Aging skin and food supplements: the myth and the truth

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Abstract The frenzied rhythm of our times leads our patients not only to resource to diet integrators—remorselessly overcoming difficulties or prejudices—to fulfill increasingly frequent nutritional needs due to decreasingly “correct” eating habits, but also to fight against a myriad of skin conditions. The rationale of a combined approach for the antiaging treatment of skin is based on the synergic effect between functional substances applied locally, where the problem arises, and other agents working from the inside to correct a need, to restore altered functions or conditions and to guarantee the correct intake of nutrients or active substances. This work discusses the active ingredients mostly used in the oral treatment of skin aging, together with the scientific evidences that do or do not support their use.

Introduction

Beginning from 1990, food loses its exclusive nutritional role, undertaking a more comprehensive one: nutrients begin to represent a prevention tool to preserve health from chronic and degenerative diseases, increasing wellness. Modern nutrition science is trying to deepen the link between food and health to highlight the biologic role that nutrients can perform on the body in general and on the skin in particular.

Cosmetic industry in turn found the opportunity to support traditional topical treatments with oral ones to strengthen the effects on the skin. Skin is actually the most visible organ and, at the same time, the first one exposed to external injury: people desire to preserve it for aesthetic and salutary concerns. Thus, the topic of nutritional supplementation invests all body components, skin being the first. Today, nutritional supplements with cosmetic aims are sought after and especially wished by those whose diet is not quite balanced. Different names are used to identify this supplementation, such as endocosmesis or nutricosmeceutics. These terms are often controversial, although denoting a new way to approach skin conditions.

Usually, food supplements consist of a nutritional component (vitamins, minerals, fibers) and a more generally salutary one (botanical or animal extracts). By a regulatory point of view, in Italy, there are no dedicated laws: food supplements are regulated as food intended for special conditions. Companies interested in the marketing of a food supplement need simply to notify to the Health Board the label of the product they are going to sell, saving time and money with respect to drugs’ market regulations.

In the last 10 years, chemists, nutritionists, and physicians have been working together to develop new nutritional applications to satisfy people’s needs and demands. People now are looking for products contributing both to skin health and disease prevention. At first, the supplements developed for such goals were those intended to stimulate exceeding fluid drainage to alleviate cellulite; since then, many different categories of supplements have been developed, coping with different skin needs, both dermocosmetic and dermatologic ones.

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This trend strongly influences the market: even pharmaceutical companies are moving to supplements to take advantage from their popularity and because the development and selling of supplements are less time- and money-consuming procedures.

Today, the cosmetic companies introduce routine topical treatments coupled with oral route products. This association is based on a strong rationale, namely, the synergy between the substances applied on the skin—where the problem arises—and the substances acting from inside that replenish gaps or support natural defense systems. The skin needs plenty of nutrients and metabolites that a topical product cannot supply by its own. We know that it is, moreover, not enough to apply a substance to the skin to be sure it will be absorbed and it will reach the target. This does not mean that cosmetics are useless, but just that they can be strengthened as to their effect. It is, however, even true that substances taken by oral route can be destroyed or can have a poor bioavailability.

So, food supplements with cosmetic aims should be considered as a nonconventional alternative or as a complementary way to approach skin problems, maintaining the skin and its appendages in a good physiologic condition and acting as a support to traditional cosmetics.

Background

In general, we have to consider that the skin is exposed to daily environmental injuries and, at same time, is connected with all parts the body. It is, therefore, reasonable to think that the combination of topical and oral treatments could be useful to protect/repair skin conditions. We should consider that the skin can have some deficiencies of particular oligoelements and vitamins, and that the supplementation is a very effective approach to recover health (scurvy, pellagra, zinc, and vitamin B_{12} deficiencies, etc). Thus, we know that some nutritional deficiencies can lead to skin diseases, but we have no evidence that it is possible to treat some of these (such as skin aging) only by oral route. A very close link exists between skin and nutritional homeostasis: this could be the rationale to develop and apply an oral route treatment to support the skin itself. Analyzing some articles, we can find a useful synergy between topical and oral treatments, acting as a support to traditional cosmetics.

