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Review Article

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Vitamin C in Therapeutic Dermatology

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Abstract

The skin is exposed to a lifetime of challenges that can alter its structure and appearance. Key challenges include the loss of elasticity due to ageing, the exposure to elements and oxidising chemicals, and damage due to direct injury. Vitamin C is recognised to play an important role in our skin; it has potent anti-oxidative, photo protecting, anti-aging and anti- pigmentary effects. This review aims to highlight the key roles of Vitamin C in skin health and function, especially regeneration and protection.

Key Words: Anti-Ageing, Antioxidants, Anti-Pigmentation, Vitamin C

Introduction

Vitamin C has different names including ascorbic acid, ascorbyl-6-palmitate, and magnesium ascorbyl phosphate. It is a charged, water-soluble molecule that gets repelled by the physical barrier of the terminally differentiated epidermal cells [1]. The skin normally has high concentrations of Vitamin C, suggestive of active accumulation from the blood circulation. Vitamin C is available in several active forms. Among all forms, L-ascorbic acid is the most biologically active and well-studied [2]. Reducing the acidity of L-ascorbic acid to a pH below 3.5 is an effective method of improving its stability and permeability [3]. The optimal concentration of Vitamin C depends on its formulation. Reputable products containing 10-20% Vitamin C tend to have significant biological effect, while concentrations above 20% can cause skin irritation [4].

The source of Vitamin C intake in humans is mainly from fruits and vegetables. It is absorbed as Ascorbic Acid (ASC), and to much lesser extent Dehydroascorbic Acid (DHA) by facilitated diffusion process via GLUT1 or GLUT3 transporters. The absorption of Vitamin C by the small intestine is helped by a system of sodium-dependent transporter (SVCT). Vitamin C is transported to plasma by diffusion or facilitated diffusion. Normally the level of ASC in plasma is significantly higher compared to intercellular concentrations [5].

Anti-Oxidation and Photo protection

Vitamin C is one of the most potent antioxidants in the skin. It neutralizes the oxidative stress by a process of electron transfer and/or donation. Environmental factors, such as solar radiation, pollution, and smoking can accelerate damage to the skin through the generation of so-called "oxidative stress" (2). Skin cells are constantly exposed to reactive oxygen species (ROS) and oxidative stress from exogenous and endogenous sources. UV radiation is the most important environmental factor in the development of skin cancer and skin aging. The primary products caused by UV exposure are generally direct DNA oxidation or generation of free radicals which form and decompose extremely quickly but can produce effects that can last for hours, days, or even years. The reduction of oxidative stress can be achieved on two levels: by lowering exposure to UVR and/or by increasing levels of antioxidant defence to remove ROS. The only endogenous protection of our skin is melanin and enzymatic antioxidants. Melanin cannot totally prevent skin damage. A second category of defence is repair processes, which removes the damaged biomolecules before they can accumulate and before their presence results in altered cell metabolism. Additional UV protection includes avoidance of sun exposure, usage of sunscreens, protective clothes, and antioxidant supplements [6].

Free radicals are highly toxic, unstable molecules that can cause damage to nucleic acids, proteins, and cell membranes. UV-induced reactive oxygen species also trigger the signal transduction cascade, which leads to up regulation of factors, such as activation protein-1 (AP-1) and nuclear factor-B, and down regulation of transforming growth factor-ß. These proteases collectively up regulate matrix metalloproteinases (MMPs), which degrade collagen, reduce collagen production, and increase elastin accumulation [7]. This leads to the clinical manifestations of photoaging

pigmentation, telangiectasias, coarse texture, deep wrinkles, and solar elastosis.

Sunscreens are only partially effective in blocking free radicals produced by UV exposure. Vitamin C has been shown to inhibit the activation of AP-1, which leads to a reduction in MMP production and collagen damage [7]. One double-blind, placebo-controlled study on 10 subjects using 10% topical vitamin C over a 12-week period showed a statistically significant reduction in photoaged scores and improvement in wrinkling in Vitamin C-treated patients as compared to placebo [8]. Vitamin C can protect against UV-induced immunosuppression. CD1a-expressing Langerhans cells are antigen-presenting cells present in the epidermis, which act by initiating a protective immune response. Their numbers are decreased upon acute and chronic UV exposure [9]. Vitamin C-containing topical solutions have been shown to prevent the reduction of CD1a-expressing Langerhans cells upon UV radiation [10].

