PRINCIPLES AND PRACTICE OF CLINICAL RESEARCH
A Global Journal of Clinical Research

The Effect of Vitamin C Supplementation in Wound Healing: A Systematic Review of Randomized Controlled Trials

Ana Derzi[1], Andressa Masson[1], Carla Chavarria[1], Caterina Paiva[1,2], Cristiane Paganoti[1], Daniel Abad[1], Daniella Audi[1,3], Dermeval Neto[1], Dominique Schakel[1], Elianet Castillo[1], Felipe Cordova[1], Fernanda Malta[1,4], Hans-Udo Richarz[1,5], Helio Grullon[1], Iloba Njokanma[1,6], Ivan Duarte[1], Jose Fermin[1], Karen Bedirian[1,7,8], Kendya Reyes[1]*, Krista Cano[1], Lucia Salgueiro[1,13], Mobolaji Jaiyesimi[1], Monaly Ribeiro[1], Nicol Ortega[1], Onyekachi Aniume[1,9], Paula Sotelo[1,10], Santiago Pastrana-Brandes[1,11], Stefania Zapata[1], Tomas Marques[1], Vanessa Lessa[1,12]

[1]Harvard T.H. Chan School of Public Health – ECPE – PPCR Program; [2]Hospital das Clínicas, Universidade de São Paulo, Brazil; [3]Breast Medicine Service, Memorial Sloan Kettering Cancer Center, New York, NY, United States; [4]D'Or Institute for Research and Education, Rio de Janeiro, Brazil. Instituto Nacional de Cardiologia, Rio de Janeiro, Brazil; [5]Fascia Research Group, Department of Experimental Anesthesia, Ulm University, Ulm, Germany; [6]Department of Surgery, Lagos State University Teaching Hospital, Ikeja, Lagos, Nigeria; [7]Immune Oncology Research Institute, Yerevan, Armenia; [8]Yeolyan Hematology and Oncology Center, Yerevan, Armenia; [9]Department of Morbid Anatomy, University of Nigeria Teaching Hospital, Enugu; [10]Department of Traumatology – Hand Surgery, Hospital del Trabajador; Hand Surgery Department, MEDS Clinic, Santiago, Chile; [11]Department of Anatomy & Neurobiology, Graduate Medical Sciences, Boston University, Boston, MA, United States; [12]Irmandade Santa Casa de Misericórdia de São Paulo, São Paulo, Brazil and Clinica Cukiert, São Paulo, Brazil; [13]Hospital General de Niños "Pedro de Elizalde", Buenos Aires, Argentina.

Abstract

Background: *Vitamin C increases the proliferation of dermal fibroblasts, favoring collagen type III, and creates an elastic network that stores kinetic energy, allowing for elastic rebound. However, there is no solid evidence to support its supplementation.*

Objective: *This review evaluates the effects of vitamin C supplementation in skin and soft tissue wound healing.*

Methods: *We searched three databases (PubMed, Embase, and Cochrane Central Register of Controlled Trials) and included randomized controlled studies until July 10th, 2024, evaluating the effect of vitamin C administered by any route on wound healing of skin and soft tissues. We excluded traumatic injuries and burns. The risk of bias was assessed using the Cochrane risk-of-bias (RoB-1) tool.*

Results: *We identified 10 relevant studies, including 599 participants. Findings were summarized qualitatively. Studies that evaluated the effect of vitamin C on healing in the dental setting, pressure sores, and foot ulcers had mostly positive results. In contrast, studies on corneal tissue and hysterectomy showed no significant effect. All articles were unicentric and small, with unclear or high risk of bias, except for one low-risk study.*

Conclusions: *The available literature studying vitamin C in wound healing is inconsistent. Few studies exist relative to each other and have a small number of participants in different clinical scenarios, mainly with a high or unclear risk of bias. Larger and higher-quality studies are warranted. Also, this intervention is simple and low-cost. Further investigation may positively impact patients' quality of life and healthcare economic burden.*

Introduction

Ensuring adequate wound healing is essential for optimal surgical recovery. Avoiding complications, like surgical site infections (SSI), osteomyelitis, dehiscence, peri-wound dermatitis, edema, hematomas, and necrosis, that can further extend the hospital stay and delay overall recovery (Scalise et al., 2016).

