The Role of Vitamins and Supplements on Skin Appearance

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PRACTICE **POINTS**

- Multiple vitamins and supplements have demonstrated evidence in improving skin appearance.
- Carotenoids, along with vitamins C and E, have been shown to protect skin from UV-induced photodamage, while supplements containing collagen decrease the appearance of wrinkles.

Skin appearance is affected by intrinsic factors (eg, aging) and extrinsic factors (eg, 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.

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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.[1] Chronologically aged skin appears dry, thin, and finely wrinkled; photoaged skin appears leathery with coarse wrinkles and uneven pigmentation.[2] 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.[3,4] Ingestion of carotenoids may play a role in photoprotection against UV radiation (UVR) by acting as acceptors of reactive oxygen species.[4-6] Stahl et al[7] 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 ($P=.02$).[7]

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.[8] 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 $P<.05$).[8]

In 2013, Meinke et al[9] 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.[9]

Vitamins C and E

Vitamin C is an essential vitamin that must be obtained through dietary sources.[10] It functions as a free radical

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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.[11] 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.[11]

In 2007, Cosgrove et al[12] 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 ($P<.009$).[12]

Vitamin E is a lipid-soluble, membrane-bound vitamin, and its most active form is α-tocopherol.[11,13] Vitamin E functions as an antioxidant and protects cellular membranes from lipid peroxidation by free radicals.[13-15] Once oxidized, vitamin E can be regenerated to its reduced form by vitamin C.[11] 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.[16] 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 96.5 mJ/cm^2 ($P<.01$) 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.[16] A prospective, randomized, placebo-controlled study by Fuchs and Kern[17] 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.[3,18,19] 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,[20] 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.[20,21] 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.[22]

A 2017 double-blind, placebo-controlled study performed by Scott et al[23] aimed to elucidate the relationship between vitamin D concentrations and sunburn. Twenty adults received either placebo or high-dose vitamin D_3 (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 D_3 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.[23]

Collagen

As humans age, the density of collagen in the dermis decreases, leading to sagging and wrinkling of skin.[24] 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[25] 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.[25]

The results of this study were replicated by Asserin et al.[26] 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.[26]

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.[27] Participants in the treatment group demonstrated significant decreases in periorbital 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 al[29] 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).

Randomized Controlled Trials Evaluating the Efficacy of Imedeen Supplements

Reference (Year)	No. of Enrolled Participants	Treatment Administered	Treatment Length	Outcome	Conclusion
Kieffer and Efsen[30] (1998)	144	Imedeen (Pfizer Inc)	1 y	Improvement compared to baseline in fine lines, overall photoaging, telangiectasia and hyperpigmentation, and self-evaluation of skin	Imedeen appears effective and safe for treatment of photoaged skin
Skovgaard et al[31] (2006)	Treatment group, 38; placebo group, 42	Imedeen Prime Renewal (Pfizer Inc)	6 mo (2 tablets twice daily)	Treatment group had greater improvement compared to placebo for the face after 6 mo for forehead, periocular and perioral wrinkles, mottled pigmentation, laxity, sagging, and overall appearance ($P<.05$)	Imedeen Prime Renewal provides improved condition, structure, and firmness of skin in postmenopausal women after 6 mo
Stephens et al[32] (2016)	Treatment group, 36; placebo group, 38	Imedeen Time Perfection (Pfizer Inc)	12 wk (2 tablets daily)	Mean difference for global facial assessment, average facial photoaging, mottled hyperpigmentation, tactile laxity, dullness, and tactile roughness significantly favored Imedeen ($P<.05$); significantly greater increases in ultrasound dermal density and stratum corneum moisturization were observed for the Imedeen group ($P<.05$)	Imedeen Time Perfection can positively affect the appearance of photoaged skin, moisturization, and skin density over 12 wk of treatment
Stephens et al[33] (2016)	Treatment group, 82; placebo group, 70	Imedeen Derma One (Pfizer Inc)	16 wk (2 tablets daily)	Significant differences in change from baseline to wk 16 for clinical grading of overall facial appearance ($P<.0001$), periocular wrinkles ($P<.05$), radiant complexion ($P<.0001$), visual and tactile roughness ($P<.0001$), and mottled hyperpigmentation ($P<.001$) favoring the patients in the treatment group	Women with photodamaged skin receiving an antiaging skin care supplement showed significant improvements in the appearance of facial photodamage ($P<.0001$)

A placebo-controlled, randomized study of 144 participants conducted by Kieffer and Efsen[30] assessed the efficacy of Imedeen supplements over 12 months. The trial included a 3-month placebo-controlled study and 9-month uncontrolled continuation. Imedeen'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.[30] Additional double-blind, placebo-controlled, randomized studies assessing the efficacy of Imedeen have shown increased dermal and epidermal thickness, improvement of stratum corneum moisturization, and improved overall facial complexion.[31-33]

