Skin appearance is affected by intrinsic factors (e.g., aging) and extrinsic factors (e.g., UV light). A myriad of treatments has been created to combat the phenotypic effects of these forces, including vitamins and supplements. This article reviews these therapies with a focus on carotenoids; vitamins C, E, and D; as well as collagen, ceramides, and mixed supplements.

As the largest and most exposed organ in the body, the skin experiences trauma from both extrinsic and intrinsic aging factors, resulting in loss of elasticity, increased laxity, wrinkling, and rough-textured appearance. Chronologically aged skin appears dry, thin, and finely wrinkled; photoaged skin appears leathery with coarse wrinkles and uneven pigmentation. In recent years, numerous systemic nutrients have been proposed to improve skin appearance. This article reviews the efficacy of these vitamins and supplements.

Carotenoids

Carotenoids are a group of lipophilic molecules derived from vitamin A. Ingestion of carotenoids may play a role in photoprotection against UV radiation (UVR) by acting as acceptors of reactive oxygen species.

Stahl et al investigated lycopene’s usefulness in protection against UVR-induced erythema. Over 10 weeks, 9 volunteers received 40 g of tomato paste containing 16 mg daily of lycopene while 10 controls received placebo. A solar simulator was used to induce erythema of the skin at weeks 0, 4, and 10. At week 10, erythema formation was 40% lower in the lycopene group compared to controls ($P = .02$).

In another study assessing the photoprotective effects of a novel nutritional and phytonutrient blend of carotenoids, 36 women with Fitzpatrick skin types I and II were treated for 8 weeks. Presupplementation, UVR-induced erythema, and skin carotenoid concentrations were determined along with facial skin attributes and characteristics. Results showed protection against UVR-induced skin damage, with reductions in erythema at 3 minimal erythema doses (MEDs) ($P = .01$). Additionally, significant improvements were noted in facial skin elasticity, radiance, and overall appearance (all $P < .05$).

In 2013, Meinke et al conducted an 8-week, double-blind, placebo-controlled study on 24 volunteers whose diets were supplemented with moderate amounts of carotenoids, including lutein, beta-carotene, and lycopene. Utilizing novel techniques to measure the skin’s ability to scavenge free radicals, they discovered that dietary carotenoids provided notable protection against stress-induced radical formation and increased baseline radical scavenging activity of the skin by 34%. The authors concluded that dietary supplementation could avoid premature skin aging.

Vitamins C and E

Vitamin C is an essential vitamin that must be obtained through dietary sources. It functions as a free radical...
scavenger and is a necessary cofactor for the synthesis and stabilization of collagen.

A study evaluated the effect of UVR-induced oxidative stress and the association with vitamin C supplementation among 20 white patients with Fitzpatrick skin types II or III. The volunteers were treated with UVR on two 1-cm sites on the buttock. Six punch biopsies of these sites and 2 control biopsies from nonexposed skin were taken. Volunteers took vitamin C supplements (500 mg) for 8 weeks, and the exposure and biopsy were repeated. Researchers concluded that supplementation with vitamin C had no effect on the MED, with identical concentrations at baseline and after 8 weeks of supplementation. Additionally, there was no evidence that vitamin C affects UVR-induced oxidative stress.

In 2007, Cosgrove et al conducted a study to assess the associations between nutrient intake and skin aging in more than 4000 women aged 40 to 74 years. Higher dietary vitamin C intakes were associated with a significantly lower likelihood of senile xerosis and wrinkled appearance (P<.009).

