REVIEW

Clinical Applications of Vitamin C in Dermatology: A Systematic Review

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J Clin Aesthet Dermatol. 2026;19(7):10–15.

OBJECTIVE: To evaluate clinical applications, efficacy profiles, and delivery strategies of vitamin C and its derivatives in dermatology. **METHODS:** A systematic review of PubMed and Scopus identified studies published from 2020 onward, evaluating topical, injectable, or systemic vitamin C formulations. Of 263 screened publications, 44 met inclusion criteria. Data were extracted regarding derivative type, delivery platform, and outcomes. **RESULTS:** Ascorbic acid remains the most clinically validated formulation, with low-pH stabilized systems and L-ascorbic acid, vitamin E, and ferulic acid–type complexes consistently improving photoaging, structural aging, pigmentary disorders, and periprocedural healing. Ascorbyl tetraisopalmitate shows superior lipophilic stability, benefiting pigmentary and structural aging. Tetrahexyldecyl ascorbate is preferred for sensitive skin but requires acetyl zingerone stabilization. Ascorbyl glucoside with or without arginine is well tolerated for chronic hyperpigmentation. Sodium ascorbyl phosphate improves texture and pigmentation, particularly when paired with microneedling. Bis-glyceryl ascorbate demonstrates niche utility for preventing tyrosine kinase inhibitor–associated hand-foot skin reaction. Ascorbyl palmitate and magnesium ascorbyl phosphate emulgels provide rapid pigment lightening. Across modalities, procedural delivery—microneedling, jet injection, and radiofrequency-assisted laser import—enhances penetration and clinical response. Dietary vitamin C at 40 to 80 mg per day offers modest systemic photoprotection, hydration, and wrinkle-smoothing benefits, even without overt deficiency. **LIMITATIONS:** Study heterogeneity and a paucity of standardized data, particularly regarding diverse phototypes, restrict direct comparison; further research is required to guide optimal dermatologic use. **CONCLUSION:** Clinical effectiveness of vitamin C depends on derivative chemistry, vehicle, pH, stabilization strategy, and delivery method. Personalized selection by skin type, treatment goals, and delivery modality is essential. **KEYWORDS:** Vitamin C derivatives, formulation stability, hyperpigmentation, photoaging, anti-aging, dietary supplementation, microneedling, systematic review

Ascorbic acid, also known as vitamin C, is an essential water-soluble antioxidant with important roles in numerous body systems, including the skin. As a cofactor for key gene regulatory enzymes, vitamin C supports immune function by promoting B-cell and T-cell proliferation.[1] In dermatology, vitamin C inhibits tyrosinase, thereby reducing melanin synthesis and improving hyperpigmentation.[2] Vitamin C also maintains activation of prolyl and lysyl hydroxylase, 2 key enzymes in collagen biosynthesis, supporting dermal repair and wound healing while mitigating age-related collagen loss.[3] As a potent antioxidant, vitamin C neutralizes reactive oxidative species via electron transfer, mitigating oxidative stress and preventing photoaging-related cellular damage.[4] Due to these diverse biological benefits, clinical interest in vitamin C spans topical, injectable, and systemic strategies.

Despite its broad dermatologic benefits, vitamin C presents notable challenges in clinical use. Ascorbic acid is hydrophilic, readily oxidized, and highly unstable, resulting in limited cutaneous penetration.[4] Effective topical delivery requires a highly acidic environment, with pH values below 3.5, to facilitate conversion to the unchanged form that permeates the stratum corneum more efficiently.[4] However, bioavailability and penetration vary greatly across formulations and delivery systems. This is further complicated by the lack of standardized outcome measures, which limits comparison across derivatives and formulations.

This review aims to summarize the clinical applications of vitamin C in dermatology, including its roles in photoaging, scarring, and hyperpigmentation. We compare the reported efficacies across formulations and treatment modalities and assess existing delivery

FUNDING: No funding was provided for this article.

DISCLOSURES: Dr. Tosti is Editor-in-Chief of *Skin Appendage Disorders* and acts as a consultant for AbbVie, Almirall, Amgen LLC, Bristol Myers Squibb, DS Laboratories, Lilly, L'Oréal/Vichy USA, Myovant, Ortho Dermatologics, Pfizer, Sun Pharmaceuticals, Tirthy Madison, Veradermics, and WellBeauty Company LLC. The remaining authors have no relevant conflicts of interest.

