



Ascorbic Acid Injection Efficacy to Increase Skin Collagen

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Received: September 11, 2023

Revised: April 10, 2024

Accepted: June 5, 2024

Published: June 30, 2024

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DOI: [10.29303/jppipa.v10i6.5282](https://doi.org/10.29303/jppipa.v10i6.5282)

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Abstract: The aging process can be delayed by antioxidant supplement such as ascorbic acid. It is useful for reducing oxidative stress, inflammation, and cellular aging so that older people will be fitter and happier. The methodological approach used in this study is Literature Review (LR). This literature review will investigate the effect of ascorbic acid on inflammaging. Google Scholar, Researchgate, and Mendeley were used as the search engine. The keywords were ascorbic acid & skin collagen. The effect of ascorbic acid on geriatric beta-endorphin were analyzed from 14 articles. Body homeostasis, organ systems, and other changes will reduce the functional capacity in the skin collagen. To delay the physiological process of aging, ascorbic acid potential to improve the skin collagen. The skin collagen can be improved by the effect of ascorbic acid for a better quality of aging process.

Keywords: Anti-aging; Ascorbic acid; Skin collagen

Introduction

Indonesia's aging demographic structure has increased significantly since 2021, with the percentage of elderly people exceeding 10%. The percentage of elderly people has increased by 3%, reaching 10.82% (Hartono, 2022; Franceschi et al., 2018). Inflammaging, a proinflammatory process, is linked to age and age-related disorders. The gut microbiota plays a crucial role in this process (Fulop et al., 2023; Neves et al., 2020).

Anti-Aging Medicine focuses on optimizing organ function to extend life expectancy (Jones, 2020). Geriatric patients in Indonesia are experiencing increased skin aging, causing abnormalities and lesions. Oxidative stress, influenced by internal and external factors, is the main culprit behind this process. Treatments for skin aging require understanding the skin's aging physiology, mechanisms, and clinical signs (Yusharyahya, 2021). Oxidative stress causes fine lines, wrinkling, loss of elasticity, and pallor, resulting in functional senescence, reduced ability to counteract infections, and increased frequency of autoimmune and neoplastic diseases (Papaccio et al., 2022).

The oxidative cleavage of carbohydrate adducts to lysine residues in glycosylated proteins, such as skin

collagen, results in the formation of N-(carboxymethyl)lysine (CML). As age increases, the concentration of CML increases significantly, while the concentration of N-(carboxymethyl)hydroxylysine (CMhL) also increases with age. This suggests that the accumulation of N-(carboxymethyl) amino acids is a general feature of the aging of long-lived proteins due to glycation and oxidation reactions (Dunn et al., 1991). Oxidative stress accelerates Ascorbic acid (AA) production, causing advanced glycation end products (AGEs), CML formation, and β 2m transformation (Miyata et al., 1997).

The electron microscope was used to investigate the structure of collagen fibrils in normal human skin corium. The fibrils ranged in width from 700 to 1,400 Å, with 1,000 Å being the most frequently observed. They showed little longitudinal fraying and fractured in planes transverse to the axis. The axial repeating periods in fibrils stained with phosphotungstic acid or shadowed with chromium or platinum ranged from 500 to 800 Å, with the average period in infant skin not significantly different from adult and aged skin (Gross et al., 1948).

Ascorbic acid, the L-enantiomer of vitamin C, is crucial for maintaining human and animal physiological

How to Cite:

Anggraini, E., & Damayanti, P. A. A. (2024). Ascorbic Acid Injection Efficacy to Increase Skin Collagen. *Jurnal Penelitian Pendidikan IPA*, 10(6), 3449–3454. <https://doi.org/10.29303/jppipa.v10i6.5282>

processes. However, some mammals, including humans, lack L-gulonolactone oxidase, affecting its de novo synthesis. Ascorbic acid's functionality has led to the development of fortified foods, protecting sensory and nutritional characteristics. Maintaining stability and improving delivery to the active site are major challenges in its utilization (Yin et al., 2022). Ascorbic acid, a vitamin derived from glucose metabolism, plays a crucial role in collagen fiber synthesis and protecting the body from free radical damage. High levels of vitamin C are found in foods like tomatoes, potatoes, and citric fruits. The recommended daily intake is 90 mg/d for men and 75 mg/d for women (Valdés, 2006).

