Astaxanthin, canthaxanthin and beta-carotene differently affect UVA-induced oxidative damage and expression of oxidative stress-responsive enzymes.

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Carotenoids are used for systemic photoprotection in humans. Regarding mechanisms underlying photoprotective effects of carotenoids, here we compared the modulation of UVA-related injury by carotenoids. Human dermal fibroblasts (HDF) were exposed to moderate doses of UVA, which stimulated apoptosis, increased levels of reactive oxygen species and thiobarbituric acid reactive substances, decreased antioxidant enzymes activities, promoted membrane perturbation, and induced the expression of heme oxygenase-1 (HO-1). The carotenoids astaxanthin (AX), canthaxanthin (CX) and beta-carotene (betaC) were delivered to HDF 24 h before exposure to UVA. Astaxanthin exhibited a pronounced photoprotective effect and counteracted all of the above-mentioned UVA-induced alterations to a significant extent. beta-Carotene only partially prevented the UVA-induced decline of catalase and superoxide dismutase activities, but it increased membrane damage and stimulated HO-1 expression. Moreover, betaC dose-dependently induced caspase-3 activity following UVA exposure. In contrast, CX had no effect on oxidative damage, except for HO-1 expression, which was augmented. Uptake of AX by fibroblasts was higher than that of the other two carotenoids. The photostability of the three compounds in fibroblasts was AX > CX >> betaC. The data indicate that the oxo-carotenoid AX has a superior preventive effect towards photo-oxidative changes in cell culture.

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Modulatory effects of an algal extract containing astaxanthin on UVA-irradiated cells in culture.

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UV radiation from sunlight is the most potent environmental risk factor in skin cancer pathogenesis. In the present study the ability of an algal extract to protect against UVA-induced DNA alterations was examined in human skin fibroblasts (1BR-3), human melanocytes (HEMAc) and human intestinal CaCo-2 cells. The protective effects of the proprietary algal extract, which contained a high level of the carotenoid astaxanthin, were compared with synthetic astaxanthin. DNA damage was assessed using the single cell gel electrophoresis or comet assay. In 1BR-3 cells, synthetic astaxanthin prevented UVA-induced DNA damage at all concentrations (10 nM, 100 nM, 10 microM) tested. In addition, the synthetic carotenoid also prevented DNA damage in both the HEMAc and CaCo-2 cells. The algal extract displayed protection against UVA-induced DNA damage when the equivalent of 10 microM astaxanthin was added to all three-cell types, however, at the lower concentrations (10 and 100 nM) no significant protection was evident. There was a 4.6-fold increase in astaxanthin content of CaCo-2 cells exposed to the synthetic compound and a 2.5-fold increase in cells exposed to algal extract. In 1BR-3 cells, exposure to UVA for 2 h resulted in a significant induction of cellular superoxide dismutase (SOD) activity, coupled with a marked decrease in cellular glutathione (GSH) content. However pre-incubation (18 h) with 10 microM of the either the synthetic astaxanthin or the algal extract prevented UVA-induced alterations in SOD activity and GSH content. Similarly, in CaCo-2 cells a significant depletion of GSH was observed following UVA-irradiation which was prevented by simultaneously incubating with 10 microM of either synthetic astaxanthin or the algal extract. SOD activity was unchanged following UVA exposure in the intestinal cell line. This work suggests a role for the algal extract as a potentially beneficial antioxidant.
Modulation of UVA light-induced oxidative stress by beta-carotene, lutein and astaxanthin in cultured fibroblasts.

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The ability of beta-carotene, lutein or astaxanthin to protect against UVA-induced oxidative stress in rat kidney fibroblasts (NRK) was assessed. Activities of the antioxidant enzymes catalase (CAT) and superoxide dismutase (SOD), and changes in thiobarbituric acid reactive substances (TBARS) were measured as indices of oxidative stress. Exposure to UVA light at a dose intensity of 5.6 mW/cm² for 4 h resulted in a significant decrease in CAT and SOD activities and a significant increase in TBARS. No cytotoxicity, as indicated by lactate dehydrogenase (LDH) release, was observed. Beta-Carotene (1 microM), lutein (1 microM) and astaxanthin (10 nM) protect against UVA light-induced oxidative stress in vitro with astaxanthin exhibiting superior protective properties.

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Vitamin A status and metabolism of cutaneous polyamines in the hairless mouse after UV irradiation: action of beta-carotene and astaxanthin.

