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REVIEW ARTICLE

Efficacy of topical vitamin C in melasma and photoaging: A systematic review

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Abstract

Background: Vitamin C is a micronutrient present in high concentrations in normal skin and a highly prescribed cosmeceutical, well known for protecting against ultraviolet-induced pigmentation and regulating collagen production. However, there is a lack of studies evaluating the efficacy of topical vitamin C in photoaging and melasma, with this systematic review being the first to assess the existing evidence.

Aim: This systematic review aims to assess whether topical vitamin C could be effective in reversing photoaging signs and treating melasma.

Methods: Prospective, randomized controlled trials assessing protocols with topically applied vitamin C in patients with melasma or photodamage were searched in Medline, CENTRAL, and Scopus databases until the 12th of May 2022. Risk of bias was conducted in accordance with Cochrane Collaboration's tool for assessing the risk of bias in randomized trials, using RevMan 5.0.

Results: Seven publications were included, with 139 volunteers in total. Studies that evaluated the topography of skin indicated that the treated skin appeared smoother and less wrinkled, which was supported by biopsies data. On objective assessments of pigmentation, there was a significant lightening of the skin treated. Hydration improved equally in the vitamin C and placebo-treated sites.

Conclusions: This study revealed that vitamin C is effective in treating uneven, wrinkled skin and has depigmenting properties, but long-term use may be needed to achieve noticeable changes. Q-switched Nd:YAG laser-associated protocols appear beneficial in enhancing vitamin C effects. Topical vitamin C may be a suitable alternative for melasma and photoaging, but more studies are needed to confirm these results and assess the ideal vitamin C concentration.

KEYWORDS
melasma, photoaging, photodamage, solar lentigines, vitamin C

1 | INTRODUCTION

Nowadays, vitamin C is one of the most prescribed cosmeceuticals in the world, being highly recommended by dermatologists. Its popularity has exponentially grown during the past 5 years and in 2020 it was the most searched cosmetic ingredient on the internet, with over a million searches, corresponding to a growth of 204% in a year. This reaffirms the established place vitamin C occupies in the average person's skincare routine.[1]

Ascorbic acid, commonly known as vitamin C, presents in high concentrations in normal skin. Its main roles include stimulating collagen biosynthesis, protecting against ultraviolet (UV)-induced damage due to its antioxidant properties, stimulating the phagocytic function of leukocytes, and proline hydroxylation.[2]

Studies have shown that vitamin C levels were lower in photoaged and naturally aged skin[3] and that it could also inhibit melanin synthesis, through downregulating monophenolase activity of tyrosinase enzyme. Moreover, its antioxidant effect prevents the production of free radicals that trigger melanogenesis.[2] These findings made it look promising for pigmentary disorders such as melasma or solar lentigos. Associated with its role in regulating collagen production, stimulating type I procollagen synthesis in skin fibroblasts, and promoting the stability of collagen molecules,[4] vitamin C was immediately defended as the perfect molecule for prevention or reversal of skin aging and, more specifically, photoaging.

Photoaging is the term used to describe the alterations in structure, function, and appearance of skin due to prolonged or repeated exposure to UV radiation. The main signs of photoaging include wrinkles, elastosis, dryness, laxity, rough-textured appearance, telangiectasis, and irregular pigmentation.[5]

UV radiation contributes to dermal structure deterioration by creating reactive oxygen species which promote collagen fragmentation, decreased collagen biosynthesis, and therefore the observable features that characterize photodamage.[6]

Melasma is an acquired hypermelanosis that is characterized by light to dark-brown symmetric macules with irregular borders that occurs mainly on the face and while it is known to affect darker skin complexions more commonly, it can occur in all skin types. The exact pathogenesis of melasma is unknown, but sun exposure seems to be the most important predisposing factor, the reason why it has been described as a photoaging disorder.[7]

This is a highly prevalent chronic disease and a leading cause of consultations that have been associated with a considerable decrease in the patient's quality of life.[8] With an unpredictable course and frequent relapses, it presents a therapeutical challenge, so alternatives must be looked onto.

