REVIEW ARTICLE

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Review of the Effects of Vitamin C on Wound Healing

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Abstract

Background: The healing process is one of the main issues for the medical and general population. Studies have shown that vitamin C can accelerate this process, in this study, we aimed to review the effects of vitamin C on wound healing.

Methods: We searched PubMed, MEDLINE, and Elsevier databases for studies with the keywords “vitamin C” OR “ascorbic acid” AND “wound healing” OR “wound repair.” Studies from the start of 2013 to the end of 2023 were reviewed.

Results: Few studies have evaluated the effects of Vitamin C on wound healing. Six studies were assessed, which found that vitamin C significantly improves wound healing, closure, post-healing appearance, decreased bacterial load, and inflammatory markers.

Conclusion: Given that only a few studies have confirmed the effects of Vitamin C on wound healing, further studies are required to appropriately confirm the association.

Conflicts of Interest: The Authors declare no conflicts of interest.
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Introduction

Wound healing represents a fundamental physiological mechanism designed to restore both the anatomical integrity and functional capacity of damaged skin. Numerous factors have been recognized as influencing the wound healing process, including age, the specific location and size of the wound, nutritional health, immune system functionality, and the presence of underlying comorbidities such as diabetes and obesity. When delayed, wound healing can cause various complications such as prolonged hospital stays, the necessity for amputations, and in severe cases, mortality. Chronic, non-healing wounds are observed in approximately 2% of the general population (1-3). Wounds induce a heightened catabolic state within the body. Following an injury, the metabolism of micronutrients escalates significantly, often resulting in critical deficiencies. Notably, the levels of vitamin C, a small, organic, water-soluble micronutrient renowned for its potent antioxidant properties, decline rapidly during inflammatory responses (4-6). Moreover, Individuals suffering from scurvy have delayed wound healing and reduced rates of collagen synthesis and maturation. In addition to its robust antioxidant capabilities, Vitamin C is a crucial co-factor in various enzymatic reactions. It has recently been demonstrated to inhibit pro-inflammatory processes through multiple mechanisms while fostering anti-inflammatory and pro-resolution effects in macrophages. Vitamin C also plays a vital role in the metabolism and regulation of collagen, prompting numerous studies to

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investigate its specific contributions to the wound healing process (7, 8). In this study, we reviewed the effects of vitamin C on wound healing.

Methods

In this study, we reviewed the wound-healing effects of vitamin C. We searched studies in PubMed, MEDLINE, and Elsevier databases with the keywords "vitamin C" AND/OR "ascorbic acid" AND/OR "wound healing" AND/OR "wound repair". Studies from the start of 2013 to the end of 2023 were reviewed. Review articles, systematic reviews, meta-analysis, and editorials not in English, were excluded. Studies that were performed on intraoral ulcers were also excluded.

Results

Four studies were found with the keywords. We have presented the results of these studies in the below. Chokesuwattanaskul et al. (9), assessed the effects of high doses of oral vitamin C + topical mesenchymal stem cells on wound healing in diabetic mice models. Mice were divided into 4 groups including control, diabetes, diabetes treated with mesenchymal stem cells, diabetes treated with vitamin C, and diabetes treated with mesenchymal stem cells + vitamin C. They made sure that wound healing occurred due to re-epithelialisation, not due to wound contraction. Daily oral vitamin C, 1.5 g/L was prescribed. It was found that although wound healing was significantly reduced in diabetic mice rather than controls, administration of topical mesenchymal stem cells, oral vitamin C, or both of them significantly improved wound healing in diabetic mice.

They found that vitamin C and mesenchymal stem cells had relatively similar effects on wound healing, but by giving these to the mice, the wound healing process significantly improved with the best effect found in the group that received both. They also determined the capillary density of the mice in the wound-healing process. They observed that vitamin C had greater effects on vascularization than other groups.

In fact, the vascularization rate in mice who received only vitamin C was higher than that of vitamin C + mesenchymal stem cells, and only mesenchymal stem cell groups (9).

