SYSTEMATIC REVIEW

The effect of beta-glucan on wound healing: a systematic review and meta-analysis

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Abstract

Background wound healing involves inflammation, proliferation and remodeling, with prolonged healing times posing significant challenges. Beta-glucans, natural polysaccharides, may enhance this process.

Objective To evaluate the impact of beta-glucan on wound healing.

Method A systematic review of MEDLINE, Embase, Scopus, and Cochrane Central databases was conducted. Eligible studies included randomised controlled trials, clinical trials, cohort, and case-control studies comparing beta-glucan to other treatments. Only English-language studies were included, with no time restrictions. Screening and assessment were independently performed by two reviewers using Rayyan. The risk of bias was evaluated using the ROB-2 tool and the Newcastle-Ottawa Scale (NOS). A meta-analysis was performed on the included studies.

Result Beta-glucans promote immune cell activation and tissue repair, accelerating inflammation resolution. The meta-analysis of chronic wounds included two studies comprising a total of 354 participants, demonstrating a twofold increase in chronic wound healing rates at 12 weeks with the application of topical beta-glucan. In contrast, the analysis of acute wounds included two studies with a combined sample size of 290 participants. However, the findings for acute wounds were inconclusive.

Conclusion Beta-glucan demonstrates potential as an adjunctive therapy for chronic wounds, significantly accelerating healing rates. Its clinical utility warrants further exploration.

Registration PROSPERO CRD42024464191

Keywords beta-glucan, chronic wounds, diabetes, healing, ulcer

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Introduction

A great number of people with wounds must confront suffering, whether it be in terms of pain, expenses and time spent on treatment or opportunities missed during treatment.[1] Minimising wound healing time would be highly beneficial for patients. Wound healing is a multifaceted biological process that comprises several stages, including inflammation, proliferation, and remodeling.[2] Numerous preclinical and clinical investigations have demonstrated the beneficial effects of beta-glucans on wound healing.[3-10]

Beta-glucans are a heterogeneous group of natural polysaccharides found in plants, bacteria, fungi and algae, which possess many biological effects, such as

immunomodulatory, anticancer, antibacterial, antiviral, blood sugar lowering, cholesterol lowering and wound healing activities.[11, 12] The healing process involves the activation of immune cells (such as macrophages), skin cells (such as keratinocytes), and connective tissue cells (such as fibroblasts) that express dectin-1 receptors on their cell surfaces[13]. This activation leads to the recruitment of inflammatory cells to the site of injury, promoting phagocytosis, cytokine production, cellular proliferation, the formation of new epithelium and collagen deposition, all of which work in concert to promote wound healing.[14-16] Moreover, beta-glucans effectively address challenges in healing hard-to-treat wounds, particularly during the inflammatory, proliferation and remodeling phases.[17-21]

Chronic wounds usually result from underlying conditions, such as obesity or diabetes, which impair the process of normal wound healing.[22] In chronic wounds, monocytes exhibit a proclivity to differentiate into inflammatory phenotype macrophages, exacerbating local inflammation,[23] while the reduced presence of anti-inflammatory macrophages impairs critical processes such as re-epithelialisation and angiogenesis [24]. Additionally, the dysfunction of neutrophils, including impaired chemotaxis and phagocytosis, further compromises the immune response, contributing to delayed wound healing.[25] Previous studies revealed that beta-glucan improves the healing of chronic ulcers by stimulating the infiltration of neutrophils during the inflammatory phase,[26,27] and enhancing the phagocytic activity of macrophages, thereby facilitating the removal of pathogens and tissue debris.[28,29] Beta-glucan has been shown to enhance cell proliferation and migration.[30] It promotes collagen synthesis through multiple pathways and modulates the ratio of collagen type I to collagen type III, which is beneficial in reducing scar formation.[21] Additionally, several studies have demonstrated its potential in promoting angiogenesis by enhancing endothelial cell proliferation and migration via various signalling pathways, including HDAC5/MEF-2, PI3K/Akt/eNOS, Src/eNOS, AMPK/DAF16 and ERK1/2.[19,31,32] These mechanisms lead to increased levels of key cytokines, such as HIF-1α and VEGF,[20] which are critical for vascularisation and tissue integration. The overall mechanism of action of beta-glucan on wound healing is summarised in Figure 1.