A meta-analysis with over 700 volunteers, assessing vitamin C on healthy skin under a UV daylight-simulated pigmentation provided clear evidence that ascorbic acid is effective in protecting from stress-induced pigmentation.[9]

However, the evidence toward its depigmenting qualities is still very fragile, with most studies being in vitro and trials having a small number of participants.

Nonetheless, the need to demonstrate the efficacy of ascorbic acid in treating melasma and photoaging is increasing as it has quickly become part of numerous cosmetic preparations, becoming an essential component in the daily skincare routine of the ordinary person.

Thus, this systematic review wants to address this issue and synthesize the current evidence on vitamin C efficacy in treating melasma and photoaging and understand what preparations and concentrations may be more beneficial.

2 | MATERIALS AND METHODS

Prospective, randomized controlled trials (RCT) assessing patients of any age or gender with melasma or photodamage were included.

Eligible interventions included the topical use of vitamin C whether alone or in formulations that are known to further stabilize/promote absorption of this molecule or its combination with iontophoresis or laser.

The desired outcomes included the Melasma Area and Severity Index, the Melasma Severity Score, Pigmentation Scores using colorimetric equipment, objective wrinkling evaluations, dermatologists' clinical evaluation, and participants' self-assessment of change in their own skin's appearance.

Studies that included patients simultaneously using other bioactive skin compounds with a possible brightening effect or using vitamin C through transdermal injections or micro-needling were excluded. Ex vivo and in vitro studies were also excluded.

The Medline, CENTRAL (Cochrane Central Register of Controlled Trials), and Scopus databases were searched until the 12th May 2022.

The terms searched to target the intervention were vitamin C, ascorbate, OR ascorbic acid AND to target the conditions in study the terms used were melasma, lentigo, hyperpigmentation, OR photodamage. The results were filtered to only present RCTs.

References of articles of interest were also checked for any RCTs that could eventually not be indexed in the searched databases.

Attempts were also made to try to obtain unpublished RCTs from the cosmeceutical industry.

Two reviewers evaluated initially both the titles and the abstracts of potentially relevant studies independently. The full paper was obtained if it was considered that the article could meet the inclusion criteria. Afterwards, the full text was screened to confirm that it met the inclusion criteria and to assess its quality. Any disagreements were resolved by discussion. The authors were not blinded to the identity of the papers.

The same reviewers independently extracted, if present: the title of publication, year of publication, first author, study design, characteristics of the participants of the trials (number of randomized subjects, number of the ones who completed the study, demographic and baseline characteristics such as age, sex, and skin phototype), treatment regimen (concentration received, frequency of intervention, and study duration) as well as the reported outcomes.

The assessment of the risk of bias was conducted for each study following the COCHRANE Risk of Bias 2.0 tool (RoB 2.0), using RevMan 5.0.

3 | RESULTS

The initial search retrieved 192 articles from the MEDLINE, CENTRAL, and EMBASE databases and 29 from the cosmeceutical industry. In all, 27 duplicates were excluded as well as 182 studies whose title and abstract did not meet the pre-established criteria. In all, 12 articles were considered relevant for a full-text review. Of these, one article was excluded for not measuring any of the outcomes of interest, three were excluded for not randomizing the intervention, and another one was excluded for not individualizing the effect of vitamin C.

Figure 1 shows the study selection flowchart, divided into the steps of identification, selection, eligibility, and inclusion, according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) recommendations for writing systematic reviews.[10]

A total of 139 volunteers with Fitzpatrick skin types I–V were included in the studies, aged from 23 to 72 years. Four of the seven studies recruited only female volunteers. The duration of the studies ranged from 2 weeks up to 6 months with different formulations and vitamin C concentrations (from 3.75% to 20%). Six of the seven studies included a placebo/control group while the one that did not, had a comparison group with hydroquinone.[7]

The main characteristics of the included studies are described in Table 1 and their outcomes are explained in Table 2.

The assessment of the risk of bias was conducted in accordance with the Cochrane Collaboration's tool for assessing the risk of bias in randomized trials,[11] using RevMan 5.0.

Six specific domains (namely random sequence generation, allocation concealment, blinding, incomplete outcome data, selective reporting, and other bias) were evaluated.

