Astaxanthin and Skin Health

Introduction

Several categories exist within the beauty industry, but none more vibrant than the anti-aging segment which includes products to reduce or reverse visible signs of aging such as wrinkles, age spots, and freckles. While aging is natural and cannot be avoided, there are factors such as solar radiation and physical and mechanical damage that accelerate the propensity of visible aging.
Today, humans face increasing exposure to chemical pollution, ultraviolet radiation and ozone levels, all of which can damage the skin's dermal layer causing wrinkles and enhancing the risk of malignant skin cancer. These negative effects are compounded with increasingly poor diets and lifestyle habits which are not conducive to maintaining the skin's natural repair process and antioxidant network. Clearly, there is opportunity for natural ingredients to help improve long term skin health management through topical application and nutritional supplementation.

In the past, Beta-carotene (provitamin A) and Vitamin E have been extensively studied.
Recent focus, however, has switched to carotenoids such as astaxanthin, (derived from the microalgae *Haematococcus pluvialis*), which is shown to have potent quenching and anti-lipid-peroxidation properties; a weakness of Beta-carotene and Vitamin E (Miki, 1991).

In human trials, astaxanthin has been shown to reduce visible signs of UV-aging through both topical and dietary supplementation within 4 to 6 weeks of use. This data is supported by a number of in-vitro and in-vivo studies. Research suggests potential skin benefits from the use of astaxanthin to maintain a youthful appearance, reverse premature signs of aging and prevent UV induced skin cancer.

Naturally, further investigation is necessary to elucidate the mechanism of action and to replicate results using significantly larger clinical trials. To date, the astaxanthin potential is promising.

Table 1. Astaxanthin maintains skin health by several methods

Benefits	Mechanism	Topical Route	Dietary Route
Increase skin's ability to resist environmental stripping of skin nutrients.	Restores skin's natural antioxidant balance (SOD, CAT, GSH). Protects cell membrane against lipid peroxidation.	✓	✓
Reduce puffiness and erythema	Suppresses the inflammatory pathway.	✓	✓
Prevent & reduce presence of UV induced wrinkles. Firmer and elastic skin. Increased moisture.	Protects the dermal layer against oxidative stress dysfunction. Allowing repair process to heal collagen network.	✓	✓
Reduce the risk of skin cancer.	Protects against accumulated DNA damage.	✓	✓

Protecting the Skin's Natural Antioxidant Network and DNA

Oxygen radicals formed from UV radiation attack skin cells in a variety of ways. As demonstrated by O'Connor & O'Brien (1998), UVA light is capable of producing oxidative stress in living cells in-vitro. By monitoring catalase (CAT), superoxide dismutase (SOD) levels and thiobarbituric acid reactive substances (TBARS), astaxanthin is capable of reducing oxidative stress ($p<0.01$, $n=6$) after UVA light irradiation at very low concentrations (5-10 nM). Astaxanthin has shown to be approximately 100-200 times more effective than other carotenoids, including lutein and beta-carotene (1.0 μM).

Similar reports by Lyons *et al*., (2002) demonstrate that UVA irradiated skin cells pretreated with astaxanthin (10 μM) suffered significantly less DNA damage. Furthermore, astaxanthin protected the skin's endogenous antioxidants SOD and glutathione (GSH) from oxygen radical attack.

Topical restoration of the skin's natural antioxidant balance is one method to maintaining healthy skin. UV radiation and air borne pollutants tend to strip away the nutrients essential to maintain the skin's hydrolipidic barrier. As a result, the skin will become dry and unhealthy in appearance.