To date, the precise mechanisms underlying beta-glucan's effects on wound healing remain unclear. However, activation of dectin-1, a primary beta-glucan receptor, is thought to play a significant role in this process, as it has been identified in several non-immune cells, including human fibroblasts, keratinocytes,[14,33,34] and endothelial cells.[19,20,31,35-38] Moreover, dectin-1 is proposed to contribute to angiogenesis through various pathways (Figure 2), including the stimulation of endothelial cell proliferation and migration. In addition to its role in wound healing, dectin-1 activation also supports peripheral nerve regeneration. In animal models of nerve injury, a correlation has been observed between dectin-1 activation and intraneural angiogenesis.[39] Additionally, a recent study explored the effects of beta-glucan in regenerative dentistry, aiming to identify supplements to repair injured dental pulp.[40] This study demonstrated that beta-glucan enhances dental pulp cell proliferation, migration and mineralisation. It also promotes integrin expression, collagen synthesis and mineralised matrix formation. Notably, previous evidence reported the expression of the dectin-1 receptor in human dental pulp,[41] suggesting that these observed effects of beta-glucan may be mediated through this specific receptor. However, further investigation is needed to elucidate the precise pathways involved in beta-glucan's actions.

More recent investigations have explored the use of beta-glucans for the treatment of hard-to-heal wounds, demonstrating that it exhibits good safety profiles and can facilitate the healing of cutaneous wounds in patients with chronic wounds or compromised healing, such as those with diabetes mellitus.[9,10,42] Due to the high costs and potential risks of antimicrobial resistance associated

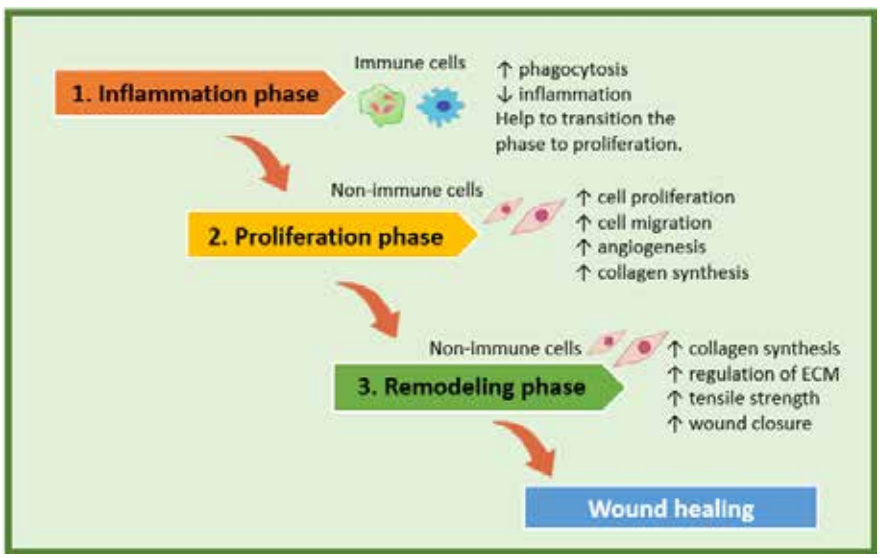

Figure 1. The role of beta-glucans in each phase of wound healing.

with conventional wound-care regimens, researchers have sought to develop alternative methods, including the use of natural bioactive extracts, to treat chronic wounds.[43] A recent clinical study evaluating the use of beta-glucan integrated gel for treating hard-to-heal wounds has reported promising results, showing that it can reduce healing time and be more cost-effective than standard treatments.[44] Furthermore, a higher percentage of wounds treated with beta-glucan gel completely healed compared to those receiving conventional care.[44,45] Taken together, these findings suggest that beta-glucan represents an effective and safe therapeutic option for the treatment of chronic wounds and offers financial advantages compared to conventional treatment methods.

