

Nutraceuticals: A Review

Skylar A. Souyoul · Katharine P. Saussy · Mary P. Lupo

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ABSTRACT

Skin aging is continuously influenced by various internal and external factors such as the biologic progression of cells, ultraviolet (UV) radiation, tobacco, nutritional deficiencies, and hormonal imbalances that lead to the degradation of skin cells. Through the degradation of skin cells, free radicals and inflammation weaken repair mechanisms and result in collagen and elastic fiber breakdown. The appearance of aging skin is highlighted by skin roughness, wrinkling, pigmentation change, telangiectasias, loss of elasticity, and decreased firmness, all of which are accelerated by these internal and external factors. Throughout the years, nutraceuticals have been studied to delay and fight against these internal and external factors, many of which are found in foods and byproducts consumed naturally. The aim of this review is to aid dermatologists in understanding the mechanism of action of popular

nutraceuticals and their possible efficacy in antiaging and skin health.

Keywords: β -Carotene; Fatty acids; Lutein; Lycopene; Minerals; Nutraceuticals; Polyphenols; Vitamin C; Vitamin E; Zeaxanthin

INTRODUCTION

The skin is the largest organ of the human body and is perpetually aging by both internal and external factors [1]. The internal factors are a part of the natural aging process within cells, but can be accelerated by external factors such as ultraviolet (UV) radiation, tobacco, inadequate nutrition, and hormonal imbalances. These external factors cause the production of free radicals and inflammation that fragment and degrade collagen and elastic fibers [2]. Over time, both these internal and external influences lead to increased skin roughness, wrinkling, pigmentation change, telangiectasias, loss of elasticity, and decreased firmness, giving skin its aged appearance [2, 3].

Nutraceuticals are oral dietary components naturally found in foods and believed to have a medical or health benefit [4]. Dr. Stephen Defelice, who combined the words “nutrition” and “pharmaceutical,” coined the term in 1989. Here, the theoretical action and clinical benefit of some dermatologic nutraceuticals are

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S. A. Souyoul (✉) · M. P. Lupo
Lupo Center for Aesthetic and General
Dermatology, New Orleans, LA, USA
e-mail: drsouyoul@drmarylupo.com

K. P. Saussy
Department of Internal Medicine, Tulane
University, New Orleans, LA, USA

reviewed. The aim of this review is to aid dermatologists in understanding the mechanism of action of popular nutraceuticals and their possible efficacy in antiaging and skin health. This article is based on previously conducted studies and does not involve any new studies of human or animal subjects performed by any of the authors.

AMINO ACIDS

N-Acetylcysteine

N-Acetylcysteine is the prodrug form of L-cysteine and has both oral and topical bioavailability [5, 6]. *N*-Acetylcysteine gives rise to glutathione, which is the most abundant endogenous intracellular antioxidant and plays a pivotal role in the body's antioxidant defense [6, 7]. The rate of glutathione synthesis decreases as humans' age, leading to glutathione deficiency, which leaves the body susceptible to oxidative stress [7]. Increased oxidative stress leads to increased DNA damage and aging [7].

A study by Sekhar et al. [7] found that elderly subjects had significantly lower intracellular glutathione synthesis and concentrations when compared to younger subjects. After 2 weeks of cysteine and glycine supplementation, elderly subjects had a significant increase in their red blood cell glycine, cysteine, and glutathione concentrations [7]. In addition, after supplementation, there was a decline in both oxidative stress and plasma markers for oxidant damage [7]. The Food and Nutrition Board of the Institute of Medicine's recommended dietary allowance (RDA) of *N*-acetylcysteine has not been established. Further clinical studies are needed to determine ideal daily consumption of *N*-acetylcysteine to achieve maximal skin benefit.