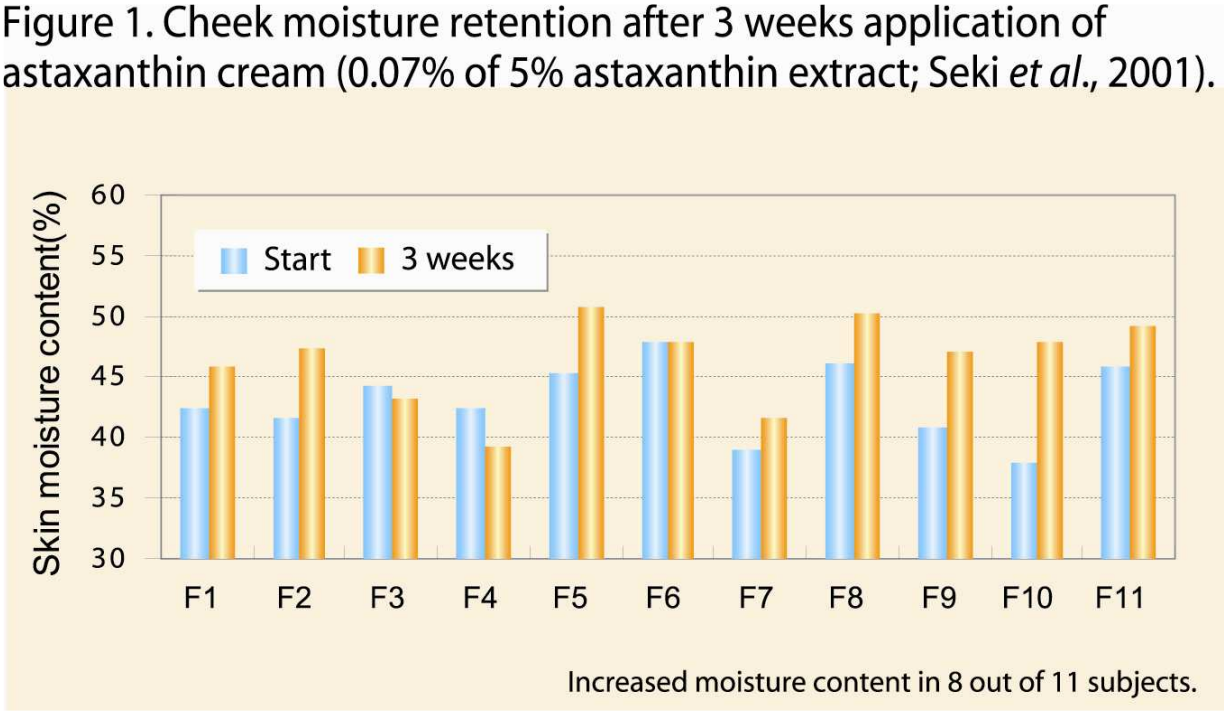
Topical Wrinkle Reduction

In a study using hairless mice, Arakane (2002) demonstrates astaxanthin's ability to suppress the formation of UVB photo-induced wrinkles. UVB doses of 65-95 mJ/cm2 were applied five times per week for 18 weeks on the back skin of the mice. After each UVB treatment, topical application of astaxanthin (350 μM) was coated on the exposed areas. After only 5 weeks, the appearance of new wrinkles were significantly reduced up until the end of the study period ($P<0.01$ at 18 weeks). Concurrently, stained skin sections revealed that astaxanthin preserved the integrity of the dermal layer by protecting the collagen network.

In a preliminary human study, Seki *et al*., (2001) demonstrates the same anti-wrinkle observations in female human subjects (n=3) using a topical cream containing astaxanthin. A dermatological assessment revealed significant reduction of wrinkles and puffiness on the lower eye and cheeks after 2 weeks of use.

In a separate test using female subjects (n=11), instrument analysis recorded significant moisture improvement ($P<0.05$) after 3 weeks of use (Figure 1).

Figure 1. Cheek moisture retention after 3 weeks application of astaxanthin cream (0.07% of 5% astaxanthin extract; Seki *et al*., 2001).



Skin Health that can be Swallowed

"Beauty from within" or improved skin condition through nutrition and supplementation is a worldwide trend that is on the increase. The market for beauty supplements is currently worth 800 million dollars, and rapid growth in this segment is expected over the next 10 years. Two human clinical trials established the use of astaxanthin to improve visible signs of premature aging and general skin health. The first, a double-blind placebo controlled study (Yamashita 2002), showed that astaxanthin in combination with tocotrienol, (a superior form of vitamin E), improved several aspects of overall skin condition. Eight female subjects with dry skin conditions (mean age 40 yrs) received daily doses containing 2 mg astaxanthin and 40 mg natural tocotrienols. Several types of data were collected at 2 and 4

weeks and compared to the initial baseline readings. Measurable differences were observed starting just 2 weeks after supplementation. By the 4th week, the treated subjects with dry skin characteristics exhibited the following: increased moisture levels ($P<0.05$), (Figure 2); consistent natural oils; reduction of fine wrinkles, (Figure 3); and a reduction in pimples ($P<0.01$).