Vitamin C is an essential nutrient that must be

*Corresponding author: kendya.reyes-2024@ppcr.org
Received: July 19, 2024 **Accepted:** November 19, 2024
Published: April 25, 2024
Editor: Felipe Fregni
Reviewers: J Fernando Camacho-Palma, Matheus Lobo, Lucas Maffioletti, Amanda Siqueira, Maria Bazan
Keywords: Vitamin C supplementation, wound healing, skin, soft tissue
DOI: https://doi.org/10.21801/ppcrj.2024.104.2

ingested as humans do not synthesize it. It plays an important role in many physiological processes, including antioxidant activity (particularly for the epidermis), immune modulation, and collagen synthesis, all vital for wound healing. Vitamin C participates explicitly as a cofactor of the enzymes prolyl-hydroxylase and lysyl-hydroxylase, facilitating proline and lysine amino-acid hydroxylation into procollagen, necessary to form mature collagen. Furthermore, there is some evidence that Vitamin C is related to an increased proliferation of dermal fibroblasts (DePhillipo et al., 2018; Bechara et al., 2022).

Considering these factors, evaluating the role of vitamin C supplementation in wound healing is important. Some preliminary studies have shown that treating deficient vitamin C in patients can quickly improve the wound-healing process, thereby minimizing hospital stay and resource expenses (Bikker et al., 2016). In addition, vitamin C supplementation's role in wound healing outcomes has not been explored thoroughly (Bechara et al., 2022). Currently, no guidelines establish the use and dose regimen of vitamin C or its prescription as an intervention in patients with wounds, leading to variation in dosages used in studies. To address this knowledge gap, this systematic review examines the evidence of vitamin C supplementation on wound healing.

Materials and Methods

This systematic review considers the recommendations of the Cochrane Handbook (J. Higgins et al., 2023) and the current Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines (Page et al., 2021).

Inclusion and Exclusion Criteria

The research question, "Does vitamin C supplementation improve wound healing?" and eligibility criteria were defined using the Population, Intervention, Comparison, Outcomes, and Study Design (PICOS) framework. Our PICOS was described as: (P) Adult patients with any type of skin and soft tissue wound, (I) Vitamin C supplementation administered by any route, (C) Placebo, (O) Skin and soft tissue healing assessed by any valid and reliable measurement and (S): Randomized Controlled Trials. We included randomized controlled trials (RCTs) with a target population of healthy or diseased patients with any type of wound, assessing vitamin C supplementation in any form, dose, or setting, using placebo or no treatment comparators as the control, and evaluating the effect on wound healing in all types of tissue as an outcome. We excluded observational studies, preclinical studies, animal studies, reviews and meta-analyses, articles without full-text availability, articles with incomplete results, and articles not in English. We also excluded studies that used other nutrient supplements together with vitamin C in the intervention arm, studies that used other nutrient supplements as the control, studies on wounds caused by traumatic injuries and burns, studies that measured inflammatory surrogates, assessed recovery that was not related to direct tissue improvement, and duplicate publications on the same study population.

Literature and Study Selection

By July 10th, 2024, based on our research question and a predefined search strategy, we had searched three databases: PubMed, Cochrane Central Register of Controlled Trials (CENTRAL), and EMBASE. The literature search was limited to publications in the English language, but no other restrictions were added. The basic concepts for our systematic electronic search were Vitamin C/Ascorbic Acid and Wound Healing/Healing/Incision(Cicatrix). A detailed search of the selected electronic databases is available in the supplementary material. Search results were imported to the Systematic Review Software Covidence (https://www.covidence.org/) for screening. After eliminating duplicates, the records were screened in titles, abstracts, and full texts. Two reviewers completed each step. When a consensus was not reached, a third reviewer resolved discrepancies.

Data Extraction and Synthesis

A data extraction form was created in Covidence, and all authors participated in manual data extraction through distribution in pairs for each article. Discrepancies in the extraction forms were resolved by consensus. The extraction form was designed to collect basic information about each study, including the year the study was published and the country where it was conducted, the methods used, the characteristics of the study population, including relevant comorbidities and vitamin C levels at baseline, information about the intervention and comparator, and wound healing outcomes and results.