CAROTENOIDS

Carotenoids are a family of over 600 fat-soluble plant pigments, approximately 20 of which are present in human tissues and blood [3, 8]. They are potent reactive oxygen species (ROS)

scavengers, protecting the skin from oxidative stress [8]. Humans and animals cannot synthesize carotenoids, so they must obtain them via ingestion of foods or supplements [8]. Skin concentrations of carotenoids increase with ingestion of the components, but decrease with oxidative stress and UV exposure [3]. Here, we focus on four of the major dietary carotenoids: β -carotene, lycopene, lutein, and zeaxanthin.

β -Carotene

β -Carotene is a precursor to vitamin A. It protects cells from damage by inhibiting free radical and singlet oxygen-induced lipid peroxidation [3]. It also has photoprotective properties, which increase the minimal erythema dose (MED), and protects against sunburn development and photosuppression of the immune system [3, 8, 9]. In mice, β -carotene has been shown to prevent wrinkle formation and decrease matrix metalloproteinase (MMP)-9 activity, protecting the extracellular matrix (ECM) from degradation [3].

Foods rich in β -carotene are green leafy vegetables, orange root vegetables, and yellow or orange fruits [3]. β -Carotene is a precursor to vitamin A; thus, the RDA is determined through consumption of vitamin A. The Food and Nutrition Board of the Institute of Medicine's RDA of vitamin A is 900 μg retinol activity equivalency (RAE) a day for men and 700 μg RAE a day for women ages 19 years and older [10]. According to the Institute of Medicine's Interconversion of Vitamin A and Carotenoid Units Table, 2 μg of supplemental all-*trans*- β -carotene is equal to 1 RAE and 12 μg of dietary all-*trans*- β -carotene is equal to 1 RAE. Thus, the RDA of supplemental all-*trans*- β -carotene is 1800 μg a day for men and 1400 μg a day for women, and the RDA for dietary all-*trans*- β -carotene is 10,800 μg a day for men and 8400 μg a day for women [10]. Long-term β -carotene supplementation has been associated with an increased risk of lung cancer, so further studies are needed to determine the optimal daily allowance while accessing for supplementation health risks [9].

Lutein and Zeaxanthin

Lutein and zeaxanthin are the two primary xanthophyll carotenoids in the retina and are generally thought to promote eye health; however, significant amounts of both are found in human skin [11]. In both the skin and eyes, these carotenoids work as a filler to block damaging blue wavelengths and as antioxidants to prevent free radical damage [11, 12].

Juturu et al. [12] evaluated a daily oral supplement containing 10 mg of lutein and 2 mg of zeaxanthin isomers. They concluded that within 12 weeks, the supplement increased the mean MED and significantly improved skin tone, luminance, and color [12]. Other studies have shown that lutein and zeaxanthin protect keratinocytes from UV radiation-induced photoaging, stop ECM degradation by inhibiting MMPs, and decrease lipid peroxidation in the skin [11, 13]. These skin effects can be seen with lutein and zeaxanthin oral supplementation, topical application, or both simultaneously for enhanced benefit [11, 13].

Humans are unable to produce lutein or zeaxanthin, so they must be obtained exogenously [10]. Both are found in highest concentration in green leafy vegetables, but are found in a more bioavailable form in eggs [13]. The Food and Nutrition Board of the Institute of Medicine's RDA of lutein and zeaxanthin has not been established; however, between 6–10 mg a day of lutein and 2 mg a day of zeaxanthin has been recommended in previous studies [10, 12, 14]. Of note, the American Optometric Association recommends taking 10 mg a day of lutein and 2 mg a day of zeaxanthin if one is not getting adequate amounts through diet alone to potentially reduce the risk of age-related macular degeneration and cataracts [15].

Lycopene

Lycopene has no vitamin A activity, but is considered the best singlet oxygen quencher in the carotenoid family [3]. Studies have shown that consumption of tomato paste, which is high in lycopene, significantly lowers UV-

induced erythema and decreases MMP-1 activity, an enzyme involved in the breakdown of collagen [16]. In vitro studies of lycopene have shown its ability to inhibit proliferation of several types of cancer cells via cell-cycle arrest and induction of apoptosis [3]. There is also a significant correlation between higher skin concentrations of lycopene and a decrease in skin roughness [3].

