose of UVB⁶. This clinical study supported previous *in vitro* findings suggesting that astaxanthin inhibited melanogenesis in both mouse study⁷ and *in vitro* study (Figure 2).

In 2012, AstaReal conducted a clinical study in which astaxanthin supplementation (6 mg daily) combined with topical application (2 mL daily) in 30 women significantly reduced the appearance of age spots on cheeks^{2,3}. The study showed that astaxanthin suppresses the secretion of two melanogenesis-promoting factors—prostaglandin-E2 and pro-opiomelanocortin—generated by keratinocytes exposed to UVB. A different study reported that astaxanthin may also suppress secretion of inflammatory mediators and cytokines by reducing NF-kB-activation upstream of the UVB-induced inflammatory reaction⁸.

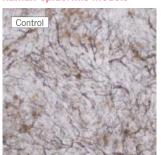
Some of the inflammatory cytokines produced by epidermal keratinocytes act on dermal fibroblasts through paracrine signaling. This promotes the expression of the enzyme matrix metalloproteinase-1 (MMP-1) by fibroblasts.

Therefore, inflammation in the epidermis disrupts the dermal elastic fibers⁵. In the study, astaxanthin indirectly suppressed MMP-1 expression in cultured fibroblasts via its anti-inflammatory effect on UVB-exposed keratinocytes³. Chronic activation of MMP-1 reduces the structural resilience of the connective tissues and results in premature sagging and wrinkling.

Experimental studies have shown that the topical application of astaxanthin can inhibit structural damage to

Figure 2. Astaxanthin inhibited melanin production in cultured human epidermis models

collagen fiber bundles after UVB exposure⁷.





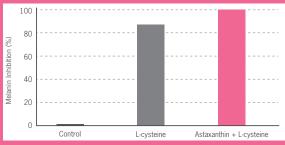
Medium for melanin production and astaxanthin were simultaneously applied to an epidermal model of melanocyte-containing three-dimensional culture, and the cells were incubated for the prescribed culture periods. After incubation, the level of melanin production was measured and compared with that of controls not treated with astaxanthin. (Photo: courtesy of AstaReal Co., Ltd.)

Synergetic Effect of Astaxanthin -1

Astaxanthin enhanced anti-melanin effect of L-cysteine

L-cysteine is known as a whitening agent. Since Astaxanthin inhibits melanin production, combined use of L-cysteine and astaxanthin shows stronger effect to skin whitening than single application of L-cysteine.

Comparison of melanin inhibition capacity







Medium for melanin production and the whitening agents were simultaneously applied to an epidermal model of melanocyte-containing three-dimensional culture, and the cells were incubated for the prescribed culture periods. After incubation, the level of melanin production was measured (Figure modified, photo: courtesy of AstaReal Co., Ltd.).

data: JP 2011-32171)



Clinical studies show astaxanthin can quench inflammatory responses and melanogenesis-promoting factors after UVB radiation and inhibit the oxidation of existing melanin. In particular, astaxanthin can greatly reduce the visual appearance and size of age spots and sunspots after 8 weeks of treatment.

Other studies show that astaxanthin alleviates the effects of UVB-induced inflammation on dermal fibroblasts by inhibiting the release of collagen-digesting enzymes. This suggests that astaxanthin can also suppress the UVB-induced degradation of dermal collagen and that it may inhibit the development of wrinkles.

3 DERMIS

Astaxanthin Fights Lines and Wrinkles

Long-term exposure of skin to UVA causes the breakdown of collagen and disrupts fibroblast activity in the dermis, leading to premature wrinkling, sagging, and loss of elasticity. Furthermore, UV radiation activates the transcription factor NF-kB, which stimulates cytokines that attract neutrophils. This causes the upregulation of MMP that then cleaves skin collagen and elastic fibers, causing the degradation of the dermal extracellular matrix.

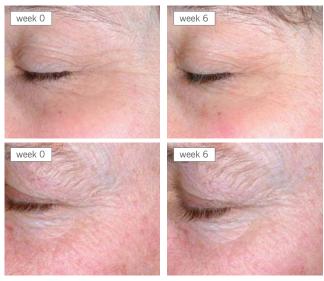
Various clinical studies have shown that astaxanthin has anti-wrinkle effects. In 2001, Fuji Chemical, the parent company of AstaReal, collaborated with Seki Dermatological clinic and Showa University School of Medicine to conduct a pilot study investigating the cosmetic efficacy of 3 weeks of treatment with cream containing astaxanthin (Figure 3)9. The study showed that women of various ages and skin types experienced a visible reduction in sagging of the skin under the eyes. The improvement in skin moisture content and retention in the outer canthus of the treated group was probably responsible for the large reduction in fine wrinkles in this delicate area.