Although all the studies were randomized, the method of randomization was not described in most trials. Most studies were double-blinded, apart from one which was single-blinded. Reporting of outcomes was mainly carried out only in those who completed the trial, and no details were available of the outcomes of participants who did not complete it, which in two studies with a more significant dropout may lead to a higher risk of attrition bias.

The risk of bias in the included studies is presented in a risk of bias graph, Figure 2, and a risk of bias summary, Figure 3.

4 | DISCUSSION

There are limited clinical trials assessing the value of ascorbic acid to improve the appearance of photoaged skin and it is being prescribed based on clinical experience, in vitro evidence of its antioxidative properties, and its protecting effect on UV-induced pigmentation. As far as we know, this is the first systematic review of RCTs assessing the efficacy of topical vitamin C in melasma and photoaging and

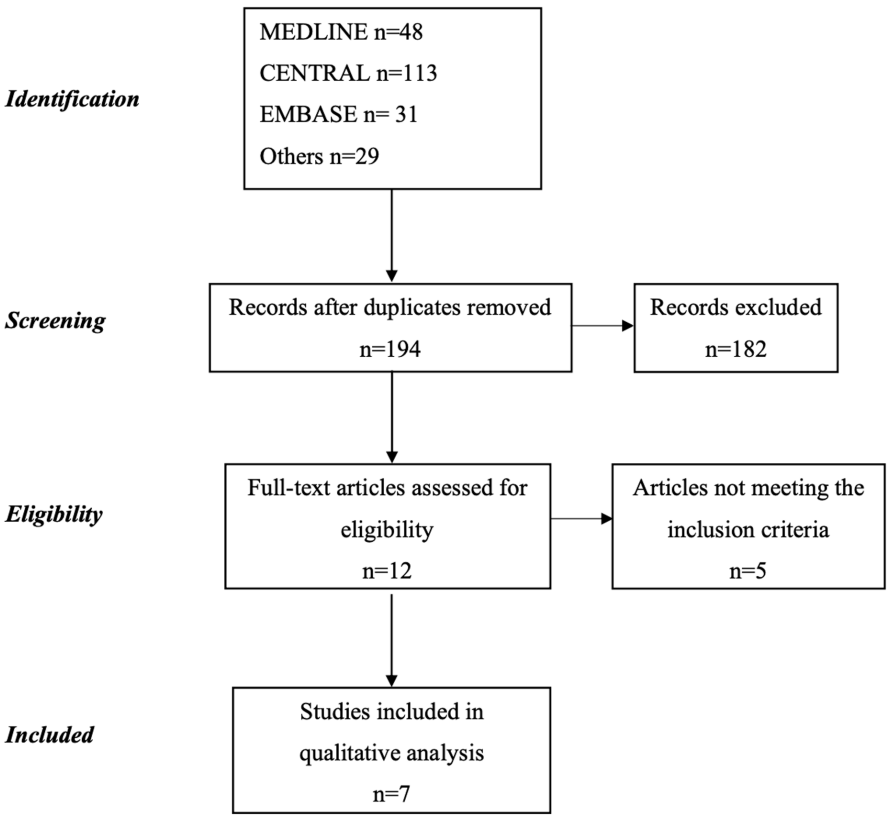

FIGURE 1 PRISMA flow diagram of included studies.

TABLE 1 Description of the included studies.