UV-induced erythema and thymine dimer mutations contribute to photo-carcinogenesis. In addition, UV-induced reactive oxygen species induce mutations on the p53 gene, which affect the repair of damaged deoxyribonucleic acid (DNA) and induce a process of programmed cell death (apoptosis) [11]. Clinical studies showed that Vitamin C-containing solutions have been shown to reduce UV-induced thymine dimers, thereby potentially reducing the risk of photo carcinogenesis [12].

Anti-aging

The role of Vitamin C in skin can be more closely understood by assessing the effects of its deficiency. Vitamin C deficiency is associated with poor wound healing, thickened stratum corneum, rapid subcutaneous bleeding. These findings suggest a role for Vitamin C in collagen formation and connective tissue morphology. The key signs of early scurvy include skin fragility, poor wound healing, and corkscrew hair growth [13]. Vitamin C plays a crucial role in reducing the effects of aging. Importantly, Vitamin C serves as a cofactor for prolyl and lysyl hydroxylase enzymes that cross-link and stabilize collagen fibers [14]. Vitamin C also directly activates the transcription factors involved in collagen synthesis and stabilizes procollagen messenger RNA (mRNA) that regulates Type I and III collagen synthesis. In addition, Vitamin C increases the gene expression of collagen and synthesis of the tissue inhibitor of matrix metalloproteinases MMP-1, which decreases collagen degradation [7]. A clinical study showed that daily application of 3% topical vitamin C over a four-month period led to a significant increase in the density of dermal papillae [15].

Anti-pigmentation

Skin pigmentation results from melanin production by melanocytes and their subsequent transfer to keratinocytes. Vitamin C plays a key role as an anti-pigmentation agent. It interacts with copper ions at tyrosinase-active sites and inhibits the action of the enzyme tyrosinase—the main enzyme responsible for the conversion of tyrosine into melanin—thereby decreasing melanin formation [16]. Although Vitamin C has been shown to suppress melanin production, its clinical effects may not be as effective as other topical products containing hydroquinone [17]. A systematic review by Saudi R et al (2020) [18] of 7 studies looking at the depigmenting effect of Vitamin C on hyperpigmented skin and gingiva. The studies strongly suggest effective response to Vitamin C, however they were associated with higher risk of bias.

Vitamin C and Inflammatory Dermatoses

There is growing evidence to suggest a link between low vitamin C status and skin inflammatory conditions, such as atopic dermatitis. This was demonstrated by Shin J et al, 2016 [19], where patients with atopic dermatitis showed lower recorded plasma levels of Vitamin C. Furthermore, Vitamin C appears to play a pivotal role in the essential hydroxylation step during synthesis of ceramide, the main lipid component of the stratum corneum layer.

Vitamin C as Treatment

Vitamin C is almost never measured in the skin and this information is needed before we can improve our understanding of what level of intake might be beneficial for skin health and protection against aging-related changes [20]. The concentration of Vitamin C varies from one area to another. In one study, Vitamin C content was measured in buccal keratinocytes, as these cells are proposed to be a good model for skin keratinocytes [1]. The keratinocyte Vitamin C concentration doubled upon supplementation of the participants with 3 g/day Vitamin C for six weeks, a dosage that is significantly higher than the recommended daily intake and would achieve plasma saturation and likely also tissue saturation [21]. Dietary supplementation is therefore only expected to be effective in elevating skin Vitamin C in individuals who have below-saturation plasma levels prior to intervention [13].

Topical delivery of Vitamin C to the skin is challenging, due to its water-solubility being repelled by the terminally charged epidermal layer [22]. Penetration becomes possible when the pH is lowered below 4 and with the active L-ascorbic Acid formulation. The use of derivatives are often needed to maintain the stability of Vitamin C and its efficient absorption into the skin. Topical formulations of Vitamin C often contain Vitamin E and a delivery vehicle. Vitamin C is the primary replenisher of vitamin E and works synergistically with vitamin E in the protection against oxidative damage [13].

Conclusion

Vitamin C plays a pivotal role in the maintenance of healthy skin. This can be demonstrated by its effects on collagen synthesis, protection from UV harm, anti-oxidation, and wound healing. Because Vitamin C deficiency results in impaired function, it is assumed that increasing intake will be beneficial. However, there are no studies that have measured Vitamin C levels or intake and associated aging changes [23]. Continuous efforts are being made

to research other benefits of vitamin C, including the effects of vitamin C on hair growth, wound healing, smoking-related skin aging, scars, and striae [13].