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.[35,36]

A study assessed the effect of BioCell Collagen (BioCell Technology, LLC), a supplement containing type II collagen, on skin aging.[37] Twenty-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=.028) as well as skin dryness and scaling (76%; P=.002). Assessment of collagen content at 6 weeks revealed a significant increase from baseline (6.3%; P=.002), though the difference after 12 weeks was not significant (3.5%; P=.134). 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.[37]

A single-blind, case-controlled study assessed a similar supplement, Celergen, that contained marine collagen peptides.[38] Forty-one adults took 2 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<.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.[39] 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≤.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.[40] 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

1. Zhang S, Duan E. Fighting against skin aging: the way from bench to bedside. *Cell Transplant.* 2018;27:729-738.
2. Rittié L, Fisher GJ. Natural and sun-induced aging of human skin. *Cold Spring Harb Perspect Med.* 2015;5:a015370.
3. Draelos ZD. Nutrition and enhancing youthful-appearing skin. *Clin Dermatol.* 2010;28:400-408.
4. Anunciato TP, da Rocha Filho PA. Carotenoids and polyphenols in nutricosmetics, nutraceuticals, and cosmeceuticals. *J Cosmet Dermatol.* 2012;11:51-54.
5. Stahl W, Heinrich U, Jungmann H, et al. Carotenoids and carotenoids plus vitamin E protect against ultraviolet light-induced erythema in humans. *Am J Clin Nutr.* 2000;71:795-798.
6. Anstey AV. Systemic photoprotection with alpha-tocopherol (vitamin E) and beta-carotene. *Clin Exp Dermatol.* 2002;27:170-176.
7. Stahl W, Heinrich U, Wiseman S, et al. Dietary tomato paste protects against ultraviolet light-induced erythema in humans. *J Nutr.* 2001;131:1449-1451.
8. Wood SM, Mastaloudis AF, Hester SN, et al. Protective effects of a novel nutritional and phytonutrient blend on ultraviolet radiation-induced skin damage and inflammatory response through aging defense mechanisms. *J Cosmet Dermatol.* 2017; 16:491-499.