Figure 2. Beauty supplement results for the cheek and eye region (Yamashita, 2002)

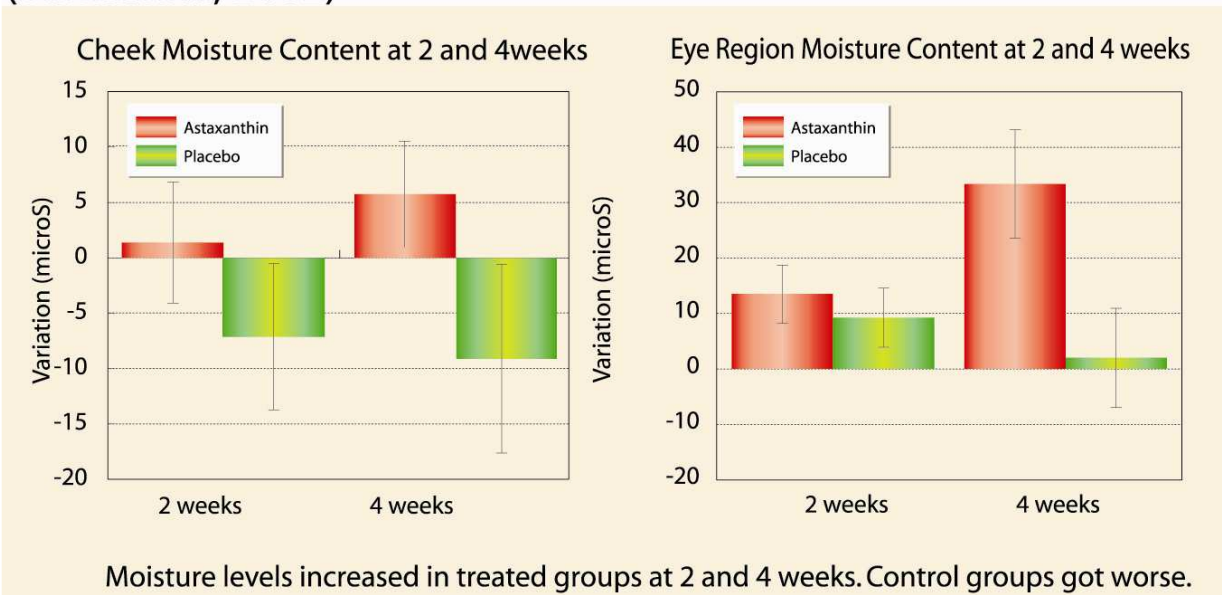
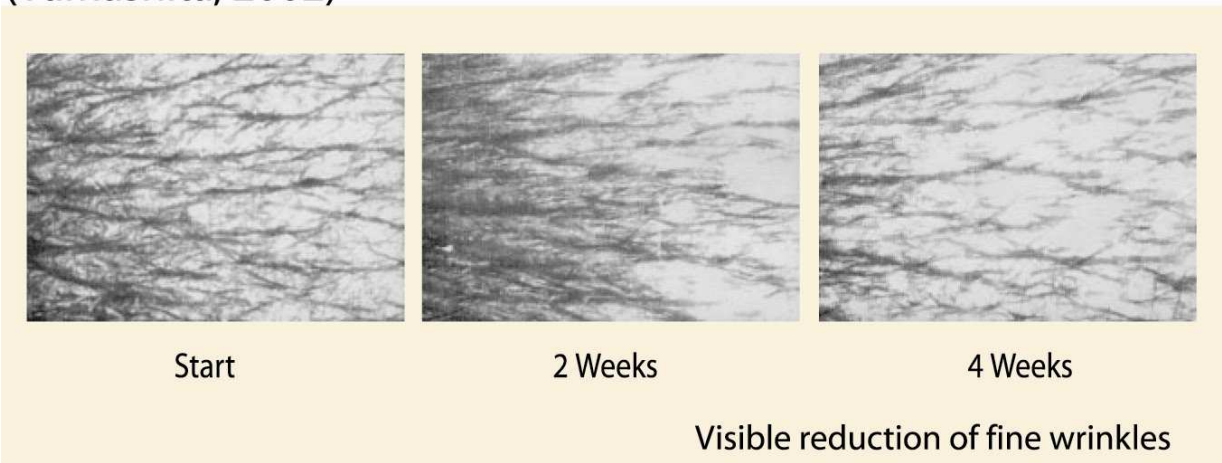
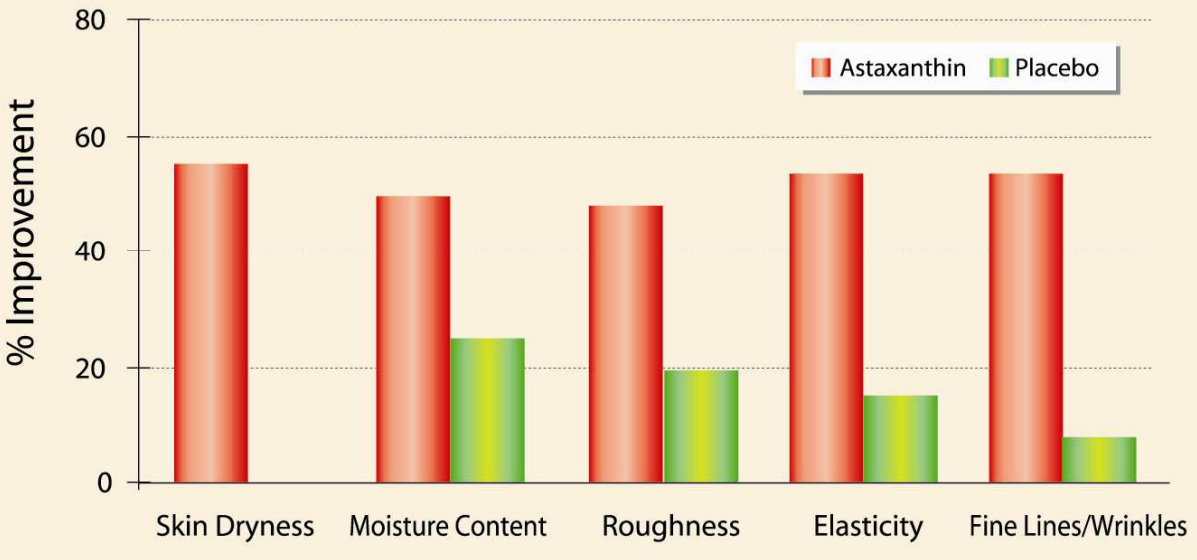


