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Clinical role of oral vitamin C and E therapy in skin and hair disorders: A systematic review

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ABSTRACT

Introduction: Vitamin C and E are generally recognized as safe dietary supplements that provide benefits for skin and hair health. However, their clinical validity in the treatment of dermatologic conditions has not been explored. It is highly important to review the current evidence on the therapeutic utility of oral vitamin C and E therapy for dermatologic disorders.

Materials and Methods: A PubMed search (between 1948-2020) was performed to identify studies that evaluated the use of vitamin C and vitamin E oral therapy for treating dermatologic conditions in humans. Articles were excluded if they examined topical formulations, if treating vitamin deficiencies, or if used in combination with other ingredients.

Results: Fifty-eight articles, encompassing only 1,669 patients, were reviewed. Evidence supports oral vitamin C therapy inpigmentary disorders, such as chloasma (600mg daily), and wound healing, such as in pressure sores (3g daily). Similarly, evidence supports oral vitamin E for pigmentary disorders, like chloasma (300mg daily), and fibrotic disorders, such as radiation-induced fibrosis (1000IU daily). Combination therapy with vitamins C and E is documentedfora variety of dermatologic disorders such aschloasma (600mg vitamin C/300mg vitamin E daily), systemic sclerosis (1000mg vitamin C/400 IU vitamin E daily), and UV-induced erythema (2-3g vitamin C/1-2g vitamin E daily).

Conclusion: The current literature offers some support of the therapeutic use of oral vitamin C and/or vitamin E inchloasma, pigmented contact dermatitis, atopic dermatitis, vitiligo, and pressure wounds. However, evidence is limited by few quality studies with contradictory results.

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Introduction

Vitamin therapy has become widely popularizedin the treatment of dermatologic conditions,[1,2] and is estimated to generate more than $30 billion dollars in the United States.[3] Moreover, vitamins C and E are well recognized for their antioxidant properties and close link to anti-aging. Vitamin C, also known as ascorbic acid, is a water-soluble nutrient that cannot be synthesized by humans, and must be obtained from dietary sources.[4] Relative to other organs, it is found in highest concentrations in the skin, where it acts as cofactor in the generation of stabilized collagen molecules within the dermis.[5] Vitamin C is integral to wound healing,[6] reducing oxidative stress from UV exposure,[7,8] and has been implicated in the inhibition of melanogenesis.[7] It is well established that vitamin C is a cofactor to stabilize collagen formation and promote the proliferation and migration of dermal fibroblasts needed for wound healing.[7] Moreover, ascorbic acid and many of its derivatives have demonstrated inhibitory effects on the enzyme tyrosinase, which catalyzes the hydroxylation of tyrosine to dihydroxyphenylalanine (DOPA). The oxidation of DOPA leads to the production of ortho-quinone, which is theorized to play a role in melanin production.[7,9]

Vitamin E, or alpha-tocopherol, is a lipid-soluble antioxidant that helps protects lipid-containing skin barriers from UV free radicals.[10] Moreover, vitamin E can modulate the inflammatory response and has been described in the inhibition

of melanogenesis.[11,12] As a potent antioxidant, vitamin E functionally reduces pigmentation by interfering in lipid peroxidation within melanocyte membranes and by increasing the melanocyte concentrations of glutathione, which has been shown to decrease tyrosinase activity and thus melanin production.[10,13] Furthermore, this antioxidant property protects the skin from photodamage by stabilizing lipid membranes.[7,10]

Aside from the basic physiological roles of vitamins C and E, numerous studies have reported on the use of vitamins C and E as treatment option in dermatologic disorders. However, the evidence for their use in dermatologic disorders is scattered. In a recent systematic review, we elucidated the role of topical vitamin C and vitamin E use in dermatologic conditions. Now, the therapeutic value of oral vitamin C and E in dermatologic diseases needs to be ascertained via a comprehensive assessment of all published studies. As such, this systematic review exploring the scientific evidence for the use of oral vitamin C and E aims to understand their therapeutic utility in skin and hair pathologies.

