Astaxanthin Technical Bulletin | Vision

VIEW YOUR WORLD WITH SHARPER EYES

The Vision Benefits of Astaxanthin



Clinical Benefits of Astaxanthin

- Relieves eye fatigue symptoms by improving capillary blood flow
- Improves quality of vision by preserving the zoom-in, zoom-out refocusing of the eye's ciliary muscle
- Relieves eye inflammation and shoulder stiffness in people who use computers extensively

Astaxanthin: The Latest Science

- Reduces UV-induced inflammation in the eyes by inhibiting activation of the signaling molecule NF-kb
- Scavenges superoxide radicals in the eyes of diabetic patients
- Delays progression of presbyopia in middle-aged and elderly people



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Astaxanthin: Seabird Sunglasses

S eabirds such as seagulls eat large amounts of fish and marine organisms that contain astaxanthin. After digestion, astaxanthin is concentrated in the eyes of seabirds¹. But why? Researchers hypothesize that as seabirds fly toward the surface of the sea to hunt fish, astaxanthin functions like a pair of sunglasses. It protects the eyes against the free radicals generated by UV glare reflected off the water surface. Astaxanthin is also thought to maintain the refocusing speed of the eye's ciliary muscle in birds. This allows the lens of the eye to follow the rapid movements of prey during hunting.

A Hidden Pandemic: Computer Vision Syndrome

On average, workers and adolescents in modern cities spend over 45 hours every week staring at computer screens, playing video games, watching television, or interacting with smart phones. The U.S. National Institute of Occupational Safety and Health found that over 88% of office workers report eyestrain. A European study showed that 23% of Swedish schoolchildren experience eye fatigue due to playing video games excessively². This widespread use of visual displays increases stress on the eyes, which leads to a complex ophthalmic and psychophysical condition called computer vision syndrome (CVS). Symptoms of CVS include eye strain, sensitivity to glare, sore eyes, blurred vision, and neck and shoulder pain. CVS also causes mood swings, irritability, physical burnout, headaches, and a consequent decline in mental performance, motivation, and interpersonal efficacy.

More seriously, Japanese researchers from Toho University School of Medicine published a study of 10,000 Japanese workers in the *Journal* of *Epidemiology and Community Health*, and found a significant

link between heavy computer use and the development of glaucoma—a serious eye condition that causes progressive and irreversible blindness if left untreated. The risk of glaucoma is higher in near-sighted individuals, who are thought to be more susceptible to computer-related eye strain³.

Over the last decade, demand has increased for clinically proven remedies, such as astaxanthin, that can effectively alleviate CVS symptoms and prevent eye diseases.

What is Computer Vision Syndrome?

CVS is a temporary condition resulting from overexposure of the eyes to a computer display for protracted, uninterrupted periods. Some symptoms of CVS include headaches, blurred vision, neck pain, difficulty refocusing the eyes, fatigue, eye strain, double vision, polyopia, and bloodshot, dry, irritated eyes.





A series of randomized double-blind placebocontrolled studies have shown that oral supplementation of natural astaxanthin from *Haematococcus pluvialis* (5-12 mg daily) can alleviate subjective symptoms typically associated with CVS. One month of treatment reduced the incidence and intensity of headaches, blurred vision, sensitivity to glare, eye fatigue and soreness, neck and shoulder pain, and psychophysical malaise. Treatment also improved visual acuity. Objective parameters measured with ophthalmic devices show that astaxanthin supplementation also improved the accommodative recovery of the eye's ciliary muscle (zoom-in, zoomout refocusing rate and accommodative amplitude), which was reduced in individuals with CVS.

C linical studies have also shown that 1 month of treatment with astaxanthin (6-12 mg daily) enhanced the eye's capillary blood flow by reducing the oxidation of red blood cells. This could prevent ocular diseases and improve the eye's internal balance, nutrition, oxygenation, waste removal, and rejuvenation. Furthermore, a one-month treatment with astaxanthin (6 mg daily) slowed down the progression of presbyopia, which is the diminished ability to focus on near objects, in middle-aged and elderly people, and improved visual acuity during athletic performance.