Figure 3. Topical application of astaxanthin twice daily for 3 weeks improved skin sagging⁹



Healthy women (n=11) applied astaxanthin containing cream (0.2g X 2 /day) from under the eyes to the cheeks daily for 3 weeks. The skin moisture retention was measured before and after the 3-week application. Photographs show skin surface in the astaxanthin group at week 3 (photo: courtesy of AstaReal Co., Ltd.).

Figure 4. Taking 4 mg of astaxanthin daily for 6 weeks improved skin elasticity, firmness and wrinkles¹⁰



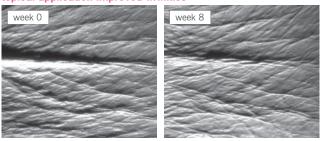
Healthy women (n=49) were randomly divided into 2 groups and received 0, 4 mg of astaxanthin daily for 6 weeks. Visual and numeral evaluations were performed at 0, 3 and 6 weeks respectively. Photographs show skin surface in the astaxanthin group at week 0 and week 6 (photo: courtesy of AstaReal Co., Ltd.).

In 2006, AstaReal conducted a single-blind, placebo-controlled study with International Research Services Inc., to investigate the effect of oral administration of astaxanthin (4 mg daily) on the skin condition of 49 middle-aged women with various skin types (Figure 4)¹⁰. In the sixth week of the study, the dermatologist's tactile and visual inspection of the skin and the self-evaluation questionnaire indicated a significant reduction in fine wrinkles and an improvement in skin suppleness in the participants treated with astaxanthin. Furthermore, instrument analysis also verified that in the astaxanthin group the hydration in the cheek areas and the elasticity in the corner of the eyes had improved.

In 2012, AstaReal conducted a randomized, doubleblind, placebo-controlled study of the nutricosmetic benefits of astaxanthin treatment on the skin of 36 men. The astaxanthin treated group (6 mg daily for 6 weeks) showed significant improvements in the total area ratio of wrinkles and the total volume ratio of wrinkles. In the same year, AstaReal conducted a second clinical study with 30 women². This study combined topical application (2 mL daily) and oral supplementation (6 mg daily) of natural astaxanthin for 8 weeks. There was a significant reduction of visible wrinkles overall. In particular, astaxanthin treatment improved the mean depth and width of crow's feet wrinkles (Figure 5)2. The study also showed a significant improvement in dermal elasticity, which was assessed with a grip meter. Those results were related to general improvements in the moisture content of the corneocyte layer in both men and women with dry skin.

Lastly, a joint study conducted by AstaReal and the Beauty Science Laboratory at the Fujisankei Research Institute showed that astaxanthin shows synergistic effects with Vitamin E (tocotrienol). In a double-blind, placebo-controlled study, 16 healthy women of about 40 years old with dry skin took astaxanthin (2 mg daily) and tocotrienol (40 mg daily) for 4 weeks. Measurements included questionnaires, inspection by a cosmetic specialist, skin moisture content assessment using a skin conductance meter, sebum content assessment using a transmission sebum meter, and observation of the skin surface using a surface microscope¹¹. The study showed a significant improvement in age spots, freckles, dark rings around the eyes, oiliness, forehead wrinkles, sagging under the eyes, smoothness, dermal elasticity, and the hydration of the outer corners of the eyes.

Figure 5. Combining astaxanthin oral supplementation and topical application improved wrinkles²



Female participants (n=30, 20-55 years old) received 6 mg of astaxanthin supplement and applied astaxanthin topical product for 8 weeks. Crow's feet condition was evaluated from replicas of the outer corners of the eye. Photographs show improvement in the astaxanthin group (photo: courtesy of AstaReal Co., Ltd.).

Astaxanthin Boosts Fibroblast and Collagen Integrity Against UV-Induced Damage

Researchers from the Dermatological Institute of San Gallicano in Italy and the University of Dusseldorf in Germany demonstrated that astaxanthin has no pro-oxidant activities unlike other carotenoids (Figure 6)^{12, 13}.



Furthermore, they also showed that astaxanthin reduced the damaging effects of UV radiation in human dermal fibroblasts better than other carotenoids¹².