Risk of Bias Assessment

The methodological quality of the studies was evaluated using version 1 of the Cochrane risk-of-bias (RoB) tool that was available and integrated into the platform used for data extraction. Two independent

reviewers conducted the RoB assessment, evaluating each domain as "low risk of bias" or "unclear risk of bias." If there was insufficient information that did not permit judgment of low risk or high risk of bias or any disagreement between the two reviewers, it was resolved by consensus.

Results

Description of the studies - selection and main characteristics

Based on an electronic literature search in PubMed, EMBASE, and Cochrane Central Register of Controlled Trials (CENTRAL), we identified 2,587 studies, and electronically exported them to Covidence. After removing 789 electronically and 41 manually identified duplicates, we screened the title and abstract of 1,757 studies. Of these, 52 were identified as relevant for conducting a full-text review to assess eligibility. Finally, ten randomized controlled studies could be included in the systematic review.

A PRISMA flow chart of the literature search is shown in Figure 1. Main study characteristics and risk of bias-scoring of each included study are shown in Tables 1 and 2.

The ten randomized controlled studies, which could be included in this review, were published between 1950 and 2022. The studies were conducted in Thailand (Pisalsitsakul et al., 2022; Yingcharoenthana et al., 2021), China (Li et al., 2018), Iran (Alishiri & Mosavi, 2019; Farahani-Jam et al., 2022), Australia (Gunton et al., 2021), The USA (Abrahmsohn et al., 1993), England (Taylor et al., 1974). Scotland (Boyd & Campbell, 1950), and India (Ramasubbu et al., 2020).

Only two studies (Farahani-Jam et al., 2022 and Gunton et al., 2021) adequately described the randomization and allocation concealment processes. Eight studies used placebo as a comparator. The control group of two trials consisted in usual care with no vitamin C supplementation (Li et al., 2018; Yingcharoenthana et al., 2021).

Five studies investigated the effect of vitamin C in the context of dental procedures or gingival healing, and three studies evaluated healing of ulcers (pressure-related, foot, and corneal). After photorefractive keratectomy, the remaining two studies evaluated wound dehiscence post hysterectomy and corneal healing.

Participants

Sample sizes varied from 16 to 161, totaling 559 participants randomly assigned to parallel groups with 2 or 3 arms. Regarding the baseline characteristics of the participants, the control and intervention groups were comparable in five of the ten studies. Across studies, the age of participants ranged between 10 years and 88 years. Two studies (Boyd & Campbell, 1950; Ramasubbu et al., 2020) did not report participant age data. The proportion between male and female participants was balanced in five studies (Abrahmsohn et al., 1993; Farahani-Jam et al., 2022; Li et al., 2018; Pisalsitsakul et al., 2022; Taylor et al., 1974) and unbalanced in three studies (Alishiri & Mosavi, 2019; Gunton et al., 2021; Yingcharoenthana et al., 2021). Two studies (Boyd & Campbell, 1950; Ramasubbu et al., 2020) did not report any data comparing the intervention and control groups. Furthermore, the survey by Gunton et al. (2021) showed further differences between the control and intervention groups in baseline characteristics beyond age, such as BMI, smoking status, and ulcer size, with higher values seen in the study subjects of the intervention group. .

Intervention and control characteristics

Route, dose, frequency, timing, and duration of vitamin C administration varied considerably across the studies. Peroral administration of vitamin C was the most frequently reported route, used in 8 studies with doses ranging from 250 mg to a maximum of 1500 mg per day. One study (Yingcharoenthana et al., 2021) administered topical vitamin C in gingival tissue in conjunction with oral administration, with no mention of dosage or concentration of the topical formulation. An intramucosal route was used in one study (Ramasubbu et al., 2020), administered in one dose of 200mg of vitamin C. Farahani-Jam et al. (2022) reported an intravenous administration of 1000 mg of vitamin C twice daily.

Regarding timing and duration of the intervention, four studies reported the administration of vitamin C after the procedure, ranging from 1 to 21 days, while 2 studies administered the vitamin C supplementation before and after the procedure (ranging from 1 to 3 days before and 1 to 4 days after) and one administered during the procedure. Three studies administered vitamin C to treat wounds unrelated to surgeries, and the intervention was initiated at the inclusion of participants in the trial for 1 to 2 months.