S tudies have also shown that astaxanthin can inhibit damage and quench inflammation of the eyes caused by heavy exposure to UV radiation. Additional experimental studies have also shown that supplemental astaxanthin could be a supportive nutrient for preventing free radical generation and neurotoxic injury of the retina, which is linked to irreversible visual field loss. Finally, astaxanthin reduces visual damage caused by free radicals and subsequent chronic inflammation in individuals with diabetes.

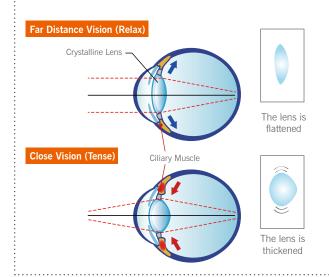
How Does Eye Fatigue Occur?

Eye fatigue is caused by straining the ciliary muscle in the eye. When looking at an object close up, this small ocular muscle contracts, making the lens of the eye thicker and more spherical. When looking at a distant object, the ciliary muscle relaxes, making the lens thinner and flatter. This muscular action facilitates the natural zoom-in, zoom-out refocusing of the eye. However, when using computers, the eyes are focused on an object at a fixed distance for many consecutive hours; therefore, the ciliary muscle is contracted for long periods. This causes spasms and strains the ciliary muscle, resulting in chronic eye fatigue.

How to Diagnose Eye Fatigue

The level of eye fatigue can be determined with ophthalmic devices found in specialized eye clinics. These devices assess the accommodative adjustment and responsiveness of the eye's ciliary muscle as it refocuses on objects at different distances. Individuals with CVS show significant worsening of the following parameters:

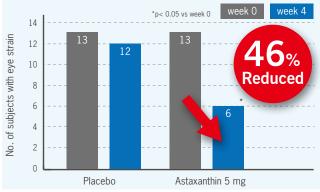
- 1. Accommodative Amplitude—how effectively the ciliary muscle tightens and stretches when facing a change in object distance. Also referred to as accommodative range.
- 2. Refocusing Rate—the time it takes for the ciliary muscle to tighten and stretch when facing sudden changes in object distance. Also referred to as accommodative response.
 - Far-to-Near Refocusing Rate (positive accommodation response) the time it takes for the ciliary muscle to contract to refocus suddenly from a far to a near object.
 - Near-to-Far Refocusing Rate (negative accommodation response) – the time it takes for the ciliary muscle to relax to refocus suddenly from a near to a far object.



Relieving Eye Fatigue with Astaxanthin

In the last decade, AstaReal Co., Ltd. has sponsored 19 clinical studies to investigate the science of eye fatigue relief using natural astaxanthin supplementation. In 2002, Toyama Medical and Pharmaceutical University in Japan conducted a randomized double-blind placebo-controlled study, which involved 26 daily computer users. Oral administration of astaxanthin (5 mg daily) for 4 weeks improved their accommodative amplitude compared with the placebo group (Figure 1)⁴. This seminal study paved the way for a series of in-depth studies of the effects of astaxanthin on visual performance in daily computer users. Two years later, Fujita Health University School of Medicine in Japan conducted another randomized double-blind placebo study to investigate the link between oral administration of astaxanthin and changes in visual function. In this clinical trial, 49 healthy volunteers aged >40 years were divided into four groups and given different doses of astaxanthin or a placebo for 28 consecutive days. Astaxanthin supplementation (4 and 12 mg daily) significantly improved the participants' far-to-near refocusing time (Figure 2)⁵.





VDT workers (n=26) were randomly divided into 2 groups and received 0, 5 mg of astaxanthin daily for 4 weeks. The number of the subjects complained about overall eye strain symptoms was assessed by a questionnaire.