Vitamin E is a lipid-soluble, membrane-bound vitamin, and its most active form is α-tocopherol. Vitamin E functions as an antioxidant and protects cellular membranes from lipid peroxidation by free radicals. Once oxidized, vitamin E can be regenerated to its reduced form by vitamin C. Their synergistic effects on skin protection have been studied extensively. A double-blind, placebo-controlled study of 10 patients compared 2 g of vitamin C combined with 1000 IU of vitamin E vs placebo. The patients’ skin reaction before and after 8 days of treatment were assessed by determination of MED and the cutaneous blood flow of skin irradiated with UV light. Results showed that the median MED of those taking vitamins increased from 80 to 56.5 ml/cm² (P<.01) and decreased for the placebo group. Investigators concluded that the combination of vitamins C and E reduces the sunburn reaction and leads to a reduction in the sequelae of UV-induced skin damage. A prospective, randomized, placebo-controlled study by Fuchs and Kern replicated these findings, also concluding that combinations of vitamins C and E provide improved photoprotective effects than either vitamin alone.

Vitamin D

Vitamin D is a fat-soluble vitamin obtained through dietary intake and exposure to UV light. Precursors of vitamin D require interaction with UV light for conversion into active forms. The highest concentrations of 7-dehydrocholesterol are found in keratinocytes in the basal cell and spinous cell layers of the skin where they are protected from UV light by melanin. As such, individuals with higher melanin content in their skin require more exposure to UV light to produce the same levels of vitamin D as those with less melanin, leading to a high rate of vitamin D deficiency in dark-skinned individuals. Because of their prodifferentiating and antiproliferative effects, vitamin D analogs have been very effective in the treatment of psoriasis. Vitamin D deficiency also has been implicated in the pathogenesis of vitiligo. A systematic review and meta-analysis conducted in 2016 found that a significant relationship existed between low 25-hydroxyvitamin D levels and vitiligo (P<.01), but no causal relationship could be established.

A 2017 double-blind, placebo-controlled study performed by Scott et al aimed to elucidate the relationship between vitamin D concentrations and sunburn. Twenty adults received either placebo or high-dose vitamin D₃ (200,000 IU) 1 hour after experimental sunburn induced by an erythemogenic dose of UVR. Investigators measured participants’ concentrations of the proinflammatory mediators tumor necrosis factor α and nitric oxide synthase via skin biopsy 48 hours later. Patients in the experimental group were found to have significantly reduced expression of both tumor necrosis factor α (P=.04) and nitric oxide synthase (P=.02). Additionally, participants with significantly higher vitamin D₃ levels following supplementation (P=.007) demonstrated increased skin expression of the anti-inflammatory marker arginase-1 (P=.005) as well as a persistent reduction in skin redness (P=.02). Investigators concluded that vitamin D plays a large role in skin homeostasis and implicated vitamin D’s upregulation of arginase-1 as a potent mechanism of its anti-inflammatory effects.

Collagen

As humans age, the density of collagen in the dermis decreases, leading to sagging and wrinkling of skin. Oral supplementation of collagen has been examined for its dermatologic benefits, primarily increasing the thickness and density of collagen in the dermal layer. In 2014, Proksch et al performed a double-blind, placebo-controlled trial in which 69 women were randomized to receive 2.5 or 5 g of collagen peptides or placebo for 8 weeks. Both treatment groups demonstrated improvements in skin elasticity as well as improved skin moisture and decreased skin evaporation; however, changes in the latter 2 qualities failed to reach statistical significance.

The results of this study were replicated by Asserin et al. One hundred six female patients were randomly assigned to receive 10 g of collagen peptides or placebo daily for 8 weeks. The collagen group demonstrated significantly improved skin hydration (P=.003) and increased density of collagen in the dermis (P=.007) relative to placebo.

In another randomized, double-blind, placebo-controlled study, 71 women consumed a 20-mL beverage containing either 3000 mg of collagen peptides or placebo for 12 weeks. Participants in the treatment group demonstrated significant decreases in periocular wrinkles (P<.05) and enhanced facial skin moisture (P<.001) and elasticity (P<.001) after 12 weeks. Researchers concluded that oral supplementation with collagen peptides holds
promise as a natural supplement to provide cutaneous antiaging properties.27

Ceramides
Ceramides are lipids composed of a sphingoid base conjugated to a fatty acid and serve as the main component of the stratum corneum of the skin. Ceramides are crucial for the maintenance of skin barrier integrity and for preventing transepidermal water loss.28 In a 3-month study of 51 women with dry skin, Guillou et al29 showed that a ceramide wheat extract capsule significantly increased corneometry measurements of skin hydration on the arms (P<.001) and the legs (P=.012) compared to placebo.