In eight studies, the control group was placebo, while only two trials reported a comparison with no additional intervention other than standard care. However, the "standard of care" is not clearly defined. The two studies that did not use placebo did not mention how the control group was treated, except for remarking that the subjects enrolled did not receive vitamin C. As they were treated with the same procedures as the intervention group, we have

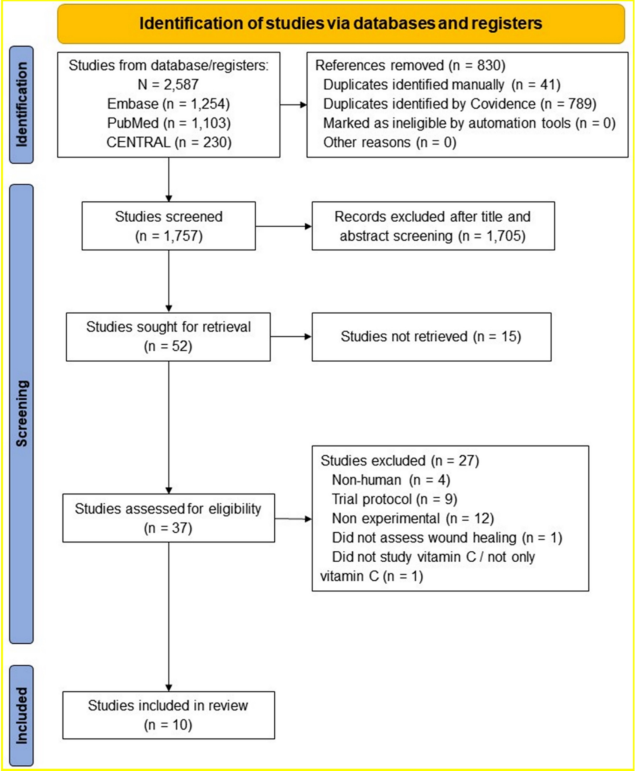

Figure 1: *PRISMA flow diagram for the systematic review.*

changed the "standard of care" to "usual care."

Outcomes

The choice of primary outcome varied across included studies. Two of the studies that evaluated dental healing (Pisalsitsakul et al., 2022; Yingcharoenthana et al., 2021) reported the percentage of reduction in the extraction wound size in three dimensions (buccolingual, mesiodistal, and depth) at three different time points (immediately to 7 days, immediately to 21 days, 7 days to 21 days). Both authors measured the bucco-lingual width and mesio-distal width with a caliper. They measured the socket depth with a periodontal probe using the cervical gingival margin of the adjacent tooth as the reference point.

Li et al. (2018) and Ramasubbu et al. (2020) assessed wound healing of dental implants using an ordinal scale (Landry index ranging from 1 to 5, with higher scores indicating better healing) at different time points (3, 7, and 14 days in the former and 7 days in the latter). Abrahmsohn et al. (1993) evaluated dental healing after extraction using a subjective dichotomous variable of healing rate (slow versus rapid healing) in one week.

From the studies addressing ulcer healing, Gunton et al. (2021) evaluated the percentage reduction of ulcer size at the closest visit of nearly 8 weeks, measured by two different methods (estimated using a silhouette 3D camera or by measuring ulcer dimensions). Taylor et al. (1974) assessed the healing of pressure sores by photography, measuring the proportion of complete wound healing and the percentage of wound area reduction after one month.

Two studies evaluated corneal epithelial healing. Alishiri & Mosavi (2019) evaluated corneal epithelial healing at 1 and 4 days after keratectomy surgery by a slit-lamp ruler, dividing into three possible healing categories (from total healing over partly healing to remaining measurable defects), Boyd and Campbell (1950) reported the time to complete epithelialization of corneal ulcers, measured by the intensity of the fluorescence of the ulcer in a dark room. Only one study evaluated the proportion of patients who developed wound dehiscence (Farahani-Jam et al., 2022); however, no specification of any time points and how the outcome was measured.