Yun et al. (10), assessed the effects of topical silicone with vitamin C gel for improving wound healing in patients who underwent head and neck surgical procedures including scar revisions, closure of lacerations, and excision of a mass on the face. The topical gel was administered starting from the removal of stitches and continued for six months post-surgery. The control group received no additional treatment. They found that the height of the scar didn't differ between the two groups, but after 6 months, there was a significant difference between the two groups in terms of the height of the scar and silicone with vitamin C group showing a significantly shorter scar height. In terms of scar erythema, there was a significant difference between the two groups after 6 months. These results were also true about scar pigmentation melanin indices, and erythema. After six months, the scar in the experimental group improved significantly rather than the control group and the scar was more similar to normal skin. Additionally, the patients were significantly more satisfied in the experimental group. It should be noted that there were no significant differences between the two groups after two months, and the effects of this gel appeared after 6 months. There was no difference between different types of surgery in terms of all evaluations (10).

Shojania et al. (11), evaluated the effects of vitamin C–loaded with 20 μg/mL vitamin C in the human serum albumin nanoparticles on wound healing. They found that this nanoparticle significantly improved the wound healing process and increased wound healing process in 12 days (11).

Voss et al. (12), studied the effects of polysaccharide-based film containing propolis and vitamin C effects on wound healing. They

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found that this film had antibacterial effects on *E. coli* and *S. aureus* in in vitro studies and polysaccharide-based film containing both propolis and vitamin C had the best antibacterial effect. This film also showed a remarkable effect on wound healing in diabetic mice and accelerated wound closure. Also, this compound decreased the bacterial counts in diabetic wound by about 94%. The combination of propolis and vitamin C increased neovascularization in the histopathology assessment (12).

Gunton et al. (13), evaluated the wound healing effects of 500 mg vitamin C on foot ulcers. 16 patients were assessed in experimental (7 patients) and placebo groups (9 patients). The blood level of vitamin C reached the optimal level in these patients. They observed that the healing was better in the experimental group after 8 weeks of daily oral 500 mg vitamin C, significantly. 44% of patients with foot ulcers underwent foot amputation, but none of the patients in the experimental group underwent amputation. Blood vitamin C level had a negative correlation with baseline ulcer size (13).

Yarahmadi et al. (14), studied the platelet-rich plasma-fibrin glue (PRP-FG) dressing with and without oral vitamin E and C effects on wound healing of diabetic foot ulcer (DFU). They found that both types of dressings significantly reduced the sizes of wounds, but the dressing that contained vitamin C and E had a better effect compared to the other. Also, PRP-FG dressing with vitamin C and E decreased the levels of prooxidant-antioxidant balance, erythrocyte sedimentation rate, and C-reactive protein, significantly (14).

Discussion

In this review, we evaluated the effects of vitamin C on wound healing. We found that vitamin C had good effects on wound healing processes especially with neovascularization and improved wound closure, post-healing appearance, decreased bacterial load, and inflammatory markers (9-14). Before performing the study, we thought that there are a lot studies on wound healing effects of vitamin C, but after searching, we observed few studies were done in this context. It seems that more studies are required on the effects of different routes and dosages of vitamin C for wound healing.

Vitamin C is a vital nutrient that humans are unable to produce due to the lack of a crucial enzyme in the biosynthetic pathway. A significant deficiency in vitamin C can lead to a life-threatening condition known as scurvy. This disease is marked by the deterioration of collagenous tissues, which leads to inadequate wound healing and compromised immune function. Those suffering from scurvy are particularly vulnerable to severe infections, such as pneumonia. Furthermore, these infections can adversely affect vitamin C levels, as they increase inflammation and metabolic demands. Historical observations have indicated that scurvy frequently emerged in populations following outbreaks of infectious diseases, with instances of scurvy documented after respiratory infections, especially among individuals who are already experiencing malnutrition (15-18).

The daily requirement of vitamin C to prevent scurvy is relatively modest, estimated at approximately 10 mg/day. However, the recommended dietary allowances for vitamin C are significantly higher, often reaching up to one hundred times the intake levels suggested for many other vitamins. A daily consumption of 100–200 mg of vitamin C is deemed sufficient to achieve optimal plasma concentrations in healthy individuals, thereby addressing general needs for mitigating the risk of chronic diseases. Given the body's limited capacity to store this water-soluble vitamin, consistent and adequate intake is essential to avoid hypovitaminosis C. Epidemiological research shows that hypovitaminosis C, characterized by plasma vitamin C levels below 23 μmol/L and is relatively prevalent in the