Figure 3. Magnified Skin Section at start, 2 and 4 weeks (Yamashita, 2002)



In the second study by Yamashita (2006), female subjects with a variety of skin types (n=49, mean age 47 yrs) were given either 4 mg (2 x 2 mg) astaxanthin or placebo in a single-blind, randomized, controlled study. After six weeks of consuming 4mg astaxanthin per day, the results of a standard questionnaire showed that the treated group of women all felt that their skin condition had improved significantly (Figure 4).

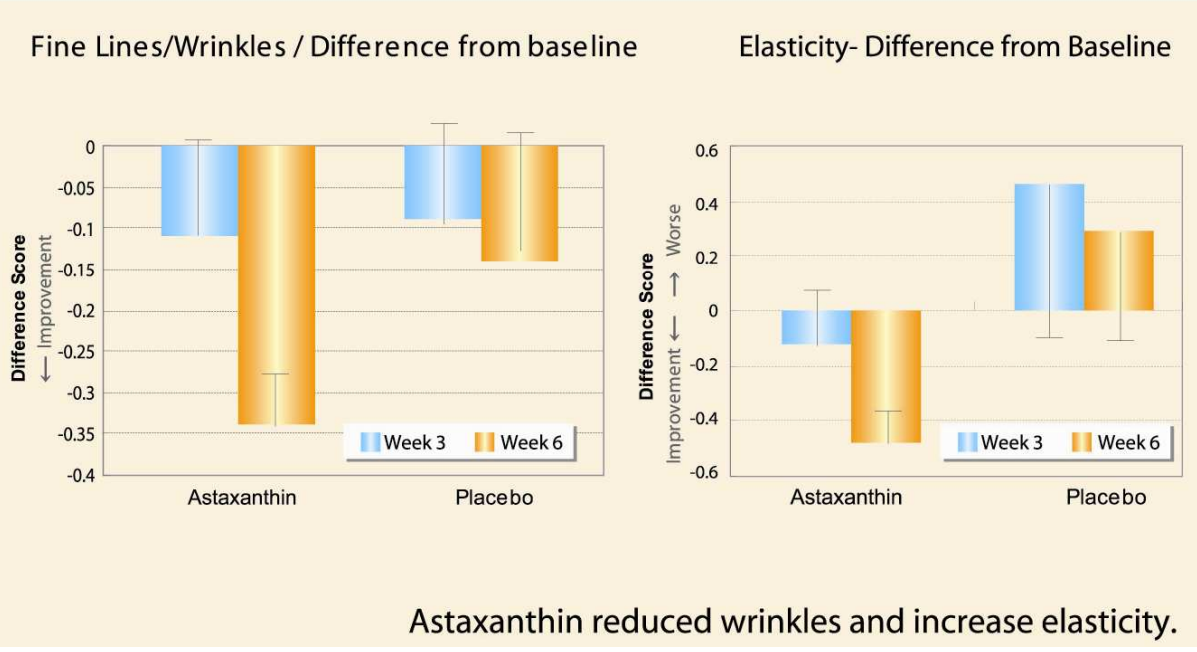
Figure 4. Subject response after 6 weeks astaxanthin supplementation (Yamashita, 2006)



Skin improvements seen in all categories after astaxanthin supplementation.

Instrument analysis proved that the treated group had indeed achieved positive results in hydration ($P<0.05$) and elasticity ($P<0.05$). Furthermore, a dermatologist's inspection showed wrinkle reduction ($P<0.05$) and improved elasticity ($P<0.05$) in the treated group especially between weeks 3 and 6 (Figure 5). The results were significant since skin regeneration usually takes between 4-5 weeks. The greatest improvement seen at week 6 supports the theory that astaxanthin protects and allows skin to regenerate.

Figure 5. Dermatologist skin analysis of moisture and elasticity at 3 and 6 weeks astaxanthin supplementation (Yamashita, 2006).



Astaxanthin reduced wrinkles and increase elasticity.