Author (year)	Participants	Intervention	Placebo	Outcome assessment
Melasma or solar lentigines				
Huh et al. (2002)[12]	29 female patients aged 24–49 with melasma	Vitamin C solution (3.75% MAP) applied to one side with iontophoresis for 8 min, 2×/a week for 12 weeks	Yes	L value of melasma measured by colorimetry; 5-graded self-assessment of the effects of treatment
Ishikawa et al. (2019)[24]	27 female patients with solar lentigos	Topical application of lotion with 6% L-ascorbate-2-phosphate trisodium salt to one-half of the face twice a day for 24 weeks.	Yes	Pigmentation levels measured by a color difference meter; melanin index measured by Mexameter MX18; pigmentation levels evaluated by a dermatologist using a photo-scale ranging from 1 to 5.
Perez et al. (2004)[7]	16 female patients aged 23–43 years old with melasma bilaterally	Topical application of lotion with 5% L-ascorbic acid on one side of the face and a 4% hydroquinone water–oil emulsion on the other for 16 weeks.	No	Evaluation of indirect pigmentary changes using a narrow-band colorimetric equipment; patient self-assessment.
Kim et al. (2020)[14]	18 patients aged 26–53, skin types II–IV, with facial lentigines and melasma	Topical application of a 20% ascorbic acid, vitamin E and ferulic acid serum on a side of the face after treatment with a 1064 nm QSNY laser and 2×/day for 2 weeks.	Yes	Digital photography and spectrometry were used to assess the melanin and erythema index; MSS; Scoring of the global improvement of skin texture and brightness by a dermatologist.
Photodamage				
Traikovich (1999)[19]	19 patients aged 36–72, with skin types I–III, with mild to moderate photodamage	Topical daily application of a high-potency serum (concentration not disclosed) containing ascorbic acid on a side of the face for 3 months.	Yes	Optical profilometry analysis was performed on skin surface replicas to measure the degree of surface irregularities; scoring by investigator of severity of wrinkling, tactile roughness, coarse rhytids, skin laxity, dryness, and sallowness; self-assessment questionnaires to rate the degree of improvement
Humbert et al. (2003)[13]	20 female patients aged 51–59 with signs of photoaging	Daily topical application of a cream containing 5% vitamin C for 6 months	Yes	Investigator assessment (parameters: hydration, roughness, laxity, wrinkles, brown spots, glare); 10-graded volunteer self-assessment; skin-relief measurements; skin biopsies.
Fitzpatrick et al. (2002)[25]	10 patients having photodamage	Daily topical application of a vitamin C complex (10% ascorbic acid and 7% tetrahexyldecyl ascorbate) for 12 weeks.	Yes	Assessment by a physician of the hydration, wrinkling and pigmentation; subjective self-assessment; Grenz zone collagen and epidermal thickness measurements and type I collagen assessment through skin biopsies.

Abbreviation: MSS, Melasma Severity Score.

our results have validated its usefulness in treating photodamaged skin and melasma.

Despite that, several questions remain unanswered. While it is frequent to see lotions or serums with concentrations of up to 30% on the market, most studies use concentrations under 10%.[7,12,13] Only one of the included RCTs assessed the effect of vitamin C in a concentration of 20%[14] which also shows the scarcity of evidence we currently have for highly prescribed high-concentration formulas. In vitro studies have also shown that the maximal concentration for optimal percutaneous absorption was 20%,[15] not supporting the routine use of products over such concentration.

Yokota et al.[16] reported no dose–response effect among a 1%, 2%, or 3% tetra-isopalmitoyl vitamin C on periorbital wrinkles, with improving effects even at a low concentration of 1% VC-IP, which

TABLE 2 Results of individual studies.