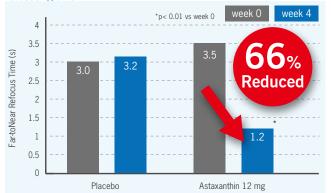


Figure 2. Taking astaxanthin daily for 4 weeks shortened far-to-near refocusing time⁵

Healthy participants (n=49) were randomly divided into 4 groups and received 0, 2, 4 or 12 mg of astaxanthin daily for 4 weeks. Far-to-near refocusing time was measured at 0 and 4 weeks. This figure shows the changes of refocusing time of the 0mg group (n=10) and 12mg group (n=13).

To investigate the specific effects of astaxanthin supplementation on eye fatigue, in 2005 Hokkaido University conducted a randomized double-blind placebocontrolled study involving 40 healthy adults with CVS symptoms. Compared with the placebo group, the group taking oral astaxanthin (6 mg daily) for 4 weeks showed improved accommodative amplitude, refocusing rate, eye irritation, and bleariness⁶.

In the same year, Hokkaido University cross-validated its previous findings by conducting a randomized doubleblind placebo-controlled study involving 30 healthy adult participants. Oral supplementation with astaxanthin (6 or 12 mg daily) for 4 weeks significantly improved participants' far-to-near refocusing rate compared with the placebo group (Figure 3)⁷. Furthermore, Kajita Eye Clinic in Japan conducted another clinical study in which taking astaxanthin (6 mg daily) for 2 weeks reduced the excessive microfluctuations and micro-spasms of the ciliary muscle in 9 participants with eye fatigue after intensive visual work. These results suggest that astaxanthin may relieve eye fatigue by improving the ability of the ciliary body to recover from stressful visual conditions⁸. A subsequent clinical study conducted by Toyama Medical and Pharmaceutical University reconfirmed these findings in 2005. In this study, oral supplementation of astaxanthin (6 mg daily) for 4 weeks significantly improved subjective symptoms linked to eye fatigue, eye irritation, and blurred vision⁹.

This preliminary research formed the basis for further Japanese studies of the clinical link between astaxanthin supplementation and relief of CVS symptoms. In 2006, Hokkaido University, in collaboration with Kyouryoukai Ichinomiya Nishi Hospital, conducted a double-blind randomized placebo-controlled study involving 48 participants to examine the effects of astaxanthin



Figure 3. Taking astaxanthin for 4 weeks improved accommodation amplitude $^{\rm 7}$

Thirty volunteers who complained of asthenopia were randomly divided into 3 groups and received 0, 6, 12 mg of astaxanthin daily for 4 weeks. Degree of asthenopia was evaluated by objective amplitude of accommodation. This figure shows the changes in objective accommodation power of the 0 mg (n=8) and the 12 mg group (n=7).

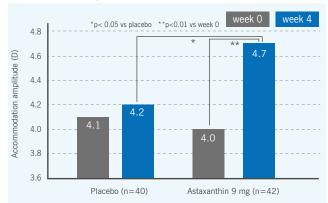
**D:The difference between the refracting power of the eye when adjusted for vision at the far and near point

supplementation on participants experiencing visual fatigue induced by heavy computer use. As in previous studies, a 6 mg daily dose of natural astaxanthin for 4 weeks improved accommodation amplitude considerably (Figure 4)¹⁰. Furthermore, despite a strong placebo effect, other CVS symptoms improved in the astaxanthin group, including eye fatigue, eye redness, blurred vision, and stiff shoulders. In the same year, the University of Occupational and Environmental Health in Japan conducted a second randomized double-blind crossover study involving 10 healthy adults who complained of CVS symptoms. The group treated with astaxanthin (6 mg daily) for 14 days reported a significant decrease in eye fatigue and heaviness¹¹. Furthermore, the far-to-near and near-tofar refocusing rate (accommodative response) in the astaxanthin group also improved.

A series of subsequent studies have also shown that astaxanthin can relieve eye fatigue in different population segments, including post-menopausal women and young adults^{12,13}.