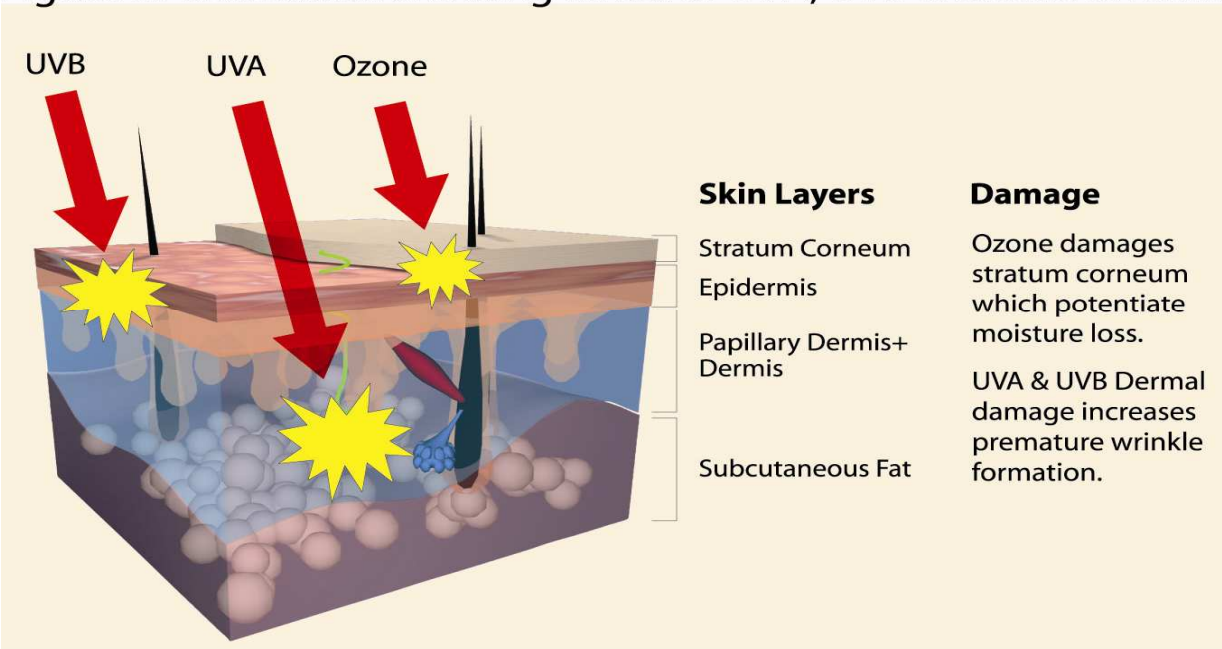
Mechanism of Action

Skin is composed of three layers: the epidermis, the dermis, and the subcutaneous fat. The dermis contains collagen, elastin, and other fibres that support the skin's structure. It is these elements that give skin its smooth and youthful appearance – and these are the parts of the skin that are damaged by UV radiation (UVR).

Anti-wrinkle

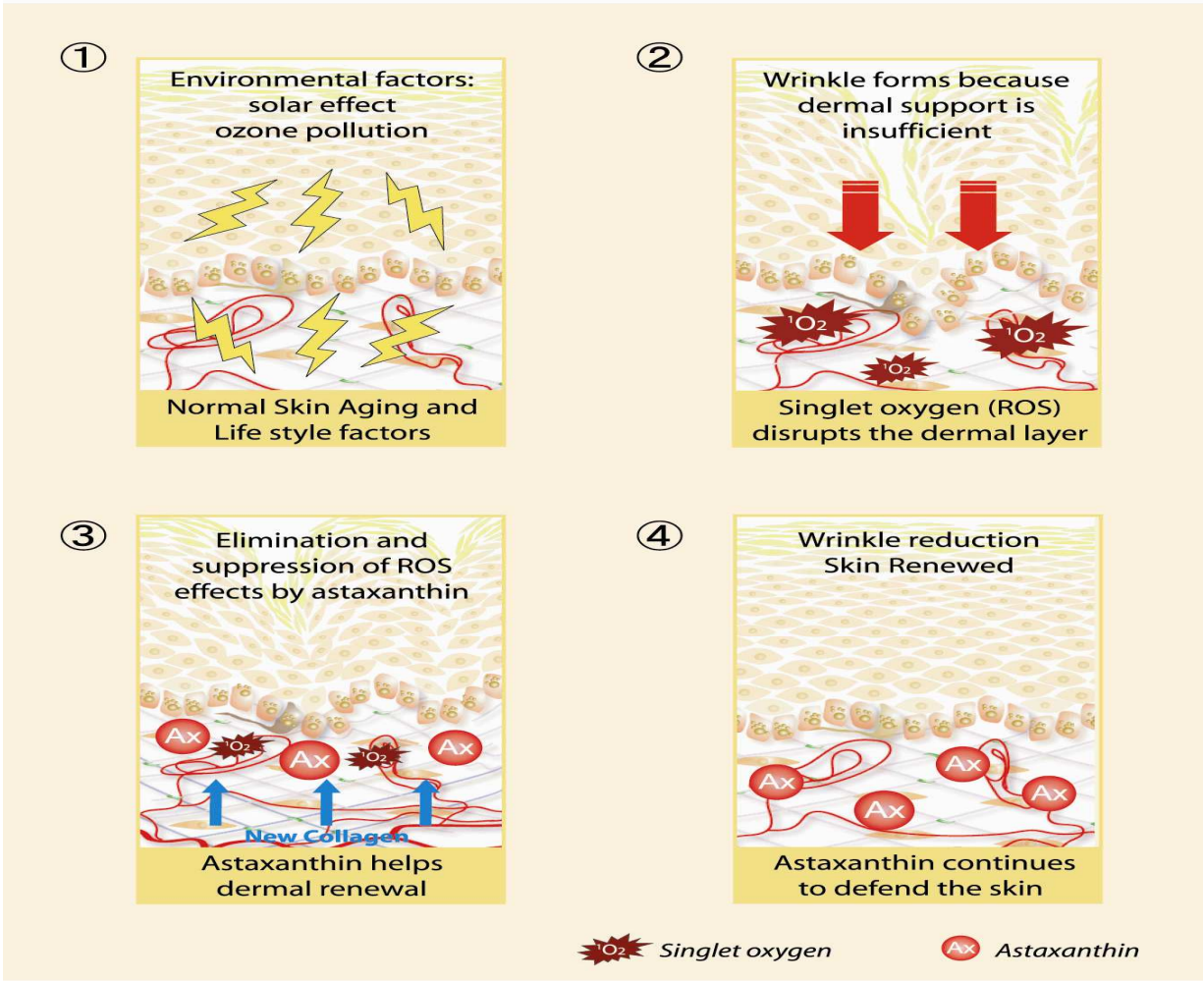
The UVR that affects the skin is composed of two types of waves; UVA and UVB. UVB rays are shorter than UVA rays, and are the main cause behind wrinkle formation and melanin production. However, it is the UVA rays, with their longer wavelength, that are responsible for much of the damage associated with photo aging. UVA rays penetrate deep into the dermis, where they damage collagen fibres, leading to wrinkle formation (Figure 6).