Foods rich in lycopene are tomatoes, pink grapefruit, and watermelon [10]. The Food and Nutrition Board of the Institute of Medicine has not established an RDA for lycopene, so further studies are needed to determine the optimal daily allowance while accessing for supplementation health risks.

FATTY ACIDS

α -Linolenic Acid, Eicosapentaenoic Acid, and Docosahexaenoic Acid

Essential fatty acids make up long-chain polyunsaturated fatty acids that can be divided into two groups, omega-3 and omega-6 [17]. Omega-3 fatty acids originate from linolenic acid, whereas omega-6 fatty acids originate from linoleic acid (LA) [17]. The three most common omega-3 essential fatty acids are alpha-linolenic acid (ALA), eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA) [17]. These three fatty acids lie on a metabolic spectrum with ALA serving as the precursor and EPA and DHA serving as ALA's metabolized products [18].

In the stratum corneum a combination of lipids serves as a protective barrier to the skin surface and cellular structure [19]. LA has the highest fatty acid concentration within the epidermis and serves as an important structural component [20], while omega-3 polyunsaturated fatty acids play an important anti-inflammatory role [20, 21]. Polyunsaturated fatty acids such ALA, EPA, and DHA hinder the formation of pro-inflammatory cytokines such as prostaglandins, leukotrienes, tumor necrosis factor- α , interferon- γ , and interleukins-12 and -6 [20, 21]. Studies have reported a significant reduction in UV-radiation-induced

inflammation when taking fatty acid supplements, attributed to the potential decrease in prostaglandin-E₂ levels during the inflammatory response [17–19]. Another study reported an increase in the MED in study participants who took 4 g of EPA daily [20].

In 2017, Wang et al. demonstrated a way to quantify the skin's fatty acid concentration and composition using gas chromatography. The study resulted in a statistically significant increase in the concentration of EPA and DHA in the skin of mice within 2 weeks of initiating a diet supplemented with fish oil [18]. Four weeks after of initiating the supplemented diet, this increase plateaued [18].

Essential fatty acids must be consumed through diet or supplementation since humans do not have the enzymes to produce them *de novo*, leading to a variation in the fatty acid make up within the skin [18, 20]. Omega-3 fatty acids, as well as omega-6 fatty acids, are found primarily in oils such as flaxseed oil, canola oil, hemp seed oil, and other foods including cold-water fish, such as salmon and trout, nuts, and seeds [17, 20]. The Food and Nutrition Board of the Institute of Medicine does not have an RDA for any of the fatty acids mentioned above because of a lack of evidence, but does have an adequate intake (AI), which is determined by the largest median intake where deficiency is extremely rare [22]. The AI for LA is 17 g per day for men and 12 g per day for women ages 19–50, and 14 and 11 g per day for men and women age 51 and above [22]. The AI for ALA is 1.6 g per day for men and 1.1 g per day for women ages 19 and older [22]. Additional studies are needed to determine the ideal daily dose of essential fatty acids to achieve maximal skin benefit.

MINERALS

Copper

Copper is a trace mineral found naturally in soil with many innate properties. Copper serves as an important cofactor in enzymatic reactions during collagen crosslinking with lysyl oxidase and skin pigmentation with tyrosinase [23, 24].

Copper promotes keratinocyte and fibroblast proliferation leading to skin rejuvenation and wound repair through its collagen crosslinking properties [25]. Lastly, copper has been used in topical treatments for wound healing to promote repair of damaged skin because of its anti-inflammatory and anti-bacterial effects [25].