The effects of ascorbic acid, TGF- β , and IFN- γ on fibroblasts in the collagen gel culture system and compared them to monolayer culture systems showed lower levels of collagenase-digestible protein synthesis in the three-dimensional culture system, but the expression of collagen mRNA increased after TGF- β treatment and decreased after IFN- γ treatment (Kim et al., 1996). So, the efficacy of ascorbic acid or vitamin C as antioxidant is studied in skin collagen.

Method

The methodological approach used in this study is Literature Review (LR). This literature search focuses on randomized controlled trials published on PubMed, Embase, Cochrane Library, and Clinical Trials.gov website from 2017 to 2022. This literature search focuses on randomized controlled trials published on website. Researcher will screen, extract data, and cross-check the results.

Result and Discussion

Sixteen articles described the efficacy of pumpkin on inflammaging. Pumpkin efficacy was studied by experimental and literature review methods. Samples varied from molecular to bedside investigation.

Table 1. The Analysis of Vitamin C Injection Effect on Skin Collagen

Author & publication year	Research Methodology	Result
(Siddeeg et al., 2020)	Article review	Nanomaterials enhance ascorbic acid detection using <i>C. elegans</i> .
(Pullar et al., 2017)	Article review	Vitamin C plays crucial role in skin health.
(Elhabak et al., 2021)	In vivo experimental study	<i>C. aprilis</i> delivers l-ascorbic acid spanlastics for UVB-induced skin stability enhancement.
(Puścion-Jakubik et al., 2021)	RCT	Vitamin C intake impacts body composition, skin hydration, and lubrication in young women.
(Prakoeswa et al., 2021)	RCT	Vitamin C-rich amniotic membrane stem cell mixture effective in photoaging patients.
(Boo, 2022)	Article review	Ascorbic acid, vitamin C, enhances dermal collagen for skin antiaging purposes.
(Casabona et al., 2017)	RCT	ascorbic acid effectively treat stretch marks
(Lee et al., 2022)	In vitro experimental study	glycinamide and ascorbic acid synergistically promote collagen production and wound healing.
(Ryu et al., 2022)	In vitro, ex vivo, and pre-post intervention clinical trial	ascorbic acid and collagen enhance anti-aging properties.
(Işin et al., 2023)	In vivo experimental study	Ascorbic acid impacts collagen and inflammation mediators in rats.
(Maekawa et al., 2022)	Article review	Ascorbic acid exhibits diverse antitumor effects on <i>C. elegans</i> .
(Dębska-Szmich et al., 2021)	Article review	Vitamin C and cancer risk: treatment options.
(Alexander et al., 2018)	In vivo experimental study	ascorbate reduces radiation-induced tissue toxicity and enhances tumor radiosensitization in pancreatic cancer.
(Gref et al., 2020)	In vivo experimental study	Collagen production in human skin enhances with Vit C-squalene bioconjugate.
(Bánvölgyi et al., 2020)	RCT	basal cell carcinoma treatment efficiency with high-dose ascorbic acid.
(Eggersdorfer, 2020)	RCT	Intake recommendations for vitamin C vary, with some countries suggesting 40-45 mg daily.

Discussion

Ascorbic acid is an important biomolecule involved in cellular metabolism, neuronal hormones, and synthesis of collagen, norepinephrine, and vitamin C. It plays a role in enzymes, intestinal iron absorption, and

carnitine biosynthesis. Nanomaterials-based sensors have recently achieved high sensitivity and selectivity for ascorbic acid detection (Siddeeg et al., 2020).

The skin's unique structure, consisting of two layers, provides a barrier against environmental insults.