Author (year)	Self and clinical assessment results	Objective assessment
Melasma or lentigines		
Huh et al. (2002)[12]	61.5% of volunteers graded both the vitamin and placebo side with a score of 4/5 or 5/5.	Gradual reduction of ΔL values in the treated site ($p=0.002$) with significant difference to the placebo-treated site ($p=0.03$); ΔL before treatment was on average 4/60; after 12 weeks ΔL = 2.78.
Ishikawa et al. (2019)[24]	No significant differences between vitamin C and placebo on photo-scale evaluation, although there was a slight decrease on both on solar lentigos (SL) and non-lesional surrounding skin (NLS).	Vitamin C treated SLs had a significantly higher ΔL value vs. placebo ($p<0.001$). 7/27 had a visibly recognizable level (ΔL >2). The ΔM (melanin index) significantly decreased for the SL (MI from 212.50 ± 33.83 to 188.65 ± 33.16) and NLS in the treated sites.
Perez et al. (2004)[7]	Vitamin C was considered excellent in 2/16, good in 8/16, moderate in 4/16, and mild in 2/16. Hydroquinone was considered excellent in 8/16, good in 7/16, moderate in 1/16, and mild in none. Data showed statistical significance for the hydroquinone side.	ΔM (melanin index difference) on the patients using vitamin C showed improvement of hyperpigmentation in 14/16 patients and worsening in 2/16. A lightening effect was noted in the third month of use. All patients on the hydroquinone had a colorimetric improvement with results noted in the first month.
Kim et al. (2020)[14]	Moderate improvement in melasma on the treated side and minimal to moderate on the non-treated side ($p<0.05$) on investigator assessment.	Significant reduction ($p<0.05$) in the MI (182.2 ± 32.97 to 160.56 ± 29.18) and the MSS score (2.22 ± 0.56 to 1.94 ± 0.64) on the treated side vs. placebo.
Photodamage		
Traikovich (1999)[19]	84.2% of the volunteers preferred the results of the treatment over placebo ($p=0.002$). Significantly more improvement with vitamin C for fine wrinkling ($p=0.002$), tactile roughness ($p=0.04$), coarse rhytids ($p=0.01$), skin laxity ($p=0.03$), sallowness ($p=0.03$), and overall assessment ($p=0.02$). No significant differences in visual dryness, telangiectasias, mottled pigmentation, or keratoses. On photographic assessment, the active side was preferred vs. placebo in 11 (57.9%) subjects ($p=0.01$)	Analysis of the skin surface impressions showed significantly more improvement with active treatment in the north–south axis in 14/19 patients ($p=0.03$). No significant differences were seen in the east–west orientation for any of the parameters.
Humbert et al. (2003)[13]	Global score (physician + volunteer assessment) was 6.7 ± 1.6 at baseline, 5.0 ± 1.0 at 3 M and 4.4 ± 0.7 at 6 M ($p<0.05$). Hydration, wrinkles, glare, and brown spots improved in both groups and roughness, suppleness and small wrinkle scores improved significantly only in the vitamin C group.	Skin relief measurements: increase in density of skin microrelief vs. placebo ($p>0.01$) and a decrease in deep furrows ($p<0.01$). On biopsy: re-appearance of composite elastic fibers in the upper dermis and more evenly distributed type I collagen. No changes in fibrocytes or dermal collagen.
Fitzpatrick et al. (2002)[25]	4/10 patients reported greater improvement of the wrinkles and 3/10 a greater improvement in hydration. No differential improvement in pigment was reported. Excluding the forehead area, average improvement of wrinkling scores was 25% vs. 7.67% placebo ($p=0.08$). All patients with dry skin improved to normal hydration bilaterally. 3/5 patients with depigmentation, improved both on the treatment and placebo-sides.	Four patients had an increase in the average epidermal thickness and Grenz zone collagen on the treated side. 3/4 patients revealed a more intense staining for type I collagen on the vitamin C side.

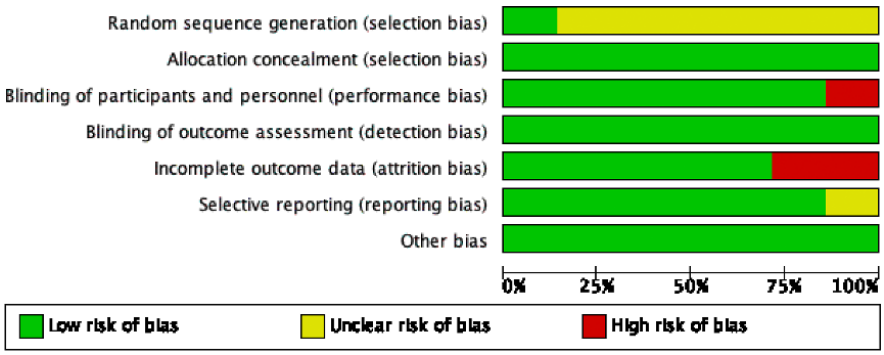

FIGURE 2 Risk of bias graph: review authors' judgments about each risk of bias item presented as percentages across all included studies.