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methods and combinations, clarifying their relevance for specific patient profiles while identifying knowledge gaps for future research.

METHODS

The authors performed a systematic literature review in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[5] PubMed and Scopus were queried in September 2025 with no language filters for studies published from January 2020 onward using key terms on skin outcomes ("skin effects,""pigmentation," "photoaging,""skin integrity") and vitamin C ("vitamin C,""ascorbic acid,""ascorbate," "magnesium ascorbyl phosphate,""sodium ascorbyl phosphate,""ascorbyl glucoside," "ascorbyl palmitate," "tetrahexyldecyl ascorbate,""ascorbyl tetraisopalmitate") for studies examining the clinical use, efficacy, and delivery of vitamin C in dermatology.

The initial search identified 271 articles (102 PubMed, 169 Scopus). After removal of 8 duplicates, 263 studies were screened for relevance by 2 independent reviewers (H.M. and N.B.). Disagreements were resolved by a third independent reviewer (T.B.). Studies were included if they investigated dermatologic outcomes related to vitamin C; reviews and nonhuman publications were excluded. Quality assessment was performed using the Quality Rating Scheme for Studies and Other Evidence.[6] A total of 44 available studies were selected for inclusion and categorized by derivative type, delivery method, and reported outcomes.

RESULTS

A total of 44 articles were included in this review, comprising 20 randomized controlled trial (Level 1), 5 prospective comparative cohort trials (Level 2), 18 case series (Level 4), and one case report (Level 5). **Table 1** details the distribution of studies by level of evidence and cumulative sample size for each derivative. **Table 2** summarizes the characteristics, benefits, limitations, and indications of each formulation.[7–50]

Ascorbic acid. L-ascorbic acid (AA) remains the most clinically validated vitamin C formulation in dermatology, with evidence across multiple vehicles, concentrations, skin types, and procedural contexts.[7–16] Classical low-pH (pH < 3.5) aqueous serums containing 10% to 15% AA, often stabilized with vitamin E, ferulic acid, peptides, or botanical antioxidants, are famously known for their superior stability and reliable penetration, with benefits in photoaged, pigmented, and structurally aged skin.[17–20]

TABLE 1. Quality of evidence of included studies

DERIVATIVE	SAMPLE SIZE	LEVEL OF EVIDENCE[a]
Ascorbic acid[17–20]	511	7 Level 1; 4 Level 2; 3 Level 4
Ascorbyl tetra-isopalmitate[21–25]	195	3 Level 1; 3 Level 4
Tetra-hexyldecyl ascorbate[27–29]	111	1 Level 1; 2 Level 4
Ascorbyl glucoside[30,31]	87	2 Level 1
Sodium ascorbyl phosphate[32,36]	84	2 Level 1
Bis-glyceryl ascorbate[33]	24	1 Level 4
Ascorbyl palmitate and magnesium ascorbyl phosphate[34,35]	60	2 Level 4
Unspecified vitamin C[37–50]	2,329	5 Level 1; 1 Level 2; 7 Level 4; 1 Level 5

[a]In accordance with the Quality Rating Scheme for Studies and Other Evidence[6]

Ascorbyl tetraisopalmitate (ATIP). ATIP is the most widely researched lipophilic vitamin C derivative and is known for its superior stability.[21–25] It may be used alone or in combination formulas, such as melatonin-bakuchiol-ATIP serums and ATIP-rice peptides creams, to improve photodamage and structural outcomes.[21,25,26]

Tetrahexyldecyl ascorbate (THDA). THDA is a lipophilic vitamin C derivative suitable for sensitive skin. Unlike low-pH AA, which may cause skin irritation, THDA remains stable at pH levels up to 6.5.[27,28] However, THDA alone is chemically unstable on skin and may rapidly degrade unless combined with acetyl zingerone (AZ), which prevents oxidation-driven breakdown.[29]

Ascorbyl glucoside (AG). AG-based formulas are promising alternatives for chronic hyperpigmentary disorders such as solar lentigines and melasma.[30,31]

Sodium ascorbyl phosphate (SAP). SAP is a phosphate-form vitamin C derivative used for photoaging and structural aging, functioning primarily through inhibition of tyrosinase and reduction of dihydroxyphenylalanine–quinone while supporting collagen remodeling.[32,36]

