

Topical Vitamin E in Modern Skin Therapy: A Comprehensive Review

Mohammed Al Abadie^{1*}, Marwah Mahfoudh², Al-Hussein Al-Rawi²

¹North Cumbria integrated care NHS foundation trust, University of Central Lancashire, UCLAN medical school, United Kingdom

²The Midlands Medical Academy

*Corresponding Author

Mohammed Al Abadie PhD FRCP, North Cumbria integrated care NHS foundation trust, University of Central Lancashire, UCLAN medical school, United Kingdom.

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Abstract

From generating millions of dollars for its positive role in skin barrier stabilization to recent advancements in burn and wound management. Vitamin E has been utilized in various experimental and clinical dermatology for more than sixty years. It has been a target for many researchers due to its role in preventing cell damage from free radical species and its unique antioxidant properties in the human body. With its importance in the cosmetic world and in clinical implications, there has been numerous research ranging from basic physiology to photoreception qualities that help shape today's use of vitamin E. This literature review aims to present the effectiveness of topical vitamin E application through a combination of recent advancements in various skin conditions and early clinical trials dating back to 1965 that helped to shape the ongoing formulation of vitamin E.

Keywords: Vitamin E, α -Tocopherol, Topical Vitamin E

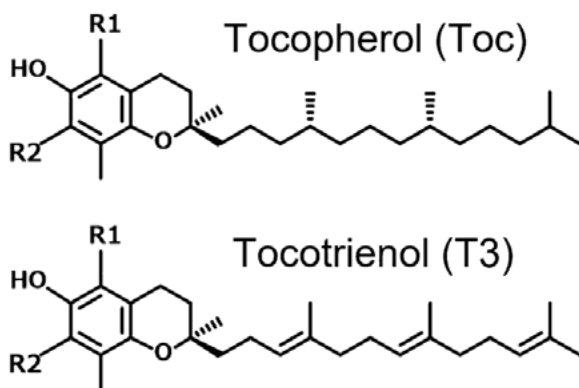
1. Topical Vitamin E in Modern Skin Therapy: A Comprehensive Review

Over the span of a lifetime, the human body encounters ongoing challenges to preserve its integrity and maintain its normal physiological functions from threats, whether its UV radiation or environmental pollutants. Oxidative stress is one of the daily challenges that can result from reactive oxygen species in response to cellular metabolism of the UV radiation [1]. As the skin organ being the first line defense, different layers of the skin (stratum corneum, epidermis, dermis, and subcutis) possess antioxidant system as a response to balance between the formation of the ROS and its activity to protect from the oxidative stress [2].

2. Antioxidant System and Vitamin E Types

Vitamins are one the integral components of the antioxidant system present in human skin. One of the most important vitamins and the main one of the human bodies is vitamin E. As it has been discovered by Evans and Bishop in 1922, during a female rat experiment to sustain pregnancy [3]. Vitamin E or tocopherols encompasses

a group of fat-soluble compounds where it is compromised into two main subclasses: Tocopherols, characterized by saturated side chains, and Tocotrienols, which have unsaturated side chains [4]. There are eight naturally occurring forms of vitamin E, including alpha, beta, gamma, and delta Tocopherols, and Tocotrienols, synthesized by plants from homogentisic acid [1]. Tocopherols, particularly alpha-Tocopherol, are the most abundant, active forms of vitamin E in the body, and the most concentrated due to its rapid metabolism and the presence of a specific transfer protein, alpha-tocopherol transfer protein, which binds strongly to alpha-Tocopherol. While Tocotrienols are found in lesser quantities [5]. Applying vitamin E topically offers a viable alternative to sustain the system's functionality. Formulation of vitamin E and its stability is important for the outcome benefit of its use. Topical preparations were commonly at <5% of concentration and in other topical application to improve the stability, 15% l-ascorbic acid is added with 1% of α -Toc to improve the outcome from fourfold to eightfold [6,7].