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Western populations, with vitamin C deficiency (levels below 11 µmol/L) ranking as the fourth most common nutrient deficiency in the United States. Several factors contribute to the failure to meet dietary recommendations for vitamin C, even in regions where the food supply is generally adequate (17-22). These factors include suboptimal dietary practices, specific life stages or lifestyles that either restrict intake or elevate micronutrient needs (such as smoking or substance abuse), various health conditions, exposure to environmental pollutants and smoke (both active and passive), and economic constraints (such as low socioeconomic status and limited access to nutritious foods). Even those considered 'healthy' in industrialized nations may be at risk due to lifestyle choices, such as following restrictive diets or consuming unbalanced meals, as well as experiencing periods of heightened physical or psychological stress (23-25). The positive effects of vitamin C on inflammatory markers were studied by Yarahmadi et al. who demonstrated that vitamin C supplementation decreased the levels of erythrocyte sedimentation rate, C-reactive protein, and prooxidant-antioxidant balance (14). The authors mentioned the anti-inflammatory effects of both vitamin C and vitamin E. Vitamin E has several anti-inflammatory effects. Some animal studies have demonstrated that vitamin E, particularly in the forms of palm-derived tocotrienol and α-tocopherol, exerts its effects by inhibiting the production of interleukins IL-1 and IL-6. As a powerful antioxidant, vitamin E has the potential to neutralize free radicals before they activate NFκB, thereby reducing cytokine synthesis. Additionally, vitamin E has been found to inhibit COX-2, an enzyme that plays a critical role in inflammatory processes (26-28). So, vitamin E may increase the anti-inflammatory effects of vitamin C in Yarahmadi et al.'s study and further study should evaluate wound healing and anti-inflammatory effects of vitamin C and vitamin E, separately. Based on the studies, vitamin C increased vascularization and wound healing in animal and human models and all of them demonstrated the positive effects of vitamin C on wound healing (9-14). Limitations of human studies mainly include a short sample size; thus, a possibility exists should larger populations be studied. Also, it seems that different routes of vitamin C prescription like topical, oral, and intravenous, should be assessed and compared in terms of wound healing.

Conclusion

Although some studies were performed on vitamin C effects on wound healing and they demonstrated positive effects of vitamin C, the number of studies is limited. Studies have shown that vitamin C increases cutaneous revascularization, accelerates wound healing, decreases scar silhouette, and decreases levels of inflammatory markers. Further studies should be done on a greater population to evaluate the effects of different routes of vitamin C administration. It should be considered that designing the studies are not hard because the use of vitamin C is acceptable for normal people and patients.

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Conflicts of Interest

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https://doi.org/10.22037/orlfps.v10i1.47017

References

1. Gupta S, Andersen C, Black J, de Leon J, Fife C, JC LI, et al. Management of Chronic Wounds: Diagnosis, Preparation, Treatment, and Follow-up. Wounds: a compendium of clinical research and practice. 2017;29(9):S19-S36.

2. Morton LM, Phillips TJ. Wound healing and treating wounds: Differential diagnosis and evaluation of chronic wounds. Journal of the American Academy of Dermatology. 2016;74(4):589-605.

3. Bryant R, Nix D. Acute and chronic wounds: current management concepts: Elsevier Health Sciences; 2015.

4. Moores J. Vitamin C: a wound healing perspective. British journal of community nursing. 2013;18(Sup12):S6-S11.

5. Fisher BJ, Seropian IM, Kraskauskas D, Thakkar JN, Voelkel NF, Natarajan R. Ascorbic acid attenuates lipopolysaccharide-induced acute lung injury. Critical care medicine. 2011;39(6):1454-60.

6. Mohammed BM, Fisher BJ, Kraskauskas D, Farkas D, Brophy DF, Fowler III AA, et al. Vitamin C: a novel regulator of neutrophil extracellular trap formation. Nutrients. 2013;5(8):3131-50.

7. Mohammed BM, Fisher BJ, Huynh QK, Wijesinghe DS, Chalfant CE, Brophy DF, et al. Resolution of sterile inflammation: role for vitamin C. Mediators of inflammation. 2014;2014(1):173403.

8. Fisher BJ, Kraskauskas D, Martin EJ, Farkas D, Puri P, Massey HD, et al. Attenuation of sepsis-induced organ injury in mice by vitamin C. Journal of Parenteral and Enteral Nutrition. 2014;38(7):825-39.