Methods

A review of PubMed database from 1948 to 2021 was completed utilizing the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocol (PRISMA-P). The search terms "((vitamin c OR ascorbic acid) OR (vitamin e OR tocopherol)) AND (skin OR hair) NOT (topical)" were used. All case reports, case series, retrospective and prospective observational studies, and clinical trials involving human subjects and written in English were included. Articles, which included other ingredients in addition to vitamin C and/or vitamin E, were included only if the effect of vitamin C and/or vitamin E could be deduced. Articles were excluded if they examined topical formulations, or if they were treating vitamin C or vitamin E deficiencies. Levels of evidence for each article was determined based on the Oxford Centre for evidence-based medicine criteria.[14]

Results

The literature search initially yielded 1,493 manuscripts. After applying the inclusion and exclusion criteria, 58 articles were reviewed (Figure 1).This included 24randomized controlled trials (RCT),six cohort studies, four case-control study, sixteen case series, and nine case reports, totaling 1,669 patients(supplemental Tables 2-4).We identified 35 unique dermatologic conditions treated with oral vitamin C and/or vitamin E in the literature. A summary of findings with level of evidence with vitamin C, vitamin E, or combination therapy by condition is included below (Table 1).

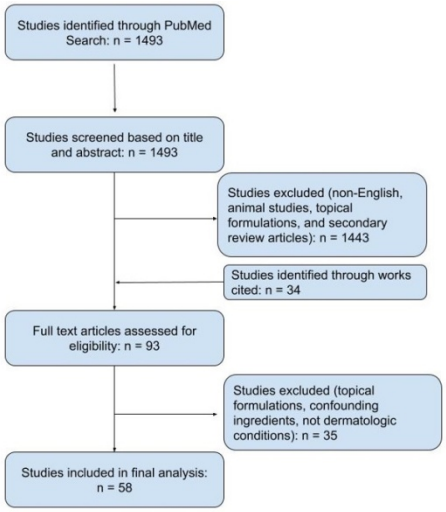

Figure 1: Preferred Reporting Items for Systematic Review and Meta-Analysis Protocol (PRISMA-P) for systemic literature review of oral vitamin C and vitamin E use in dermatology.

Oral Vitamin C Therapy

There were total of 16 studies examining treatment with oral vitamin C (200-4,000 mg daily) in skin conditions, with eight studies supporting its efficacy.

Pigmentary Disorders

In chloasma and pigmented contract dermatitis (PCD), a triple-armed RCT compared the use of 300mg vitamin C, 150 mg d 1-α-tocopheryl acetate, and combination therapy for 4-12 weeks in patients with facial PCD (n = 15) or chloasma (n = 45). For the vitamin C group, significant clinical improvement in discoloration was noted among 40%of subjects with PCD and 50% with chloasma. Side effects were noted among 11.7% of subjects, and included acne, hot flushes, upset stomach, hypermenorrhea, and seborrheic dermatitis of the scalp.[15]

Vitamin C therapy(up to 1g of vitamin C daily) was found ineffective for pigmented purpuric dermatosis in a retrospective cohort study of 53 patients after median duration of 3.1 months.[16]

Inflammatory Conditions

In inflammatory conditions, vitamin C therapy is supported for the treatment off urunculosis, pediatric miliaria rubra, and by a single case report inlichen spinulosus. In recurrent furunculosis, one prospective cohort study (n = 23)from 1975 described the use of 1g of vitamin C for up to six weeks with significant clinical improvement and enhanced neutrophil function (n =12/23).[17]For pediatric miliaria rubra, one non-randomized clinical trial from 1968 described the use of 15mg/kg of ascorbic acid in children (n = 30) for two weeks, with clinical improvement among 93% of those treated versus 27% of those receiving placebo.[18] For lichen spinulosus, one case from 1964 reported clinical improvement after eight months of 500mg of vitamin C therapy.[19]

Vitamin C therapy (1-4g ascorbic acid daily)was found ineffective in the treatment of cutaneous hypersensitivity reactions in a RCT (n=14).[20]

Table 1. Summary of dermatologic conditions treated with oral vitamin C, vitamin E, or combination therapy based on efficacy of treatment and categorized by level of evidence based on the Oxford Centre for evidence-based medicine criteria.

