Vitamin E in dermatology

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ABSTRACT

Vitamin E is an important fat-soluble antioxidant and has been in use for more than 50 years in dermatology. It is an important ingredient in many cosmetic products. It protects the skin from various deleterious effects due to solar radiation by acting as a free-radical scavenger. Experimental studies suggest that vitamin E has antitumorigenic and photoprotective properties. There is a paucity of controlled clinical studies providing a rationale for well-defined dosages and clinical indications of vitamin E usage in dermatological practice. The aim of this article is to review the cosmetic as well as clinical implications of vitamin E in dermatology.

Key words: Cosmetic, dermatology, vitamin E

HISTORICAL PERSPECTIVE

Vitamin E was first described in 1922 by Herbert M Evans and Katherine Bishop. In 1936, it was biochemically characterized and named tocopherol (Greek: "tocos" meaning offspring and "phero" meaning to bring forth).[1,2]

SOURCES AND FORMS OF VITAMIN E

Vitamin E is synthesized by plants and must be obtained through dietary sources. Richest sources are nuts, spinach, whole grains, olive oil, and sunflower oil.[3]

There are eight types of vitamin E (α-,β-,γ-, and σ-tocopherols and their related corresponding tocotrienols), γ-tocopherol being the most abundant tocopherol in diet, whereas α-tocopherol (α-Toc) is the most abundant vitamin E derivative in human tissues and sera.

VITAMIN E AND EPIDERMIS: MOLECULAR ASPECTS

γ-Tocopherol levels exceeding those of α-Toc in human skin,[4] inhibits the production of PGE2 and nitric oxide, and also prevents sunburn cell formation, ultraviolet (UV) B-induced lipid peroxidation and edema,[5,6] wherefore it has a role in epidermal protection from oxidative stress. Vitamin E also has a role in photoadduct formation and immunosuppression.[7]

STABILITY OF VITAMIN E

Stability of vitamin E depends on its form, dl-α-Toc acetate being the most stable.

Vitamin E, occurring naturally in food in the form of α-Toc oxidizes slowly when exposed to air. The stability of topical vitamin E may be increased by the use of vitamin E conjugates, which are esters of tocopherol, resistant to oxidation but can still penetrate skin layers.[8]

Although many cosmeceuticals contain vitamins C and E, very few are actually effective in topical application because the stability is compromised as soon as the product is opened and exposed to air and light.

However when a stable formulation delivers a high concentration of nonesterified, optimal isomer of the antioxidant, vitamins C and E inhibit the acute UV damage as well as chronic UV photoaging and skin cancer.[9]

Ferulic acid is a ubiquitous plant antioxidant and its incorporation into a topical solution of

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15% l-ascorbic acid and 1% of α-Toc improves chemical stability of the vitamins (C + E) and doubles photoprotection to solar-stimulated irradiation of skin from fourfold to eightfold.[10]

DERMATOLOGIC INDICATIONS

Yellow nail syndrome: (Level of evidence IV)

The yellow nail syndrome includes slow growing, opaque yellow nails with exaggerated yellow curvature, lymphedema, and chronic respiratory disorders such as chronic bronchitis, pleural effusions, and chronic sinusitis.[11] Vitamin E is one of the treatment modalities for yellow nail syndrome,[12] in a dosage of 1000 IU once a day for a period of 6 months.[13]

Dapsone-induced hemolysis and headache: (Level of evidence IV)

In various studies to ascertain the protective effect of Vitamin E on the hemolysis associated with dapsone treatment, it was seen that (dl-α-tocopheryl acetate) in a dose of 800 IU/day confers a partial protective effect against dapsone-induced hemolysis in patients with dermatitis herpetiformis.[14,15] Vitamin E has also been used in dapsone-induced headache.[16]

Headache is a recognized effect of methemoglobinemia, and reduction of previously elevated methemoglobin concentration is presumably the mechanism by which vitamin E improves this symptom, as improved methemoglobin concentration seems to be the most consistent laboratory parameter in studies of vitamin E for protection against dapsone side effects.[14]

Subcorneal pustular dermatoses: (Level of evidence IV)

Vitamin E (d-α-tocopheryl acetate) 100 IU/day, gradually increasing to 400 IU/day for 4 weeks is one of the therapeutic modalities in subcorneal pustular dermatoses, particularly those showing unsatisfactory response to conventional medications.[17]

Cutaneous amyloidosis: (Level of evidence IV)

Tocoretinate is a hybrid compound of retinoic acid and tocopherol. In a study designed to evaluate the effects of topical tocoretinate on lichen amyloidosis and macular amyloidosis, it was concluded that topical tocoretinate reduces the clinical symptoms of lichen and macular amyloidosis.[18]

Other dermatological indications for which there is little utility for the use of Vitamin E

Atopic dermatitis

A single-blind, placebo-controlled study was performed by Tsoureli-Nikita *et al*. in which 96 atopic dermatitis patients were treated with either placebo or oral vitamin E (400 IE/day) for 8 months. They found an improvement and near remission of atopic dermatitis and a 62% decrease in serum IgE levels in the vitamin E-treated group. Vitamin E decreases serum levels of IgE in atopic subjects.[19] The correlation between vitamin E intake, IgE levels, and the clinical manifestations of atopy indicate that vitamin E could be a therapeutic tool for atopic dermatitis.