Effect of intervention on the outcome - main results

Regarding the main results from the studies included, most of them demonstrated significant effects of vitamin C in wound healing, except for the 2 studies that evaluated corneal healing (Alishiri & Mosavi, 2019; Boyd & Campbell, 1950) and one study that addressed wound dehiscence after hysterectomy (Farahani-Jam et al., 2022).

The studies that evaluated the effect of vitamin

Study Identifier	Design	Intervention	Control	Time-points and duration of follow-up	Total sample size	Baseline Age (years)	Baseline Gender (M/F)*	Wound type / procedure	Baseline vitamin C measured?	Primary outcome and outcome measure	Statistical methods employed	Main results
Yingcharoenthana 2021 Thailand	RCT, parallel group, split-mouth, 3 arms[#]	PO, 200mg t.i.d for 14 days with or without local vitamin C (no dosage information)	Usual care[§]	Immediately, 7 and 21 days	30	20.90 ± 2.47[1] 19.3±2.54[1] 20.0±2.98[1]	30/70	Dental extraction	No	Percentage of reduction in the extraction wound size between the extraction sites in three dimensions	Wilcoxon signed-rank test	The local and systemic administration of vitamin C lead to a reduction of socket depth at 21 days after extraction compared with control (p < 0.05)
Pisalsitsakul 2022 Thailand	RCT, parallel group, 3 arms	PO, 600 mg or 1500 mg, t.i.d., daily, for 10 days after extraction	Placebo[£]	Immediately, 7 and 21 days	32	18.68 ± 3.95[1]	41/59	Dental extraction	No	Percentage of reduction in the extraction wound size between the extraction sites in two dimension	Wilcoxon signed-rank test	Taking oral vitamin C 600 mg/d, t.i.d -enhances extraction wound healing by reducing mesiodistal extraction wound and reduces postoperative pain
Abrahmsohn 1993 USA	RCT, parallel group, 2 arms	PO, 500mg t.i.d, daily, for 3 weeks after surgery	Placebo[£]	1 week	161	10 - 39: n = 105 (65)[2] 40 - 89: n = 56 (35)	49 / 51	Dental extraction	No	Rapid healing Healing rates (2 categories: slow and rapid healing), based on criteria suggested by Dubois et al.	Chi-square and paired t-test	A greater proportion of patients in the vitamin C group had rapid healing compared to placebo (87.7% versus 62.5%), with statistical significance (p<0.01)
Li 2018 China	RCT, parallel group, 2 arms	PO, 300mg per day for 7 days after surgery	Usual care[§]	3, 7 and 14 days	128	A: 41.23[3] (19; 76) B: 46.00 (28; 64) C: 48.72 (29; 66) D: 43.83 (21; 68)	47/53	Dental implants	No	Wound healing assessed by ordinal scale (Landry index)	Mann-Whitney U test Generalized estimating equations	The experimental subgroups had significantly higher healing indices than the controls (p<0.05) at day 7 postsurgery for group B and day 14 postsurgery for groups A, B, and C. Group D displayed no difference between the experimental and control groups at any time point.
Ramasubbu et al., 2022 India	RCT, parallel group, 2 arms	Intramucosal, 200 mg, single dose	Placebo[£]	3 and 7 days after surgery	30	Not mentioned	Not mentioned	Wound healing after trans alveolar extraction of third molar teeth	No	Healing index score (Landry)	Not mentioned	L-ascorbic acid injection provides satisfactory healing after the 7th postoperative day of the dental extraction.
Gunton 2021 Australia	RCT, parallel group, 2 arms	PO, 500mg per day for 8 weeks	Placebo[£]	nearest appointment to 8 weeks	16	63.9 ± 22.2[1] 57.7±13.8	87.5/12.5[*]	Foot ulcers	30.5 µmol/L (IQR 4-52)[4]	Percentage of wound healing (reduction in ulcer size, measured using a silhouette 3D camera or by measuring ulcer dimensions)	Analysis was by ITT. Values not normally distributed – non-parametric test Kaplan-Meier analysis	Healing was significantly better in the vitamin C group (median 100% versus -14%, p=0.041). Healing without amputation occurred in all patients in the vitamin C group, while, 44% of controls had not healed their ulcer at the end of the study period.
Taylor 1974 England	RCT, parallel group, 2 arms	PO, 1000mg/day for 1 month after surgery	Placebo[£]	1 month	20	74.5 (54 - 88)[3]	40 /60	Pressure ulcers	Intervention: 22 µg Control: 24µg	Percentage of reduction in area of pressure sores**	Not Mentioned	Subjects in the vitamin C group had a higher percentage of wound area reduction compared to placebo (84% vs 42.7%) (p<0.05).
Farahani-Jam 2022 Iran	RCT, parallel group, 2 arms	IV, 1000mg/day for 2 days (one day before and one day during surgery)	Placebo[£]	Not mentioned	80	38.47 ± 3.8[1] 37.25 ± 5.6	0/100	Hysterectomy	Intervention: 4.77 ± 1.9 mg/dL Control: 5.37 ± 2.2 mg/dL	Wound dehiscence	Chi-square test or Fisher's Exact test	Although the rate of infection, wound dehiscence and the duration of hospitalization were lower in the vitamin C group, the difference was not
Alishiri 2019 Iran	RCT, parallel group, 2 arms	PO, 250mg/day, 3 days before and 4 days after surgery	Placebo[£]	1 and 4 days after surgery	51	29.34 ± 8.97 27.76 ± 7.21	36/64	Keratectomy	No	Complete corneal epithelial healing	t-test, Chi-square test, paired t-test Mann–Whitney	Complete corneal epithelial healing was more frequent in the vitamin C group (84%) than in the placebo group (65%), with no statistical significance (p=0.127).
Boyd et al., 1950 Scotland	RCT, parallel group, 2 arms	PO, 500mg t.i.d until complete healing	Placebo[£]	10 days	51	Not mentioned	Not mentioned	Corneal Ulcers	No	Time to corneal epithelization	Not mentioned	The administration of large doses of ascorbic acid had no significant effect on the healing time of superficial ulcers, but significantly accelerated the healing of deep ulcers.