Oxford Level of Evidence	Vitamin C	Vitamin E	Vitamins C and E
Effective			
Level 1	Chloasma	Atopic Dermatitis[2]	Chloasma
	Pigmented Contact Dermatitis	Chloasma	Pigmented Contact Dermatitis
	Pressure Sores[2]	Pigmented Contact Dermatitis	UV-Induced Erythema[3]
		Radiation-Induced Fibrosis	
		UV-Induced Erythema[2,3]	
		Vitiligo[2]	
Level 2	Furunculosis	Epidermolysis Bullosa[2,3]	Systemic Sclerosis
	Thalassemia Leg Ulcers	Leprosy (as adjunct)	
		Retinoid Toxicity	
Level 3	Miliaria Rubra	Actinic Prurigo	
		Yellow Nail Syndrome[2,3]	
Level 4	Staphylococcal Pyoderma	Cutaneous Lupus[2]	
		Chemotherapy-Induced Alopecia[2]	
		Porphyria Cutanea Tarda	
		Acrodermatitis atrophicans	
Level 5	Inherited Human Collagen Lysyl Hydroxylase Deficiency	Necrobiosis LipoidicaDiabeticorum	Pseudoxanthoma Elasticum
	Lichen Spinulosus		
Ineffective or Not Statistically Significant			
	Achromotrichia	Acne Vulgaris	Polymorphous Light Eruption
	Cutaneous Hypersensitivity Reaction	Arsenic-Induced Skin Lesions[1]	
	Erythropoietic Protoporphyria[1]	Granuloma Annulare[1]	
	Pigmented Purpuric Dermatosis	Leukoplakia[1]	
	UV-Induced Erythema	Psoriasis	

[1]Studies which showed improvement, but not statistically significant
[2]Disease for which multiple studies exist and demonstrate conflicting results
[3]Disease for which multiple studies exist and are entered here based on the study with highest level of evidence.

Wound Healing

In wound healing studies**,** there is evidence to support vitamin C therapy inthalassemia leg ulcers, but the evidence in pressure wounds and pyoderma is not as strong. Inthalassemia leg ulcers, which are a chronic complication of this hereditary hemolytic anemia, one crossover RCT from the United Kingdom in 1975 described eight subjects treated with 3g of ascorbic acid for eight weeks who experienced higher rates of healing with vitamin C therapy compared to placebo. Adverse side effects included "heartburn" and increased diuresis.[21]Regarding pressure wounds, in one RCT from 1974, subjects (n = 20) were divided into two groups (1g ascorbic acid versus placebo), of which the treatment group demonstrated significant reduction in ulcer size after onemonth.[22] A second RCT divided subjects (n = 88) into two groups (1g ascorbic acid versus 20mg ascorbic acid) for 12 weeks, but noticed no significant difference in healing rates nor healing velocities (measured in centimeters per week).[23]Lastly, regarding staphylococcal pyoderma, one case series demonstrated improvement of patients (n = 2) with recurrent wounds on the buttocks and genitalia with 1.5g ascorbic acid for six months.[24]

Hair and Nail Disorders

Vitamin C therapy was found to be ineffective in one case series from 1950of patients(n= 24) treated for achromotrichia (200-600mg vitamin C daily) with treatment duration ranging from fewer than seven days to seven months.[25]

Photosensitivity/ UV Exposure

Therapy with vitamin C was found ineffective in the treatment of erythropoietic protoporphyria in one low-quality RCT (n=12) using 1g ascorbic acid daily,[26] and the treatment

or prevention of UV-induced erythema in two RCTs and one prospective cohort study(500mg-3g ascorbic acid daily).[27–29]

Genetic Disorders

One case report from 1978 supports use of vitamin C therapy (4g ascorbic acid daily) for inherited human collagen lysyl hydroxylase deficiency, a genetic collagen disorder, demonstrated by improved wound healing, corneal growth, muscle strength, and pulmonary function.[30]

Oral Vitamin E therapy

There were a total of 41 studies utilizing oral vitamin E in dermatologic disease, in doses ranging from 10 – 2000mg/100 - 10,000 IU, with 25 studies demonstrating some efficacy.