Vitamin C, found in normal skin, supports collagen synthesis and antioxidant protection. However, the efficacy of topical vitamin C treatments compared to dietary vitamin C intake is poorly understood. This review explores the potential roles of vitamin C in skin health, comparing nutritional intake versus topical application, and suggesting which skin properties benefit from improved vitamin C intake (Pullar et al., 2017).

L-Ascorbic acid (LAA) is a powerful antioxidant that protects skin from premature aging. To maintain vitamin C stability, LAA-loaded spanlastics were prepared using ethanol injection methods. The selected formula showed high entrapment efficiency, high deformability, and good physical and chemical stability for 6 months. LAA-loaded spanlastics significantly suppressed MMP2 and MMP9 levels in rats exposed to UV irradiation, providing the highest skin protection compared to UVB and LAA solution-treated groups (Elhabak et al., 2021).

To estimate the consumption of dietary components with antioxidant properties, assess body composition, and assess skin hydration and lubrication, results showed that 172 young women had insufficient vitamin C, vitamin E, zinc, and vitamin D levels. The highest hydration was observed in eyelids, neckline, and chin areas, while the greatest sebum was found in nose and forehead areas. To properly moisturize and lubricate the skin, young women should consume products rich in antioxidant properties, particularly fat-soluble vitamins A and E, and copper (Puścion-Jakubik et al., 2021).

Extrinsic factor-related aging leads to degradation of skin structure, with amniotic membranes being promising candidates for cellular therapy and regenerative medicine. Vitamin C, a water-soluble vitamin, is used in dermatology as an antioxidant and promotes depigmentation and collagen synthesis. Microneedling facilitates the penetration of these molecules, improving the efficacy of a mixture of amniotic membrane stem cells (AMSC)-metabolic products and vitamin C in skin rejuvenation. A study of 60 photoaging women showed significant improvement in wrinkles, ultraviolet spots, and pores, suggesting that the combination of AMSC-MPs and vitamin C is an effective treatment for photoaging (Prakoeswa et al., 2021).

Ascorbic acid (AA) is a cosmeceutical that can protect skin health and beauty by attenuating photoaging and natural aging. It promotes collagen synthesis and increases dermal collagen, inhibiting skin aging. However, AA's biochemical basis and clinical evidence suggest that it can be a limiting factor for collagen synthesis. Combining AA analogs with amino acid analogs can enhance collagen production, making it a promising approach for skin antiaging (Boo, 2022).

A study found that combined treatment with microneedling, topical ascorbic acid, calcium hydroxylapatite (CaHA), and microfocused ultrasound with visualization (MFU-V) improved striae appearance. Results showed increased collagen and elastin fibers in the dermis, with most subjects satisfied. MFU-V may achieve additional improvements in striae appearance (Casabona et al., 2017).

This study presents a novel strategy to enhance collagen production in cells by combining glycinamide and ascorbic acid (AA). Human dermal fibroblasts (HDFs) were treated with 20 amidated amino acids and 20 free amino acids at 1 mM. Glycinamide significantly enhanced collagen production, while AA increased COL1A1 and COL3A1 mRNA and collagen I protein levels. The combination of AA and glycinamide synergistically enhanced collagen production and wound closure in HDFs, similar to TGF- β cells treated with TGF- β . MAP, a derivative of AA, had a similar effect on wound closure, which was further enhanced by glycinamide (Lee et al., 2022).

Collagen synthesis and ascorbic acid are essential substances for skin aging prevention and wound healing. A product was developed to achieve a synergistic effect of collagen and ascorbic acid on all skin types. The product was tested in fibroblasts, keratinocytes, melanocytes, and human skin tissues. Results showed that the product improved skin wrinkles, lifting, and pigmentation areas, with a sustained improvement even after discontinuing use. The combination of ascorbic acid and collagen effectively alleviates skin aging (Ryu et al., 2022).

The effects of ascorbic acid administration on the repair process after muscle injury showed that ascorbic acid reduced serum IL-6 and muscle tissue TNF- α levels, increased liver tissue IL-10 levels, and increased muscle tissue collagen levels. Vitamin C has effects on inflammatory mediators during muscle tissue repair, but further molecular analyses are needed to understand the mechanism (Işin et al., 2023).

