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REVIEW

# Systemic Vitamin E in Modern Skin Therapy: A Comprehensive Review

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## ABSTRACT

**With its strong line defense and an essential nutrient in the dermatological field in treating various skin conditions. Antioxidants have always been a topic of interest with their antitumorigenic effects or in protecting cells from reactive oxygen species. One of the most important antioxidants in the body is vitamin E, with its lipid-solubility and regenerative mechanism. This article review focuses on various uses of vitamin E in its systemic form. Numerous clinical trials have been testing various dosages across all ages of the population, such as atopic dermatitis, vitiligo, and other diseases, along with the newest technologies used to bring out the effectiveness of this unique molecule.**

**Keywords:** Systemic Vitamin E, Vitamin E, $\alpha$-Tocopherol.

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## 1. Systemic Vitamin E in Modern Skin Therapy: A Comprehensive Review

Oral Vitamin E has always been a field of continued research as formulations of the dosages differ among the population age groups as well as certain disease responses. Various studies have shown the effectiveness of vitamin E, yet further investigations are needed for other dermatologic diseases to provide more evidence for its use. In the field of cosmetics, the use of oral supplementation of vitamin E in experiments has been large in trials, especially in photoprotection against UV radiation [1]. Other studies have shown that vitamin E can surpass the purpose of cosmetics and extend to the field of cosmeceuticals. Vitamin E is considered one of the main potent antioxidants in the body with its fat solubility and eight natural present forms (four tocopherols and four tocotrienols) that act as a photoprotector in healthy skin [2]. With their limiting effects of oxidative stress, which is known to be the leading cause of cancer, ageing, arthritis, and other diseases, balances the cellular metabolism production of free radicals.

### *1.1. Vitamin E Biological Activity*

Vitamin E or Tocochromanols, is a term used to define lipid-soluble compounds that was discovered by Evans and Bishop in 1922 [3]. The most common form is tocopherols, methyl-substituted derivatives of "tocol", being the most abundant in the skin cutaneous and most prevalent in the body as whole as well as in the serum levels compared to the other forms of vitamin E. In contrast to tocopherol, tocotrienol is less prevalent and studies have shown it to be more potent where further research is needed for its use. Tocotrienols are distinct from tocopherols because they have a farnesyl side chain instead of a saturated isoprenoid C16 side chain, yet they have the same basic chemical structure [4]. The distribution of the tocopherol forms of vitamin E differs among the others; beta-, gamma-, and delta-tocopherols have a faster distribution, where they are secreted into the bile and excreted through faeces. Whereas alpha-tocopherol is excreted in urine and has the possibility to accumulate in areas where free radical production is the highest, such as in the mitochondria and endoplasmic membranes of the lungs and heart [2].

### *1.2. Vitamin E and Skin Cellular Functions*

Vitamin E has multiple functions that protect the human skin from altering changes. One of the prominent functions is cellular membrane protection, which involves anti-inflammatory effects by protecting the cell membrane through reducing prostaglandin synthesis, interleukin production, the induction of cyclooxygenase-2 and NADPH oxidase by UV light and promoting membrane repair by preventing the formation of oxidized phospholipids [5], [6]. In addition to cellular membrane protection, other functions known for vitamin E include preventing oxidative stress through lipid peroxidation and peroxyl radical scavenging activity, as well as regulating platelet aggregation through an increase in alpha-tocopherol concentration in the endothelial cells [7].

### *1.3. Pharmaceutical Preparations of Vitamin E*

Many preparations are available for systemic applications. Systemic use includes soft gel capsules for oral use as a supplement. Oral vitamin E doses come in 500 and 1000 IU/d have been tolerated with almost no adverse effects, as well as in the pregnancy group, although smaller doses have been tested out [1]. Institute of Medicine. Food and Nutrition Board recommended daily 15 g of vitamin E for adults and for lactating mothers up to 19 mg [8].

## 2. Diet: Vitamin E Nutritional Value

The impact of vitamin E on skin function is diverse, from its cellular function to the outcome of diseases. With the protection it provides for cells from damage and from producing free radicals or oxidative stress, vitamin E can play a role in the prognosis of diseases [9]. Vitamin E dietary effects are commonly seen in skin disorders of photocarcinogenesis such as nonmelanoma skin cancer, aging of the skin, atopic dermatitis, and acne [10].