Pigmentary Disorders

In chloasma and PCD, a RCT utilized 150 mg d1-α-tocopheryl acetate for 4-12 weeks in patients with PCD (n = 10) or chloasma (n =50) and showed significant improvement in33% ofsubjects with PCD and 60% with chloasma. Side effects were noted in 11.7% of subjects, and included acne, stomach discomfort, excessive perspiration, menstrual abnormalities, and shortened menstrual cycles.[15]

In a vitiligo trial, subjects (n =24)who had UVB phototherapy plus 400 IU α-tocopherol versus UVB alone needed significantly fewer UV treatments to achieve 50% repigmentation.[31] In another RCT, subjects(n = 30) were divided into two groups (UVA phototherapy versus UVA phototherapy plus 900 IU vitamin E) for six months, however no significant difference in treatment efficacy was demonstrated, and similar adverse effects were noted, including erythema, nausea, and headache.[32]

Inflammatory Disorders

In atopic dermatitis, one RCT from 1989 separated subjects (n = 60) into three groups (600μg selenium, 600μg selenium plus 600 IU vitamin E, and placebo) and demonstrated no clinically significant difference between the three groups after 12 weeks of treatment.[33] A second RCT from 2011 divided subjects (n = 45) into four groups (vitamin D, 600 IU all-rac-alpha-tocopherol, 600 IU all-rac-α-tocopherol plus vitamin D, and placebo), demonstrating clinical SCORAD improvement with vitamin E therapy after 60 days, with vitamin D and vitamin E combination being the most effective.[34] A third RCT from 2002 separated subjects (n = 96)into two groups (400 IU R,R,R-α-tocopherol versus placebo) and noted 66% SCORAD improvement with vitamin E versus 20% with placebo after eight months.[35]

Five old case series have studied the role of vitamin E therapy in cutaneous lupus. One case series from 1948 described the use of 50mg-2000mg mixed tocopherols daily which significantly improved lesion regression in all eleven subjects.[36] A second case series from 1952 noted subjects (n = 47) received 50-300mg of L-tocopherol for 3-6 weeks, followed by 50mg daily as a maintenance dose, showing significant improvement among 87% of patients. Rare side effects included urticarial eruptions, nausea, and constipation, and severe leg pain.[37]Among the three studies which showed negligible or no improvement, one case series from 1992 examined the use of 400mg vitamin E among seven subjects, and demonstrated no improvement based on clinical assessment after 12 weeks.[38]In an additional case series from1950, subjects (n =45) received treatment with 600mg vitamin E for 2-9 months, with some clinical improvement in 11% of subjects, no significant improvement in 87% of subjects, and rapid relapse in one individual after discontinuing treatment. Adverse effects of vitamin E therapy included fever, chills, flushing, nausea, and vomiting.[39] A third case series from 1951 gave subjects(n =10) 600mg mixed tocopherols for five months without noting improvement based on clinical assessment.[40]

The use of vitamin E therapy was not found to be of benefitfor the treatment of isotretinoin-related side effects in acne vulgaris (800 IU d-L-alpha-tocopherol) as noted in two RCTs (n=222),[41,42]or psoriasis (600 IU d-α-tocopherol and 600 μg selenium) in one RCT (n=69).[43]