Experimental evidence

In the field of skin aging, a problem that concerns both man and woman, we can find plenty of trials about the opportunity of using the oral route alone or in association with the topical one, both showing very good results. Likewise, lacking data or divergent results arise when we review articles testing ingredients alone or in combination, for example, combinations of traditional antioxidant molecules.

In particular, a study conducted on 453 volunteers revealed that skin wrinkling (measured by a cutaneous microtopographic method in a sun-exposed site in older people of various ethnic backgrounds) may be influenced by the types of food taken.

Namely, a high intake of vegetables, legumes, and olive oil appeared to be protective against cutaneous actinic damage thanks to their high content in antioxidant actives. So, the rationale in using the oral route to treat skin conditions is quite strong.

Now, the question is whether oral supplements do really exert the effect they are designed and intended for. Hundreds of supplements to specific skin conditions have been developed. In general, oral supplements contain ingredients (especially antioxidants) for the protection of the skin against environmental injuries and for the repairing of senescence feature, although only few of them have been assessed as their real efficacy, besides a simple placebo effect. Reactive oxygen species can cause harmful effects in keratinocytes and fibroblasts when the antioxidative defense mechanisms are exhausted. It would be, therefore, reasonable to prove if oral supplementation with various nutrient antioxidants could be useful in the prevention or treatment of skin disorders, especially those mediated by UV irradiation. Beta-carotene, ascorbic acid, and tocopherol have been tested alone or in combination in the prevention of sunburns, photodermatoses, and photocarcinogenesis, with divergent results. Other candidates for oral antioxidative supplementation in humans are selenium and polyphenols. Clinical data are, however, limited or lacking at present.
erythema, although the extent of the protective effect is modest. Other results do not show an antioxidant efficacy in the photoprotection of oral vitamin E and β-carotene in human skin. The authors examined the ability of 2 liposoluble antioxidants, vitamin E and β-carotene, to reduce the markers of oxidative stress and erythema after UV irradiation (UVR) skin exposure in 16 healthy subjects who received either α-tocopherol (n = 8, 400 IU/d) or β-carotene (n = 8, 15 mg/d) for 8 weeks. Biopsy samples before and after supplementation were taken from unexposed skin and from skin 6 hours after 120 mJ/cm² UVR exposure. Vitamin E or β-carotene supplementation had no effect on skin sensitivity to UVR. Although vitamin E supplements significantly decreased skin malondialdehyde concentration, none of the supplements affected other parameters of UVR-induced oxidative stress in human skin, suggesting that the supplementation did not induce photoprotection.

The same authors studied also the effects of vitamin C supplementation on UVR-induced damages in human skin. They hypothesized that an acute exposure of human skin to UVR in vivo would lead to oxidation of cell biomolecules, which could be prevented by prior vitamin C treatment. So, they examined in detail a time course of the changes of oxidative stress markers in the skin after exposure to physiologic amounts of UVR in vivo. Oral vitamin C supplements (500 mg/d) were taken by 12 volunteers for 8 weeks, resulting in a significant increase of vitamin C level in plasma and skin. The supplementation had no effect on the UVR-induced erythemal response. The malondialdehyde skin content was reduced by vitamin C supplementation, but surprisingly, reductions in the skin content of total glutathione and protein thiols were also observed. They speculated that this apparently paradoxical effect could be due to the regulation of the total reductant capacity by skin cells, such that vitamin C may have replaced other reductants in these cells. No evidence was obtained for an effect of supplementary vitamin C on the mild oxidative stress seen in human skin after UVR exposure.

There is increasing evidence that reactive oxygen species play a pivotal role in the process of aging. The skin, as the outermost barrier of the body, is exposed to various exogenous sources of oxidative stress, in particular, UV irradiation. These are believed to be responsible for the extrinsic type of skin aging, termed photaging. It seems reasonable, therefore, to try to increase the levels of protective low molecular weight antioxidants through a diet rich in fruits and vegetables or by direct topical application. Indeed, various in vitro and animal studies proved that low molecular weight antioxidants, especially vitamins C and E, ascorbate and tocopherol, as well as lipoic acid, exert protective effects against oxidative stress. Controlled long-term studies on the efficacy of low molecular weight antioxidants in the prevention or treatment of skin aging in humans are, however, still lacking.

