Carotenoids: Red, Orange, and Yellow Wonders

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Carotenoids are derivatives of vitamin A and have widespread use in cosmeceuticals due to the established topical antiaging benefits associated with the prescription tretinoin. Cosmetic chemists are searching for ingredients that can rival the topical effects of tretinoin in terms of collagen production, wrinkle reduction, and pigmentation improvement. Because tretinoin has a poor tolerability profile due to the unwanted side effects of erythema and peeling, perhaps a lower potency, over-the-counter (OTC) carotenoid could produce some of the same benefits.

The carotenoids are a large family of red, orange, and yellow substances that perform vital antioxidant roles when ingested and are less well established as topical antioxidants. There are more than 600 known naturally occurring carotenoids. Carotenoids are found in numerous fruits and vegetables and are consumed in large quantities in the Western diet. The most notable source is tomatoes. Topically, carotenoids are difficult to formulate in creams because they impart a characteristic color to the product; however, colorless carotenoids have been developed. Removing one double bond in the carotenoid can decrease the color and improve product aesthetics.

This article examines the commonly used topical carotenoids, including astaxanthin, lutein, lycopene, mangosteen, and pomegranate. These raw materials are rapidly finding their way into moisturizing cosmeceuticals because they are relatively inexpensive and have great consumer appeal. It is clear that much of their efficacy data are from ingestion studies. Nevertheless, if it can be ingested, it can be applied to the skin.

Astaxanthin

Astaxanthin is a pink carotenoid found in high concentration in salmon, accounting for the characteristic pink color of the fish. This is the rationale for antiaging diets that recommend ingesting salmon 5 times per week.[1] For topical application purposes, astaxanthin is obtained from the marine microalgae *Haematococcus pluvialis*. The efficacy of astaxanthin is attributed to its cell membrane, composed of 2 external lipid layers, which has been touted to possess stronger antioxidant abilities than vitamin E.[2] The astaxanthin produced by algae is both water and oil soluble when exposed to intense UV radiation.

Few studies exist to confirm the topical effects of astaxanthin,[3] but it has been studied extensively as an oral supplement.[4] It is used as a homeopathic treatment for macular degeneration because, unlike the carotenoid canthaxanthin, it does not crystallize in the eye. It crosses the blood-brain barrier and has been studied in brain dysfunction to include spinal cord injuries and Parkinson disease.[5] Even though other carotenoids, such as β-carotene, have been proven ineffective in reducing the oxidative stress associated with cardiovascular disease, astaxanthin is currently undergoing further investigation.[6]

Astaxanthin in concentrations of 0.03% to 0.07% produces a pink cream. This limits the concentration that can be used, but no topical adverse reactions have been associated with astaxanthin. The topical antioxidant benefits of astaxanthin have not been established, but it is showing up in creams launched this year that are sold in skin care boutiques.

Lutein

Another carotenoid found in topical cosmeceuticals is lutein. It is naturally found in green leafy vegetables, such as spinach and kale. Lutein is an antioxidant in the plant kingdom and is also used for blue light absorption. In the animal kingdom, lutein is found in egg yolks, animal fats, and the corpus luteum. It is a lipophilic molecule, which makes it not soluble in water, and is characterized by a long polyene side chain composed of conjugated double bonds. These double bonds are degraded by light and heat, which is a universal characteristic of carotenoids to a greater or lesser degree.[7]

Lutein is used as a natural colorant due to its orange-red color resulting from the absorption of blue light. Its

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largest use is as a food supplement for chickens, which results in more vivid yellow yolks. In humans, lutein is concentrated in the macula and has been linked to the prevention of macular degeneration.[8] It has been available as a nutritional supplement since 1996 and can be administered as a sublingual spray for elderly patients with macular degeneration. Most well-conducted studies evaluating the benefits of lutein for macular degeneration have been inconclusive.[9] No recommended daily allowance has been established for lutein, but 6 mg/d has been published.[10] Most of the lutein used for food additives is derived from marigolds.

The question remains as to whether using lutein topically is of value. Again, data are lacking, but excessive lutein intake can result in carotenodermia, and excessive topical applications can result in bronzing of the skin. It may be of interest that when lutein is fed to chickens, the result is the characteristic yellow appearance of chicken skin, which is felt to be more attractive than the natural white skin. This may not be the case in humans.