Hair and Nail Disorders

Low-level evidence supports vitamin E therapy in two hair and nail disorders: chemotherapy-induced alopecia and yellow nail syndrome. Two case series explore the use of 1600 IU α-tocopherol in the reduction of chemotherapy-induced alopecia. In one case series, 20 patients were treated for one week prior to beginning chemotherapy, of which 90% reported significant hair loss.[44] The second case series (n = 16) demonstrated that longer periods of vitamin E intake was associated with less hair loss while undergoing doxorubicin therapy, and 69% of patients did not experience significant alopecia, based on clinical assessment.[45]

For yellow nail syndrome, a retrospective observational study (n = 11) reported that 27% of subjects taking 1200 IU vitamin E completely recovered, 27% with clinical improvement, and 45% of subjects with no response; treatment duration ranged from one month to nine years.[46] In one case series, two patients were treated with 800 IU oral α-tocopherol for at least four months, however only one demonstrated clinical improvement.[47] A second case series (n =2) described the use of 800-1200 IU vitamin E for 12-13 months, with one subject noting complete resolution of nail discoloration.[48] Another case report from 1973 described a patient taking 800 IU d-α-tocopherol for 6.5 months and showed clinical improvement with occasional bronchial coughing.[49] In a second case report, a patient is described taking 300mg tocopherol nicotinate for nine months with clinical improvement. However, the patient experienced sudden weight gain and generalized fatigue.[50]

Photosensitivity/ UV Exposure

The evidence to support vitamin E therapy in UV-induced erythema is inconsistent. One cohort study divided subjects (n

=16) into two groups, (400 IU α-tocopherol versus 15mg β-carotene), with no improvement in either group in skin sensitivity to UV radiation based on markers of oxidative stress, histology, and minimal erythema dose (MED) assessments after eight weeks.[51] In a RCT, subjects (n = 20) were divided into two groups (25mg carotenoids versus 25mg carotenoids plus 500 IU tocopherol), with erythema reduction over the course of 12 weeks with combination therapy, as assessed by reflection photometry.[52] In another study (n=16), two groups (400 IU α-tocopherol acetate versus placebo) were treated over six months, with a 6% decrease in overall erythema in the vitamin E group.[53] In a trial with 40 subjects placed on different vitamin therapies (3g L-ascorbic acid, 2g D-α-tocopherol, 3g L-ascorbic acid and 2g D-α-tocopherol, and placebo) for 50 days, there was no significant reduction of erythema in the D-α-tocopherol group.[28] Similar lack of improvement was noted in a trial that divided subjects (n = 45) into three groups (2g ascorbic acid, 1200 IU D-α-tocopherol, and combination of 2g ascorbic acid plus 1200 IU D-α-tocopherol).[29]

In actinic prurigo, efficacy of tetracycline versus 100 IU vitamin E for six months among 16 subjects was assessed, with significant clinical improvement from baseline, and no significant difference in the efficacy between the two treatments.[54]

Fibrotic/Sclerotic Disorders

The use of vitamin E therapy for radiation-induced fibrosis is supported by a small RCT with subjects (n = 22) in four groups (pentoxifylline, 1000 IU vitamin E, pentoxifylline and 1000 IU vitamin E, and placebo). Significant improvement of fibrosis with pentoxifylline and vitamin E was noted after six months, based on ultrasound measurements of the affected areas. Neither pentoxifylline nor vitamin E demonstrated an effect individually. Adverse side effects included hot flushes, nausea, asthenia, vertigo, and headache; though, attribution of side effects to vitamin E or pentoxifylline is unclear.[55]

Bullous Disorders

Few dated studies conducted between 1964 – 1976 provide support for vitamin E therapy inepidermolysis bullosa (EB). Indystrophic EB, one low quality clinical trial administered 400 IU vitamin E to subjects (n = 2) for eight weeks, noting reduced numbers of bullae.[56]Treatment with doses of 300-600 IU d-L-α-tocopherylin dystrophic EB for 30 days to 4 months lead to varying degrees of bullae regression (n = 6), with two subjects experiencing relapse after treatment discontinuation.[57,58]Other reports ofdystrophic and hereditary EB patients (n = 2)given1600-6000 IU and 300 mg-1800 mg α-tocopherol, respectively, over a three month period demonstrated clinical improvement with fewer and smaller bullae.[59,60]In contrast, a patient with dystrophic EB treated with 10,000 IU D-L-α-tocopheryl acetate for seven weeks showed no clinical improvement.[61]