In 2010, Dr. Nagaki's research group conducted a larger scale double-blind placebo-controlled study in collaboration with Ichinomiya Nishi Hospital in Japan involving 82 heavy computer users. The study showed that the refocusing rate (accommodative response rate) improved significantly after taking astaxanthin (9 mg daily) for 4 weeks compared with the placebo group. In addition, administration of astaxanthin substantially improved conditions linked to eye strain, blurred vision, and shoulder and back stiffness (Figure 5)¹⁴.

Figure 5.Taking 9mg of astaxanthin for 4 weeks improved accommodation amplitude¹⁴

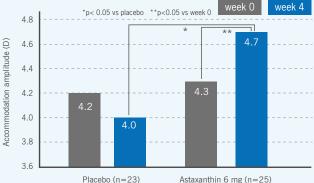


VDT workers were randomly divided into 2 groups and received 0, 9 mg of astaxanthin daily for 4 weeks. Objective accommodation was examined before and after supplementation. Subjective eyestrain evaluation was also conducted by using a questionnaire before and after supplementation.



Various clinical studies have shown that supplementation with astaxanthin for 1 month improves subjective symptoms and objective parameters linked to CVS in different population segments. Astaxanthin is thought to help maintain the accommodative amplitude and accommodative response of the ciliary muscle. This improves both far-tonear and near-to-far refocusing of the eyes. Clinical studies also showed that astaxanthin supplementation alleviated eye fatigue by quenching the cellular inflammation that emerges during persistent visual stress and contraction of the ciliary muscle.

Figure 4. Taking 6mg of astaxanthin for 4 weeks improved accommodation amplitude¹⁰



VDT workers were randomly divided into 2 groups and received 0, 6 mg of astaxanthin daily for 4 weeks. Objective accommodation was examined before and after supplementation. Subjective eyestrain evaluation was also conducted by using a questionnaire before and after supplementation.



Delaying the Progression of Presbyopia with Astaxanthin



Presbyopia is an age-related condition where the eye exhibits a progressive reduction in its ability to focus on near objects. The first signs of

presbyopia include eyestrain, difficulty seeing in dim light, and problems focusing on small objects. These usually begin between the ages of 40 and 50 years. Presbyopia has been linked to loss of elasticity of the crystalline lens and loss of accommodative amplitude of the ciliary muscle. So individuals with presbyopia are more vulnerable to CVS.

In 2009, Kajita Eye Clinic investigated the effects of astaxanthin supplementation (6 mg daily) in 22 elderly participants with presbyopia¹⁵. After 4 weeks of treatment, the participants experienced a subjective improvement in their presbyopia symptoms. Participants felt an improvement when looking at close objects and found their vision was less blurred. In addition, the pupillary constriction ratio, which is used to assess the accommodative function of the eye, showed an overall improvement of 12.5% after supplementation with astaxanthin. This improvement was also accompanied by an improvement in eye fatigue symptoms¹⁵.

Improving Visual Acuity with Astaxanthin

Visual acuity, which is the clearness of vision, plays a crucial role in athletic performance, because it improves responsiveness, adaption, and accuracy when athletes encounter sudden changes in their immediate environment. Depth perception and critical flicker fusion are particularly relevant to athletes' visual acuity. Depth perception is the ability to judge the distances between objects as well as the ability to perceive them in three dimensions. Depth perception affects how accurately a baseball player can move to catch a ball. Critical flicker fusion indicates how quickly the central nervous system generates a clear picture when receiving signals from the eyes.

The effects of astaxanthin supplementation on visual acuity were investigated by Juntendo University, in Japan, which conducted a double-blind placebo-controlled study involving 18 handball players¹⁶. Supplementation with astaxanthin (6 mg daily) for 4 weeks improved deep vision and critical flicker fusion compared with the placebo group¹⁶.



A clinical study suggests that astaxanthin may enhance athletic performance by improving visual acuity, depth perception, and critical flicker fusion.



6

Clinical studies suggest that astaxanthin may improve the accommodative function of the eye and alleviate symptoms such as eye fatigue and blurred vision in elderly subjects with presbyopia by improving pupillary constriction.