CLSA – combination of local and systemic administration; CSA – control and systemic administration; F- female; IQR – interquartile range; ITT: Intention to treat; IV – intravenous; M- male; PO – orally; RCT – randomized clinical trial; TID – three times a day;

*data were presented as percentages

** - Assessed weekly in 3 ways: 1)subjectively by one of the researchers a purely clinical basis; 2)by pressure-area tracings performed independently by the department of physiotherapy; 3)photographic assessment

[#] - 3 arms:

a) Yingcharoenthana et al: Control and systemic administration / Control and combination of local and systemic administration / Systemic and combination of local and systemic administration

b) Pisalsitsakul et al.: Placebo vs. 600mg vitamin C / placebo vs. 1,500mg vitamin C / 60mmg vs. 1,500mg vitamin C.

[£] - Placebo:

a) Pisalsitsakul et al: calcium carbonate, sucrose, and carnauba wax coating;

b) Abrahmsohn et al.: did not specify what type of oral placebo was used;

c) Gunton et al.: inactive comparator which was identical-appearing glucosamine sulfate capsules (1000mg).

d) Taylor et al.: white tablets, inert placebo

e) Farahani-Jam et al: 100mL normal saline therapy.

f) Alishiri et al. and Ramasubbu et al.: did not provide additional information about placebo

g) Boyd et al.: tablet of identical appearance and taste

[§] - standard of care not specified by the author, it is only specified that a control group did not received vitamin C by any route.

[1] - mean ± standard-deviation

[2] - absolute and relative frequencies (N(%))