Clinical investigations have demonstrated the efficacy of beta-glucans in promoting wound closure and reducing the cost of wound treatment.[44,46] Some studies have confirmed the beneficial effects of beta-glucans on wound healing, whether applied in the form of electrospun nanofibers or hydrogels.[10,47] Presently, commercial beta-glucan products are available in the form of semi-solid hydrogel that can be applied directly to the wound by finger. Consequently, wound dressings containing beta-glucans may represent a promising therapeutic approach for wound healing, with potential applications in medicine. However, reviews of studies on the effects of beta-glucan on wound healing in clinical settings still yield inconclusive results.[9, 10, 42, 48, 49] This systematic review and meta-analysis aimed to investigate the effect of beta-glucan on wound healing.

Methods

This systematic review and meta-analysis was conducted using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[50] This review was registered in the PROSPERO International Prospective Register of Systematic Reviews (CRD42024464191).

Literature search

A comprehensive, systematic search was conducted in four international electronic databases including MEDLINE, Embase, Scopus, and Cochrane Library using keywords extracted from Medical Subject Headings such as “wound healing” and “beta-glucan” from the earliest to December 2024. For example, the search strategy was in the Scopus database, including (beta-glucan OR β-glucan OR beta glucan OR β glucan) AND (wound AND healing). To combine phrases, the Boolean operators “OR” and “AND” were used. Two researchers independently searched extensively.

Inclusion and exclusion criteria

The inclusion criteria for this review were clinical studies, including observational studies, clinical trials, and randomised controlled trials, which compared the duration of wound healing treated with any formulas of beta-glucan and any other procedures, irrespective of the type of wound. Duplicate publications were excluded. Studies in which complete data could not be obtained, duplicate studies, in vitro studies, animal experiments, conference abstracts, reviews, case series and case reports were excluded.