Presumably, the question about the efficacy of oral supplementation directed to skin conditions lies in the features of the formulation: the choice, the concentration, and the quality of the active ingredients, as well as the kinetics—which depend on the drug delivery system—and so on. Most natural antioxidants such as α-tocopherol, ascorbic acid, and others are biologically unstable, poorly soluble in water, and poorly distributed to target sites. Because of these shortcomings, further prophylactic applications of dietary supplements have stagnated. This is partially due to a lack of basic knowledge of the delivery mechanisms of these dietary supplements and nutrients. Some authors in this regard strongly advocate a serious consideration of the bioavailability of dietary supplements, and some others, not finding a significant difference in the clinical and histologic appearance of photaging skin after placebo and treatment with green tea extracts in a double-blinded placebo-controlled trial, proposed an interesting hypothesis. It has been postulated that green tea polyphenols protect human skin from the cutaneous signs of photaging, although no significant changes could be clinically detected, suggesting that maybe a longer supplementation could be required for clinically observable improvements.

There are some reports of publications supporting the use of supplements specifically formulated with ingredients selected to help skin trophic, defense, or repair systems. These authors strongly supported by their experimental experience, suggested the opportunity to trust natural carotenoids antioxidant effects: for a successful intervention, a treatment with carotenoids is needed for a period of at least 10 weeks.

**Protoprotection**

The photoprotection exerted by a pool of antioxidants was investigated in a study of the effects of oral supplementation with carotenoids and a combination of carotenoids and vitamin E against the development of erythema in humans over 12 weeks. Erythema was induced by a "blue-light solar simulator. β-Carotene and α-tocopherol serum concentrations and carotenoid skin levels were assessed by high-performance liquid chromatography and reflection photometry. β-Carotene and α-tocopherol serum concentrations increased after the supplementation. Erythema on dorsal skin (back) was significantly diminished (P < .01) after 8 weeks, and erythema suppression was greater with the combination of carotenoids and vitamin E than with carotenoids alone. The antioxidants used in this study provided a protection against erythema in humans, and they can be useful to decrease sensitivity to UV light. Regarding the synergic effect of a pool and the possible enhancing effect of the excipient of a commercial product, another author reported a randomized, double-blind, placebo-controlled study on the clinical efficacy of an oral treatment of skin aging symptoms. Forty women with skin aging symptoms were randomized to receive a formulation containing marine proteins, α-lipoic acid, pine bark extract, vitamins and...
minerals (n = 20), or placebo (n = 20), twice daily for 6 months. Objective measurements of skin thickness and elasticity, together with subjective clinical assessments of various parameters (fine wrinkles, coarse wrinkles, tactile roughness, and telangiectasia), were performed. Self-evaluations were also made by the study participants. There was a significant improvement in skin quality in both objective and subjective parameters after treatment with the product compared with placebo. Participants’ self-evaluations also showed a statistically significant difference in favor of the active treatment.

Procyanidins from French maritime pine bark (Pycnogenol) are among the most powerful natural antioxidants that recycle and prolong vitamin C and E effects. These bioflavonoids neutralize collagenases and elastases, improving skin aging features. Used since 1853, Pycnogenol as a health supplement is a proven free radical scavenger, according to European researchers. It also efficiently protects from oxidative stress injury (lipid peroxidation and cytotoxicity) induced by UVR. The protective effects are dose related, with the highest concentration providing the greatest benefits. The ingredient is effective even in protecting the skin from erythema induced by UV-B rays.