### *2.1. Sources of Vitamin E*

Since vitamin E is an extrinsic nutrient, it is important to have a balanced diet with foods such as avocados, fish, seafood such as salmon, and fruits such as kiwi, mango, and papaya. Natural sources that are rich in vitamin E particularly alpha-tocopherol include nuts, seeds and vegetable oils such as olive oil, wheatgerm oil, sunflower oil, hazelnuts, and almonds. Additionally, it is also available in green leafy vegetables such as broccoli and spinach as well as fortified cereals [1].

### *2.2. Diet: Photo Carcinogenesis and Aging*

UV radiation is the most common cause of skin cancer, specifically nonmelanoma skin carcinogenesis, as well as accelerating the natural process of aging. Finding treatment for such a condition has always been under study for decades. In 1994, a study was conducted to determine whether supplementation with dietary a-tocopheryl acetate was able to be a tumor-preventive agent and reduce the chances of carcinogenesis. Three groups of mice were divided based on the calorie intake and the dosage of a-tocopheryl acetate, respectively: group 1 no basal diet with vitamin E, group 2 basal diet and 100 IU/KG of vitamin E, and Group 3 basal diet and 200 IU/KG of vitamin E. Outcomes stated groups 2 and 3 had results of 46% and 19% of tumor formation, respectively [11]. The result is promising, and further experiments are needed to differentiate between skin tumors and the influence of diet on the disease prognosis.

In antiaging defense, vitamin E has been known for its ability to protect against collagen cross-linking as well as lipid peroxidation in the cell membranes [12]. One of the signs of antiaging is wrinkling of the skin, specifically the face region. An oral supplementation of vitamin E, vitamin C, and pycnogenol oil has given encouraging results in inhibiting wrinkle formation through enhancing collagen synthesis and suppressing matrix metalloproteinase (MMP) activity in hairless mice [13]. Furthermore, a deficiency in vitamin E can cause premature aging, keratoses, and difficulty in wound healing [14]. Clinical trials and further studies are needed to explore the benefits that can come from a vitamin E diet.

## 3. Systemic Vitamin E in UV Photodamage Protection

Exposure to ultraviolet (UV) radiation, whether from sunlight or tanning beds, can result in skin photodamage. This damage can trigger the production of free radicals, also called reactive oxygen species (ROS), leading to oxidative stress and alterations in cellular function.

Formulas of vitamin E with other antioxidants show impressive results in protecting the skin from photodamage. A mixture of vitamin E, vitamin C, lycopene, B-carotene, and carnosic acid in oral form has shown a photoprotective effect, with vitamin E preventing the formation of oxidative stress from UVA in skin fibroblasts [15], [16]. Furthermore, a combination of b-carotene and a-tocopherol has proven positive results in decreasing phototoxicity and erythema [17], while others reveal no photoprotection in supplementation [18]–[20]. A combination of oral intake with vitamin C (3 g), and vitamin E (2 g) has shown a 1.5-fold protection increase against phototoxicity [21]. Others have shown adding melatonin increased the protection and erythemal reaction [22].

## 4. Vitiligo Treatment: Vitamin E as an Adjuvant and in Combination Therapy

With the increased trend on social media of celebrities with vitiligo, only 0.5% to 2% of the world population has been recorded to have this skin condition [23]. Vitiligo is a skin disorder where the epidermis loses its melanin, and forms patches due to the death of melanocytes. It is mostly prevalent in the dark-skinned population, and the mechanism of the disease is not yet fully understood. Various causes can trigger the skin reaction, whether it is a combination of autoimmune, environmental, or genetic pathways. Treatment options have different approaches, from medication to phototherapy, such as narrow-band UVB (NBUVB) and surgical procedures.