	R1	R2
α -	-CH ₃	-CH ₃
β -	-CH ₃	-H
γ -	-H	-CH ₃
δ -	-H	-H

Figure 1: Tocopherol and Tocotrienol

Figure 1 adapted from- The difference in the cellular uptake of tocopherol and tocotrienol is influenced by their affinities to albumin [8]

3. Topical Vitamin E in UV Photodamage Protection

From sunlight radiation to tanning beds, exposure to UV can lead to photodamage of the skin. This damage can lead to the formation of free radicals, known as reactive oxygen species (ROS), and oxidizing stress which causes changes in the cellular function. Various studies have shown positive results for the effectivity of topical vitamin E from UV radiation protection from UV radiation. Combination of vitamin E, vitamin C, and oxybenzone (UVA sunscreen) results in greater adaptivity for phototoxic damage [9,10]. Other solutions, such as 15% L-ascorbic acid and 1% alpha-tocopherol, have been proven to decrease cellular apoptosis in sunburn cells and provide fourfold protection against UV radiation [11]. Topical vitamin E, vitamin C, and ferulic acid show improved results in protection from photodamage and DNA mutations against skin cancer [11]. Q10 and Vitamin E have also been shown to reduce UVB irradiation and have an interesting formula for anti-aging, as well as NAC and Vitamin E [12-14].

4. Vitamin E Use in Cosmetics

Antioxidants have increased in their use and effectiveness in the last 50 years [15]. Vitamin E is known for its crucial role in the cosmetics and skin care worlds. It has been sourced from wheat grams and sunflowers to be used in the form of a pure compound, isolated, or from plant oils [16]. Vitamin E uses the glutathione pathway and chain-breaking lipid peroxidation for its physiology in the skin. Numerous benefits from vitamin E have been found to be moisturizing for the skin and strengthening the hair follicles [17]. In recent years, it has been used in makeup products to enhance their stability and effect on skin and has been found to be favored in the market for skin care products, specifically anti-aging products. In addition to skincare products, it is important to understand the physiology of the skin, from the penetration of the percutaneous to the oral delivery pathway, for the benefit of skin treatment or in the prevention of acute and chronic skin diseases [18]. The following segments will discuss the possible uses of vitamin E in the cosmetic world.

5. Skincare Treatments

One of the various uses of vitamin E is in the formulation of over-the-counter products that have been commercially used in recent years, where it's found to be commonly used in the form of 0.5% to 1% of vitamin E in the use of anti-aging [19]. The nonantioxidant function of vitamin E helps in the integrity of the skin, while the antioxidant function helps in protecting the skin from side effects that can result from exposure to UV radiation or oxidative stress through the inhibition of prostaglandin E2 and nitric oxide [20].

Tocopheryl acetate is one of the common forms of vitamin E that have been used in skincare treatments, as results indicate excellence in protecting the stability of the product used in the moisturizing effects on the skin [21]. One of the effective uses of vitamin E has been shown in facial cleansers when combined with aloe vera and glycolic acid in treating acne or in acne management. It has been shown that with its physiological activity of protecting the skin from free radicals, it can protect the skin types of oily and mixed skin from forming acne spots and hyperpigmentation by reducing inflammation in sebaceous glands and follicles by stopping the leakage of serum lipids into those areas [22]. A recent study has shown the use of vitamin E and kenaf seed oil (*Hibiscus cannabinus* L.) can help in stabilizing the product by making the pH value closer to the skin pH, as well as in microbiologic stability [23]. Furthermore, another study shows the brightening effect of vitamin E in use with vitamin C and raspberry leaf cell culture in improving the appearance of hyperpigmentation along with elasticity, radiance, and smoothness of the skin [24].