Another study supporting the effects attributable to the synergism of a pool was performed on a combination of vitamins C and E, carotenoids, selenium, zinc, amino acids and glycosaminoglycans, blueberry extract, and Pycnogenol. The pool induced an improvement in skin smoothness and elasticity in a double-blind placebo-controlled study involving 62 women. Another study showed further evidence about the effect of an oral supplement containing glucosamine, amino acids, minerals, and antioxidants on cutaneous aging in a 5-week treatment of 53 female volunteers. The hydration properties of the skin as well as the textural analysis of women’s fine lines and wrinkles were assessed and compared with those of a control group of 12 individuals who did not receive the supplement. There was a statistically significant reduction (34%) in the number of visible wrinkles, as measured by the Silflo replicas, and a reduction (34%) in the number of fine lines in the group of women who took the supplement. No significant changes in epidermal hydration were observed in either the control or study groups.

As regards the sun protective effect of supplements, the literature reports a lot of evidence about the efficacy of antioxidant ingredients, though mixed. About this, there are very interesting results regarding some new stronger and longer-lasting sun protectors, thanks to the presence of carotenoids and vitamins. Even strong smokers and people undergoing severe sun exposure could benefit from taking oral carotenoids: after 60 days, the plasmatic levels of free radicals were proportionally lower with respect to type, dose, and combination of carotenoids, being their association with vitamins E and C the best treatment than single ingredients alone. The study protocol used for carrying out the evaluations let the authors determine the radical protective factor, which is a very useful parameter to calibrate supplements assumption, adapting their use to the real individual needs. Further evidence from the same authors concerned the protective effects of oral antioxidants on skin and eye function. They conclude that carotenoids used as nutritional supplements can play an interesting photoprotective role for both skin and eyes, increasing the activity of topical sunscreens.

The role of the traditional molecules lutein and astaxanthine—which have been used for years in eye care—is today under investigation for the potential application to skin care, thanks to the antioxidant properties these molecules are endorsed with.

Some interesting results about the photoprotective effects of lutein on the skin, besides its effects on the eyes, are disclosed by Krieger and Alves-Rodrigues. In turn, lycopene has recently been the object of a patent. After its linkage to lactoglobulin (lactolycopene), the lycopene was made hydrosoluble, thus, becoming easier to handle in cosmetic/oral formulations. Then, its combination with soy isoflavones and vitamin C has been studied in a 6-month treatment of 90 menopausal women taking 3 tablets a day (6 mg lycopene, 50 mg isoflavones, 60 mg vitamin C), revealing a significant improvement in some biophysical properties of the skin, such as density, viscoelasticity, microrelief as average depth of fine lines, hydration, and radiance, as indicated by instrumental evaluation.

**Vitamin E**

We should spend a few words for vitamin E also, traditionally used for topical applications, but more recently, as a precious ingredient of “cosmetofoods.” In particular, the term vitamin E is a generic word indicating a family of substances endorsed with antioxidant activity, involving 2 classes of agents: tocopherols and tocotrienols. Generally, if we speak about vitamin E, we refer to the tocopherol group.

![Skin thickness (mean ± SD).](image)

Fig. 1 Skin thickness (mean ± SD). Significant increase in dermal thickness (P < .0001) in the active-treated group. bas indicates baseline; fin, final.
and, in particular, to α-tocopherol, but tocotrienols are gaining increasing popularity in dermocosmetic applications, thus, being considered the third millennium vitamin E form. They are stronger antioxidant than tocopherols and show a better cutaneous bioavailability. They accumulate, moreover, in the stratum corneum, and they exert a very important action against free radicals elicited by actinic damage and injury caused by environmental pollutants; the δ-tocotrienol form is particularly effective. They were born as nutraceuticals, but they are suitable to be formulated both as topical products and cosmecofoods, or as food supplements that claim specific and positive effects on the skin, intended for skin aging prevention or treatment.29-34

Starting from the studies conducted on Imedeen,35 to prevent/treat skin aging, we have today more scientific evidence of the protective and regenerative role on the skin exerted by fish polysaccharides in association with antioxidants and capillary protectors.36

