Vitamin E and Skin Health

Contents

Overview

Vitamin E is a fat-soluble antioxidant that is essential for the maintenance of healthy skin. Naturally occurring vitamin E is not a single compound; instead, vitamin E is a group of molecules with related structures, some of which may have unique properties in skin. Vitamin E is also found as vitamin E conjugates that increase stability but require cellular metabolism for activation. Vitamin E is normally provided to the skin through the sebum. Topical application can also supply the skin with vitamin E and may provide specific vitamin E forms that are not available from the diet. As an antioxidant, vitamin E primarily reacts with reactive oxygen species. In addition, vitamin E can also absorb the energy from ultraviolet (UV) light. Thus, it plays important roles in photoprotection, preventing UV-induced free radical damage to skin. Vitamin E may also have related anti-inflammatory roles in the skin. Other roles of vitamin E in the skin are poorly understood because research is limited. This article discusses the roles of vitamin E in the skin and summarizes the current knowledge about vitamin E in skin health.

Forms of vitamin E

The term "vitamin E" does not refer to a single molecule but to two classes of molecules with similar structures and antioxidant properties, comprising a family of eight substances. Tocopherols are the most abundant form of vitamin E in the body, consisting of four different forms (α-, β-, γ-, and δ-tocopherol). Tocotrienols, which are found in the body to a lesser extent, also exist in four different forms (α-, β-, γ-, and δ-tocotrienol). Although tocopherols and tocotrienols are available from the diet, α-tocopherol is the primary form of vitamin E found and maintained in the body, due to the specificity of a transport protein for α-tocopherol (see the article on Vitamin E).

Naturally occurring vitamin E is usually labeled as "natural" or "d" vitamin E, while synthetic vitamin E is a mixture of eight isomeric forms, usually labeled "all-rac" or "dl." Tocopherols and tocotrienols are also available as ester derivatives that increase molecular stability upon exposure to heat, light, and air. Conjugated vitamin E molecules are typically used in dietary supplements; the esterified molecule is removed by cellular metabolism in the intestine. However, metabolism of vitamin E conjugates in skin is low; therefore, the availability of unesterified or "free" vitamin E from cutaneous application of conjugates may be limited (see Topical application).

Content and availability

Vitamin E is the most abundant lipophilic antioxidant found in human skin (1, 2). In humans, levels of vitamin E in the epidermis are higher than the dermis (1). Although the predominant form of vitamin E in skin of unsupplemented individuals is α-tocopherol, skin may also contain measurable amounts of γ-tocopherol (3) and other diet-derived tocopherols and tocotrienols (4).

Vitamin E first accumulates in the sebaceous glands before it is delivered to the skin surface through sebum (5, 6). Following oral ingestion, it takes at least seven days before the vitamin E content of sebum is altered (5, 7). There are no transport proteins specific for vitamin E in the skin. Sebum is secreted to the surface of the stratum corneum, where it concentrates in the lipid-rich extracellular matrix of this layer (3). Due to its lipophilic nature, vitamin E can also penetrate into all underlying layers of skin (8). Skin vitamin E levels are higher in individuals with increased sebum production, as well as in skin types that naturally produce more sebum (e.g., "oily" skin on the face vs. drier skin on the arm) (1, 8).

Exposures to UV light (3, 9, 10) or ozone (6, 11, 12) lower the vitamin E content in skin, primarily in the stratum corneum. Vitamin E concentrations in the human epidermis also decline with age (1). Since epidermal structure changes with age (13), this may be due to increased UV penetration of this layer.