Bis-glyceryl ascorbate (DGA). DGA is a novel topical ascorbic acid derivative formulated as a 1% cream, characterized by improved cutaneous permeability and stability within the epidermis compared to conventional vitamin C forms.[33]

Ascorbyl palmitate (AP) and magnesium ascorbyl phosphate (MAP). AP and MAP can be effectively delivered through emulgel, systems that incorporate hydrophobic actives into a water-soluble gel base to enhance shelf life, create smoother application, and improve patient compliance.[34,35]

Novel uses of vitamin C. Vitamin C is increasingly delivered through devices rather than as simple pre- or postprocedure topicals,[7,11–13,36] with consistent pigmentary and textural benefits.

In women with photoaging, microneedling with SAP serum, 3%, every 2 weeks for 3 sessions improved pigmentation more than microneedling with saline, with no procedure-related adverse events.[32] For melasma, microneedling-assisted vitamin C delivered over 3 biweekly sessions consistently reduced modified melasma severity indices (MASI) and enhanced both physician and patient assessments.[37] For sensitive erythematous skin, low depth (0.2 mm) microneedle mesotherapy or sonophoresis using injectable AA (500 mg) in 6 sessions at 2-week intervals improved elasticity, pigmentation, erythema, and hydration with excellent tolerability.[9] Transient postprocedure redness and irritation typically resolved within hours, and most patients reported brighter, less reactive skin.[9]

Other modalities also showed benefit. Intradermal mesotherapy combining vitamin C and tranexamic acid reduced periorbital hyperpigmentation, producing moderate lightening effects and only mild, self-limited adverse effects.[38] Needle-free delivery with high-velocity transdermal injections, weekly for 8 treatments, significantly reduced hemi-MASI scores, with only brief erythema or stuffiness during application.[39] Radiofrequency (RF)-assisted delivery offers another effective route: combining a 1064-nm Q-switched Nd:YAG laser with RF-assisted import of injectable vitamin C reduced the appearance of infraorbital dark circles, with durable lightening at 1

TABLE 2. Characteristics and clinical uses of vitamin C derivatives[7–50]

DERIVATIVE	STABILITY	SOLUBILITY	COMMON COMPLEXES	DELIVERY	CLINICAL USES	KEY CONSIDERATIONS
Ascorbic acid (AA)	Stable only at low pH (<3.5); efficacy maintained in stabilized or anhydrous/ginger extract systems at physiologic pH (~pH 6)	Hydrophilic	• Vitamin E • Ferulic acid • Peptides • Botanicals • Ginger extract	Topical	• Aging of face/neck/hands (radiance, fine lines, texture, firmness, dyschromia) • Pigment clearance (lentigines, melasma, PIE, PIH) • Pollution-induced oxi-inflammaging (pigment/barrier damage) • Adjunct to QSNY, fractional CO_2, nonablative fractional lasers, MNRF (↓ pigment and wrinkles postprocedure; ↑ elastin after MNRF) • Early evidence for superficial BCC with 30% AA in DMSO (histologic clearance in small trials)	• Most clinically validated derivative • L-ascorbic acid, vitamin E, ferulic acid is gold standard • AA + ginger extract best for sensitive skin • Immediate postprocedure use can leverage barrier permeability to accelerate pigment clearance • Many studies are open label, single center, and industry sponsored
Ascorbyl tetraisopalmitate (ATIP)	Stable as single active	Lipophilic	• Melatonin • Bakuchiol • Rice peptides	Topical	• Photoaging treatment and prevention • Pigment clearance (↓ basal hyperreflexive pixels on confocal microscopy) • Wrinkles (↑ collagen III, ↑ dermal and epidermal thickness; improvement in periorbital wrinkles with 1%–3% ATIP after 4–8 weeks) • Hydration (↓ lipid peroxidation)	• Most researched lipophilic derivative • Used in sunscreen formulations
Tetrahexyldecyl ascorbate (THDA)	Stable up to pH 6.5 (when paired with AZ)	Lipophilic	• AZ	Topical	• Photoaging treatment • Improves tone and pigment • Fine lines, deep wrinkles, texture (↑ firmness, elasticity, and smoothness) • Reduces erythema	• Suitable for sensitive skin • THDA alone may worsen wrinkles via oxidative pathways • Requires stabilization with AZ (yields superior pigment and wrinkle improvement than THDA alone)
Ascorbyl glucoside (AG)	Generally stable	Hydrophilic	• Arginine (raises pH to 6.5)	Topical	• Pigment clearance (lentigines, melasma) • Nonlesional pigmentation; ↑ brightness • Reduces erythema	• Less irritating alternative to hydroquinone with similar efficacy in comparative trials (AG maintains hydration and reduces erythema) • AGAC improves tolerability and allows concentrations up to 28%
Sodium ascorbyl phosphate	Not specified	Hydrophilic	• Amniotic membrane metabolites	Topical	• Photoaging (dark spots, uneven tone), including in Fitzpatrick IV–V • Fine lines (supports collagen remodeling) • Refines pores and texture • Postmicroneedling as 3% standalone serum	• Studied only as postmicroneedling adjunct
Bis-glyceryl ascorbate	Stabilized derivative	Hydrophilic	• None reported	Topical	• Prophylaxis for TKI-related hand-foot skin reaction (applied multiple times daily to palms/soles alongside urea- or heparinoid-based moisturizers)	• Novel derivative with enhanced permeability and stability • Maximal efficacy/penetration at 1%
Ascorbyl palmitate (AP) and magnesium ascorbyl phosphate (MAP)	MAP: highly stable; AP: moderately stable	AP: lipophilic; MAP: hydrophilic	• None reported	Topical	• Reduce melanin index and brightens skin (within 7 days of use in some trials) • Enhance hydration	• Delivered via emulgel systems for improved penetration and cosmetic elegance • MAP most stable among lipophilic derivatives due to its magnesium salt