9. Chokesuwattanaskul S, Sukpat S, Duangpatra J, Buppajarntham S, Decharatanachart P, Mutirangura A, et al. High dose oral vitamin C and mesenchymal stem cells aid wound healing in a diabetic mouse model. Journal of Wound Care. 2018;27(5):334-9.

10. Yun IS, Yoo H-S, Kim YO, Rah DK. Improved scar appearance with combined use of silicone gel and vitamin C for Asian patients: A comparative case series. Aesthetic plastic surgery. 2013;37:1176-81.

11. Shojania HR, Momeni-Moghaddam M, Hossini S-e, Armin M, Omrani Bidi J. MicroRNA 155 Downregulation by Vitamin C–Loaded Human Serum Albumin Nanoparticles During Cutaneous Wound Healing in Mice. The international journal of lower extremity wounds. 2019;18(2):143-52.

12. Voss GT, Gularte MS, Vogt AG, Giongo JL, Vaucher RA, Echenique JV, et al. Polysaccharide-based film loaded with vitamin C and propolis: A promising device to accelerate diabetic wound healing. International journal of pharmaceutics. 2018;552(1-2):340-51.

13. Gunton JE, Girgis CM, Lau T, Vicaretti M, Begg L, Flood V. Vitamin C improves healing of foot ulcers: A randomised, double-blind, placebo-controlled trial. British Journal of Nutrition. 2021;126(10):1451-8.

14. Yarahmadi A, Saeed Modaghegh M-H, Mostafavi-Pour Z, Azarpira N, Mousavian A, Bonakdaran S, et al. The effect of platelet-rich plasma-fibrin glue dressing in combination with oral vitamin E and C for treatment of non-healing diabetic foot ulcers: a randomized, double-blind, parallel-group, clinical trial. Expert Opinion on Biological Therapy. 2021;21(5):687-96.

15. Hemilä H. Vitamin C and infections. Nutrients. 2017;9(4):339.

16. Carr AC, McCall C. The role of vitamin C in the treatment of pain: new insights. Journal of translational medicine. 2017;15(1):77.

17. Magiorkinis E, Beloukas A, Diamantis A. Scurvy: past, present and future. European journal of internal medicine. 2011;22(2):147-52.

18. Dresen E, Lee ZY, Hill A, Notz Q, Patel JJ, Stoppe C. History of scurvy and use of vitamin C in critical illness: A narrative review. Nutrition in Clinical Practice. 2023;38(1):46-54.

19. Hambidge KM. Micronutrient bioavailability: Dietary Reference Intakes and a future perspective. The American journal of clinical nutrition. 2010;91(5):1430S-2S.

20. Schleicher RL, Carroll MD, Ford ES, Lacher DA. Serum vitamin C and the prevalence of vitamin C deficiency in the United States: 2003–2004 National Health and Nutrition Examination Survey (NHANES). The American journal of clinical nutrition. 2009;90(5):1252-63.

21. Carr AC, Lykkesfeldt J. Factors affecting the vitamin C dose-concentration relationship: Implications for global vitamin C dietary recommendations. Nutrients. 2023;15(7):1657.

22. Carr AC, Rowe S. Factors affecting vitamin C status and prevalence of deficiency: A global health perspective. Nutrients. 2020;12(7):1963.

23. Marcos A. A review of micronutrients and the immune system—Working in harmony to reduce the risk of infection. MDPI; 2021. p. 4180.

24. Percival SS. Nutrition and immunity: balancing diet and immune function. Nutrition Today. 2011;46(1):12-7.

25. Oz HS. Nutrients, infectious and inflammatory diseases. MDPI; 2017. p. 1085.

26. Jiang Q. Natural forms of vitamin E: metabolism, antioxidant, and anti-inflammatory activities and their role in disease prevention and therapy. Free Radical Biology and Medicine. 2014;72:76-90.

27. Nazrun A, Norazlina M, Norliza M, Nirwana SI. The anti-inflammatory role of vitamin e in prevention of osteoporosis. Advances in Pharmacological and Pharmaceutical Sciences. 2012;2012(1):142702.

28. Wallert M, Börmel L, Lorkowski S. Inflammatory diseases and vitamin E—what do we know and where do we go? Molecular Nutrition & Food Research. 2021;65(1):2000097.