Improving Retinal Blood Flow with Astaxanthin

Retinal blood flow is crucial to vision, because it governs the eye's internal balance, nutrition, oxygenation, waste removal, and tissue rejuvenation. Therefore, lower blood antioxidant capacity and blood fluidity reduces eye capillary circulation, which can severely affect the accommodative and ocular functioning of the eye. Poor circulation in the choroidal area has been linked to the development of ocular diseases and choroidal neovascularization. Poor circulation to the ciliary muscle may also be associated with loss of accommodative performance, eye fatigue, and early onset of presbyopia.

In 2005, Toyama Medical and Pharmaceutical University in Japan conducted a randomized placebo-controlled study in which 36 healthy subjects took either astaxanthin (6 mg daily) or a placebo for 4 weeks⁹. Retinal blood flow was measured and found to be significantly higher in the astaxanthin group than in the placebo group (Figure 6)⁹. These findings indicate that astaxanthin could be a circulatory failure in the retina that is associated with glaucoma. Additionally, astaxanthin increased blood flow in ophthalmic arteries supplying the ciliary body⁹. Improving capillary blood flow to the ciliary body could improve the eye's accommodative function and reduce symptoms of eye fatigue.

In 2011, Hokkaido University conducted a randomized double-blind placebo-controlled study to investigate the effects of astaxanthin on choroidal blood flow in 20 healthy participants. Supplementation with astaxanthin (12 mg daily) for 4 weeks significantly increased blood

flow velocity¹⁷. The data were converted into the square blur rate (SBR), which is a quantitative index of relative blood flow velocity. The SBR values increased 15% after 4 weeks of astaxanthin supplementation compared with initial levels, whereas no significant change occurred in the placebo group. Interestingly, although the capillary blood flow increased, blood pressure indices did not change. This suggests that astaxanthin may improve nitric oxide-induced blood vessel relaxation and blood antioxidant capacity and may inhibit oxidation of red blood cells. These three factors are thought to be the main causes of lower quality capillary circulation (Figure 7)¹⁷.

Subsequently, supporting clinical studies have validated the earlier findings that astaxanthin supplementation improves capillary blood flow^{17,18}.

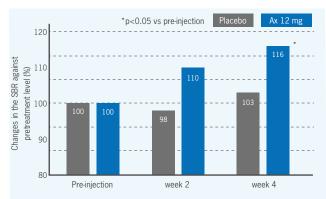


Figure 7. Astaxanthin supplementation increased the choroidal blood flow velocity $^{17}\,$

Twenty healthy volunteers were randomly divided into 2 groups and received 0, 12 mg of astaxanthin daily for 4 weeks. Square blur rate (SBR) was measured in the right eyes of all participants at pre-ingestion, and at 2 and 4 weeks after starting ingestion by using laser speckle flowgraphy (LSFG). (Figure modified).

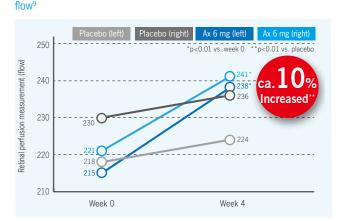


Figure 6. Astaxanthin supplementation increased retinal capillary blood

Double-blind study. Thirty six volunteers were randomly divided into two groups. After 4-week- supplementation, retinal blood flow was measured by using Laser Doppler Retina Flowmete. Astaxanthin group was significantly higher than before supplementation in the both eyes.



Various clinical studies show that astaxanthin improves the blood capillary circulation of the eyes and consequently combats development of ocular diseases and symptoms linked to CVS. These effects are achieved through an increase in antioxidant concentration in the blood and a reduction in red blood cell oxidation. Therefore, astaxanthin supplementation improves the nutrition, oxygenation, waste-removal, and tissue rejuvenation of the eye.