AGAC: AG-arginine complex; AZ: acetyl zingerone; BCC: basal cell carcinoma; DMSO: dimethylsulfoxide; MNRF: microneedling radiofrequency; PIE: postinflammatory erythema; PIH: postinflammatory hyperpigmentation; QSNY: Q-switched Nd:YAG laser; TKI: tyrosine kinase inhibitor

year posttreatment.[40] This modality has been shown to decrease melanin particle density on reflectance confocal microscopy and has only mild, transient tingling, erythema, and edema with no downtime.[40] Together, these approaches show that microneedling, mesotherapy, jet injection, and RF-assisted laser protocols can reliably deliver vitamin C into targeted tissue with improvements in pigmentation, erythema, and texture and with an excellent safety profile.

Dietary supplementation. Dietary vitamin C supports skin health by strengthening the extracellular matrix, enhancing photoprotection, and preventing deficiency-related dermatoses.[41–44] A dose of 80 mg of oral vitamin C daily for 16 weeks was shown to promote collagen synthesis and contribute to improvements in dermal density, texture, and wrinkle appearance, particularly when combined with collagen peptides or other bioactive nutrients.[41] Antioxidant complexes containing 40 to 80 mg of vitamin C, alongside vitamins A and E, carotenoids, selenium, or botanical extracts, increased minimal erythema dose, reduced malondialdehyde levels, and improved hydration and elasticity, offering systemic photoprotection that is meaningful for patients with photoaging or high UV exposure.[42,43] These effects generally appeared after 8 to 12 weeks of daily use.[42,43] Adequate dietary intake is also essential for maintaining vascular and follicular integrity, as deficiency can lead to perifollicular hemorrhage, corkscrew hairs, gingival bleeding, and impaired wound healing, all of which resolved with intensive repletion doses of up to 1,000 mg daily.[44]