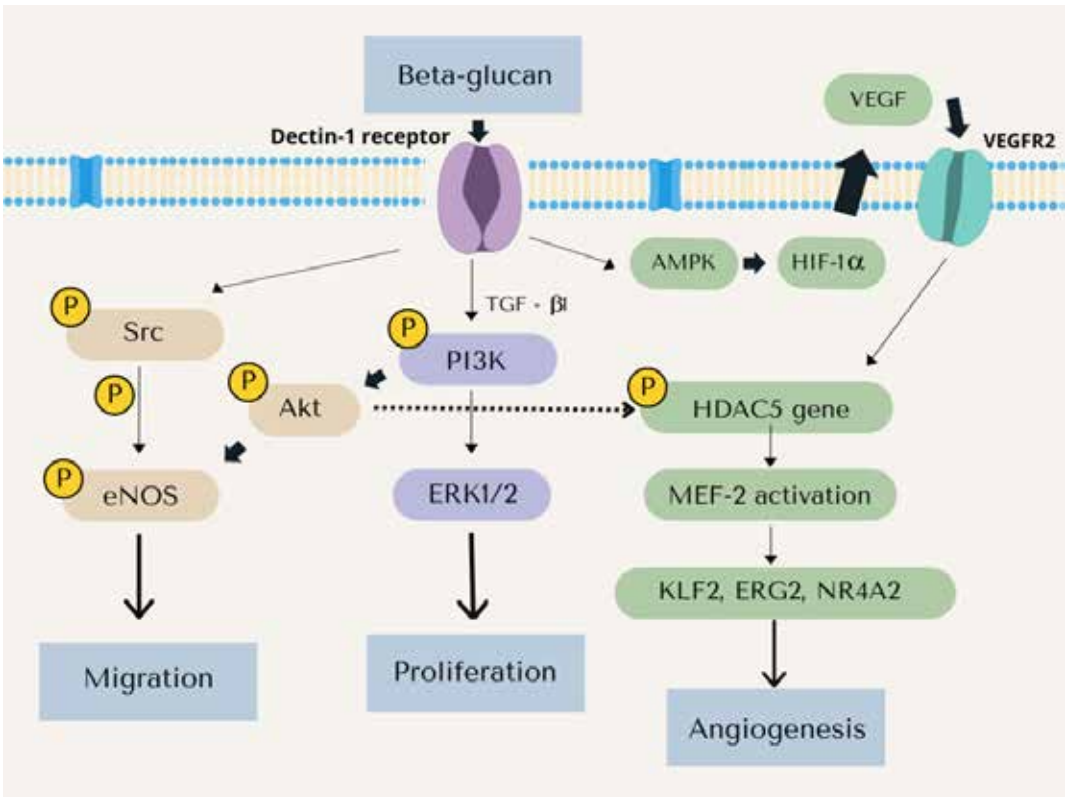

Figure 2. The mechanism of beta-glucan-induced angiogenesis

Articles screening and data extraction

Rayyan software was used to manage and organise the data during the screening process. Two researchers independently screened the study titles and abstracts, removed duplicate studies, and assessed them based on the predefined inclusion and exclusion criteria. While choosing the studies, any different opinions were resolved by discussion. Subsequently, the abstracts and full contents were examined to finalise the studies to be included. The extracted data included the following information: first author, publication year, sample size, types of beta-glucan, types of treatment used as control, the duration of healing, and types of wounds. Statistical data not reported in the articles. such as mean and standard deviation, were estimated using statistical method[51] prior to meta-analysis.

Quality assessment

Newcastle-Ottawa quality assessment scales were used to independently evaluate the quality of the included observational studies by two researchers. There are eight items consisting of four for selection, one for comparability, and three for outcome. Each study could be awarded a maximum of one star for each numbered item within the selection and outcome. A revised Cochrane Risk of Bias tool for randomised trials (RoB2) was used for the randomised controlled trials that were included. The five domains of bias were assessed. They are: randomisation processes; deviations from intended inventions; missing outcome data; measurement of outcomes; and selection of the reported results.

Statistical analysis

Data analysis was carried out using STATA V.14 software. Odds ratio (OR) and 95% CI were obtained by mean and standard deviation. Heterogeneity was assessed using the I^2 statistic, with significant heterogeneity was defined as an I^2 greater than 50%. In the analysis, random effects models were used. Wound healing rates for patients treated with beta-glucan and for the non-beta glucan groups, along with sample sizes for each group from the studies, were sourced to report the healing rate difference between beta-glucan and non-beta glucan groups.

Results

The process of the literature search is shown in Figure 3. From four databases, 618 studies were found after an extensive search of electronic resources, however, due to duplication, 288 articles were excluded from the study. The remaining 330 studies were further subdivided into 317 studies that did not align with our inclusion criteria by screening title and abstract. The full texts of the remaining 13 studies were then thoroughly assessed. Among these, three studies