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Solar radiations (UV A and B) can cause epidermis photoaging and skin cancers. These frequently irreversible effects result from the in situ generation of free radicals. However, it has been noted that nutritional factors can modulate photochemical damage, in particular the common carotenoids present in food, which can be considered as potential prophylactic agents against carcinogenesis. We investigated the effect of UV A and B radiations on the skin of the SKH1 hairless mouse fed a diet either lacking in vitamin A or supplemented with retinol, beta-carotene or astaxanthin. The latter is an oxygenated carotenoid (like canthaxanthin) without provitamin A activity and with strong singlet oxygen quenching ability. After analysing of vitamin status of each group (plasma retinol concentrations and hepatic reserves), we searched for UV-induced modifications of polyamine metabolism by measuring epidermal ornithine decarboxylase (ODC) activity and free polyamines concentration (putrescine, spermidine and spermine). In the basal state without irradiation, differences in ODC activity between groups were nonsignificant; but after UV stimulation, ODC increased markedly in the skin of vitamin A-deficient animals, much more than in other groups. Curiously, the addition of astaxanthin or beta-carotene to the regimen containing retinol reduced the protective effect of retinol alone. Regarding polyamines after irradiation, putrescine was significantly increased in the skin of deficient animals, in parallel with ODC activity. However, astaxanthin had a stronger inhibitory effect on putrescine accumulation than retinol, and decreased spermidine and spermine concentrations: this suggests a specific action on transglutaminases.

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Beauty From Within: A Synergistic Combination Of Astaxanthin And Tocotrienol For Beauty Supplements
Yamashita, E.


Previously reported dermatological benefits of natural astaxanthin included anti-hyperpigmentation, melanin synthesis inhibition, and reduced photo-skin aging. Hence, the potency of astaxanthin for cosmetic effect is “clearly visible”. Another class of natural compounds called tocotrienols also offer cosmetic benefits. A member of the vitamin E family, its isomeric form (chemically identical, but structurally different) imparts greater protection against free radicals than its popular cousin, alpha-tocopherol. Tocotrienols are generally 40-60 times more powerful than alpha-tocopherols in terms of free radical protection. Both astaxanthin and tocotrienols are found naturally in daily foods we consume. By concentrating these into an oral beauty supplement, it can provide an excellent source of protection in addition to the daily skincare regime. Results in 4 weeks supplementation indicated reduction in fine wrinkles, increased skin moisture and increased skin elasticity compared to placebo.
Beauty clinical: Astaxanthin with Omega 3 and Marine Glycosaminoglycans

Alain Thibodeau, Director of Scientific Affairs for Atrium Biotechnologies Inc. in Quebec, Canada published results of a blinded parallel group clinical trial on topical and supplemental forms of a product they call MRT2 (Matrix Rejuvenation Technology 2). The trial was done using both a topical product containing marine glycosaminoglycans and a supplement containing marine glycosaminoglycans, astaxanthin and omega-3 fatty acids. The trial involved 100 subjects.

Significant improvements were measured in skin hydration and elasticity. Skin appearance (including skin tone, fine lines and sallowness) also showed benefits, with the strongest improvements made in subjects using both the supplement and the topical products.

“We can demonstrate a synergistic activity between the topical product and the dietary supplement…The topical product works. The supplement works as well, but you get much better results from using both” said Thibodeau.
Dietary /Nutritional Supplements: The New Ally to Topical Cosmetic Formulations?
Alain Thibodeau and Edouard lauzler

Dietary/Nutritional Supplements

Dietary/nutritional supplements can be used to make active nutrients available to all organs of the body. As mentioned earlier, skin is an organ and may therefore benefit from active nutrients conveyed by dietary/nutritional supplements. The repercussions of nutrient on skin health are well exemplified by the fact that some skin disorders are directly linked to nutritional deficiencies.

Conversely, skin plays a major role in maintaining bone health through the synthesis of vitamin D. the interrelation between skin and the nutritional homeostasis has been recently highlighted and calls upon the understanding of the cellular and molecular processes in play.