Astaxanthin and Glaucoma

Premature death of retinal ganglion cells (RGCs) is a common feature of many ophthalmic disorders such as glaucoma and retino-vascular diseases. RGCs are neurons located near the inner surface of the retina. They receive visual information and transmit it to the brain. Damage to RGCs affects communication between the brain and the eye and results in loss of visual quality and neural responsiveness. Abnormal RGC death leads to the thinning of the inner nuclear and neural loss in the ganglion cell layer.

In an experimental study conducted by Gifu Pharmaceutical University, astaxanthin was found to decrease RGC shrinkage and cell death after 24 h exposure to hydrogen peroxide radicals. Furthermore, oral administration of astaxanthin (100 mg/kg 4 times daily) decreased retinal damage caused by the neurotoxic injury of *N*-methyl-Daspartate (NMDA), presumably by scavenging hydrogen peroxide radicals, superoxide anions, and hydroxyl radicals. NMDA activates glutamate receptors, and the over-activation of these receptors causes neural cell death, which is believed to play a major role in many neurological disorders and retinal diseases (Figure 8)²⁰.

Astaxanthin treatment inhibited lipid peroxidation, oxidative DNA damage, and eventual ganglion cell death in the ganglion cell layer and inner plexiform layer. Those two layers are essential for healthy functioning of the retina and maintenance of good-quality vision.

In a second experimental study conducted by Akdeniz University in Turkey, astaxanthin treatment (5 mg/kg daily) for 8 weeks decreased lipid peroxidation, protein oxidation, and eventual cell death in the retinas caused by ocular hypertension (OH). Ocular hypertension can cause persistent damage to the optic nerve fibers and consequent degeneration of retinal ganglion cells in the inner retina. This progressive condition is called glaucoma, and is the second leading cause of visual field loss and blindness worldwide²¹.

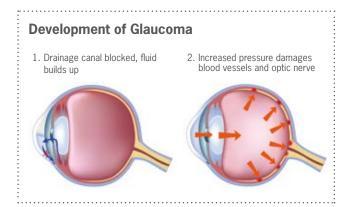
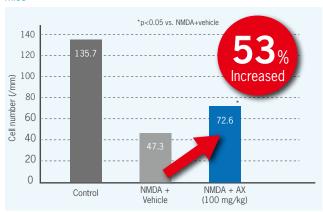


Figure 8. Astaxanthin suppressed NMDA induced retinal damage in ${\rm mice}^{\rm 20}$



Retinal damage (a decrease in retinal ganglion cells) induced by injection of N-methyl-D-aspartate (NMDA) into the vitreous body of the left eye (ganglion cell layer). Damage was assessed by cell number count. Astaxanthin was orally administrered fourtimes for histological analysis. (Figure modified)



Experimental studies show that supplemental astaxanthin could be a supportive nutrient that mitigates damages caused by the development of glaucoma. Astaxanthin inhibits oxidative DNA damage, lipid peroxidation, and premature retinal cell death. These results suggest that astaxanthin preserves the integrity and neural responsiveness of the eye-to-brain pathway.

Quenching Eye Inflammation with Astaxanthin



The aqueous humor is a transparent, gelatinous fluid located between the lens and the cornea. It serves a very important function because it provides

nutrients to the lens, maintains the convex shape of the cornea, carries away waste products from ocular tissues, and modulates the immune response to pathogens. Degeneration of the aqueous humor has been linked to formation of cataracts and progressive vision loss.

In 2009, Tsukuba Hashimoto Optical Clinic found that taking astaxanthin (6 mg daily) for 2 weeks increased free radical scavenging activity in the aqueous humor by 10% in 19

non-diabetic male patients and by 15% in 16 diabetic male patients who underwent cataract surgery. Free radicals attack and deplete natural antioxidant enzymes in the eye lenses and cause chronic inflammation in the aqueous humor²².