Lycopene

Lycopene is a potent carotenoid found in most fruits and vegetables with a red color, including tomatoes, watermelons, pink grapefruits, papayas, gac, red bell peppers, and pink guavas. The highest lycopene-containing food is ketchup, but lycopene is not an essential human nutrient. The Mayo Clinic Web site grades the effectiveness of lycopene as an antioxidant as grade C because it is not clear if lycopene has an effect on the human body.[11] Lycopene oral supplements have been purported to reduce the risk for prostate cancer, but the US Food and Drug Administration concludes there is little scientific evidence to support this claim.[12]

Lycopene is a highly unsaturated hydrocarbon containing 11 conjugated and 2 unconjugated double bonds, which makes it a longer molecule than any other carotenoid. This makes its absorption into the skin doubtful. It undergoes trans-cis isomerization when exposed to sunlight. Even though lycopene was the oral supplement added to many commercial multivitamins in 2008, its topical value has never been documented. It is safe for topical application, but may stain the skin in high concentration.

Retinol

Of all the topical carotenoids, retinol is the best understood because it is necessary for vision and possesses a well-characterized skin receptor.[13] Prescription retinoids, such as tazarotene and tretinoin, are well studied for their ability to induce the skin changes noted in Table 1; however, OTC retinoids may demonstrate some of the same effects to a lesser degree.[14,15]

It is theoretically possible to interconvert the retinoids from one form to another. For example, retinyl palmitate and retinyl propionate, chemically known as retinyl esters, can become biologically active following cutaneous enzymatic cleavage of the ester bond and subsequent conversion to retinol. Retinol is the naturally occurring vitamin A form found in red, orange, and yellow fruits and vegetables. It is the pigment responsible for vision, but is highly unstable. Retinol can be oxidized to retinaldehyde and then oxidized to retinoic acid, also known as prescription tretinoin. It is this cutaneous conversion of retinol to retinoic acid that is responsible for the biologic activity of some of the new stabilized OTC vitamin A preparations designed to improve the appearance of benign photodamaged skin.[16] Unfortunately, only small amounts of retinyl

Cutaneous Effects of Topical Retinoids

Gross Dermatologic Effects

- Improvement in fine and coarse facial wrinkling
- Decreased tactile roughness
- Reduction of actinic keratoses
- Lightening of solar lentigenes

Histologic Dermatologic Effects

- Reduction in stratum corneum cohesion
- Decreased epidermal hyperplasia
- Increased production of collagen, elastin, and fibronectin
- Reduction in tonofilaments, desmosomes, melanosomes
- Numerous Langerhans cells
- Angiogenesis
- Decreased glycosaminoglycans
- Reduced activity of collagenase and gelatinase
- Normalization of keratinization of the pilosebaceous unit

palmitate and retinol can be converted by the skin, which accounts for the increased efficacy seen with prescription preparations containing retinoic acid.

The main problem with prescription retinoids is their irritancy. Unfortunately, as the biological efficacy of the retinoid increases, so does the irritancy. This is also the case with OTC retinoids. Retinol is more irritating than the retinyl esters and also more unstable. It is for this reason that cosmeceutical formulations not manufactured under strict oxygen-free conditions prefer to add retinyl palmitate to moisturizing creams. However, the retinyl palmitate may present to act as an antioxidant for the lipids present in the moisturizer.

The topical benefit of retinol has been documented by well-controlled studies.[17] It is commonly felt among dermatologists that retinol is of benefit,[18] but it is difficult in studies on moisturizers that do not include vehicle control to separate the retinol benefit from the moisturizer benefit. Nevertheless, of all the carotenoids available for formulation, retinol has the most evidence to support topical application efficacy.

Summary

Carotenoids are an interesting family of substances, of which only a few have been discussed. Many well-controlled studies have tried to show their oral benefit in everything from cardiovascular disease, cancer prevention, and brain trauma to their topical application benefit for photodamaged skin. It is interesting to note that all of these studies have been inconclusive to date. Could it be that carotenoids do not have the same protective antioxidant effect in humans as in fruits, vegetables, and algae? Or, is it that the right model or indication for study has not been identified? It seems to make intuitive sense that carotenoids should have some human benefit, but the data have not been forthcoming. Carotenoids are a large part of the Western diet, yet they are not an essential nutrient.

I must admit that my favorite summertime lunch is a freshly picked tomato sliced thinly on a potato flour roll. The tangy bite of the tomato is clearly due to ascorbic acid, while the red stain on my white blouse is from the carotenoids. Something so tasty must have some benefit. However, it remains to be proven.

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