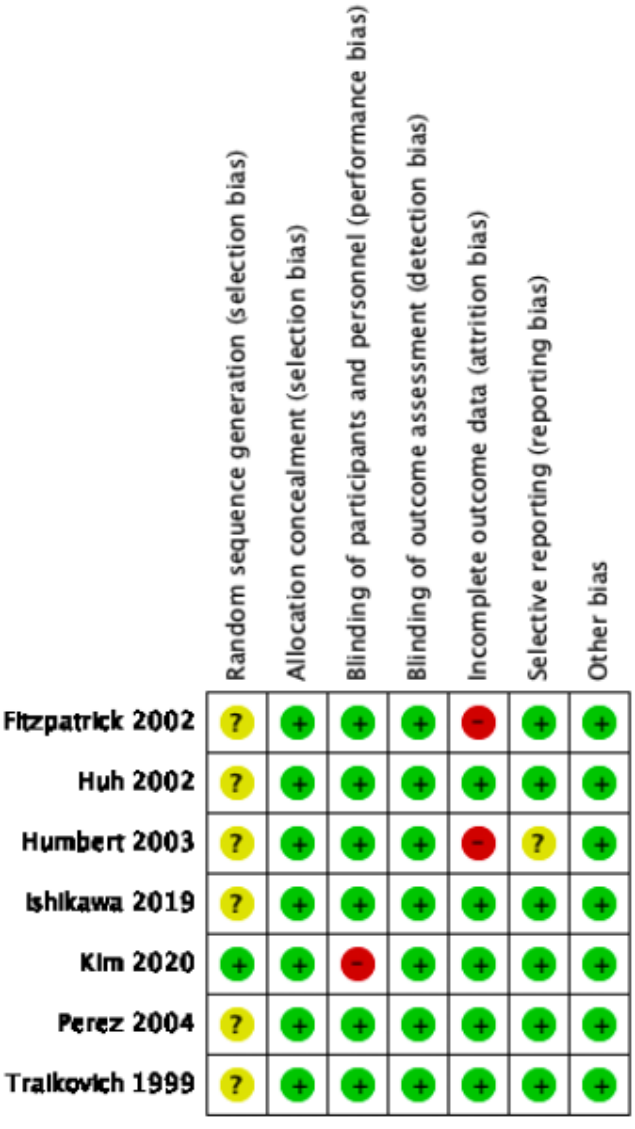

FIGURE 3 Risk of bias summary: review authors' judgments about each risk of bias item for each included studies.

reiterates the need to design comparative studies to find the ideal concentration.

Since the levels of vitamin C available in the skin after oral ingestion are limited by regulatory mechanisms, topical delivery became attractive.[13] However, vitamin C is a water-soluble and charged molecule that is repelled by the epidermal cells.[2] To overcome this challenge, it is necessary that the pH level is below 4 and that the molecule is stable enough not to oxidate.[17] To overcome this challenge, several derivatives, lipid-soluble analogues, conjugates, and protocols have been created to assist the transport into the epidermis. There is currently a huge variety of protocols, combining vitamin C with procedures such as iontophoresis, ultrasound, laser, or micro-needling. However, these studies remain small, and there are no comparative studies to determine the optimal delivery method.

All of the three RCTs included in this systematic review that evaluated the topography of skin treated with topical ascorbic acid indicated that the skin treated appeared smoother and less wrinkled compared with placebo/control. Humbert et al.'s[13] study corroborates in vitro studies that showed topical ascorbic acid may promote the activation of a dermal synthesis of elastic fibers.[18] In this study, there were no changes in dermal collagen, but Traikovich et al.[19] revealed an increase in collagen in the dermal–epidermal junction. Hence, these studies support what was primarily found in cultures of fibroblasts derived from normal human skin[18] and provide evidence that topical vitamin C helps restore the elasticity of photodamaged skin and reduce wrinkling.

Hydration improved both in the vitamin C and placebo areas in the three studies where this was an assessed parameter, which suggests that enhanced hydration is not an effect of vitamin C but instead a result of more regular skincare.

On objective assessments of pigmentation, both in patients with melasma and with solar lentigines, there was a significant lightening of the skin treated with ascorbic acid. Nonetheless, clinical and self-assessment results did not corroborate this, as vitamin C was only preferred to placebo concerning hyperpigmentation reversal in one of the five studies that included this outcome. Besides that, although these studies were mainly double-blinded, it is worth mentioning that because it is common for patients to feel a small stinging in the area where vitamin C is applied, there may be some distortion in patient appraisal scores, leading them to overestimate the treated-site changes.

This discrepancy between pigmentation levels and clinical or self-assessments might have occurred because, within the timeframe of the studies, the decrease was not distinct in visible skin pigmentation and longer studies are needed to determine how long the protocols must be to result in a visible change.