We have performed a clinical trail in which a topical cream formulation and a dietary/nutritional supplement were concomitantly administered. The dietary/nutritional supplement provided proteoglycans, collagen, glucosamine, carotenoid pigment (astaxanthin esters) and omega-3 essential fatty acids (EPA and DHA). The efficacy of this regimen was demonstrated on the visual appearance of signs of aging as well as by the amelioration of functional properties of the skin.
A novel micronutrient supplement in skin aging: a randomized placebo-controlled double-blind study

Alain Béguin

Summary

Background: Skin aging, a combination of intrinsic and environmentally induced processes, predominantly ultraviolet (UV) light from the sun, results in characteristic tissue alterations, such as the degradation of collagen and the formation of visible fine lines and wrinkles.

Objective To test the efficacy and safety of a novel micronutrient supplement (Estime® containing BioAstin Natural Astaxanthin) in skin aging.

Methods A 4-month randomized double-blind controlled study including 40 subjects where the supplement was tested against placebo for 3 months followed by a 1-month supplement-free period for both groups to assess lasting effects. Efficacy measurements included skin surface evaluation, ultrasound measurement of sun-exposed and protected areas of the skin (back of the hand and ventral forearms, respectively), and photographic assessment.

Results All investigated parameters showed a continuous and significant improvement in the active group during the 3 months of supplementation as compared to placebo. Photographs showed visible improvement of the overall skin appearance and reduction of fine lines. Ultrasound measurements showed an increase in dermis density of up to 78% in the active group (P < 0.0001). The final assessment after 1 month without supplementation showed no further improvements, but a slight decrease was observed in most improved parameters. No treatment-related side effects were reported.

Conclusion The study demonstrated that the supplement appears to be effective and safe as an oral supplement to protect the skin and support its repair process. Recommendations are made for further evaluations.
The Effects of a Dietary Supplement Containing Astaxanthin on Skin Condition
Eiji Yamashita

The somatic effects on human skin by 4mg per day astaxanthin supplementation were demonstrated in a single blind placebo controlled study using forty-nine US healthy middle-aged women. There were significant improvements in fine lines/wrinkles and elasticity by dermatologist’s assessment and in the moisture content by instrumental assessment at week 6 compared to base-line initial values.

Astaxanthin, widely and naturally distributed in marine organisms, including Crustacea such as shrimps and crabs and such fish as salmon and sea bream exhibits a strong anti-oxidative effect, and its action is reported to 1,000 times stronger than alpha-tocopherol and approximately 40 times stronger than beta-carotene. It has also been reported that astaxanthin doesn’t have any pro-oxidative nature like beta-carotene and lycopene and its potent anti-oxidant property is exhibited at the cell membrane. Although used only as a coloring in the past (either as a food additive or a dye-up agent for cultured fish), astaxanthin has become one of the major materials eagerly anticipated by industries for dietary supplements and personal care products.

Furthermore its other various important benefits to date have suggested for human health such as anti-inflammation, LDL cholesterol oxidation suppression, immunomodulation, anti-stress, limiting diabetic nephropathy, improved semen quality, attenuating eye fatigue, sport performance and endurance, limiting exercised induced muscle damage and improving hypertension.

In terms of dermatological actions, suppression of hyper-pigmentation, inhibitions of melanin synthesis and photo-aging have been reported. We have also reported visual wrinkled reduction by topical astaxanthin. However, only one study for internal use about cosmetic benefit of a dietary supplement including astaxanthin and tocotrienol on human skin has been reported.

Here we report the effects of a dietary supplement containing astaxanthin on skin condition performed in the United States of America.
Biological activities of astaxanthin and its cosmeceutical application.

YAMASHITA EIJI

The present review covers cosmeceutical benefits of astaxanthin that is one of the most abundant carotenoids in nature, particularly in marine based life. The antioxidant properties of astaxanthin without any pro-oxidative nature working at cell membrane and cosmeceutical effects such as anti-hyperpigmentation, anti-photoaging, melanin inhibition and visual wrinkle reduction by topical or internal use and one of the action mechanisms of astaxanthin on NF-κB dependent inflammation are introduced. And current and future cosmeceutical applications of astaxanthin particularly from a green microalgae Haematococcus pluvialis that is the most ideal source in the earth are discussed describing actual examples of astaxanthin containing skin care products in Japanese market.
Photoprotective Effect of Astaxanthin Applied to the Skin

Arakane, K. 2002. KOSE Corporation

Reactive oxygen species generated by exposing the skin to sunlight are responsible for sunburn, lipid peroxidation and degenerative changes in dermal connective tissues. This causes premature aging of the skin.