Vitamin E antioxidant attributes have gained attention in studies experimenting with their therapeutic effectiveness. One trial experimented with two groups of twenty-four patients using NBUVB, which is considered a valuable therapeutic option, and oral supplementation of vitamin E (400 IU). Group A consisted of twelve patients and used NBUVB and oral vitamin E, while group B consisted of twelve patients but only used NVUVB. Group A started with vitamin E supplements two weeks before the use of NVUVB, and for both groups, the course was conducted over six months. The results were impressive, as group A had 72.7% repigmentation compared to group B with 55.6%. Mild erythema was less common in group A post-NVUVB. These outcomes show that oral vitamin E can work best as an adjuvant to NBUVB [24]. A similar study used a combination of antioxidant therapy with vitamin E, vitamin C, a-lipoic acid, and NBUVB. Results were present with positive adjuvant therapy, specifically synergetic between vitamin E and a-lipoic acid, which provided

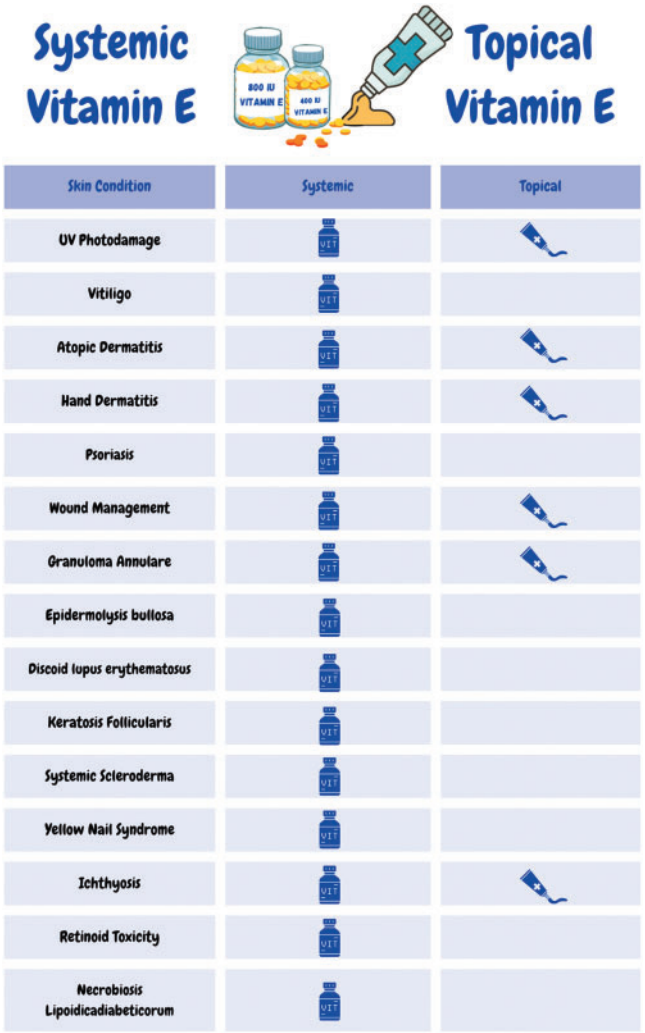


Fig. 1. Other uses of vitamin E in the form of topical vitamin E compared to systemic vitamin E in treating skin conditions.

a reduction in the number of vitiligo lesions [25]. Furthermore, a study demonstrating the use of oral vitamin E, carotenoids, and P. emblica fruit showed promising results in treating three patients with vitiligo as repigmentation has been reported [26]. In contrast to the positive results of the combination of vitamin E and NVUVB, a study was conducted between two groups using psoralen plus UV-A (PUVA) and oral vitamin E (900 IU daily) over a course of six months. The outcome did not show any significant difference between the two groups in the improvement of the vitiligo lesions, yet vitamin E may be used as adjuvant therapy for oxidative distress from PUVA therapy [27].

## 5. Eczema: Vitamin E in Atopic Dermatitis and Hand Dermatitis

Eczema has tripled in prevalence in the past three decades. Children tend to experience eczema more commonly than adults, with results stating 20% to 21%, respectively [28]. One of the most common examples of eczema is atopic dermatitis (AD), which is a chronic inflammatory skin reaction that presents with itchiness and inflamed red patches on the skin. Atopic dermatitis is more commonly found in developed countries compared to developing countries due to factors such as hygiene, lower infection rates, and childhood vaccines. Furthermore, there are common genetic predispositions for atopic dermatitis with asthma and hay fever due to their allergic reactions.