Mixed Supplements
The discovery that nutritional contents can affect skin appearance has energized the development of combination supplements containing multiple vitamins and micronutrients. Imedeen is a biomarine complex and antioxidant supplement with several different formulations, including Prime Renewal, Time Perfection, and Derma One (Pfizer Inc). The ingredients include a combination of a biomarine complex (blend of fish proteins and polysaccharides), lycopene, grape seed extract, vitamin C, vitamin E, and zinc. Several trials have been conducted to assess the efficacy of the supplements on improving the appearance of photodamaged and aged skin (Table).

<table>
<thead>
<tr>
<th>Reference (Year)</th>
<th>No. of Enrolled Participants</th>
<th>Treatment Administered</th>
<th>Treatment Length</th>
<th>Outcome</th>
<th>Conclusion</th>
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<tr>
<td>Kieffer and Efsen30 (1998)</td>
<td>144</td>
<td>Imedeen (Pfizer Inc)</td>
<td>1 y</td>
<td>Improvement compared to baseline in fine lines, overall photaging, telangiectasia and hyperpigmentation, and self-evaluation of skin</td>
<td>Imedeen appears effective and safe for treatment of photoaged skin</td>
</tr>
<tr>
<td>Skovgaard et al31 (2006)</td>
<td>Treatment group, 38; placebo group, 42</td>
<td>Imedeen Prime Renewal (Pfizer Inc)</td>
<td>6 mo (2 tablets twice daily)</td>
<td>Treatment group had greater improvement compared to placebo for the face after 6 mo for forehead, periorcular and perioral wrinkles, mottled pigmentation, laxity, sagging, and overall appearance (P&lt;.05)</td>
<td>Imedeen Prime Renewal provides improved condition, structure, and firmness of skin in postmenopausal women after 6 mo</td>
</tr>
<tr>
<td>Stephens et al32 (2016)</td>
<td>Treatment group, 36; placebo group, 38</td>
<td>Imedeen Time Perfection (Pfizer Inc)</td>
<td>12 wk (2 tablets daily)</td>
<td>Mean difference for global facial assessment, average facial photaging, mottled hyperpigmentation, tactile laxity, dullness, and tactile roughness significantly favored Imedeen (P&lt;.05); significantly greater increases in ultrasound dermal density and stratum corneum moisturization were observed for the Imedeen group (P&lt;.05)</td>
<td>Imedeen Time Perfection can positively affect the appearance of photoaged skin, moisturization, and skin density over 12 wk of treatment</td>
</tr>
<tr>
<td>Stephens et al33 (2016)</td>
<td>Treatment group, 82; placebo group, 70</td>
<td>Imedeen Derma One (Pfizer Inc)</td>
<td>16 wk (2 tablets daily)</td>
<td>Significant differences in change from baseline to wk 16 for clinical grading of overall facial appearance (P&lt;.0001), periorcular wrinkles (P&lt;.05), radiant complexion (P&lt;.0001), visual and tactile roughness (P&lt;.0001), and mottled hyperpigmentation (P&lt;.001) favoring the patients in the treatment group</td>
<td>Women with photodamaged skin receiving an antiaging skin care supplement showed significant improvements in the appearance of facial photodamage (P&lt;.0001)</td>
</tr>
</tbody>
</table>
A placebo-controlled, randomized study of 144 participants conducted by Kieffer and Efsen assessed the efficacy of Im美德安 supplements over 12 months. The trial included a 3-month placebo-controlled study and a 9-month uncontrolled continuation. Im美德安’s efficacy was measured using clinical evaluation, transepidermal water loss, self-evaluation, and photograph evaluation. After 1 year of treatment, improvement occurred in photograph evaluation of fine lines, overall photoaging, telangiectasia and hyperpigmentation, and self-evaluation of skin condition. Additional double-blind, placebo-controlled, randomized studies assessing the efficacy of Im美德安 have shown increased dermal and epidermal thickness, improvement of stratum corneum moisturization, and improved overall facial complexion.30-33