Hailey–Hailey disease

In 1975, Ayres and Mihan reported control of the condition of three patients with Hailey–Hailey disease by oral administration of vitamin E in the form of d-α-tocopheryl acetate in doses of 800–1200 IU/L.[20] The exact mechanism by which Vitamin E controls this disease is unknown, but its antioxidant action in protecting cell membrane from lipid peroxidation, thus perhaps preventing the formation of autoimmune antibodies, may be an important factor.[21]

Epidermolysis bullosa

Several case reports suggest efficacy of vitamin E (300–600 IU/day) for the management of epidermolysis bullosa.[22,23] Vitamin E acts as an antioxidant, thus protecting the cell membranes and intracellular organelles from lipid peroxidation.[24] It is possible that in case of epidermolysis bullosa, there is a genetic defect that effects the storage of Vitamin E in the tissues or in the ability of tissues to use it, which necessitates an additional supply.[24]

Psoriasis

A natural product, called "Mirak," for the treatment of psoriasis has recently become available in many European countries. Mirak consists of natural spring water, valconic earth, and vitamin E cream. It induces a modest therapeutic effect compared with placebo, without any significant side effects, but may not be able to compete with the already existing treatment options for psoriasis.[25]

Cutaneous ulcers

Vitamin E has been seen to be useful in the treatment of pressure sores in doses of 800 IU/L gradually increasing to 1600 IU/L in four patients.[26]

Skin cancer prevention

Mouse studies reported inhibition of UV-induced tumors in mice fed with α-tocopherol acetate.[27] Multiple human studies have shown no effects of vitamin E on the prevention or development of skin cancers.[28,29]

Wound healing

Vitamin E along with zinc and vitamin C, is included in oral therapies for pressure ulcers and burns.[30] The antioxidant supplementation through vitamins E and C and the mineral zinc has been seen to apparently enhance the antioxidant protection against oxidative stress and allow less time for wound healing.[31]

Melasma

Vitamin E alone has shown minimal efficacy in the treatment of melasma.[32] It has been shown to cause depigmentation by interference with lipid peroxidation of melanocyte membranes, increase in intracellular glutathione content, and inhibition of tyrosinase.[33]

In a randomized, double-bind, placebo-controlled trial, a combination of oral proanthocyanidin plus vitamin A, C, and E was assessed in 60 Phillipino females with bilateral epidermal melasma. The antioxidants were taken twice a day for 8 weeks and were compared with placebo intake by mexametric and Melasma Area and Severity (MASI) score analysis.[34] There was a significant reduction in MASI scores and pigmentation by mexametry in malar regions.

Pycnogenol is a standardized extract of the bark of the French maritime pine (*Pinus pinaster*), a well-known, potent antioxidant, several times more powerful than vitamin E and in addition, regenerates vitamin E and increases the endogenous antioxidant enzyme system. Therefore its efficacy in the treatment of melasma was investigated in a clinical study in which 30 women with melasma took one 25 mg tablet of pycnogenol with meals three times daily, that is, 75 mg pycnogenol per day for a period of 30 days. These patients were evaluated clinically by parameters such as the melasma area index, pigmentary intensity index, and by routine blood and urine tests. After a 30-day treatment, the average melasma area of the patients decreased by 25.86 ± 20.39 mm (2) ($P < 0.001$) and the average pigmentary intensity decreased by 0.47 ± 0.51 unit ($P < 0.001$).[35]

α-Toc derivatives inhibit tyrosinase *in vitro*[36] and melanogenesis in epidermal melanocytes.[37] The antioxidant properties of α-Toc, which interferes with lipid peroxidation of melanocyte membranes and increases the intracellular glutathione content, could explain its depigmenting effect.[38]

Acne vulgaris

In one of the studies conducted in a series of 98 patients, the emphasis was based on the correction of the defective keratinization of sebaceous follicles with a combination of vitamin E and vitamin C.[39] This was seen to prevent the formation of comedones, thus depriving the *Propionibacterium acnes* of a culture medium. Vitamin E prevents lipid peroxidation of serum from bacterial-induced leakage through follicles and sebaceous glands, thus preventing inflammation due to peroxide irritation.