[3] - mean and minimum and maximum age in each group

[4] – median and IQR

Table 1: *Characteristics of the included studies.*

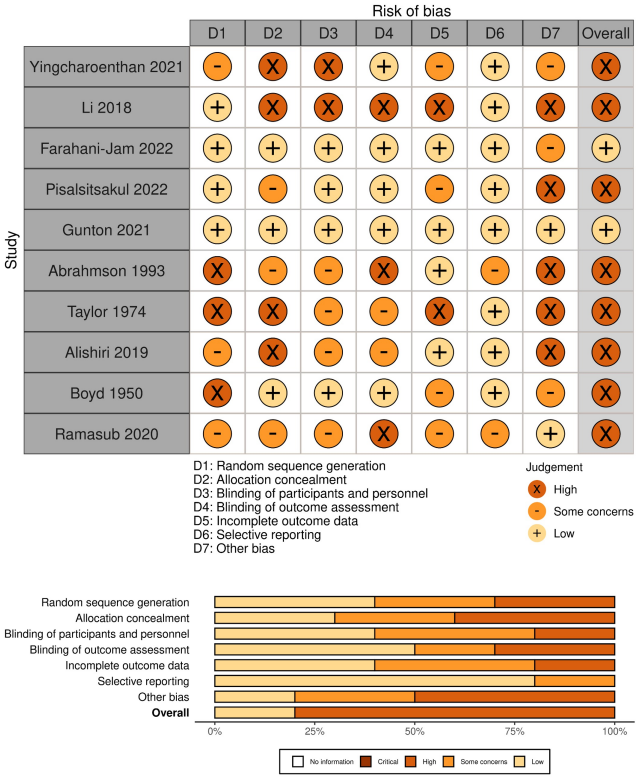

Table 2: *Risk of bias assessment.*

C on different outcomes related to gingival healing after dental extraction or implant reported positive effects. Regarding dental extraction, Yingcharoenthana et al. (2021) showed that local and systemic administration of vitamin C led to an improvement in soft tissue healing based on a reduction of socket depth at 21 days after extraction compared with control ($p<0.05$). Pisalsitsakul et al. (2022) showed enhanced tooth extraction wound healing in the 600 mg vitamin C group compared to placebo (57.3% vs. 48.3%) between day 0 and day 7 ($p=0.036$). However, the percentage of wound size reduction between the two extraction sites comparing placebo with vitamin C 1,500mg/day and vitamin C 600mg/day with 1,500mg/day were not significantly different ($p>0.05$).

Abrahmsohn et al. (1993) reported that the wounds of subjects who were administered vitamin C after dental extraction healed faster than those of the subjects in the placebo group and that the differences were statistically significant ($p<0.01$). Ramasubbu et al. (2020) reported statistically significant better healing index scores after the third molar extraction on the 7th postoperative day in the group that received a submucosal vitamin C injection compared to the placebo ($p=0.036$). The study that evaluated wound healing after dental implant (Li et al., 2018) reported results for 4 different subgroups, showing statistically significant benefit of vitamin C in at least one time-point in 3 of the 4 subgroups ($p<0.05$), with no difference in patients who received implants without bone grafting and in the absence of periodontitis. Both studies investigating the healing of ulcers also showed positive results: Gunton et al.,2021 demonstrated that reduction in ulcer size at 8 weeks was significantly better in the vitamin C group than in the glucosamine group (median 100% versus –14%, $p=0.041$). Similarly, Taylor et al. (1974) showed that the vitamin C group had a higher percentage of pressure-sores reduction one month after the start of treatment compared to placebo (84% vs 42.7%), a statistically significant difference ($p<0.005$).

In contrast, Farahani-Jam et al., 2022 could not show statistically significant differences in the rate of wound dehiscence after hysterectomy between the vitamin C group and the control group ($p=0.35$). Similarly, Alishiri et al. (2019) showed that complete corneal epithelial healing after keratectomy was more frequent in the vitamin C group (84%) than in the placebo group (65%), Still, they reported that the difference didn't reach the statistical significance ($p=0.127$). Boyd and Campbell (1950) also showed no significant difference in corneal ulcer epithelization with oral vitamin C.

Assessment of risk of bias in individual studies

Using the Cochrane RoB II tool, the quality as-

sessment of the reviewed studies revealed varying methodological levels of potential bias. Yingcharoenthana et al., 2021; Li et al., 2018; Abrahmsohn et al., 1993; Taylor et al., 1974; Boyd & Campbell et al., 1950; Ramasubbu et al., 2022; Pisalsitsakul et al., 2022; and Alishri et al., 2019 were rated with a high risk of bias, and their findings should therefore be interpreted with caution. Gunton et al., 2021 and Farahani-Jam et al., 2022 were the only studies that could be rated with a low risk of bias. The predominance of study designs with a high risk of bias highlights the importance of scrutinizing study designs and methodologies when evaluating the effects of vitamin C on wound healing and tissue recovery.