Astaxanthin decreased caspase-3 activity, which is an indicator of apoptosis (cell death) dose-dependently, whereas the levels of β-carotene caused caspase-3 activity up-regulation (Figure 6)¹². Meanwhile, astaxanthin treatment may inhibit the depletion of two endogenous antioxidant enzymes—catalase and superoxide dismutase—even after 24 hours of consecutive UVA exposure. The effect of astaxanthin was the opposite that of the carotenoids β-carotene and cantaxanthin, for which concentrations

of both catalase and superoxide dismutase dropped

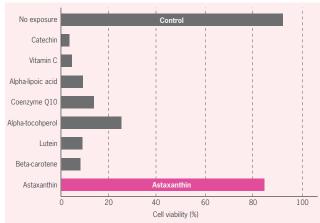
dramatically¹².

Figure 6. Astaxanthin may have the stronger protective effect on human fibroblasts than other carotenoids¹²



Human dermal fibroblasts (HDF) were loaded with 3 types of carotenoids (astaxanthin, cantaxanthin, β -carotene) at different concentrations 24 hours prior to UVA irradiation. This figure shows the changes in caspase-3 activity of astaxanthin and β -carotene (Figure modified).

Figure 7. Astaxanthin may have the stronger protective effect on human fibroblasts than other antioxidants¹⁷



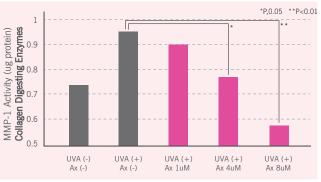
Human dermal fibroblasts (HDF) were pre-incubated with antioxidants before exposure to singlet oxygen, and cell viability was measured to compare the protective efficacy.

In a subsequent study conducted by a team of Japanese researchers from AstaReal, astaxanthin boosted the fibroblast survival rate after persistent exposure to singlet oxygen attack. The performance of astaxanthin was considerably better than most common antioxidants (Figure 7)¹⁴¹⁷. Astaxanthin preserved the ability of the fibroblasts to synthesize collagen, despite the attack of singlet oxygen on their cell structure. Even more remarkably, astaxanthin restored the ability of vitamin C to protect and promote the production of collagen by fibroblasts under oxidative stress (see synergetic effect of astaxanthin-2)¹⁸.

Other researchers from Jichi Medical University and Tokyo University of Technology showed that astaxanthin can also suppress UVA-induced matrix metalloproteinase-1 (MMP-1) and skin fibroblast elastase both in the protein level and the gene expression level after irradiation. Especially MMP-1 activity was suppressed in a dose dependent manner (Figure 8)¹⁹. Both MMP-1 and skin fibroblast elastase are enzymes that breakdown elastin and collagen in the dermis. Chronic activation of these enzymes causes a loss of structural resilience of the connective tissues, resulting in premature sagging and wrinkling.

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Figure 8. Astaxanthin attenuated the UVA-induced up-regulation of MMP-1 in human dermal fibroblasts¹⁹



Human dermal fibroblasts (HDF) were washed with phosphate-buffered saline (PBS), then subjected to UVA irradiation. Astaxanthin was added to HDF immediately after the UVA irradiation. MMP-1 activity was assessed by ELISA at 48 hours post-irradiation.

Astaxanthin works with vitamin C and other whitening agents to help collagen synthesis Vitamin C, retinoic acid and collagen peptides are commonly known as a promoting agent of collagen synthesis. The truth is, however, each agent can't fully act under oxidative stress. Astaxanthin improves its synthesis by quenching oxidative stress. Comparison of collagen production under conditions of oxidative stress Comparison of collagen production under conditions of oxidative stress Vitamin C Vitamin C Retinoic Acid Retinoic Acid Retinoic Acid Retinoic Acid

Collagen peptides

Singlet oxygen-exposed cells were incubated with vitamin C, retinoic acid and collagen peptides (known to promote collagen synthesis) for 72 hours. After incubation, type I collagen production was examined respectively using a PIP EIA kit* (data: JP 2011-63563)
*PIP EIA kit: Test kit for detecting and quantitating Procollagen Type IC-peptide.



- 1. Clinical studies show that astaxanthin can improve dermal wrinkles caused by the degeneration of elastic fibers and the collagen network, as well as epidermal fine lines caused by dryness of the corneum layer. The effects were particularly strong in the corner of the eyes, on the cheeks, and the forehead.
- Astaxanthin may inhibit the gene overexpression of collagen-digesting enzymes and protect the fibroblast synthesis of collagen from oxidative stress. Therefore, astaxanthin treatment can reduce premature sagging and wrinkling caused by excessing exposure to UVA radiation.
- 3. The astaxanthin quenching potency for singlet oxygen is much greater than that of other antioxidants and it shows no proxidant activity, even after 24 hours of continuous UVA exposure.