Topical application

Topical application of vitamin E has been used in a wide variety of forms throughout history, ranging from the application of oils to the skin surface to the use of modern cosmetic formulations. Just as sebum provides a delivery mechanism for vitamin E to the stratum corneum, topical applications of vitamin E permeate the epidermis and dermis (14, 15). The rate of percutaneous vitamin E absorption and factors that influence its penetration are largely unknown in humans, with a large range of concentrations and times used in various studies. It is generally assumed that solutions with vitamin E concentrations as low as 0.1% can increase vitamin E levels in the skin (16). Interestingly, vitamin E levels in the dermis increase greatly after topical application, likely accumulating in the sebaceous glands (15). However, although it is increased after topical delivery, the concentration of vitamin E in the dermis is lower than in the stratum corneum. Skin supplied only with dietary vitamin E primarily contains α- and γ-tocopherol (3, 7, 8); by contrast, skin supplied with synthetic vitamin E topically can contain a mixture of different tocopherols and/or tocotrienols (10, 15). In terms of penetration and absorption following topical application, tocotrienols and tocopherols accumulate in skin at varying rates, but the mechanisms governing these differences are unclear (15).

After topical application, vitamin E accumulates not only in cell membranes but also in the extracellular lipid matrix of the stratum corneum, where vitamin E contributes to antioxidant defenses. However, much of a topically applied dose of vitamin E alone will be destroyed in the skin following exposure to UV light (10). This suggests that although vitamin E is working as an antioxidant, it is unstable on its own and easily lost from the skin. Thus, improving the stability of topical applications with vitamin E is important. Products containing both vitamin C and vitamin E have shown greater efficacy in photoprotection than either antioxidant alone (see Photoprotection).

The stability of topical vitamin E solutions may also be increased by the use of vitamin E conjugates. These vitamin E derivatives are usually commercially produced esters of tocopherol (although tocotrienol esters have been formulated) that are resistant to oxidation but can still penetrate the skin layers. Vitamin E conjugates, however, do not have antioxidant functions. To be effective, the molecule conjugated to vitamin E must be removed by enzymes within a cell. Since the stratum corneum contains metabolically inactive cells and the remaining layers of the epidermis and dermis may contain a large volume of extracellular proteins, it is unclear how efficiently ester conjugates are converted to "free" vitamin E in skin. Depending on the compound and the model system used, the effectiveness of these formulations can vary greatly (16-20), and studies often do not compare the application of vitamin E conjugates to the application of unmodified vitamin E molecules.

Because vitamin E can absorb UV light to produce free radicals (see Photoprotection), there is the possibility that heavy sunlight exposure after topical application can cause skin reactions. However, concentrations of vitamin E between 0.1%-1.0% are generally considered safe and effective to increase vitamin E levels in the skin, but higher levels of α-tocopherol have been used with no apparent side effects (16). On the other hand, studies of dose-dependent vitamin E accumulation and effectiveness in skin protection are lacking. Some forms of vitamin E, especially ester conjugates, have led to adverse reactions in the skin, including allergic contact dermatitis and erythema. Although such reactions may be due to oxidation by-products, the emulsion creams used for topical delivery of compounds may also contribute to the observed effects (21).

Deficiency

Vitamin E deficiency may affect skin function, but there is little evidence from human studies. Vitamin E deficiency in rats has been reported to cause skin ulcerations (22) and changes in skin collagen cross-linking (23, 24), but the underlying cause of these effects is unknown.

Functions in Healthy Skin

Photoprotection

The primary role of vitamin E in the skin is to prevent damage induced by free radicals and reactive oxygen species; therefore, the use of vitamin E in the prevention of UV-induced damage has been extensively studied. Although molecules in the vitamin E family can absorb light in the UVB spectrum, the "sunscreen" activity of vitamin E is considered limited since it cannot absorb UVA light or light in higher wavelengths of the UVB spectrum (25). Thus, the primary photoprotective effect of vitamin E is attributed to its role as a lipid-soluble antioxidant.

Many studies in cell culture models (*in vitro* studies) have found protective effects of vitamin E molecules on skin cells (26-28), but these models do not recreate the complex structure of skin tissues. Therefore, *in vivo* studies are needed.