Dietary copper is found in highest concentration in nuts, seeds, seafood, meat, and grains [10]. Human deficiencies are rare and are most commonly seen in people with intestinal malabsorption [10]. The Food and Nutrition Board of the Institute of Medicine's recommended dietary allowance of copper is 900 µg a day for men and women ages 19 and older [10]. Additional studies are needed to determine the ideal daily dose of copper to achieve maximal skin benefit.

Selenium

Selenium is a trace element, also referred to as an essential mineral, found in soil, water, and specific foods. It exists in multiple forms, but predominantly found in humans as selenomethionine [26]. It plays an important role in DNA synthesis and repair, cell apoptosis, and guarding against oxidative damage [26]. Selenium works through glutathione peroxidases and thioredoxin reductases, which remove damaging lipid hydroperoxides, hydrogen peroxide, and peroxynitrite formed during oxidative stress, leading to cell membrane stabilization and defense against DNA damage [27, 28].

Selenium, in multiple forms, is found in highest concentration in animal proteins such as meat and seafood, the majority of which are highly bioavailable [29]. The precise concentration of selenium is dependent on the selenium concentration within the soil where those animals and plants were produced, which varies between land sources [29]. The Food and Nutrition Board of the Institute of Medicine's RDA of selenium is 55 µg a day for men and women ages 19 years and older [29]. Additional studies are needed to determine the ideal daily dose of selenium to achieve maximal skin benefit.

Zinc

Zinc is an essential mineral found naturally in whole grains, red meat, seafood, and fortified in products such as cereal [10]. Zinc is an important cofactor for cellular activity and defense. It protects against lipid peroxidation, UV-induced cytotoxicity, and oxidative stress induced by ROS made and distributed within the cytosol by macrophages [27, 28].

The majority of the skin's zinc stores are found in the epidermis, where it is a necessary element for epidermal proliferation and keratinocyte differentiation [30]. Zinc plays a major role in wound healing and keratinocyte cell survival [30]. It is also anti-inflammatory by hindering intercellular adhesion molecule 1, a pro-inflammatory marker of keratinocytes, and decreasing the production of nitric oxide [30].

In 2001, it was estimated that 10% of the US population consumes less than 50% of the recommend daily allowance of zinc [31]. The bioavailability of zinc is mainly dependent on zinc's absorption and reabsorption properties found within the human intestines [10]. Varying concentrations of elements such as iron, copper, calcium, phosphate, and folate influence the bioavailability of zinc in the body [10]. Zinc is found in highest dietary concentrations in foods such as non-milled whole grains, red meats, and seafood [10]. The Food and Nutrition Board of the Institute of Medicine's RDA of zinc is 11 mg a day for men and 8 mg a day for women ages 19 years and older [10]. Additional studies are needed to determine the ideal daily dose of zinc to achieve maximal skin benefit.

POLYPHENOLS

Polyphenols are secondary metabolites of plants and are found predominately in fruits, vegetables, cereals, and beverages [32]. For years, polyphenols have been of interest for their antimutagenic, anticarcinogenic, anti-inflammatory, and antioxidant properties [28, 33]. Extensive research has shown that through these properties different polyphenols can be protective against numerous health concerns including cancer, hypertension, asthma,

diabetes, cardiovascular disease, and infection [32]. Over eight thousand different polyphenol compounds have been identified, but here only two will be discussed: curcumin and epigallocatechin gallate (EGCG) [32].

Curcumin

Curcumin is a polyphenol derived from the turmeric spice. It has a yellow pigment, which is responsible for the characteristic yellow color of curry [34]. Curcumin serves many biologically active roles, as does EGCG, including the alike anticarcinogenic, anti-inflammatory, and antioxidant roles [33].

Similarity to EGCG, curcumin has been suggested as a potential treatment for cancer because of its ability to hinder the production of cancer cells and encourage apoptosis [35]. It has been shown to promote cell death by influencing the expression of p53 and decreasing the production of nuclear factor kappa B [33].