In Kim et al.'s study,[14] the only RCT demonstrating a visible lightening of facial lentigines and melasma assessed by two blinded dermatologists after the 2-week protocol was also the only one that included a Q-switched 1064-nm Nd:YAG laser pre-treatment. Studies have demonstrated that laser pretreatment could increase the permeability and depth of penetration of topically applied molecules so the better absorption of vitamin C and the melanin granule dispersion caused by the selective photothermolysis could explain the improved results.[14,20] However, a study comparing this protocol without the laser pre-treatment is necessary to understand its role in these results and do a risk–benefit analysis that considers the hypopigmentation, rebound hyperpigmentation, and ochronosis that has been reported in other studies using the Q-switched 1064-nm Nd:YAG laser.[20]

In addition, Perez et al.[7] showed that there were no differences in colorimetric assessment between hydroquinone and vitamin C, with the latter presenting fewer adverse effects and raising fewer safety concerns. This suggests that ascorbic acid may be used as part of the melasma treatment, and more studies need to be conducted to confirm these findings and identify compounds that can have an additive lightening effect and thus create a better treatment option for melasma.

Concerning photoaging, retinoids have been a mainstay and although there is indeed robust evidence of its efficacy, it is also true that it is accompanied by several adverse effects such as pruritus, erythema, peeling, and photosensitization.[21] Moreover, its use is contraindicated in pregnant and women trying to conceive and therefore vitamin C may be an alternative for long-term use, as it carries fewer risks, has a shorter range of side effects, and toxicity was only documented under laboratory conditions with 100–200 times the daily recommended dose, giving vitamin C a very high safety profile.[22] Moreover, it is safe to use during pregnancy which is very important considering female sex hormones that are increased during gestation accelerate the development and aggravate melasma.[7]

Herndon et al.[23] tested an 0.5% retinol treatment combined with a moisturizer with 30% vitamin C in 44 women which revealed an improvement in clinical grading scores for all parameters assessed including hyperpigmentation, wrinkles, and overall photodamage, as soon as in the 4th week of evaluation This suggests that these two compounds can even be used simultaneously to improve outcomes, using a lower concentration of retinol, and therefore having better tolerability.

Despite the limitations regarding the heterogeneity of the studies included in this systematic review, overall, this work supports the use of vitamin C to treat uneven, wrinkled skin and demonstrates that ascorbic acid has depigmenting properties, useful in photodamaged skin and melasma, but long-term use is needed to achieve noticeable changes. Therefore, topical vitamin C seems to be a suitable compound to improve skin photodamage and treat melasma.

CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest to declare that are relevant to the content of this article.

DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no datasets were generated or analysed during the current study.

ETHICS STATEMENT

The authors confirm that the ethical policies of the journal, as noted on the journal's author guidelines page, have been adhered to. No ethical approval was required as this is a review article with no research data.