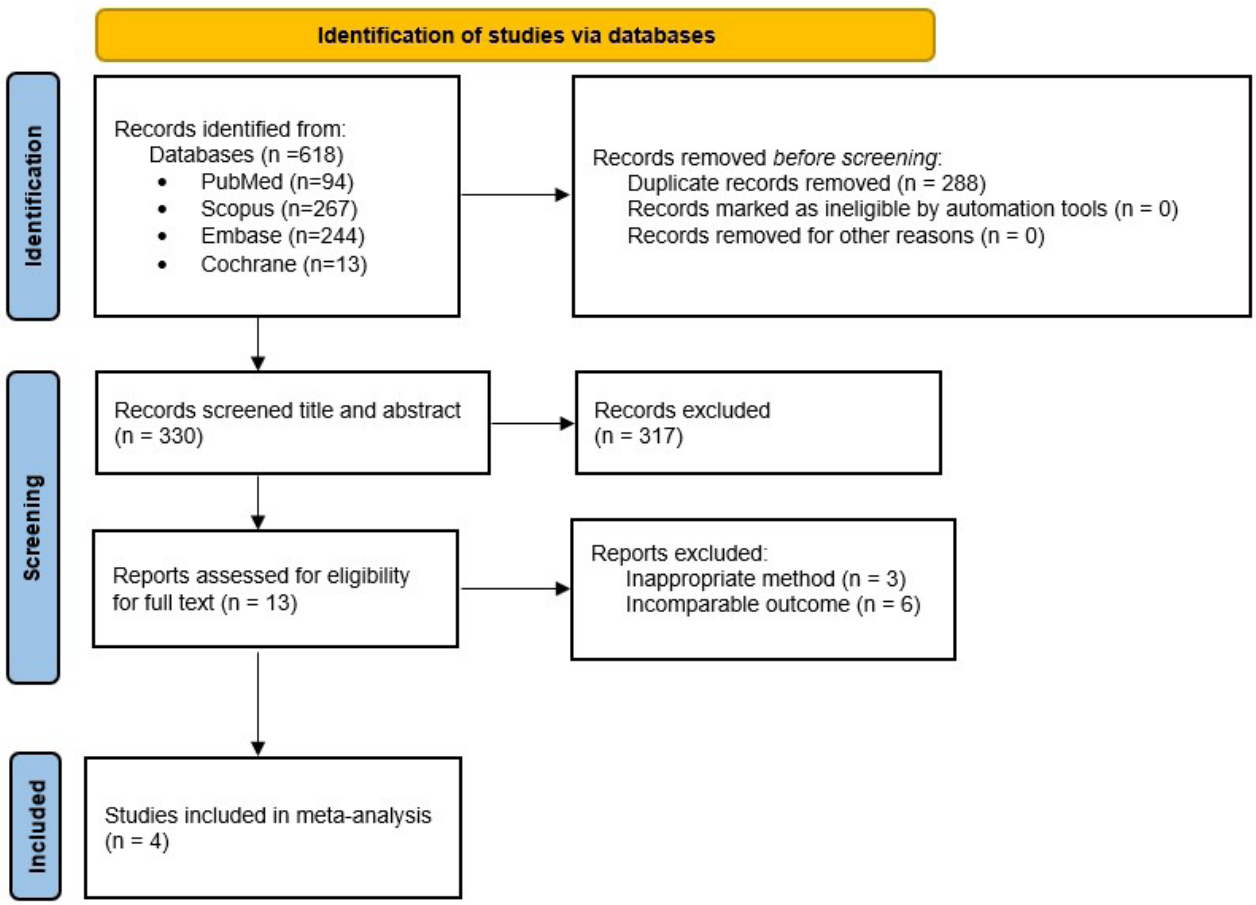

Figure 3. Flow diagram of the studies selection process

were excluded due to inappropriate methodologies, and six studies were excluded due to incomparable outcomes. Ultimately, this systematic review and meta-analysis included four articles.[9,10,48,49]

Characteristics of the included studies

Among the four studies included in this analysis, two are randomised controlled trials (RCT) while the other two are retrospective cohort studies. These studies are categorised according to the type of wound examined: two studies focus on the healing of burn wounds, which are classified as acute wounds, and the other two investigate chronic wounds, which are likely attributable to diabetes mellitus. In each study, beta-glucan was used as a wound dressing, and compared with alternative dressings, such as Biobrane® and methylcellulose. The average age of participants varied between studies, reflecting the differing etiologies of the wounds. The studies addressing acute wounds reported mean participant ages of 5.8 and 33.5 years, whereas those concerning chronic wounds reported mean ages of 54.5 and 61.7 years. Furthermore, the studies employed distinct outcome measures: those investigating acute wounds reported the time to complete healing (Table 1), while the studies focusing on chronic wounds assessed the number of wounds healed at a 12-week interval (Table 2).

Quality assessment

The quality assessment using a revised Cochrane RoB2 tool reveals that both RCTs included had a high risk of bias (Supporting information, Table S1). Nevertheless, Newcastle-Ottawa quality assessment scales results were six and seven out of nine for the remaining two cohort studies, recruited as shown in Supporting information, Table S2.

After extracting the data, we conducted a comparative analysis of various outcome measurements that exhibit intersections across the studies. In the studies of acute wounds, particular emphasis was placed on assessing the time required for complete epitheliali sation. In the studies of chronic wounds, it was observed that the comparable outcome measure was the number of wounds healed at 12-weeks.

The effect of beta-glucan on chronic wound healing

The two studies of chronic wounds compared the number of wounds healed at 12-weeks from the beta-glucan and placebo treated groups. There was no heterogeneity among these two studies ($I^2 = 0\%$, $p = 0.99$). A significantly increased number of healed wounds was observed in the beta-glucan group (OR = 2.14, 95% CI [1.31, 3.47]), $p < 0.01$; Figure 4).