Astaxanthin Improves the Supply of Nutrients to Skin Tissues

A decrease in the antioxidant concentration in the circulatory system increases the oxidation of red blood cells and exacerbates oxidative stress and inflammation in all skin layers. This worsens capillary circulation and capillary integrity, and increases lipid oxidation in the hypodermis, which is particularly rich in vessels and adipose cells. Photoaged skin shows an age-dependent reduction in micro-vasculature and vessel size, resulting in decreased skin temperature, waste-removal, and nutrient supply.

Clinical studies suggest that astaxanthin can improve blood antioxidant activity²⁰, capillary blood flow²¹⁻²³, and blood lipid profile²⁴. Other studies confirmed that astaxanthin can reduce oxidative byproducts and DNA damage in red blood cells^{25, 26}, and consequently inhibits inflammation and glycosylated byproducts in the circulatory system²⁷. This clinical evidence indicates astaxanthin improves the nutrient supply to cells, waste-removal from tissues, the maintenance of natural antioxidant enzymes that protect cells against ROS, and helps to maintain a healthy immuno-inflammatory response in all skin layers²¹.

Free Radical Assault from All Sides: The Root of Skin Aging

The skin is the largest, most visible organ in the body, and it is the organ that is most exposed to the harsh external environment. The skin is also a complex and dynamic organ. Every square centimeter of skin contains 14 cm of blood vessels and over 6 million cells. Because the skin is so rich in cellular activity and capillary distribution, doctors know that the appearance of the skin is an immediate indication of a person's psychophysical health.

Loss of skin vitality is linked to the constant attack of millions of free radical species generated inside the body or from the environment. Sources of free radicals include poor diet, alcohol, medication, psychophysical stress, X-rays, pollution, and exposure to UV-radiation. Free radicals cause oxidative stress, which progressively damages the skin's cell walls (membranes); their energy system (mitochondria), and their DNA. This causes chronic inflammation and weakens the skin cells. All of these factors contribute to premature photoaging and cellular senescence in all skin layers.



Nicholas Perricone, M.D.,

Dr. Nicholas Perricone is a board-certified dermatologist, award-winning inventor, research scientist, and internationally renowned anti-aging expert. He is the author of various New York Times bestsellers.

In his book, *Forever Young*, Dr. Perricone called natural astaxanthin "the king of



carotenoids; an irreplaceable and exceptionally powerful nutrient that is necessary for any successful anti-aging regimen." According to Dr. Perricone, taking astaxanthin supplements is of critical importance to keeping the skin youthful and supple. This is because astaxanthin supports skin renewal by reducing factors that contribute to the formation of wrinkles. This includes the powerful scavenging of free radicals both inside and outside cellular membranes, suppression of enzymes that destroy the collagen matrix, and effective inhibition of pro-inflammatory chemicals that accelerate skin aging²⁸.

Outlook

Astaxanthin shows various positive effects in all skin layers, including the corneum, epidermis, and dermis. Evidence shows that daily astaxanthin supplementation



Repairs wrinkles by protecting the collagen network and dermal fibroblasts, and maintains collagen production



Improves skin texture and roughness by protecting the corneum cell layer and its hydration capacity



Reduces hyperpigmentation and age-spots by inhibiting melanin overproduction and oxidation after excessive exposure to sunlight



ul>
 Restores oil balance and skin radiance by inhibiting sebum oxidation in the skin surface induced by ozone and pollution



Reduces the chronic inflammation and autoimmune symptoms of atopic dermatitis

Recommended daily dosage: 2-6 mg

Warning: Consult your physician prior to use if you are pregnant or nursing, or if you have any medical condition or are taking any medication or other dietary supplements.

AstaREAL® Natural Algae Astaxanthin

Astaxanthin is a naturally occurring pigment that gives the reddish pink color to marine organisms such as crabs, shrimp, and salmon. It is often called the King of Carotenoids because of its powerful antioxidant potency. Astaxanthin also possesses a unique molecular structure that spans the cell membrane's hydrophillic and hydrophobic layers, attracting and quenching free radicals. AstaREAL® astaxanthin is derived from wholly natural source, the microalgae Haematococcus pluvialis, and contains the same form of astaxanthin found in wild salmon.