In another bullous condition porphyria cutanea tarda, a case series from 1978 demonstrated complete resolution of lesions in two subjects with 400-1600IU d-α-tocopherol for at least 2 months of treatment.[62]

Infections

There is support for the use of vitamin E therapy (400 IU) in the treatment of leprosy from a comparative cohort studyin India. Patientswith leprosy (n = 50) receiving multi-drug therapy (MDT) wereseparated into two groups (MDT versus MDT plus vitamin E), with the latter noting significantly reduced oxidative stress in blood samples and skin.[63]

Inacrodermatitis atrophicans, a case series (n =11)from 1952 showed significant clinical improvementwith treatment of 10-150 mg L-tocopherol. Side effects included urticarial eruptions, nausea, and constipation.[37]

Other

There is no evidence to support vitamin E therapy in arsenic-induced skin lesions. One RCT from Bangladesh utilizing 400mg racemic alpha-tocopherol daily for six months showed clinical improvement compared to placebo, however results were not statistically significant.[64]

Vitamin E therapy for retinoid toxicity is supported by a comparative cohort study which divided subjects (n = 66) into two groups (13-cis-retinoic acid versus 13-cis-retinoid acid plus 800 mg d-α-tocopherol); there were reduced rates of hyperkeratosis and dryness of mucous membranes following treatment with d-α-tocopherol after a minimum of six months.[65]

One case report from 1948 supports vitamin E therapy for necrobiosis lipoidicadiabeticorum, as the patient experienced significant clinical improvement with 100-250mg mixed tocopherols.[66]

Vitamin E therapy was found to be ineffective in one observational cohort study for granuloma annulare (n=38) (400-600 IU vitamin E for 3-12 months)[67]and one single-arm study with intervention for leukoplakia (n=43) (800 IU vitamin E for 24 weeks).[68]

Oral Vitamins C and E Therapy

There were total of seven studies with combination oral vitamin C (600 - 3,000mg) and vitamin E (90 - 2,000mg / 400 – 1,500 IU) therapy, with six studies demonstrating efficacy.

Pigmentary Disorders

The previously mentioned triple-armed RCT by Hayakawa et al. utilizing 300mg of vitamin C and 150 mg d 1-α-tocopheryl acetate twice daily for 4-12 weeks in patients with PCD (n =17) and chloasma (n = 41) noted87% ofsubjects with PCD and 69% with chloasma experienced significant improvement in discoloration, and significantly greater improvement with combination therapy than with either vitamin alone. Adverse events were noted in 8.6% of subjects,

including acne, xerosis, mild stomach disturbance, and metrorrhagia.[15]

Photosensitivity/ UV Exposure

The combination vitamin C and vitamin E therapy in the treatment of UV-induced erythema has been studied in three small RCTs. Subjects (n=10) who were treated with 2g ascorbic acid and 1000 IU D-α-tocopherol for eight days experienced significantly reduced erythema compared to placebo.[69] In a second RCT (n = 40), there was a significant decrease in erythema among the group taking both vitamins (3g L-ascorbic acid plus 2g D-α-tocopherol) compared to placebo after 50 days.[28] In a third RCT, subjects (n =45) were divided into three groups (2g ascorbic acid, 1200 IU D-α-tocopherol, and combination of 2g ascorbic acid plus 1200 IU D-α-tocopherol). Combination therapy with vitamin C and E demonstrated a clinically significant decrease in erythema after only one week.[29]

Conversely, combination therapy with vitamin C (3g) and vitamin E (1500 IU) in the treatment of nine patients with polymorphous light eruption for eight days was ineffective.[70]