Curcumin's anti-inflammatory properties are exhibited through its ability to suppress pro-inflammatory cytokines including chemokines, cyclooxygenase-2, prostaglandin E₂, MMPs, interleukins (IL) such as IL-6 and IL-12, and tumor necrosis factor- α [34, 35]. In addition, curcumin serves as an antioxidant by suppressing ROS production, scavenging free oxygen radicals, and inhibiting lipid peroxidation [34, 35].

In 2017, Shailaja et al. studied curcumin's anti-inflammatory properties in albino rats as a potential anti-aging nutraceutical. The study compared three dosages of oral daily curcumin supplementation against two different standard rat feed and water diets. They report a statistically significant decrease in the C-reactive protein levels in the curcumin-supplemented group compared with the two control groups [36].

The Food and Nutrition Board of the Institute of Medicine's RDA of curcumin has not been established; however, the United States Food and Drug Administration (FDA) has labeled curcumin safe for ingestion and pharmacologic use [35]. In 2016, Pal et al. [33] reported two studies of safe oral

supplementation of curcumin between 2–8 g per kg daily. Further studies are needed to determine the optimal daily allowance while accessing for supplementation health risks.

Epigallocatechin Gallate (Egcg)

Tea polyphenols inhibit lipid peroxidation, limit the amount of UV radiation-induced DNA damage, and reduce the amount ROS and free radicals produced in the skin [28, 34]. EGCG is the most potent tea polyphenol and is commonly found in green tea [17, 28]. EGCG has anti-inflammatory effects via the suppression of pro-inflammatory inducers such as cyclooxygenase-2, MMPs, tumor necrosis factor- α , and IL-6, 8, and 12 [33]. Studies have also shown that EGCG can diminish melanoma cell growth in humans by supporting cell cycle arrest and apoptosis [33].

Health benefits of EGCG have been shown with both topical application and ingestion, although some benefits are only seen with one delivery method and not the other. In mice, studies have shown diminished radiation-induced effects with topical application. These effects include decreased edema and erythema, preservation of skin antioxidant stores, and reduction of UV-induced skin tumors [3, 17].

Green tea has been reported to consist of the most polyphenol antioxidants, and the highest concentration of EGCG is found within green tea leaves [17]. It is commercially available as a white powder for oral consumption [17]. The Food and Nutrition Board of the Institute of Medicine's RDA of EGCG has not been established. In 2017, Yates et al. completed an extensive literature search evaluating the toxicity level of EGCG in daily human consumption. The results were inconclusive and need future investigation; however, publications by France and Italy report a proposed upper limit of approximately 300 mg per day of EGCG [37]. Pal et al. report a phase I clinical study with 200–1200 mg of daily consumption being well tolerated [33]. Further studies are needed to determine the optimal daily allowance while accessing for supplementation health risks.

VITAMINS

Vitamin C

Vitamin C is a water-soluble compound. Bodily concentrations are maintained through consumption of vitamin C, as humans cannot synthesize ascorbic acid *de novo*. Oxidation of vitamin C produces dehydroxy ascorbic acid, which is shifted into our cells via glucose transporters and then reduced back to ascorbic acid for cellular use [38]. Studies have shown that oral vitamin C supplementation leads to an increase in its plasma and skin content [39].

Vitamin C is a powerful antioxidant and free radical scavenger that protects our tissues, cell membranes, and DNA from oxidative damage. It also serves as an essential cofactor and electron donor during collagen hydroxylation, encouraging the maturation of intracellular and extracellular collagen [26]. Vitamin C has been shown to reduce UVB-induced oxidative damage and UV radiation-induced skin neoplasms in mice and protect human keratinocytes from UVA-induced lipid peroxidation [39, 40]. Vitamin C also decreases the malondialdehyde content in the skin, which is a marker of oxidative stress [39, 40].