DISCUSSION

Current literature indicates that clinical outcomes with vitamin C hinge primarily on formulation chemistry rather than the presence of ascorbate alone.[51] Across most formulations, vitamin C improves photoaging through antioxidant and photoprotective effects and supports structural aging through promotion of collagen synthesis, preservation of dermal matrix integrity, and reduction of wrinkle formation.[11,21,25,26,28,29,36] AA remains the gold standard, clinically validated formulation, famously complexed with vitamin E and ferulic acid, with reproducible improvements in photoaging, pigmentary disorders, and periprocedural recovery in multiple controlled studies.[11,12,16] ATIP is the most stable lipophilic derivative, incorporated into creams and sunscreens targeting both pigmentary and structural components of photoaging, with particular strengths in collagen support and wrinkle reduction.[21,25,26] THDA is best for sensitive skin but requires stabilization with AZ, with emerging evidence of its benefits for photoaging of the face, neck, and chest.[28,29] AG offers a well-tolerated alternative to hydroquinone for chronic hyperpigmentation, with arginine-complexed AG (AGAC) allowing for use at higher concentrations.[30,31] SAP functions as a pigment- and texture-correcting derivative optimized by microneedling-assisted delivery,[36] while DGA has a niche supportive role in oncology.[33] Specifically, in patients with metastatic renal cell carcinoma receiving the tyrosine kinase inhibitor sunitinib, a DGA cream, 1%, applied several times daily to the palms and soles, together with standard urea- or heparinoid-based moisturizers, has been shown to significantly reduce the incidence of sunitinib-induced hand-foot skin reaction (HFSR), defined as posttherapy dryness, pruritus, maculopapular erythema, purpura, bulla/vesicles, erythroderma, or hyper-/hypopigmentation.[33] The benefit is hypothesized to reflect the ability of DGA to counteract sunitinib-induced keratinocyte growth inhibition.[33] Finally, evidence is emerging regarding combined AP and MAP emulgel systems for rapid pigmentlightening.[34] Overall, clinicians should assess vitamin C regimens by derivative, pH, vehicle, stabilization strategy, and intended clinical target rather than by the generic "vitamin C" label.

Periprocedural use of vitamin C presents unique opportunities and challenges for dermatologists. When procedures such as fractional lasers or microneedling already induce neocollagenesis, appropriately formulated vitamin C could potentially augment the quality of remodeling rather than function only as a generic antioxidant.[52] Fractional CO_2 laser pretreatment can increase transdermal delivery of several topical agents, including vitamin C derivatives.[11] These lasers create microthermal zones that act as conduits through the stratum corneum, with evidence demonstrating up to a 10- to 21-fold increase in uptake of vitamin C serums, 10% to 15%, when applied following laser treatments in ex vivo human skin.[53] Similarly, microneedle technologies enhance transdermal drug delivery by bypassing the stratum corneum barrier, with evidence supporting greater improvements in wrinkles, pores, and pigmentation with microneedling combined with topical vitamin C compared to microneedling alone.[32] However, these findings remain preliminary, and there is a lack of studies evaluating these combinations across different vitamin C formulations and diverse phototypes. Dermatologists should incorporate these uncertainties into procedural planning, tailoring product selection and timing to mitigate irritation risk and optimize treatment outcomes.

Phototype-related biology further underscores the need for individualized decision making. Patients with skin of color have higher eumelanin content, which confers increased resistance to UV-B–induced damage and more efficient DNA repair, but also greater susceptibility to visible light-induced pigmentation and oxidative stress, which drives common pigmentary disorders in this population.[54] Vitamin C may offer antimelanogenic and antioxidative benefits for hyperpigmentation and photoprotection in these patients.[55] However, clinical trial data specifically addressing topical vitamin C in darker phototypes are limited. Most studies use antioxidant blends rather than isolated vitamin C and lack adequate representation of skin of color,[56] leaving significant gaps in evidence regarding efficacy, optimal formulation, and long-term safety.

This review is limited by the heterogeneity of study designs and outcome measures across included trials, which precluded direct comparison between derivatives. Many studies were open label, short in duration, industry-sponsored, or conducted in small, homogeneous cohorts, limiting external validity. Phototype reporting was limited, leaving sparse data for diverse skin types. Procedural studies frequently combined vitamin C with additional modalities, complicating attribution of therapeutic effect. Finally, variations in pH, vehicle, concentration, and stabilization strategies were inconsistently reported, restricting the ability to standardize recommendations across products.

CONCLUSION

Vitamin C remains a versatile therapy in dermatology, but its therapeutic success is determined by formulation chemistry rather than ascorbate content alone. Evidence supports AA as the most reliable option for broad-

spectrum photoaging, structural aging, and pigmentary concerns, while derivatives such as ATIP, THDA, AG/AGAC, SAP, DGA, and AP/MAP offer targeted benefits based on stability and intended use. Procedural delivery can further expand the applications of vitamin C but requires individualized planning to balance efficacy with tolerability. Ongoing research, especially across diverse skin types and with standardized outcome measures, is needed to refine best practices and guide precise, patient-specific use of vitamin C in clinical dermatology.

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