Several combined supplements containing collagen peptide as the main ingredient have been created for use in skin care. Collagen is found in the extracellular matrix of the dermis and is responsible for the resiliency and strength of skin.34,35 Damage to the dermis can occur with prolonged UV light exposure and is seen histologically as disorganized collagen fibrils and grossly as wrinkles and photoaged skin.36

A study assessed the effect of BioCell Collagen (BioCell Technology, LLC), a supplement containing type II collagen, on skin aging. Thirty-six women underwent baseline visual assessments of their skin before taking 2 tablets of the supplement daily. Twelve weeks of supplementation led to significant reduction in global lines and wrinkles (13.2%; P=0.028) as well as skin dryness and scaling (76%; P=0.002). Assessment of collagen content at 6 weeks revealed a significant increase from baseline (6.3%; P=0.002), though the difference after 12 weeks was not significant (3.5%; P=1.34). The authors concluded that although preliminary data suggested that BioCell Collagen may reduce visible signs of aging, a controlled study was necessary to verify this finding.38

A single-blind, case-controlled study assessed a similar supplement, Celergen, that contained marine collagen peptides. Forty-one adults took 4 capsules each day for 60 days. Assessment of their skin physiology was conducted at the enrollment visit, 2 months later, and after the treatment period ended. Skin elasticity, transepidermal water loss, epidermal and dermal thickness, and density were measured. Investigators found that Celergen administration significantly enhanced skin elasticity and sebum production (P<0.0001) but did not influence cutaneous moisture. The dermal thickness and homogenous distribution of collagen fibers were enhanced in 11 patients while properties of the epidermis remained unchanged. The study determined that supplementation remarkably improved skin elasticity, sebum production, and dermal ultrasonic markers.38

A double-blind, randomized, placebo-controlled study assessed a collagen- and antioxidant-containing supplement, Gold Collagen Forte, on skin properties. The treatment and placebo groups each consisted of 60 patients who consumed 1 bottle (50 mL) of the product each day for 90 days. Patients completed a self-assessment of their skin regarding photoaging, focusing on the crow’s-feet area and nasolabial folds, while skin elasticity was assessed with the SkinLab USB elasticity module. Results showed a significant increase in skin elasticity (+7.5%; P≤0.001). Self-assessment results showed improvements in both the treatment and placebo groups, and investigators concluded that Gold Collagen Forte may have photoprotective effects and help improve skin health.39

Safety
Although trials have demonstrated vitamin supplementation to be safe and effective for skin enhancement, it is important to consider potential vitamin toxicities. High doses of vitamin C supplementation have been shown to cause damage via lipid peroxidation.30 In a study assessing if high levels of beta-carotene and vitamin E were associated with a lower risk for lung cancer, data showed that these supplements may actually have harmful effects.40-41 Additionally, consumption of high-dose dietary supplements has been associated with an increased risk for severe medical events, including disability and death among adolescents and young adults.42

Conclusion
Numerous trials have indicated that the use of systemic vitamins can have beneficial effects on the protection and appearance of skin. Photodamage from UV light–induced erythema can be decreased by carotenoids and vitamins C and E. Similarly, supplements that combine multiple nutrients with collagen have been shown to improve the appearance of aging skin by decreasing the prominence of wrinkles. Given the growing number of products and advertisements that exist in the supplement marketplace, it is crucial for clinicians to ground their recommendations to patients in the scientific data of robust studies.

REFERENCES

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