Figure 6. Illustration showing effect of UVA, UVB & Ozone on skin



UV rays induce the production of in situ radical oxygen species (ROS) and matrix metalloproteinases (MMP). These factors are the root of wrinkle formation because they destroy the collagen matrix in the dermis. Fortunately, the skin's repair mechanism will rebuild the damage collagen. However, the hindrance of skin renewal by repeated exposure to uncontrolled levels of ROS and MMP leads to the formation of wrinkles. The presence of astaxanthin attenuates the effects of reactive oxygen and MMP and therefore, it allows the skin to regenerate properly (Figure 7).

Figure 7. Astaxanthin supports skin renewal by attenuating factors which contribute to wrinkle formation



Astaxanthin defends against Reactive Oxygen Species (ROS).

Oxygen present in our cells can form harmful radicals known as ROS or active oxygen when sufficient energy from UV rays is applied. ROS include singlet oxygen, superoxides and hydroxyl radicals (leading to peroxyl radicals) and they attempt to steal electrons from neighbouring molecules such as DNA, phospholipids, enzymes and protein in order to stabilize.
Fortunately, astaxanthin is able to quench singlet oxygen reactions and suppress lipid peroxidation much more effectively than other well known antioxidants and thus control the presence of ROS.

Anti-inflammatory Action

Inflammation that normally follows sun exposure can be modulated by a powerful antioxidant. Yamashita (1995) shows in healthy male subjects (n=7), that topical natural astaxanthin significantly reduces burn level (erythema) by 60% at 98 hours after UVB exposure. We now know that astaxanthin works by suppressing the proinflammatory mediators and cytokines via the IκB kinase dependant NF-κB activation pathway (Lee *et al*., 2003).

Safety for Topical & Nutritional Use

Astaxanthin is determined safe for topical use. A total of forty-five subjects (males and females) were exposed to the Standard Japanese Patch test and results were reported 24 and 48 hours after application. Dermatitis was only induced by the adhesive plaster and not astaxanthin itself (Seki *et al*. 2002).
Furthermore, Koura (2005) reports no adverse topical reactions in animal sensitization models.
Astaxanthin is listed in the JP Cosmetics and INCI name as *Haematococcus pluvialis* extract.

Outlook

Naturally, the best way to avoid photo-aging is through prevention of the solar effects on skin by applying sunscreen to areas vulnerable to increased exposure. However, recent surveys reveal that people in general are not doing enough to protect their skin. The use of powerful carotenoids like astaxanthin in topical and nutritional skin products can help deliver the benefits against the risk of accelerated photo-aging and skin cancer.

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Patent

Method of inhibitating the expression of inflammatory cytokines
and chemokines, US7078040.