6. Wrinkles Minimization

With its antioxidant effect, vitamin E continues its use in protecting the skin from various chronic damages, and one of those is skin wrinkles. Despite it being a natural process of antiaging, wrinkles form when the skin loses its elasticity and collagen production. Causes of wrinkles range from sun exposure, repeated facial expressions, smoking and environmental changes such as pollution. Various studies have shown vitamin E's potential in minimizing wrinkles appearance [25]. One study has shown noticeable results with the daily use of 5% d- α -tocopherol cream over a course of four months for periorbital wrinkles [26][27][28]. Another study has shown that combining vitamin E, vitamin C, phytonadione,

and retinol has proven to decrease not only wrinkles in the lower orbital area but also the dark pigmentation known as dark circles in the periorbital area over a course of 8 weeks [29].

7. Stretch Marks and Vitamin E

Few studies have shown the effect of vitamin E on striae distensae (SD) or stretch marks, as many treatments were performed but none were able to eradicate them. In 1996, a study was conducted on a group of pregnant women applying vitamin E ointment and massaging it in the abdomen, thighs, and breast areas resulted in a decrease in stretch mark numbers [30]. However, the study was considered poor in randomizing and without blinding the groups for it to be efficient. Another study shows the effect of vitamin E on rehydration, and the results were insignificant compared to the other group of placebos [31]. Furthermore, studies are needed for combining vitamin E and other antioxidants, as it can be the future treatment of stretch marks with the potential of their synergetic nature.

8. Vitamin E Oils and Hair Follicles

From alopecia to cosmetic needs, the appearance of hair has always been one of the concerns in the dermatology field. When it comes to the role of vitamin E, studies have shown potential for its use in growing hair and appearance. A study showed that the combination of 0.5% alpha-tocopherol and tocopherol acetate had positive results in hair growth from 2 weeks to 4 weeks [32]. Another interesting study based on two groups of chemotherapy-induced alopecia found that the group that used vitamin E prior to chemotherapy long-term resulted in 69% of hair loss compared to the other group of 90% [33]. Furthermore, a recent study done on rabbit hair using a mixture of egg yolk, coconut oil, and vitamin E showed a significant increase in hair growth at 2 weeks; however, the author mentions that further studies are needed regarding the action mechanism of the oils used [34].

9. Vitamin E and Melasma

Skin pigmentation has been one of the symptoms that has increased within the dermatological cosmetic interests and its underlying systemic causes in treating it. Hyperpigmentation is a universal description for when skin produces melanin excessively, which leads to the formation of dark patches. Melasma is one of the most common causes of hyperpigmentation. They tend to be in dark gray patches, specifically on the face region. It is known as a “black spot” or “chloasma” in pregnant women. UV radiation, genetics, ethnicity, and hormonal changes are some of the common causes of melasma.

Melasma treatment comes with a combination of approaches that include avoiding sun exposure and hormonal management. One of the common therapeutics given to melasma patients is oral procyanidin, which is known for its anti-inflammatory and antioxidant properties that help reduce the appearance of melasma and its safety in use. Furthermore, antioxidants such as vitamin E, vitamin A, and vitamin C share these common features [35]. Vitamin E can have a positive effect in therapeutics for this skin condition as it can provide protection for the melanocyte membrane

from lipid peroxidation [36]. A trial was performed on fifty-six Filipino women, where they presented with melasma and used a combination therapy of oral procyanidin and vitamin A, C, and E. The results were effective and promising in brightening the dark patches, but further study is needed to determine the effectiveness of the treatment [37].

10. Newest Laser Treatment and Combination of Vitamin E

When combining vitamin E with other antioxidants, results tend to be dramatic and positive compared to when applied alone. One of the synergistic effects of vitamin E use is when combined with the laser treatment, such as Q-switched Nd:YAG laser (QSNY). A study has shown that when combining vitamin E, vitamin C, and ferulic acid, skin pigmentation such as melasma has shown great improvement, although after 5 sessions [38].