Atopic dermatitis has been known for the unavailability of a long-term cure, and common drugs used are antihistamines, corticosteroids, and calcineurin inhibitors [29]. With vitamin E's role as an antioxidant in the skin barrier, it has been receiving attention in the skincare field due to its therapeutic properties [30]. With its phenolic nature, vitamin E can be a possible therapeutic agent for AD in the sense that it can decrease inflammation, stimulate gene expression of keratinocyte differentiation markers, and promote water loss through a functional biomarker called transepidermal water loss (TEWL) that is expressed in low levels when skin barrier integrity is high [29]. Moreover, on water loss quality, one study examined moisturizing effects on the stratum corneum of hairless mice by using sodium DL-$\alpha$-tocopheryl-6-O-phosphate. The results revealed the effectiveness of holding water up to 1.5-fold, and when enhanced with ceramide, it increased to 1.7-fold. These results are promising for using vitamin E as a moisturizer for atopic dermatitis cases [31].

In terms of vitamin E use in atopic dermatitis, various studies and articles have shown positive results when supplemented orally, from its effects on the pediatric group to the pregnancy group [32]. A study has found that children who consume a higher vitamin E diet are at lower risk compared to other groups that have a lower intake [33]. Furthermore, a study was conducted based on $\alpha$ and $\gamma$-TP serum levels between the mothers who were in their last weeks of gestation and their infants. Results have shown that mothers who had higher serum levels affected children's prevalence of acquiring AD in their first two years [34].

In relation to vitamin E and the levels of atopic dermatitis, an investigation was conducted to ensure its effectiveness. The clinical trial started with a daily treatment of 400 IU over a course of eight months compared to a placebo group. The outcome showed that the group that used vitamin E reduced serum IgE levels and achieved a complete reduction of the disease [35]. A similar study was conducted on AD patients by using 400 IU of vitamin E over 4 months, and the results were encouraging in reducing symptoms and maintaining quality of life [36].

A combination therapy of oral vitamin E and vitamin D was found to be effective for the treatment of atopic dermatitis, as well as a combination of vitamin B12 and vitamin E, which had positive outcomes for treating atopic dermatitis [37], [38].

### *5.1. Hand Dermatitis and Vitamin E*

A study was conducted in 1993 by a 38-year-old physician who presented with hyperkeratosis and fissure of the palmar side in both his hands, with no family history of atopic dermatitis. He initiated the use of over-the-counter oral vitamin E at 400 IU daily, and his hands cleared after 4 months. The outcome needs further investigation in a larger-scale group to prove the efficiency of its use. However, the results are hopeful for vitamin E to be used as a therapeutic model [39].

## 6. Vitamin E in Psoriasis

Psoriasis is a chronic autoimmune skin disease in which skin cells multiply rapidly, leading to scaly and inflamed patches of skin mainly on the knees, elbows, and scalp, as well as other parts of the body. Vitamin E was demonstrated to be useful in combating the oxidative burden that accompanies psoriasis [40]. In addition, nano-transferosome pharmaceutical formulations of vitamin E with aloe vera showed more permeability and high efficacy in the treatment of psoriasis [41]. Furthermore, supplementation with vitamin E could aid in the management of severe psoriasis. A study compared the combination of vitamin E, selenium, and coenzyme Q10 between two groups. The first group consisted of fifty-eight patients with arthropathic (PsA) and severe erythrodermic (EP) forms of psoriasis. Whereas the control group consisted of twenty-four healthy patients. Outcomes were significantly positive compared to the placebo group, where the healing process was faster and can prove to be a future treatment option for severe psoriasis cases [42].

## 7. Vitamin E's Wound Management

Wounds range from surface-level injuries affecting the outer skin layer to deeper wounds involving inner tissues or organs, characterized by a disruption in skin or tissue integrity. Given vitamin E's known abilities to aid in tissue repair and healing, there is growing attention towards its role in wound management. Evaluating the success of wound management typically involves ensuring no infection is present and monitoring cell proliferation.

Vitamin E has known antioxidant activity that can be favored in various skin treatments, including wounds. For instance, vitamin E not only influences cell signaling, but it can also modulate CTGF, a connective tissue growth factor, to protect the wounds from infections such as MRSA (methicillin-resistant Staphylococcus aureus) [43]. A study has demonstrated the use of vitamin E as a potential antimicrobial agent when added to daptomycin and tigecycline results in effectivity against MRSA infection in wound treatment by inhibiting bacterial action and increasing fibronectin and IL-24 expression [44]. Another study has shown promising results for future patients with hyperglycemia when being treated for their wound using vitamin E supplementation in an experiment with rats induced by streptozotocin injection [45].