Studies using orally administered vitamin E have reported mixed results on its photoprotective potential. An early study of vitamin E supplementation in hairless mice found no effect of dietary α-tocopherol acetate on UV-induced carcinogenesis (29). Three other mouse studies reported inhibition of UV-induced tumors in mice fed α-tocopherol acetate (30-32), but one of these studies utilized vitamin E doses that were toxic to animals when combined with the UV treatment (30). Another study in mice found a reduction of UV-induced DNA damage with dietary α-tocopherol acetate, but no effects on other free radical damage were observed in the skin (33). One human study reported that subjects taking 400 IU/day of α-tocopherol had reduced UV-induced lipid peroxidation in the skin but concluded there was no overall photoprotective effect (34). This was supported by another human study that found that 400 IU/day of α-tocopherol for six months provided no meaningful protection to skin (35). Furthermore, multiple human studies have shown no effect of vitamin E on the prevention or development of skin cancers (36, 37).

In contrast to oral supplementation with α-tocopherol alone, multiple studies have found that the combination of vitamin C and vitamin E protects the skin against UV damage. Human subjects orally co-supplemented with vitamins C and E show increased Minimal Erythemal Dose (MED), a measure of photoprotection from UV light in skin (38, 39). The combination of the two vitamins was associated with lower amounts of DNA damage after UV exposure (40). Results of another study suggest a mixture of tocopherols and tocotrienols may be superior to α-tocopherol alone, as the mixture showed reduced sunburn reactions and tumor incidence after UV exposure in mice (41). However, further trials with dietary tocotrienol/tocopherol mixtures are needed in human subjects.

Topical application of vitamin E is generally effective for increasing photoprotection of the skin. In rodent models, the application of α-tocopherol or α-tocopherol acetate before UV exposure reduces UV-induced skin damage by reducing lipid peroxidation (33, 42-44), limiting DNA damage (33, 45-47), and reducing the many chemical and structural changes to skin after UV exposure (14, 48-50). Vitamin E topical applications have also been shown to reduce UV-induced tumor formation in multiple mouse studies (14, 31, 51) and to reduce the effects of photo-activated toxins in the skin (52-55). Topical application of vitamin E also reduces the effects of UV radiation when applied after the initial exposure. In mice, α-tocopherol acetate prevents some of the erythema, edema, skin swelling, and skin thickening if applied immediately after UV exposure (49, 50). A similar effect has been shown in rabbits, where applying α-tocopherol to skin immediately after UV increased the MED (56). While the greatest effect was seen when vitamin E was applied immediately after UV exposure, one study showed a significant effect of application eight hours after the insult (49). In human subjects, the use of vitamin E on skin lowers peroxidation of skin surface lipids (57), decreases erythema (58, 59), and limits immune cell activation after UV exposure (60).

Like oral supplementation with vitamin C and vitamin E, topical preparations with both vitamins have also been successful. Together, the application of these antioxidants to the skin of animals before UV exposure has been shown to decrease sunburned cells (61, 62), decrease DNA damage (61, 63), inhibit erythema (61, 64), and decrease skin pigmentation after UV exposure (64). Similar effects have been seen in human subjects (65-67).

While a majority of studies have found benefit of topical α-tocopherol, there is much less evidence for the activity of esters of vitamin E in photoprotection (57). As described above, vitamin E esters require cellular metabolism to produce "free" vitamin E. Thus, topical use of vitamin E esters may provide only limited benefit or may require a delay after administration to provide significant UV protection.

Anti-inflammatory effects

Vitamin E has been considered an anti-inflammatory agent in the skin, as several studies have supported its prevention of inflammatory damage after UV exposure. As mentioned above, topical vitamin E can reduce UV-induced skin swelling, skin thickness, erythema, and edema — all signs of skin inflammation. In cultured keratinocytes, α-tocopherol and γ-tocotrienol have been shown to decrease inflammatory prostaglandin synthesis, interleukin production, and the induction of cyclooxygenase-2 (COX-2) and NADPH oxidase by UV light (68-70), as well as limit inflammatory responses to lipid hydroperoxide exposure (71). In mice, dietary γ-tocotrienol suppresses UV-induced COX-2 expression in the skin (70). Furthermore, topical application of α-tocopherol acetate or a γ-tocopherol derivative inhibited the induction of COX-2 and nitric oxide synthase (iNOS) following UV exposure (72). *In vitro* studies have shown similar anti-inflammatory effects of α- and γ-tocopherol on immune cells (73-75).