Fibrotic/Sclerotic Disorders

In a low-quality clinical trial, thirteen subjects with systemic sclerosis were divided into two groups (1000mg ascorbic acid plus 400 IU α-tocopherol versus placebo) and experienced a significant decrease in the rate of skin thickening following 6-months of treatment, as assessed clinically and using the Rodnan skin thickness score.[71]

Genetic Disorders

Vitamin C (900 mg ascorbic acid) and vitamin E (90 mg tocopherol acetate) therapy for at least two years in a pseudoxanthoma elasticum case report showed regression of papules within six months of treatment and total clearance of lesions within two years.[72]

Discussion

This in-depth review found that the use of oral vitamin C and vitamin E therapy in dermatologic conditions has limited support by small and dated studies with inconsistent results. There is evidence to support the use of oral vitamin C (600 mg ascorbic acid) and vitamin E (300mg D-1-α-tocopherol acetate) therapy for 4 -12 weeks in the treatment of pigmentary disorders such as pigmented contact dermatitis or chloasma, with greatest efficacy from combination therapy. Similarly, combination therapy with vitamin C and vitamin E for 7 – 50 days may be beneficial in UV-induced erythema (2 – 3g vitamin C; 1000 – 1200 IU/ 2g vitamin E). There is some evidence to support vitamin C therapy in wound healing such as in pressure wounds (1g ascorbic acid for 1 month) and vitamin E therapy in fibrotic disorders like radiation-induced fibrosis (1,000 IU vitamin E in conjunction with pentoxifylline for 6 months).

There are several dermatologic conditions which do not benefit from oral vitamin C or vitamin E therapy. There is no evidence to support the use of vitamin C in the treatment of achromotrichia, cutaneous hypersensitivity reaction,erythropoietic protoporphyria, pigmented purpuric dermatosis, or UV-induced erythema. For vitamin E, there is no evidence to support its use in acne vulgaris, arsenic-induced skin lesions, leukoplakia, granuloma annulare, or psoriasis. Also, there is no evidence to support the use of combination therapy for polymorphous light eruption.

As mentioned above, vitamin C and vitamin E are each believed to have a role in the inhibition of melanogenesis, which may explain their synergistic efficacy in the treatment of pigmentary disorders such as chloasma and pigmented contact dermatitis. Moreover, the antioxidant properties of vitamin C and vitamin E protects reasonable explain how their use in combination protect the skin from photodamage.[7,10] Regarding fibrotic diseases, vitamin E has been shown to reduce fibrosis in other disorders, such as with non-alcoholic steatohepatitis and liver transplant. It is conjectured that its role in lipid peroxidation and oxidative stress reduction minimizes fibrotic changes within the tissue.[73] However, it must be noted that high doses of vitamin E (greater than 400 IU per day) are associated with an increase in all-cause mortality[74], and thus should be used with caution.

Our review was limited by the use of a single publication database and insufficient high-quality evidence. Most studies included in this review had small sample sizes (less than 100 subjects) and demonstrated inconsistent results. Moreover, many studies were conducted before 1980, particularly those lending support to vitamin therapy for cutaneous lupus and epidermolysis bullosa. Based on the quality of evidence currently in the literature, future studies should focus on the use of large (greater than 100 subjects) randomized-controlled trials with standardized dosing regimens, and long-term clinical and patient-reported evaluations. Lastly, authors of 10 studies had an affiliation with pharmaceutical companies (denoted in supplemental Tables 2-4).

Conclusions

The current literature supports oral vitamin C and vitamin E therapy in the treatment of pigmentary disorders (chloasma and pigmented contact dermatitis), inflammatory disorders (atopic dermatitis and vitiligo), and wounds (pressure sores). However, the evidence is limited by a small number of quality studies with inconsistent results. Larger studies are needed to provide definitive support for the roles of vitamin C and vitamin E in the treatment of these conditions, recommended doses, and potential adverse events.

Authorship Confirmation Statement

All coauthors have reviewed and approved of the manuscript prior to submission.

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