Singlet Oxygen Quenching Power

Astaxanthin is

500 times stronger than Vitamin E

560 times stronger than Green tea catechins

800 times stronger than CoQ 10

3000 times stronger than Resveratrol

6000 times stronger than Vitamin C

References

- Wisthaler CJ et al., Reactions of ozone with human skin lipids: Sources of carbonyls, dicarbonyls, and hydroxycarbonyls in indoor air. Proc Natl Acad Sci USA. 2010:107(15):6568-75.
- Tominaga K et al., Cosmetic benefits of astaxanthin on humans subjects. Acta Biochim Pol. 2012;59(1):43-7.
- 3 Yamashita E, Jpn Food Style 21. 2012;16(5):69-74.
- Ichihashi M et al., Photoaging of the skin. Anti-Aging Medicine. 2009;6:46-59. Fagot D et al., Direct role of human dermal fibroblasts and indirect participation of epidermal keratinocytes in MMP-1 production after UV-B irradiation. Arch Dermatol Res. 2002:293(11):576-83.
- Yamashita E, Suppression of post-UVB hyperpigmentation by topical astaxanthin from krill. Fragrance Journal. 1995;14:180-5.
- Arakane K, Superior Skin Protection via astaxanthin. Carotenoid Science. 2002;5:21-5
- Terazawa S et al., 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. Exp Dermatol. 2012;21 Suppl 1:11-7
- Seki T et al., Effects of astaxanthin from Haematococcus pluvialis on human skin. Fragrance Journal. 2001;12:98-103.
- 10. Yamashita E, The effects of a dietary supplement containing astaxanthin on skin condition. Carotenoid Science. 2006;10:91-5.
- 11. Yamashita E, Cosmetic benefit of dietary supplements containing astaxanthin and tocotrienol on human skin. Food Style 21. 2002;6(6):112-7. 12. Camera E et al., Astaxanthin, canthaxanthin and beta-carotene differently affect UVA-
- induced oxidative damage and expression of oxidative stress-responsive enzymes. Exp Dermatol. 2008;18(3):222-31.
- 13. Martin HD et al., Chemistry of carotenoid oxidation and free radical reactions. Pure Appl Chem. 1999:71(12):2253-62.
- 14. Krutmann J, Ultraviolet A radiation-induced biological effects in human skin: relevance for photoaging and photodermatosis. J Dermatol Sci. 2000;23(1):S22-6.
- 15. Nishida Y et al., Quenching activities of common hydrophilic and lipophilic antioxidants against singlet oxygen using chemiluminescence detection system. Carotenoid Science. 2007:11:16-20
- 16. Shimidzu N et al., Carotenoids as singlet oxygen quenchers in marine organisms. Fisheries Science. 1996;62(1):134-7
- 17. Tominaga K et al., Protective effects of astaxanthin against singlet oxygen induced damage in human dermal fibroblasts in-vitro. Food Style 21. 2009;13(1):84-6
- 18. Tominaga K et al., Cosmetic effects of astaxanthin for all layers of skin. Food Style 21. 2009:13(10):25-9
- 19. Suganuma K et al., Astaxanthin attenuates the UVA-induced up-regulation of matrix-met alloproteinase-1 and skin fibroblast elastase in human dermal fibroblasts. J Dermatol Sci. 2010;58(2):136-42.
- 20 Kim JH et al. Protective effects of Haematococcus astaxanthin on oxidative stress in healthy smokers. J Med Food. 2011;14(11):1469-75.
- 21. Saito M et al., Astaxanthin increases choroidal blood flow velocity. Graefes Arch Clin Exp Ophthalmol. 2012;250(2):239-45.
- 22. Miyawaki H et al., Effects of astaxanthin on human blood rheology. J Clin Biochem Nutr. 2008;43(2):69-74.
- 23. Tsukahara H et al., Supplementation effect of astaxanthin on blood flow and shoulder
- stiffness. Medical Consultation & New Remedies. 2009;46(4):427-32. 24. Yoshida H et al., Administration of natural astaxanthin increases serum HDL-cholesterol and adiponectin in subjects with mild hyperlipidemia. Atherosclerosis. 2010;209(2):520-3.
- 25. Nakagawa K et al., Antioxidant effect of astaxanthin on phospholipid peroxidation in human erythrocytes. Br J Nutr. 2011;105(11):1563-71.
- 26. Park JS et al., Astaxanthin decreased oxidative stress and inflammation and enhanced immune response in humans. Nutr Metab (Lond). 2010;7:18.
- 27. Uchiyama A et al., Clinical efficacy of astaxanthin-containing Haematococcus pluvialis extract for the volunteers at risk of metabolic syndrome. J Clin Biochem Nutr. 2008;43 (1):38-43.
- 28. Perricone, Forever young: the science of nutrigenomics for glowing, wrinkle-free skin and radiant health at every age. Atria Books. 2010.

Patent: Immunomodulation-autoimmune diseases, chronic viral and intracellular bacterial infections: US Pat. 6,773,708

Inhibiting the expression of inflammatory cytokines and chemokines: US Pat. 7,078,040



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