11. Vitamin E's Wound Management

From superficial wounds that can disrupt the outermost layer of the skin to the deepest lower layer, Wounds are described as a disruption in the skin's integrity, mucous membrane, or organ tissue. With vitamin E's properties in promoting healing and tissue repair, there has been an increased interest in the field of wound management. To assess the overall effectiveness of the management, there should be no infection or cell proliferation.

Chitosan/alginate hydrogels that contain vitamin E proved to be successful in terms of higher proliferation and closure of the wound compared to a gauze-treated wound [39]. However, in terms of application, studies tend to favor oral supplementation of vitamin E to be more effective than topical application of vitamin E in wound management [40]. In contrast to the use of vitamin E systemically, a study compared the efficacy of the most used isomer, α -Toc, with tocotrienols in topical application. Results favored the use of tocotrienols as they proved their potency in accelerating antioxidant enzymatic activity in the wounds of diabetic rats [41]. Furthermore, an experiment has shown vitamin E effectivity in treating wounds that were caused by laser injury by reducing healing mean time to 1-week post-exposure [42].

New studies have used a combination of C.E. FERULIC and fractional ablative laser to understand the mechanism of decreasing the time of postoperative wound healing [43]. Another study has shown the effect of using topical alpha-tocopherol on delayed wound healing, and the results were successful with no sepsis or tissue necrosis [44].

12. Vitamin E's Burn Management

Burn injury is considered one of the most global health concerns because it poses serious challenges physiologically and psychologically to wellbeing. There are four degrees of burn, and with each degree, it requires further medical attention as it can be life-threatening. Burns have various causes, ranging from thermal, chemical, friction, electrical, and radiation. Burn management has a protocol for assessing and treating the injury, as well as a multidisciplinary approach for recovering the patient.

The physiologic changes that occur after burn injury are oxidative stress and the production of free radicals and reactive nitrogen species (RNS) that exceed the innate defense system. The potential role of vitamin E as an antioxidant is that it protects the mitochondria from oxidative stress. A conjugated form of vitamin E known as triphenyl phosphonium (TPP) has been used in burn injuries, which helps in reducing pain and bacterial exudates [45]. The use of vitamin E in burn injuries can be both through supplementation and topical administration, as burn injuries can cause systemic disruption to the body as well as to the local site of injury. One study stated that the use of polymeric films containing vitamin E acetate and aloe vera provided a faster healing process and reduced damage since vitamin E is present in the deepest layers of stratum corneum [46]. In addition to polymeric films, another study has used microparticles loaded with aloe vera, chitosan, and vitamin E, which provided good mucoadhesive properties to burn wounds [47].

13. Vitamin E's Scar Management

Scar management has always been one of the topics of interest in the dermatological and plastic surgery fields, from the healing process to the cosmetic visibility for the patient's self-esteem. There are four known types of scars, which include hypertrophic scars, atrophic scars, keloid scars, and contracture scars. Several medications have been recommended to patients, from steroids to moisturizers and antioxidants, including vitamin E topical creams. The use of these products is aimed at reducing the visibility of the scar, relieving symptoms, and preventing further complications, such as transforming into a keloid scar.

Vitamin E is preferred by many medical professionals due to its physiological activity in remodeling scars, speeding the healing process, and avoiding hypertrophic scar transformation [48]. It works by acting on the phospholipid in the cell membrane and helps with its biologic stability [49]. Mixed studies have shown the ineffectiveness of vitamin E in scar management ranging from insignificant results to developing contact dermatitis as adverse effects [50]. One study has shown the use of vitamin E as a combination therapy with silicone gel sheets and had promising results [51]; the second study used hydrocortisone with silicone gel sheets [52]. However, others have shown no significant changes [53], while a study resulted with adverse effects such as contact dermatitis, itching, and rash [54]. In addition to combination therapy for treating scars, a study in Bangladesh found supplementation of vitamin E and selenium helped improve skin lesions caused by arsenic exposure [55].