Vitamin E has also been used with high doses of isotretinoin to ameliorate isotretinoin-induced side effects. However, studies have demonstrated that vitamin E does not significantly ameliorate retinoid side effects when combined with isotretinoin in the treatment of acne.[40,41]

Scleroderma

Oxidative stress is significantly increased in patients with scleroderma when compared with the healthy controls, suggesting that free radical induced oxidative injury occurs in scleroderma.[42] Antioxidants such as vitamin E might, therefore, be beneficial. Vitamin E is also believed to stabilize lysosomal membranes, potentially inhibiting events involved in the autoimmune process.[21]

Vitamin E supplementation has resulted in improvement in the skin of scleroderma patients, although nondermatological aspects of scleroderma did not improve.[43]

Various components of scleroderma, including morphea, calcinosis cutis, and Raynaud's phenomenon respond to vitamin E.[44] The dose of vitamin E in these reports ranged from 200 to 1200 IU per day.

One patient successfully treated was a 45-year-old man with Raynaud's phenomenon, probable early scleroderma, and ulceration and gangrene of the fingertips. He received 800 IU oral vitamin E daily and applied the vitamin (50 IU per mL) to the ulcerated fingers twice daily. The ulcerations became less painful after two weeks and healed almost completely within one month.[45]

Dermatological indications for which there are anecdotal reports of beneficial effects of vitamin E

Chronic cutaneous lupus erythematosus[46]
Keratosis follicularis[47]
Postherpetic neuralgia[48]
Pseudoxanthoma elasticum[49]
Porphyria cutanea tarda.[50]

Recommended dose of vitamin E

In case of vitamin E, the recommended intake (6–10 mg of α-tocopherol or the equivalent) is based solely on an estimate of how much tocopherol the average person consumes.[51] In a healthy adult who had been on a normal diet it would take an estimated 4 years to fully deplete body stores of vitamin E.[52]

TOPICAL VITAMIN E IN DERMATOLOGY

Topical vitamin E has emerged as a popular treatment for a number of skin disorders owing to its antioxidant properties. It has been seen that reactive oxygen species have the ability to alter the biosynthesis of collagen and glycosaminoglycans in skin.[53] Most of the over-the-counter antiaging creams contain 0.5%–1% of vitamin E.

One of the most popular applications of vitamin E is the treatment of burns, surgical scars, and wounds. However, studies looking at the efficacy of vitamin E in the treatment of burns and scars have been disappointing.[54,55]

Topical vitamin E has also been found to be effective in granuloma annulare.[56] Vitamin E is one of the ingredients in over-the-counter treatments of skin aging.[57] Topical application of the gel containing 2% phytonadione, 0.1% retinol, 0.1% vitamin C, and 0.1% vitamin E has been seen to be fairly or moderately effective in reducing dark under-eye circles, especially in cases of hemostasis.[58]

VITAMIN E INTAKE DURING PREGNANCY AND CHILDHOOD

Vitamin E supplements in pregnancy usually contain only small doses of vitamin E, although adverse effects have not been observed even at higher doses.[59] Theoretically, however, due to the involvement of cytochrome P450 system in the metabolism of orally supplemented RRR-α-tocopherol, drug interactions have to be taken into account when supranutritional doses of Vitamin E are provided. There is no published report documenting adverse fetal effects due to use of topical vitamin products.

SIDE EFFECTS

Most of the people do not experience any side effects when taking the recommended daily dose. High dose can cause nausea, diarrhea, stomach cramps, fatigue, weakness, headache, blurred vision, rash, bruising, and bleeding.

Vitamin E being a fat-soluble vitamin, administration of a dose higher than daily requirement results in accumulation inside the body, resulting in hypervitaminosis E. Healthy adults taking vitamin E daily at a dose of 100 mg for more than 1 year are likely to get hypervitaminosis E, manifesting as reduced platelet aggregation and interference with vitamin K metabolism resulting in bleeding tendencies.[60]

Topical application of vitamin E can rarely cause contact dermatitis,[61] erythema multiforme,[62] and xanthomatous reaction.[63]

CONTRAINDICATIONS OR SPECIAL PRECAUTIONS

There are no contraindications to the use of vitamin E. Patients with coagulation disorders or taking anticoagulant medications should be monitored for increased bleeding tendencies.

CONCLUSION

Despite development of new formulations for use in cosmetics and skin care products, there is a lack of controlled clinical trials providing a rationale for well-defined dosages and clinical indications for oral and topical vitamin E. After so many years of research on vitamin E, it is still unclear as to whether millions of dollars worth of vitamin E products paid for by patients and consumers have been of any benefit. A better understanding of this vitamin may help in evaluating the indications and dosage regimens for the prevention and treatment of acute and chronic skin disorders.

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Conflicts of interest
There are no conflicts of interest.

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