Discussion

This systematic review effectively highlights the potential advantages of Vitamin C supplementation to improve wound healing across various medical contexts, including surgery, dental extractions, pressure sores, foot ulcers, and corneal ulcers. The findings from the included studies reveal considerable variability, reflecting the complex interplay of factors involved in wound healing.

Importantly, the evidence suggests that Vitamin C can lead to significant improvements in specific types of wounds. Research focusing on pressure sores, foot ulcers, dental extractions, and implants indicates positive outcomes associated with Vitamin C supplementation. Conversely, there is limited efficacy for corneal ulcers and certain surgical procedures, such as hysterectomy and keratectomy. These contrasting results underscore that the effectiveness of Vitamin C may be context-dependent, influenced by the type of wound and individual patient factors.

A comprehensive analysis of the ten randomized controlled trials (RCTs) featured in this review identified notable inconsistencies in study designs, settings, sample sizes, participant characteristics, dosages, and routes of Vitamin C administration. This variability complicates the ability to generalize findings and draw definitive conclusions regarding its role in wound healing. While eight studies reported a beneficial effect of Vitamin C supplementation, the two studies showing adverse outcomes may have been underpowered, highlighting the need for cautious interpretation of the results. Further research is essential to fully explore and optimize the potential of Vitamin C in the healing process.

The review reveals considerable variation in Vitamin C supplementation protocols, with dosages ranging from 200 mg to 2 grams daily and encompassing various administration routes, including oral, topical, and intravenous methods. This variability underscores the pressing need for standardized protocols in future research, as inconsistent dosing and delivery methods may significantly contribute to the divergent outcomes observed across studies.

A notable strength of this review is its focused analysis of the isolated effects of Vitamin C in a clinical post-surgical context. By excluding studies that incorporated multi-nutrient supplementation, we effectively reduced confounding variables, allowing for a more precise evaluation of Vitamin C's role in wound healing. Furthermore, the majority of the included trials employed a double-blind design, which enhances the reliability of the findings, unlike the systematic review by Bechara et al. (2021). However, several limitations warrant consideration. A high risk of bias was identified in eight out of the ten studies, potentially undermining the internal validity of the results. Additionally, the small sample sizes in many studies restrict the generalizability of the findings to broader populations. The variability in participant characteristics such as health status and comorbidities complicates the interpretation of results, as baseline differences may influence healing outcomes. Moreover, the majority of studies did not assess baseline Vitamin C levels, which is essential for understanding the effects of supplementation in populations with varying nutritional statuses.

To maximize the benefits of future research, we must focus on several crucial areas: standardizing optimal Vitamin C dosages to establish clear and consistent dosages and administration routes for Vitamin C is vital. This standardization will facilitate meaningful comparisons across studies and improve the reliability of results. Controlling baseline levels by accounting for baseline Vitamin C levels, we can gain a more accurate understanding of the nutrient's impact on different patient populations, leading to more targeted interventions. Larger sample sizes expanding sample sizes to include various age groups and health conditions is essential for enhancing the robustness of findings, ensuring that the results apply to a broader spectrum of patients. Extended treatment periods by investigating longer treatment durations are important to truly assess the sustained benefits of Vitamin C on wound healing, providing insights that short-term studies may overlook (Li et al., 2018).

To conclude, despite identified limitations, the findings strongly indicate that Vitamin C supplementation can significantly improve post-surgery wound healing. This enhancement not only elevates patients' quality of life but also reduces hospitalization lengths. Considering the low cost and excellent safety profile of Vitamin C, particularly at doses of at least 500 mg per day (Gunton et al., 2021), it deserves further exploration as a valuable option in wound healing

protocols.

Conclusion

This systematic review assessed the effect of vitamin C supplementation on skin and soft tissue wound healing. The positive effects of vitamin C supplementation on wound healing across various clinical settings were promising and clinically important. More adequately powered, high-quality randomized controlled trials (RCTs) and, if necessary, controlled observational studies and quasi-experimental studies with longer study periods are needed.

Supplementary Materials

Search strategies

Funding

This research received no external funding.

Conflicts of Interest

The authors declare no conflict of interest.

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