14. Surgery in Dermatology: The Use of Vitamin E

From mole removal to skin cancer intervention, surgery in dermatology encompasses a wide range of procedures, and with the technological advancements available, it makes it a rich area for research to evolve in the upcoming years. The following studies

are the most recent for the use of vitamin E in the surgical field.

A study carried out in 2017 was conducted on a healing graft site by donors using silicone vitamin E gauze and α -tocopherol acetate oil. The method consisted of two groups, each consisting of thirty patients, and the difference was between using normal moist gauzes and the other group using vitamin E gauzes and α -tocopherol acetate oil. The outcomes were compared on four variables that is healing time, infection, pain, and costs. In terms of healing time, no significant difference was found between the two groups. In terms of infection, three patients were reported in group 2 to develop infection compared to group 1 with no wound infection. Whereas in terms of pain, visual analog scale (VAS) was used to measure acute to chronic pain and the score in group 2 was significantly lower compared to group 1. Furthermore, regarding the cost, group 2 costs were reduced by 75% compared to group 1 [56].

Another study was conducted on the pediatric group to see the effect of topical vitamin E pre- and post-surgery on the surgical incision. It was monitored in two groups and controlled in two groups. Group A was given topical vitamin E to be administered 30 days before surgery, twice a day, and 15 days post-surgery, thrice a day. Group B was the control group where only petroleum-based ointment was given. Results came out particularly good, as 96% of group A patients did not develop keloid scars and no patient experienced infection, whereas in the control group, 76% of patients were satisfied with the cosmetic results and thirteen patients developed keloid scar [57]. The use of vitamin E seems encouraging for future use in surgical cosmetics.

15. Miscellaneous Uses of Topical Vitamin E

15.1. Actinic Keratoses

Actinic keratosis or "solar keratoses" are dry, flaky patches that have been caused by sun radiation damage. Few studies have been conducted to demonstrate the effect of topical vitamin E in this skin condition. One study shows the use of topical DL- α -Tocopherol helped to reduce polyamine (AK phenotype) concentration in the skin. However, no reduction in the number of AK lesions has been resulted [58].

15.2. Cheilitis

Cheilitis is known to be the inflammation of the lips ranging from acute to chronic due to the dryness of the skin and the onset of infection. One study has shown the effectiveness of topical vitamin E acetate in its toleration of this skin condition [59].

15.3. Systemic Sclerosis

Systemic Sclerosis or scleroderma is a rare disease that results in the hardening and thickening of the skin and may later cause problems in the blood vessels and internal organs. One study has shown the effectiveness of using topical gel of α -Tocopherol in reducing the peripheral blood flow through its application [60].

Topical Vitamin E Systemic Vitamin E

Skin Condition	Topical	Systemic
UV Photodamage		
Acne		
Wrinkles		
Striae Distensae (Stretch Marks)		
Hair Growth		
Chloasma (Melasma)		
Scar Management		
Wound Management		
Burn Management		
Surgery In Dermatology		
Actinic Keratoses		
Cheilitis		
Systemic Sclerosis		

Figure 2: Other uses of vitamin E in the form of systemic vitamin E compared to topical vitamin E in treating skin conditions.

16. Conclusion

After a century of discovery, vitamin E studies and articles are endless, yet we need further information for the effective use of it. As many studies have been conducted, there are even more skin diseases whose vitamin E effectiveness has not been tested yet. With the studies that have been performed, we can elevate the data with technology and the combination of other antioxidants to extract as much benefit as possible. Controlled clinical trials that support precise dosages and clinical indications for oral and topical vitamin E are scarce, despite the development of novel formulations for use in cosmetics and skin care products. From nanotechnology to newly developed gauzes, the future use of vitamin E is promising, further data for other skin diseases and

their mechanisms of action is required. With its low cost, future research and studies are warranted to gain knowledge of vitamin E use, whether as a pretreatment or as a secondary treatment, and to learn more about its dosage formulas. Therefore, this nutrient that has been discovered through food, despite its extrinsic nature, is still a rich experiment area for evolution in all branches of medicine.

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