A researcher from a Japanese company called KOSE Corporation compared astaxanthin to other commonly used ingredients in cosmetics that are thought to protect the skin from the damaging effects of sunlight. He found that astaxanthin potentially offers greater antioxidant protection against premature signs of aging.
Superior Skin Protection via Astaxanthin

Kumi Arakane

It has been believed for a long time that the skin exists only for the purpose of merely protecting our body by physically shielding it from outside factors. But in recent years, along with the radical progress in the field of dermatological science studies, it is known that the skin does actually indicate various responses and accept acute and chronic damages under UV irradiation. According to the enthusiastic studies to clarify the mechanism leading to the skin damages, nowadays the reactive oxygen species generated by UV irradiation is considered to be an important factor mediating photo-induced skin damages. Accumulation skin damages by reactive oxygen species such as lipid peroxidation, sunburn and degenerative changes in dermal connective tissues induce the skin aging. To protect skin from reactive oxygen species, many cosmetics contain nowadays both naturally occurring molecules and synthetic compounds as antioxidant. However, β-carotene was the only carotenoid for cosmetics among more than 600 carotenoids which had been isolated from nature, until astaxanthin from Antarctic krill was approved for cosmetics in 1997. In this paper, I would like to show the possibility of astaxanthin as a cosmetic ingredient and the useful formula for maintaining the stability of astaxanthin in the preparation.
Preventive Effects of Carotenoids on Photoaging and Its Application for Cosmetics

MIZUTANI YUKI; SAKATA OSAMU; HOSHINO TAKU; HONDA YOSHIKO; YAMASHITA MIKA; ARAKANE KUMI; SUZUKI TADASHI

Carotenoids are functional materials and more than 650 kinds of carotenoids are isolated from nature. They have been applied for foods, but most of these carotenoids have not been studied in terms of their effects on skin functions, and because of their instability under light exposure they were hardly used in the cosmetics field until now. Using hairless mice irradiated with UVB to produce photoaged skin, we investigated the inhibitory effect of astaxanthin on wrinkle formation, decrease of skin elasticity, ultrastructural change of dermal collagen fiber bundles and elastic fibers and the level of matrix metalloproteinase-1 (MMP-1) activity. These results indicated that the astaxanthin had the superior protection effect on photoaging as a ROS scavenger. It is well known that carotenoids are easy to decompose during storage by UV light and oxygen. We found that the incorporation of dl-ALPHA.-tocopherol and .ALPHA.-glucosyl rutin was able to maintain long-term stability of astaxanthin in preparation. This research demonstrated the superior anti-aging effects by carotenoids and this is the first time for carotenoids to be practically applicable to cosmetic formulation.
Effects of astaxanthin from Haematococcus pluvialis on human skin.
Patch testing Skin repeated application test Effect on wrinkle reduction.

SEKI TAI SUKE; SUEKI HIROHIKO; KONO HIROMI; SUGANUMA KAORU; YAMASHITA EIJI

Astaxanthin is a natural color carotenoid found in salmon, salmon eggs, krill, and crab. Therefore, astaxanthin has been contained in the human diet for a long time. Astaxanthin from krill has been used for cosmetics to suppress post-UVB hyperpigmentation in human skin and food color additives. Recently, astaxanthin from Haematococcus pluvialis is available using new fermentation technology of H. pluvialis and it is used for dietary supplements, food color additives and cosmetics. Effects of astaxanthin from Haematococcus pluvialis on human subjects were tested. No serious adverse effects were observed by patch testing and sequencing applied test on human skin. In a pilot study, the skin repeated application test of cream containing astaxanthin on human skin showed the visual wrinkle reduction. The present paper described about patch testing, skin repeated application test, and a pilot study evaluating the wrinkle reduction effect on human skin.
Effect of Antioxidant to Inhibit UV-Induced Wrinkles