**Topical agents**

Topically applied cosmetic products can ameliorate aging skin condition. Our study shows that an oral supplementation with fish cartilage can be helpful in improving the treatment of aging skin. We enrolled 30 healthy women with signs of skin aging. Fifteen women were treated for 2 months with a food supplement based on polysaccharides derived from cartilage and a natural mix of antioxidants, whereas the other 15 with a placebo. We performed a clinical evaluation and measured some biophysical parameters related to skin function and wrinkle severity, such as silicone replica, skin thickness, mechanical properties, skin color, and capacitance. The results showed statistically significant changes in the active-treated group in comparison to the placebo. In particular, dermal thickness (treatment, 1.13-1.23 mm; $P < .001$), skin wrinkling (treatment, 9.5-3.5 Ra; $P < .002$), viscoelasticity (treatment, 0.70-0.97%; $P < .02$), and skin color (treatment, brighter and less pigmented; $P < .02$) showed a considerable improvement. Most of these parameters were related to changes occurring within the dermal matrix, which improved after the treatment, whereas we know that most of the topically applied cosmetic products have a short-term effect only on superficial structures. So, the oral supplementation can be integrated with topical products to obtain an even more effective result.

**Fig. 2** Mechanical properties. Skin viscoelasticity—R6 (mean ± SD). Statistically significant increase in dermal viscoelasticity after treatment in the active-treated group ($P < .02$).

**Fig. 3** Elasticity—R2 (mean ± SD). Improvement in skin elasticity, although not statistically significant, after an 8-week treatment of the active group ($P = .07$).

**Fig. 4** Skin replica. Ra-3D-roughness and waviness (mean ± SD). Relative changes in roughness (Ra) due to microrelief and waviness-related deeper wrinkles (data expressed in % of improvement). In the group supplemented with fish cartilage, we recorded improvements of 9.5% and 13.5% in microrelief ($P < .02$) and waviness ($P < .002$).

**Fig. 5** Skin color (mean ± SD) luminosity or brightness. Significant improvement in skin brightness ($P < .006$) in the active group due to increased skin reflectance.
On the basis of our results, we can suggest the prescription of this product for skin protection against aging and for the recovering of its properties after an injury, in dermocosmetic treatments, to prepare skin to plastic surgery, as well as sun protector.

We report, hereafter, some graphics to show the data trend (Figs. 1-5).

These results confirm that fish polysaccharides taken orally can be helpful in ameliorating some aspects of skin aging because of their peculiar properties. It could be interesting to investigate a combination treatment with topical retinoids/alpha hydroxyacids.

Another important skin feature is hydration, normally affected because of aging.

A recent study carried out an interesting application for ceramides formulated with lycopene, vitamin E, borago oil rich in polyunsaturated fatty acids, and the amino acidic precursors of collagen synthesis, such as lysine and proline. The study showed the effects of oral supplementation in improving and preventing skin dehydration. A total of 32 healthy female volunteers entered the study, 16 of which were treated for 40 days with a food supplement (vegetable ceramides, amino acids, fish cartilage, antioxidants, and essential fatty acids) and 16 of them with placebo. At the beginning and at the end of the treatment skin hydration, smoothness and desquamation were assessed both instrumentally (Corneometer, Visioscan) and by self-assessment. The results of the clinical and instrumental evaluations carried out in this study have highlighted how the active treatment is effective in improving skin hydration and in reducing the cutaneous roughness and the depth of furrows, in comparison to the placebo. In fact, concerning several important parameters such as the stratum corneum hydration and skin roughness, the improvements measured exceeded 25%.

Conclusions

On the basis of the data here reported, there is strong evidence and rationale in using food supplements to support traditional dermocosmetic treatments when approaching skin conditions. Perhaps the divergent data about efficacy on skin conditions are linked to the differences in the starting experimental conditions: dosage, duration, combination of ingredients, kind of excipients, skin conditions, and so on. To face up to skin problems, we suggest that a complete approach to skin dermocosmetic conditions could be represented by the correct association of a topical treatment with an oral one on the basis of their synergy, thus, fighting both symptoms and their causes.

In the future, we can hypothesize even other opportunities, such as the possibility to implement the scientific research on functional ingredients, both new and newly associated, and to screen some new potentially useful natural ingredients.

References