REFERENCES

1. Murray B. These are the most searched-for beauty ingredients of 2020, in Harper's Bazaar. 2020: United Kingdom.
2. Pullar JM, Carr AC, Vissers MCM. The roles of vitamin C in skin health. *Nutrients*. 2017;9(8):866.
3. Rhie G, Shin MH, Seo JY, et al. Aging- and photoaging-dependent changes of enzymic and nonenzymic antioxidants in the epidermis and dermis of human skin in vivo. *J Invest Dermatol*. 2001;117(5):1212-1217.
4. Dumas M, Chaudagne C, Bonté F, Meybeck A. Age-related response of human dermal fibroblasts to L-ascorbic acid: study of type I and III collagen synthesis. *C R Acad Sci III*. 1996;319(12):1127-1132.
5. Situm M, Buljan M, Cavka V, Bulat V, Krolo I, Mihić LL. Skin changes in the elderly people – how strong is the influence of the UV radiation on skin aging? *Coll Antropol*. 2010;34(Suppl 2):9-13.
6. Shin JW, Kwon SH, Choi JY, et al. Molecular mechanisms of dermal aging and antiaging approaches. *Int J Mol Sci*. 2019;20(9):2126.
7. Espinal-Perez LE, Moncada B, Castanedo-Cazares JP. A double-blind randomized trial of 5% ascorbic acid vs. 4% hydroquinone in melasma. *Int J Dermatol*. 2004;43(8):604-607.
8. Zhu Y, Zeng X, Ying J, Cai Y, Qiu Y, Xiang W. Evaluating the quality of life among melasma patients using the MELASQoL scale: a systematic review and meta-analysis. *PLoS One*. 2022;17(1):e0262833.
9. De Dormael R, Bastien P, Sextius P, et al. Vitamin C prevents ultraviolet-induced pigmentation in healthy volunteers: Bayesian meta-analysis results from 31 randomized controlled versus vehicle clinical studies. *J Clin Aesthet Dermatol*. 2019;12(2):E53-E59.
10. Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. *BMJ*. 2009;339:b2700.
11. Higgins JP, Altman DG, Gøtzsche PC, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ*. 2011;343:d5928.
12. Huh CH, Seo KI, Park JY, Lim JG, Eun HC, Park KC. A randomized, double-blind, placebo-controlled trial of vitamin C iontophoresis in melasma. *Dermatology*. 2003;206(4):316-320.
13. Humbert PG, Haftek M, Creidi P, et al. Topical ascorbic acid on photoaged skin. Clinical, topographical and ultrastructural evaluation: double-blind study vs. placebo. *Exp Dermatol*. 2003;12(3):237-244.
14. Kim J, Kim J, Lee YI, Almurayshid A, Jung JY, Lee JH. Effect of a topical antioxidant serum containing vitamin C, vitamin E, and ferulic acid after Q-switched 1064-nm Nd:YAG laser for treatment of environment-induced skin pigmentation. *J Cosmet Dermatol*. 2020;19(10):2576-2582.
15. Al-Niaimi F, Chiang NYZ. Topical vitamin C and the skin: mechanisms of action and clinical applications. *J Clin Aesthet Dermatol*. 2017;10(7):14-17.
16. Yokota M, Yahagi S. Evaluation of the anti-wrinkle effect of a lipophilic pro-vitamin C derivative, tetra-isopalmitoyl ascorbic acid. *J Cosmet Dermatol*. 2022;21(8):3503-3514.

17. Stamford NP. Stability, transdermal penetration, and cutaneous effects of ascorbic acid and its derivatives. *J Cosmet Dermatol*. 2012;11(4):310-317.
18. Hinek A, Kim HJ, Wang Y, Wang A, Mitts TF. Sodium L-ascorbate enhances elastic fibers deposition by fibroblasts from normal and pathologic human skin. *J Dermatol Sci*. 2014;75(3):173-182.
19. Traikovich SS. Use of topical ascorbic acid and its effects on photodamaged skin topography. *Arch Otolaryngol Head Neck Surg*. 1999;125(10):1091-1098.
20. Wattanakrai P, Mornchan R, Eimpunth S. Low-fluence Q-switched neodymium-doped yttrium aluminum garnet (1,064 nm) laser for the treatment of facial melasma in Asians. *Dermatol Surg*. 2010;36(1):76-87.
21. Mukherjee S, Date A, Patravale V, Korting HC, Roeder A, Weindl G. Retinoids in the treatment of skin aging: an overview of clinical efficacy and safety. *Clin Interv Aging*. 2006;1(4):327-348.
22. Telang PS. Vitamin C in dermatology. *Indian Dermatol Online J*. 2013;4(2):143-146.
23. Herndon JH Jr, Jiang LI, Kononov T, Fox T. An open label clinical trial to evaluate the efficacy and tolerance of a retinol and vitamin C facial regimen in women with mild-to-moderate hyperpigmentation and photodamaged facial skin. *J Drugs Dermatol*. 2016;15(4):476-482.
24. Ishikawa Y, Niwano T, Hirano S, Numano K, Takasima K, Imokawa G. Whitening effect of L-ascorbate-2-phosphate trisodium salt on solar lentigos. *Arch Dermatol Res*. 2019;311(3):183-191.
25. Fitzpatrick RE, Rostan EF. Double-blind, half-face study comparing topical vitamin C and vehicle for rejuvenation of photodamage. *Dermatol Surg*. 2002;28(3):231-236.

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