9. Meinke MC, Friedrich A, Tscherch K, et al. Influence of dietary carotenoids on radical scavenging capacity of the skin and skin lipids. *Eur J Pharm Biopharm.* 2013;84:365-373.
10. Manela-Azulay M, Bagatin E. Cosmeceuticals vitamins. *Clin Dermatol.* 2009;27:469-474.
11. McArdle F, Rhodes LE, Parslew R, et al. UVR-induced oxidative stress in human skin in vivo: effects of oral vitamin C supplementation. *Free Radic Biol Med.* 2002;33:1355-1362.
12. Cosgrove MC, Franco OH, Granger SP, et al. Dietary nutrient intakes and skin-aging appearance among middle-aged American women. *Am J Clin Nutr.* 2007;86:1225-1231.
13. Thiele JJ, Ekanayake-Mudiyanselage S. Vitamin E in human skin: organ-specific physiology and considerations for its use in dermatology. *Mol Aspects Med.* 2007;28:646-667.
14. Schagen SK, Zampeli VA, Makrantonaki E, et al. Discovering the link between nutrition and skin aging. *Dermatoendocrinol.* 2012;4:298-307.
15. Chan AC. Partners in defense, vitamin E and vitamin C. *Can J Physiol Pharmacol.* 1993;71:725-731.
16. Eberlein-Konig B, Placzek M, Przybilla B. Protective effect against sunburn of combined systemic ascorbic acid (vitamin C) and d-alpha-tocopherol (vitamin E). *J Am Acad Dermatol.* 1998;38:45-48.
17. Fuchs J, Kern H. Modulation of UV-light-induced skin inflammation by D-alpha-tocopherol and L-ascorbic acid: a clinical study using solar simulated radiation. *Free Radic Biol Med.* 1998;25:1006-1012.
18. Shahriari M, Kerr PE, Slade K, et al. Vitamin D and the skin. *Clin Dermatol.* 2010;28:663-668.
19. Soleymani T, Hung T, Soung J. The role of vitamin D in psoriasis: a review. *Int J Dermatol.* 2015;54:383-392.
20. Lehmann B, Querings K, Reichrath J. Vitamin D and skin: new aspects for dermatology. *Exp Dermatol.* 2004;13(suppl 4):11-15.
21. Kannan S, Lim HW. Photoprotection and vitamin D: a review. *Photodermatol Photoimmunol Photomed.* 2014;30:137-145.
22. Upala S, Sanguankeo A. Low 25-hydroxyvitamin D levels are associated with vitiligo: a systematic review and meta-analysis. *Photodermatol Photoimmunol Photomed.* 2016;32:181-190.
23. Scott JF, Das LM, Ahsanuddin S, et al. Oral vitamin D rapidly attenuates inflammation from sunburn: an interventional study. *J Invest Dermatol.* 2017;137:2078-2086.
24. Varani J, Dame MK, Rittie L, et al. Decreased collagen production in chronologically aged skin: roles of age-dependent alteration in fibroblast function and defective mechanical stimulation. *Am J Pathol.* 2006;168:1861-1868.
25. Proksch E, Segger D, Degwert J, et al. Oral supplementation of specific collagen peptides has beneficial effects on human skin physiology: a double-blind, placebo-controlled study. *Skin Pharmacol Physiol.* 2014;27:47-55.
26. Asserin J, Lati E, Shioya T, et al. The effect of oral collagen peptide supplementation on skin moisture and the dermal collagen network: evidence from an ex vivo model and randomized, placebo-controlled clinical trials. *J Cosmet Dermatol.* 2015;14:291-301.
27. Koizumi S, Inoue N, Shimizu M, et al. Effects of dietary supplementation with fish scales-derived collagen peptides on skin parameters and condition: a randomized, placebo-controlled, double-blind study. *Int J Peptide Res Ther.* 2018;24:397-402.
28. Vollmer DL, West VA, Lephart ED. Enhancing skin health: by oral administration of natural compounds and minerals with implications to the dermal microbiome. *Int J Mol Sci.* 2018;19. doi:10.3390/ijms19103059.
29. Guillou S, Ghabri S, Jannot C, et al. The moisturizing effect of a wheat extract food supplement on women's skin: a randomized, double-blind placebo-controlled trial. *Int J Cosmet Sci.* 2011;33:138-143.
30. Kieffer ME, Efsen J. Imedeen in the treatment of photoaged skin: an efficacy and safety trial over 12 months. *J Eur Acad Dermatol Venereol.* 1998;11:129-136.
31. Skovgaard GR, Jensen AS, Sigler ML. Effect of a novel dietary supplement on skin aging in post-menopausal women. *Eur J Clin Nutr.* 2006;60:1201-1206.
32. Stephens TJ, Sigler ML, Herndon JH Jr, et al. A placebo-controlled, double-blind clinical trial to evaluate the efficacy of Imedeen(®) Time Perfection(®) for improving the appearance of photodamaged skin. *Clin Cosmet Investig Dermatol.* 2016;9:63-70.
33. Stephens TJ, Sigler ML, Hino PD, et al. A randomized, double-blind, placebo-controlled clinical trial evaluating an oral anti-aging skin care supplement for treating photodamaged skin. *J Clin Aesthet Dermatol.* 2016;9:25-32.
34. El-Domyati M, Attia S, Saleh F, et al. Intrinsic aging vs. photoaging: a comparative histopathological, immunohistochemical, and ultrastructural study of skin. *Exp Dermatol.* 2002;11:398-405.
35. Fisher GJ, Wang ZQ, Datta SC, et al. Pathophysiology of premature skin aging induced by ultraviolet light. *N Engl J Med.* 1997;337:1419-1428.
36. Kang MC, Yumnam S, Kim SY. Oral intake of collagen peptide attenuates ultraviolet B irradiation-induced skin dehydration in vivo by regulating hyaluronic acid synthesis. *Int J Mol Sci.* 2018;19. doi:10.3390/ijms19113551.
37. Schwartz SR, Park J. Ingestion of BioCell Collagen(®), a novel hydrolyzed chicken sternal cartilage extract; enhanced blood microcirculation and reduced facial aging signs. *Clin Interv Aging.* 2012;7:267-273.
38. De Luca C, Mikhal'chik EV, Suprun MV, et al. Skin antiageing and systemic redox effects of supplementation with marine collagen peptides and plant-derived antioxidants: a single-blind case-control clinical study. *Oxid Med Cell Longev.* 2016;2016:4389410.
39. Genovese L, Corbo A, Sibilla S. An insight into the changes in skin texture and properties following dietary intervention with a nutricosmeceutical containing a blend of collagen bioactive peptides and antioxidants. *Skin Pharmacol Physiol.* 2017;30:146-158.
40. Hamishehkar H, Ranjdoost F, Asgharian P, et al. Vitamins, are they safe? *Adv Pharm Bull.* 2016;6:467-477.
41. Alpha-Tocopherol, Beta Carotene Cancer Prevention Study Group. The effect of vitamin E and beta carotene on the incidence of lung cancer and other cancers in male smokers. *N Engl J Med.* 1994;330:1029-1035.
42. Or F, Yongjoo K, Simms J, et al. Taking stock of dietary supplements' harmful effects on children, adolescents, and young adults [published online June 3, 2019]. *J Adolesc Health.* S1054-139X(19)30163-6. doi:10.1016/j.jadohealth.2019.03.005.