This clinical study is supported by a series of experimental studies conducted in Japan. In 2006, Hokkaido University demonstrated that astaxanthin could suppress an inflammatory response, known as uveitis, in a dosedependent manner in the aqueous humor after exposure to lipopolysaccharide (LPS), which induces eye inflammation. Furthermore, astaxanthin significantly reduced the concentration of the signaling molecules nitric oxide, tumor necrosis factor alpha, and prostaglandin that perpetuate inflammation in the aqueous humor. The anti-inflammatory effects of astaxanthin arise from the inactivation of the proinflammatory transcription factor NF-kB signaling pathway, thereby preventing the overall inflammatory cascade in the eyes, even after 3 h exposure to LPS²³. This study replicated findings of the same research team published in 2003, where the anti-inflammatory effects of astaxanthin were comparable to those of prednisolone, a common antiinflammatory drug²⁴.



Clinical and experimental studies indicate that astaxanthin boosts antioxidant and antiinflammatory activity in the aqueous humor and ciliary muscle, through the inactivation of the transcription factor NF-kB. The anti-inflammatory effects of astaxanthin were comparable to the well-known antiinflammatory drug, prednisolone. These findings suggest that astaxanthin could combat the premature formation of cataracts and vision loss, especially in individuals with diabetes.

Quenching UVB Inflammation with Astaxanthin

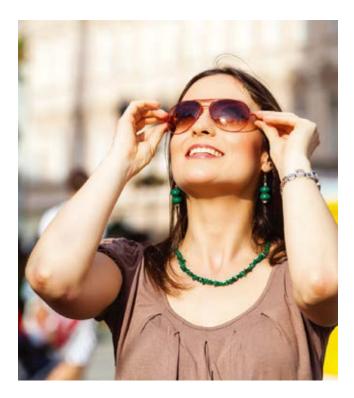
UVB radiation and the persistent attack of free radicals can cause acute and chronic inflammation in the cornea, lens, and retina, leading to physical damage and premature cell death in all ocular tissues. The acute effects of UVB radiation include photokeratitis and photoconjunctivitis, which are UV light-induced inflammation of the cornea and conjunctiva, respectively. Furthermore, chronic UVB exposure can cause cataract formation and carcinoma.

In 2012, Hokkaido University conducted an experimental study on the therapeutic effects of astaxanthin eye drops on UVB-induced inflammation. Astaxanthin eye drops with concentrations of 1, 0.1, and 0.01 mg/mL were administered to the right eye and the left eye was the control. The epithelia of the astaxanthin-treated corneas were morphologically preserved and significantly thicker after UVB irradiation (400 mJ/cm²) compared to the control and the effect was dose-dependent²⁵.

The amount of corneal cell death, free radicals, and NF-kB expression were reduced considerably, in a dose-dependent manner. An *in vitro* study using corneal epithelial cells showed that astaxanthin produced a dose-dependent increase in cell resilience to UVB-irradiation.

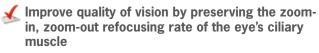


Experimental studies have shown that ocular administration of astaxanthin prevents general eye damage and degenerative conditions of the cornea caused by exposure to UVB radiation.



Outlook

Various clinical studies have shown that astaxanthin supplementation has beneficial effects on different eye conditions in different population segments. In summary, administration of 6 to 12 mg daily of natural astaxanthin for 4-8 weeks can do the following:



🖌 Improve the subjective symptoms linked to CVS

Combat premature formation of cataracts and vision loss, especially in diabetic patients

Reduce retinal neural cell death and damage to the eye's circulatory system caused by glaucoma

Lelay progression of presbyopia in middle-aged and elderly individuals

Improve capillary blood flow, thus improving nutrition, oxygenation, and waste removal in ocular tissues

Reduce UVB-induced inflammation and oxidative damage in eyes

Recommended daily dosage: 6-12 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



6000 times stronger than Vitamin C

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Patent: Medicament for improving the failure of accommodation (Eye fatigue): WO 02/094253



The Front Tower Shiba Koen 12th Floor, 2-6-3 Shiba Koen, Minato-ku, Tokyo 105-0011 Japan TEL: +81-3-3437-2353 FAX: +81-3-3437-2348 WEB: www.astareal.com E-MAIL: international@astareal.co.jp

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