Food sources containing the highest concentrations of vitamin C are raw red and green peppers, oranges, grapefruits, kiwifruit, broccoli, strawberries, and Brussels sprouts [41]. The Food and Nutrition Board of the Institute of Medicine's RDA of vitamin C is 90 mg a day for men and 75 mg a day for women ages 19 years and older [29]. National surveys indicate that most adults and children in the US consume their RDA of vitamin C [41]. Additional studies are needed to determine the ideal daily dose of vitamin C to achieve maximal skin benefit.

Vitamin E

Vitamin E is a group of fat-soluble compounds. The most abundant and biologically active form of vitamin E, alpha-tocopherol (α T), is the leading form used in human metabolism [3, 42]. α T protects the skin from UVB damage by halting the formation of ROS, scavenging free

radicals, stabilizing the surface and membranes of cells, reducing the number of apoptotic cells, and minimizing the activation of nuclear factor kappa B [26, 43]. α T is also believed to be photoprotective as multiple studies have shown that α T in combination with vitamin C supplementation increases the MED [3].

UV light reduces the skin's concentration of α T, promoting skin aging [3]. Luckily, the skin's concentration of α T can be increased with oral or topical delivery [3]. Naturally occurring oral sources of vitamin E are found in highest concentrations in plant seeds such as sunflower seeds, peanuts, almonds, walnuts, pecans, pistachios, and sesame seeds and in lesser amounts in fruits and vegetables [44, 45]. The Food and Nutrition Board of the Institute of Medicine's RDA of vitamin E is 15 mg a day for men and women ages 19 years and older [29]. National surveys have found that most Americans consume less than their RDA of vitamin E [46]. However, these intake estimates might be low because they did not account for the fats added while cooking [46]. No adverse effects have been reported from consuming vitamin E in food; however, hemorrhage and altered blood coagulation were reported in animals who consumed supplements containing high doses of α T [46]. Additional studies are needed to determine the ideal daily allowance of vitamin E to achieve maximal skin benefit.

POTENTIAL FUTURE NUTRACEUTICALS

Aloe Sterol

Collagen and elastin are the two main fibers in the dermis and together makeup and maintain the majority of the skin's structure [47]. Degradation of these fibers, which is seen in chronologically aged skin, leads to a decrease in cutaneous elasticity and an increase in cutaneous fragility [47]. Oral *Aloe* sterols have been shown to encourage the formation of type I and type III collagen in human dermal fibroblasts, leading to increased collagen production and improved skin elasticity [48]. They have also been found to decrease the expression of MMP-2 and MMP-9,

protecting collagen and the ECM from degradation, in UVB-irradiated hairless mice [47]. In addition, studies have showed that oral *Aloe* sterol may encourage the production of hyaluronic acid in human dermal fibroblasts [49]. Further studies are needed to determine the role of oral *Aloe* sterols and optimal daily allowance while accessing for supplementation health risks.

Serenoa Repens

Serenoa repens, also known as saw palmetto, is a low-growing palm tree native to the Southeast US and West Indies [50]. The berries of the palm tree contain fatty acids and phytosterols that have antiandrogenic activity through inhibition of 5-alpha reductase [51]. It is well known as an herbal treatment of benign prostatic hyperplasia and lower urinary symptoms such as weak urine flow, hesitancy, incomplete emptying, frequency, urgency, and nocturia [50]. Over the past few years, *Serenoa repens* has become of interest for potentially treating androgenetic alopecia (AGA).

One study found that 320 mg a day of *Serenoa repens* improved AGA in 38% of patients and stabilized AGA in 52% of the patients, but on the vertex scalp [51]. It is important to mention that this improvement was not as significant as that in patients treated with finasteride. In the same study, 68% of patients who took 1 mg a day of finasteride had improvement of their AGA in both the vertex and anterior scalp regions [51].

Serenoa repens is generally tolerated well and has not been associated with any serious adverse events [50]. The most common adverse events reported are abdominal pain, diarrhea, nausea, vomiting, headache, decreased libido, and rhinitis [50]. *Serenoa repens*, like other 5-alpha reductase inhibitors, reduces prostate-specific antigen levels by 50% after 6–12 months of treatment [51]. More studies are needed to assess the role of *Serenoa repens* in the treatment of AGA.