References

1. Fuchs J, Kern H (1998) Modulation of UV-light-induced skin inflammation by D-alpha-tocopherol and L-ascorbic acid: A clinical study using solar simulated radiation. Free Radic. Biol. Med. 25: 1006-1012.
2. Farris PK, Draelos ZD, Dover JS, Alam M, (2009) Cosmetical vitamins: vitamin C. In: editors. Cosmoceuticals. Procedures in Cosmetic Dermatology. 2nd ed. New York: Saunders Elsevier; 2009: 51-56.
3. Lin FH, Lin JY, Gupta RD, et al. (2005) Ferulic acid stabilizes a solution of vitamins C and E and doubles its photoprotection of skin. J Invest Dermatol. 125: 826-832.
4. Pinnell SR, Yang H, Omar M, et al. (2001) Topical L-ascorbic acid: percutaneous absorption studies. Dermatol Surg. 27: 137-142.
5. Jens Lykkesfeldt, Pernille Sveden-Nyborg (2018) The Pharmacokinetics of Vitamin C. Nutrients 2018 Oct; 11: 2412.
6. Godic A, Poljšak B, Adamic M, Dahmane R (2014) The role of antioxidants in skin cancer prevention and treatment. Oxid Med Cell Longev. 860479.
7. Chen L, Hu JY, Wang SQ (2012) The role of antioxidants in photoprotection: a critical review. J Am Acad Dermatol. 67: 1013-1024.
8. Fitzpatrick RE, Rostan EF (2002) Double-blind, half-face study comparing topical vitamin C and vehicle for rejuvenation of photodamage. Dermatol Surg. 28: 231-236.
9. Toyoda M, Bhawan J (1997) Ultrastructural evidence for the participation of Langerhans cells in cutaneous photoaging processes: a quantitative comparative study. J Dermatol Sci. 14: 87-100.
10. Matsui MS, Hsia A, Miller JD, et al. (2009) Non-sunscreen photoprotection: antioxidants add value to a sunscreen. J Investig Dermatol Symp Proc. 14: 56-59.
11. Meplan C, Richard MJ, Hainaut P (2000) Redox signaling and transition metals in the control of the p53 pathway. Biochem Pharmacol. 59: 25-33.
12. Murray JC, Burch JA, Streilein RD, Iannacchione MA, Hall RP, et al. (2008) A topical antioxidant solution containing vitamins C and E stabilized by ferulic acid provides protection for human skin against damage caused by ultraviolet irradiation. J Am Acad Dermatol. 59: 418-425.
13. Al-Niaimi F, Chiang NYZ (2017) Topical Vitamin C and the Skin: Mechanisms of Action and Clinical Applications. J Clin Aesthet Dermatol. 10: 14-17.
14. Rhie G, Shin MH Seo JY, et al. (2001) Aging-and photoaging –dependent changes of enzymic and nonenzymic antioxidants in the epidermis and dermis of human skin in vivo. J Invest Dermatol. 117: 1212-1217.
15. Lin JY, Selim MA, Shea CR, et al. (2003) UV photoprotection by combination topical antioxidants vitamin C and vitamin E. J Am Acad Dermatol. 48: 866-874.
16. Ando H, Kondoh H, Ichihashi M, Hearing VJ (2007) Approaches to identify inhibitors of melanin biosynthesis via the quality control of tyrosinase. J Invest Dermatol. 127: 751-761.
17. Espinal-Perez LE, Moncada B, Castanedo-Cazares JP (2004) A double- blind randomized trial of 5% ascorbic acid vs. 4% hydroquinone in melasma. Int J Dermatol. 43: 604-607.
18. Sanadi R, Deshmukh R (2020) The effect of Vitamin C on melanin pigmentation – A systematic review. Journal of Oral and Maxillofacial Pathology, 24: 374.
19. Shin J, Kim Y, Kwon O, Kim N, Cho Y, et al. (2016) Associations among plasma vitamin C, epidermal ceramide and clinical severity of atopic dermatitis. Nutrition Research and Practice, 10: 398.
20. Pullar JM, Carr AC, Visser MC (2017) The roles of Vitamin C in Skin Health. Nutrient. Aug 9: 866.
21. Levine M, Conry-Cantilena C, Wang Y, Welch RW, Washko PW, et al. (1996) Vitamin C pharmacokinetics in healthy volunteers: Evidence for a recommended dietary allowance. Proc. Natl. Acad. Sci. USA. 93: 3704-3709.
22. Stamford N (2012) Stability, transdermal penetration, and cutaneous effects of ascorbic acid and its derivatives. Journal of Cosmetic Dermatology, 11: 310-317.
23. Rinnerthaler M, Bischof J, Streubel M K, Trost A, Richter K, et al. (2015) Oxidative stress in aging human skin. Biomolecules. 5: 545-589.