ARAKANE KUMI

Living organisms are protected from harmful ultraviolet (UV) rays by the ozone layer surrounding the earth. However, depletion of the ozone layer and an increase in the amount of UV rays in sunlight reaching the earth's surface have been recently reported. As a result, social concerns over the effects of UV on living organisms have been increasing year by year. The skin covers the outer surface of the body, and so it is most vulnerable to UV. Because UV-induced wrinkles are prominently observed only in sun-exposed areas, they are apparently caused by chronic damage due to accumulated UV exposure. In addition to a change in appearance (large deep wrinkles), histological changes including thickening of the epidermis and dermis, elastin fiber deposition and decreased collagen fibers are observed as a result of continuous UV irradiation. Many reports indicate the involvement of action of reactive oxygen species in UV-induced wrinkles formation. Reactive oxygen species are known to damage essential elements including collagen and elastin which maintain elasticity and firmness of the skin, and also damage the function of fibroblasts producing these elements. It goes without saying that application of UV-absorbing agents is effective in preventing changes associated with photoaging. It is also reported that antioxidants such as vitamins C, E and iron chelators are effective for photoaging. We demonstrate that reactive oxygen species quenchers play an important role in reduction of UV-induced wrinkles formation using a carotenoid, astaxanthin, which has no pro-vitamin A activity unlike .BETA.-carotene, and a new iron chelator, N-(4-pyridoxylmethylene)-L-serine (PYSer), which consists of biomimetic molecules and effectively suppresses production of hydroxyl radical by chelating iron in skin. The demonstrable and potential roles of antioxidants for suppression of UV-induced wrinkles formation effectively are summarized here.

Skin Health
Austaxanthin attenuates the UVA-induced up-regulation of matrix-metalloproteinase-1 and skin fibroblast elastase in human dermal fibroblasts.

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Abstract
BACKGROUND: Repetitive exposure of the skin to UVA radiation elicits sagging more frequently than wrinkling, which is mainly attributed to its biochemical mechanism to up-regulate the expression of matrix-metalloproteinase (MMP)-1 and skin fibroblast elastase (SFE)/neutral endopeptidase (NEP), respectively. OBJECTIVE: In this study, we examined the effects of a potent antioxidant, astaxanthin (AX), on the induction of MMP-1 and SFE by UVA treatment of cultured human dermal fibroblasts. METHODS: Those effects were assessed by real-time RT-PCR, Western blotting and enzymic activity assays. RESULTS: UVA radiation elicited a significant increase in the gene expression of MMP-1 as well as SFE/NEP (to a lesser extent) which was followed by distinct increases in their protein and enzymatic activity levels. The addition of AX at concentrations of 4-8 microM immediately after UVA exposure significantly attenuated the induction of MMP-1 and SFE/NEP expression elicited by UVA at the gene, protein and activity levels although both the UVA stimulation and the subsequent AX inhibition were greater for MMP-1 than for SFE/NEP. Analysis of the UVA-induced release of cytokines revealed that UVA significantly stimulated only the secretion of IL-6 among the cytokines tested and that AX significantly diminished only the IL-6 secretion. CONCLUSION: These findings indicate that, based on different effective concentrations of AX, a major mode of action leading to the inhibition elicited by AX depends on inhibition of UVA effects of the reactive oxygen species-directed signaling cascade, but not on interruption of the IL-6-mediated signaling cascade. We hypothesize that AX would have a significant benefit on protecting against UVA-induced skin photo-aging such as sagging and wrinkles. 2010 Japanese Society for Investigative Dermatology.

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Transgenic carrot plants accumulating ketocarotenoids show tolerance to UV and oxidative stresses.

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Ketocarotenoids are strong antioxidant compounds which accumulate in salmon, shrimp, crustaceans and algae, but are rarely found naturally in higher plants. In this study, we engineered constitutive expression of an algal beta-carotene ketolase gene (bkt) in carrot plants to produce a number of ketocarotenoids from beta-carotene. These included astaxanthin, adonirubin, canthaxanthin, echinenone, adonixanthin and beta-cryptoxanthin. Leaves accumulated up to 56 microg/g total ketocarotenoids and contained higher beta-carotene levels but lower levels of alpha-carotene and lutein. The photosynthetic capacity of transgenic plants was not significantly altered by these changes. However, when high-expressing transgenic plants were exposed to UV-B irradiation, they grew significantly better than the wild-type controls. Similarly, leaf tissues exposed to various oxidative stresses including treatment with H(2)O(2) and methyl viologen showed less injury and retained higher levels of chlorophyll a+b. Total carotenoid extracts from transgenic leaves had higher antioxidant and free-radical scavenging activity in vitro compared to control leaves. Transgenic tissues also accumulated lower amounts of H(2)O(2) following exposure to oxidative stresses, suggesting that free radical and reactive oxygen species were quenched by the ketocarotenoids.

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