CONCLUSIONS

The aim of this review was to aid dermatologists in better understanding the mechanism of

action, efficacy, and potential dermatologic benefits of popular nutraceuticals. For the majority of nutraceuticals mentioned here, patients who consume a healthy balanced diet are most likely obtaining adequate amounts of these nutrients to receive the aforementioned skin benefits. However, if diets are lacking key nutritional components, supplementation may be of benefit to those patients. It is important for providers to discuss the benefits and

consequences of nutraceuticals with patients and to mention the importance of a recommended daily allowance as most things consumed in excess have the potential to cause adverse effects. With advances in technology and the expansion of the online consumer market, it is vital that providers offer an authenticated, medically certified, and safe avenue to purchasing the recommended nutraceuticals.

Major subtype of nutraceutical	Nutraceutical	MOA	RDA	Oral source	Skin function
Amino acids	<i>N</i> -Acetylcysteine	Increase in red blood cell glycine, cysteine, glutathione concentrations; decline in oxidative stress and plasma markers for oxidant damage	Not yet established by FNBIM. Further studies needed	Cysteine and glycine supplementation	Protects against oxidative stress (i.e., DNA damage and aging)
Carotenoids	β -Carotene	Inhibits free radicals and singlet oxygen-induced lipid peroxidation; decreases MMP-9 activity	Supplemental all-trans- β -carotene: 1800 μ g/day for men; 1400 μ g/day for women. Dietary all-trans- β -carotene is 10,800 μ g/day for men; 8400 μ g/day for women	Green leafy vegetables, orange root vegetables, yellow or orange fruits	Scavenges ROS to protect against oxidative stress and decrease UV exposure; protects against ECM degradation
Carotenoids	Lutein and zeaxanthin	Blocks damaging blue wavelengths and prevents free radical damage	Not yet established by FNBIM. Proposed quantity: lutein 6–10 mg/day and zeaxanthin 2 mg/day	Green leafy vegetables, eggs	Antioxidant and decrease UV exposure
Carotenoids	Lycopene	Singlet oxygen quencher; decreases MMP-1 activity; induces cell-cycle arrest and induces apoptosis	Not yet established by FNBIM. Further studies needed	Tomato paste, tomatoes, pink grapefruit, watermelon	Lowers UV-induced erythema; decreases collagen breakdown; inhibits proliferation of certain cancer cells; decreases skin roughness
Fatty acids	α -Linolenic acid (ALA), eicosapentaenoic acid, and docosahexaenoic acid	Inhibits formation of pro-inflammatory cytokines (i.e., prostaglandins, leukotrienes); decreases prostaglandin- E_2 production	Not yet established by FNBIM. Adequate intake for linoleic acid: 17 g/day for men and 12 g/day for women ages 19–50; 14 g/day men and 11 g/day women ages 51+. AI for ALA 1.6 g/day men and 1.1 g/day women, ages 19+	Flaxseed oil, canola oil, hemp seed oil, cold-water fish (salmon, trout), nuts, seeds	Anti-inflammatory; reduces UVR-induced inflammation; increases MED
Minerals	Copper	Cofactor in enzymatic reactions for collagen crosslinking with lysyl oxidase and skin pigmentation with tyrosinase; promotes keratinocyte and fibroblast proliferation	900 μ g for men and women ages 19+	Nuts, seeds, seafood, meat, grains	Collagen crosslinking, skin pigmentation, skin rejuvenation, wound repair, anti-inflammatory, and antibacterial properties
Minerals	Selenium	Aids glutathione peroxidases and thioredoxin reductases, removing damaging lipid hydroperoxides, hydrogen peroxide, peroxynitrites	55 μ g/day men and women 19+	Meat and seafood	Supports DNA synthesis and repair, cell apoptosis and guards against oxidative damage, leading to cell membrane stabilization and protects against DNA damage