Ascorbic acid, an antioxidant and cofactor in various enzymatic reactions, has potential antitumor effects. However, its clinical efficacy against cancer and its mechanism remain unclear. Cancer-associated fibroblasts (CAFs) form cancer-specific microenvironments, and the effect of ascorbic acid on these cells is unclear. Oral administration of ascorbic acid results in low blood concentrations, while intravenous treatment achieves high concentrations and oxidative-promoting actions (Maekawa et al., 2022).

L-ascorbic acid, a crucial antioxidant, protects cell membranes in tissues and extracellular fluid from peroxidative damage. It plays a role in collagen synthesis, enzyme activity, and immune system function. Low intake increases cancer risk, but no clinical evidence supports antioxidant supplements' cancer prevention

(Dębska-Szmich et al., 2021). Ascorbic acid (P-AsCH), is used to treat advanced pancreatic cancer. This results in enhanced clonogenic survival and double-stranded DNA breaks in tumor cells, while reducing radiation-induced intestinal damage, collagen deposition, and oxidative stress in normal tissue (Alexander et al., 2018).

Fibrin-coated membranes showed higher cell spreading, mitochondrial activity, and population density, with ascorbic acid improving cell performance. Fibrin stimulated collagen I expression in human dermal fibroblasts, and ascorbic acid slightly enhanced beta1-integrins expression. Combining nanofibrous membranes with fibrin nanocoating and ascorbic acid is advantageous for skin tissue engineering (Bacakova et al., 2016).

Vitamin C (Vit C) plays a crucial role in human skin physiology by stimulating collagen biosynthesis. However, it struggles to bypass the epidermis stratum corneum barrier. A lipophilic version of Vit C was developed by conjugating it to squalene (SQ), a natural lipid of the skin. The study found that Vit C-SQ significantly increased epidermal thickness and favored collagen III production in human skin. It also promoted glycosaminoglycans production. The strongest effects were observed with Vit C-SQ (Gref et al., 2020).

High-dose intravenous ascorbic acid has anti-cancer properties and has been tested for treating basal cell carcinoma (BCC). Studies show alterations in collagen structure between tumor nests during IVA therapy, suggesting it is well-tolerated in a small group of patients with extensive BCCs. However, it may only be considered as an adjuvant therapy in treatment-resistant cases (Bánvölgyi et al., 2020).

Intake recommendations for vitamin C are set at a minimum of 10 mg/day to prevent scurvy, while some countries like the UK, Australia, and the FAO/WHO recommend 40-45 mg/day. Recent studies have shown that higher intakes of vitamin C are essential for the immune system's functions, and some countries have increased their vitamin C recommendations. However, there is currently no sufficient evidence for a functional parameter, and recent research suggests increasing the intake recommendation to 200 mg/day for healthy individuals (Eggersdorfer, 2020).

The study evaluated percutaneous collagen induction (PCI) in post-burn scarring, focusing on patients with residual cicatricial deformity. The ideal treatment would preserve the epidermis and promote normal collagen and elastin formation in the dermis. A total of 16 patients in Germany with post-burn scarring underwent PCI. Results showed an average improvement of 80% better than before treatment, with a significant increase in collagen and elastin deposition 12 months postoperatively. The epidermis showed 45% thickening of stratum spinosum and normal rete ridges,

and normalization of the collagen matrix in the reticular dermis at 1 year postoperatively (Aust et al., 2010).

Conclusion

Vitamin C injection effectively regulates skin collagen in the elderly, making it an alternative supplement for an anti-aging lifestyle. Further research is needed to expand the sample size and age-specific criteria.

Acknowledgments

The authors appreciate the support and guidance of the Head and all staff of the Biomedical Department Medical Faculty Universitas Udayana, Denpasar, Indonesia.

Author Contributions

All authors contributed to writing this article.

Funding

No external funding.

Conflicts of Interest

Nothing is considered as the conflict of interest.

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