## 8. Epidermolysis Bullosa and Vitamin E

Epidermolysis bullosa (EB) is a rare genetic disorder that causes fragile and blistering skin as a response to trauma in the form of painful sores. The use of vitamin E in this case has been positive, whether in systemic use or topical application. A study was conducted on the use of vitamin E in the form of d-$\alpha$-tocopherol acetate in three pediatric patients with EB and has shown dramatic results, from returning to their daily habits to going back to their hobbies such as football with no recurrences. The method that was used in the previous study was a dose of vitamin E (400 IU) given three to four times a day before bedtime [46], [47]. Another study has shown that combining topical vitamin E and systemic oral olopatadine hydrochloride can reduce pruritus and improve the prognosis of the disease [48].

## 9. Miscellaneous Uses of Vitamin E in Skin Diseases

Variety of skin diseases need further studies to ensure the effectiveness of vitamin E in its therapeutic use. There are anecdotal reports of successful results from the use

TABLE I: Miscellaneous Dermatological Indications

| Dermatologic disorders | Vitamin E isoform | Efficacy | Reference |
|---|---|---|---|
| Granuloma Annulare | Oral 180 mg<br>$\alpha$-Tocopherol | Results were positive, lesions flattened and faded. | [49] |
| Systemic Scleroderma | Oral<br>D-$\alpha$-tocopheryl acetate | Acceleration in healing time and pain reduction | [50] |
| Yellow Nail Syndrome | Oral 400 IU<br>D-$\alpha$-tocopheryl acetate<br>2,000 IU tocopherol acetate per ounce of safflower oil | Reduction in tingling and numbness in the fingertips.<br>No significant changes were found. | [51], [52] |
| Keratosis Follicularis | Oral 1600 IU<br>$\alpha$-Tocopherol<br>Remarked inhibition of eruption and recurrence. | Worked synergistically with Vitamin A of 100,000 IU | [53] |
| Ichthyosis | Oral 800 to 1600 IU<br>$\alpha$-Tocopherol | Treatment was successful with vitamin A 100,000 IU/d with no side effects. | [54] |
| Discoid lupus erythematosus | Oral<br>1200 to 2000 mg/d &<br>300 to 400 mg/d<br>L-tocopherol | Two studies have presented the effectiveness of vitamin E on the recovery from the condition through collagen regeneration as its primary effect. | [55], [56] |
| Retinoid toxicity | Oral 800 IU<br>$\alpha$-tocopherol | Reduction of retinoid side effects with no intervention in retinoid efficacy. | [57] |
| Necrobiosis Lipoidicadiabeticorum | Oral 100–250 mg<br>Mixed tocopherols | Significant clinical improvement | [58] |

of systemic vitamin E in dermatological conditions. The Table 1 contains the listing of dermatological conditions where they encourage the use of systemic vitamin E. Other methods of vitamin E use, such as in the form of topical vitamin E compared to systemic vitamin E, are in Fig. 1, where it shows the mentioned skin conditions and their other applicable method of use.

## 10. Conclusion

After a century of research and exploration, there is still a lot we do not know about the effective use of vitamin E, especially in treating various skin diseases that have not been thoroughly studied yet. While numerous studies exist, there is a need to leverage technology and combine vitamin E with other antioxidants to maximize its benefits. Controlled clinical trials that provide precise dosing guidelines and clinical indications for both oral and topical vitamin E remain limited, despite advancements in formulations for cosmetics and skincare products. The future of vitamin E holds promise, especially with innovations like nanotechnology and new wound dressings, yet there is a call for more data on its efficacy against different skin conditions and the underlying mechanisms. Given its affordability, further research is warranted to understand vitamin E's potential as a preventive or adjunctive treatment and to refine dosage recommendations. Thus, despite being a nutrient initially discovered in food, vitamin E continues to be a fertile ground for advancements in medical science across various domains.

## Conflicts of Interest

Authors declare that they do not have any conflict of interest.

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