continued

Major subtype of nutraceutical	Nutraceutical	MOA	RDA	Oral source	Skin function
Minerals	Zinc	Protects against lipid peroxidation, UVR-induced cytotoxicity, and oxidative stress. Necessary for epidermal proliferation and keratinocyte differentiation. Hinders intracellular adhesion molecule 1; decreases nitric oxide production	11 mg/day men; 8 mg/day women 19+	Non-milled whole grains, red meat, seafood, fortified products (i.e., cereal)	Cofactor for cellular activity and defense; skin cell proliferation; wound healing; anti-inflammatory properties
Polyphenols	Curcumin	Hinders production of cancer cells, encourages apoptosis, promotes cell death by influencing p53 expression and decreases NF- κ B production. Suppresses pro-inflammatory cytokines. Suppresses ROS production by scavenging free oxygen radicals; inhibits lipid peroxidation. Decreases C-reactive protein	Not yet established by FNBIM. 2–8 g/kg/day has been suggested	Turmeric spice, curry	Anticarcinogenic, anti-inflammatory, and antioxidant properties
Polyphenols	Epigallocatechin gallate (EGCG)	Inhibits lipid peroxidation, limits UVR-induced DNA damage, reduces ROS and free radical production. Suppresses pro-inflammatory inducers (i.e., cyclooxygenase-2, MMPs). Supports cell cycle arrest and apoptosis	Not yet established by FNBIM. Proposed upper limit of approximately 300 mg/day	Green tea leaves, green tea, commercially available in white powder form	Antioxidant, anti-inflammatory, and anticarcinogenic properties; reduces UVR-induced erythema/edema
Vitamins; water-soluble	Vitamin C	Free radical scavenger; essential cofactor and electron donor during collagen hydroxylation. Reduces UVB-induced oxidative damage. Protects against UVA-induced lipid peroxidation. Decreases malondialdehyde	90 mg/day men; 75 mg/day women 19+	Raw red and green peppers, oranges, grapefruits, kiwifruit, broccoli, strawberries, Brussels sprouts	Powerful antioxidant; encourages intracellular and extracellular collagen production
Vitamins; fat-soluble	Vitamin E; α -tocopherol (α T)	Halts formation of reactive oxygen species, scavenges free radicals, stabilizes cell membranes, reduces apoptotic cells, minimizes activation of nuclear factor kappa B (NF- κ B)	15 mg/day men and women 19+	Sunflower seeds, peanuts, almonds, walnuts, pecans, pistachios, sesame seeds, fruits, and vegetables	Protects against UVB damage; photo-protective properties; increases MED

FNBIM The Food and Nutrition Board of the Institute of Medicine, *MED* minimal erythema dose, *MMP* matrix metalloproteinase, *UVR* ultraviolet radiation

Potential future nutraceuticals

Nutraceutical	MOA	RDA	Oral source	Skin function
Aloe sterol	Encourage formation of type I and III collagen in dermal fibroblasts; decrease expression of MMP-2 and MMP-9; potentially increases hyaluronic acid in dermal fibroblasts	Not yet established by FNBIM. Further studies needed	Not yet commercially available	Increase collagen production, improve skin elasticity; protects against collagen and ECM degradation; potentially increases hyaluronic acid in dermis

continued

Nutraceutical	MOA	RDA	Oral source	Skin function
<i>Serenoa repens</i> (saw palmetto)	Inhibits 5-alpha reductase	Not yet established by FNBIM. Proposed studied amounts range from 320 mg/day–1 g/day	Supplementation	Antiandrogenic activity, potential treatment of androgenetic alopecia

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Compliance with Ethics Guidelines. This article is based on previously conducted studies, and does not involve any new studies of human or animal subjects performed by any of the authors.

Data Availability. This manuscript has no associated data to be deposited.

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