Many of these anti-inflammatory effects of vitamin E supplementation have been reported in combination with its photoprotective effects, making it difficult to distinguish an anti-inflammatory action from an antioxidant action that would prevent inflammation from initially occurring. Despite these limitations, there are many reports of vitamin E being used successfully in chronic inflammatory skin conditions, either alone (76, 77) or in combination with vitamin C (78) or vitamin D (79), thus suggesting a true anti-inflammatory action.

Wound healing

As mentioned above, skin lesions have been reported in rats suffering from vitamin E deficiency, although their origin is unclear. Vitamin E levels decrease rapidly at the site of a cutaneous wound, along with other skin antioxidants, such as vitamin C or glutathione (80). Since skin antioxidants slowly increase during normal wound healing, these observations have stimulated additional studies on the effect of vitamin E on the wound healing process. However, no studies have demonstrated a positive effect of vitamin E supplementation on wound repair in normal skin. Studies have shown that α-tocopherol supplementation decreases wound closure time in diabetic mice, but no effects have been observed in normal mice (81, 82). Vitamin E increases the breaking strength of wounds pre-treated with ionizing radiation (83), but this is likely due to antioxidant functions at the wound site akin to a photoprotective effect. In contrast, intramuscular injection of α-tocopherol acetate in rats has been suggested to decrease collagen synthesis and inhibit wound repair (84).

In humans, studies with topical α-tocopherol have either found no effects on wound healing or appearance or have found negative effects on the appearance of scar tissue (85, 86). However, these studies are complicated by a high number of skin reactions to the vitamin E preparations, possibly due to uncontrolled formation of tocopherol radicals in the solutions used. Despite these results, vitamin E, along with zinc and vitamin C, is included in oral therapies for pressure ulcers (bed sores) and burns (87, 88).

Other functions

There is limited information concerning the effects of vitamin E supplementation on photodamage, which is commonly observed as skin wrinkling. Although vitamin E can protect mice exposed to UV from excessive skin wrinkling, this is a photoprotective effect rather than treatment of pre-existing wrinkles. Other reports using vitamin E to treat photodamage or reduce wrinkles are poorly controlled studies or unpublished observations (89, 90). An analysis of the dietary intake of Japanese women showed no correlation between vitamin E consumption and skin wrinkling (91).

Vitamin E and oils containing tocopherols or tocotrienols have been reported to have moisturizing properties, but data supporting these roles are limited. Cross-sectional studies have shown no association between vitamin E consumption and skin hydration in healthy men and women (91, 92). However, two small studies have shown topical application of vitamin E can improve skin water-binding capacity after two to four weeks of use (93, 94). Long-term studies with topical vitamin E are needed to establish if these moisturizing effects can be sustained.

Environmental pollutants like ozone can decrease vitamin E levels in the skin (6, 11, 12) and lead to free radical damage that may compound the effects of UV exposure (12). Although not well studied, topical applications of vitamin E may reduce pollution-related free radical damage (11).

Conclusion

Vitamin E is an integral part of the skin's antioxidant defenses, primarily providing protection against UV radiation and other free radicals that may come in contact with the epidermis. Oral supplementation with only vitamin E may not provide adequate protection for the skin, and co-supplementation of vitamin E and vitamin C may be warranted to effectively increase the photoprotection of skin through the diet. However, topical vitamin E seems to be an effective mechanism for both delivery to the skin and providing a photoprotective effect. Additional anti-inflammatory effects of topical vitamin E have been seen in the skin, although more studies are needed to determine if vitamin E primarily works as a free-radical scavenger or can have other effects on inflammatory signaling. Vitamin E is available commercially as a variety of synthetic derivatives, but the limited cellular metabolism in skin layers makes the use of such products problematic. Use of unesterified vitamin E, similar to that found in natural sources, has provided the most consistent data concerning its topical efficacy. The vitamin E family consists of eight different tocopherols and tocotrienols, and it will be important for future studies to determine if one or more of these molecules can have unique effects on skin function.

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