In the study by Zykova et al[10] of diabetic foot ulcers, beta-glucan treatment led to significantly higher healing rates compared to the control group. By week 12, 81% of wounds in the beta-glucan group were fully healed, compared to 66% in the control group; this advantage was sustained through

Table 1. Baseline characteristics of the two studies included in the meta-analysis for acute wounds

Author, year	Type of study	Sample size	Formula of beta glucan	Formula of competitor	Wound type	Mean age (years)	Mean of days to heal (beta-glucan)	Mean of days to heal (Competitor)
Yang et al, 2003	Randomised controlled trials	12	B.G.C.®	Biobrane®	Acute	33.5	14.5	14.0
Lesher et al, 2011	Retrospective	278	B.G.C.®	Biobrane®	Acute	5.8	18.5	15.0

Table 2. Baseline characteristics of the two studies included in the meta-analysis for chronic wounds

First Author/ year	Type of study	Sample size	Formula of Beta glucan	Formula of competitor	Wound type	Mean age (years)	Healed rate of beta-glucan*	Healed rate of competitor*
Zykova et al, 2014	Randomised controlled trials	54	Soluble b-1,3/1,6-glucan	Methylcellulose	Chronic	61.7	15/27	10/27
Hunt et al, 2018	Retrospective	300	Bioactive soluble beta-glucan gel	Standard care	Chronic	54.5	116/144	91/138

*Healed rates were observed at a 12-week time point

week 24 (96% versus 75%). Beta-glucan also significantly accelerated wound size reduction, showing a 33% greater healing response by week 24 in chronic ulcers. The study by Hunt et al[9] included a variety of chronic wound types, such as venous leg ulcers, pressure ulcers and diabetic foot ulcers, all of which had been non-healing for over eight weeks. Despite standard care wound healing outcomes were initially reported as wound size reduction percentages rather than the proportion of fully healed wounds. For consistency with the other included study, we used the 12-week data which reported that 81% of wounds in the beta-glucan group were fully healed, compared to 66% in the control group. Additionally, Hunt et al[9] highlighted early healing progress, with 80% of wounds achieving ≥40% wound size reduction by week four in the beta-glucan group, compared to 62% in the control group. These findings demonstrate both the accelerated initial response and the sustained healing benefits of beta-glucan in chronic wounds. Patients treated with hydroigel reported high satisfaction and ease of use, with scores averaging 8.9 and 9.6 out of 10, respectively. The study also highlighted the cost-effectiveness of hydrogel, noting significant savings in patient care and wound management, making it a valuable option for chronic wound treatment, particularly in resource-limited settings.

The effect of beta-glucan on acute wound healing

On the other hand, two studies reported the effect of beta-glucan on time to complete epithelisation of acute wounds. Due to the lack of comparable data, the mean and standard deviation for the study by Lesher et al[48] were estimated from the reported median and range using a validated mathematical method.[51] There was considerable heterogeneity among these two studies ($I^2 = 76\%$, $p = 0.04$), but no significant relationship between use of beta-glucan and time-to-healed in this type of wound (MD=-1.70, 95% CI [-4.58, 1.18]), p = 0.25; Figure 5).

In the study by Yang et al[49] comparing Biobrane® and beta-glucan collagen (BGC) for split-thickness skin graft (STSG) donor sites, the results indicated no statistically significant difference in healing times between the two treatments. The Biobrane® dressing facilitated an average healing time of 14 days, while BGC showed a comparable healing time of 14.5 days. These findings suggest that BGC performs similarly to Biobrane® in terms of healing time for acute wounds. Similarly, the study by Lesher et al[48] evaluated the efficacy of Biobrane® versus BGC in treating pediatric partial-thickness burns and found that Biobrane® significantly reduced the median healing time to 9 days, compared to 13 days with BGC. These findings suggest that Biobrane® may provide a more effective and cost-efficient alternative for specific wound types.

Discussion

This meta-analysis evaluated the effect of topical beta-glucan on wound healing across various wound types. The results of our meta-analysis indicate that the topical application of beta-glucan significantly increases the number of wounds healed at the 12-week mark by twofold compared to non-beta-glucan treatments in chronic wounds. This finding highlights its potential benefit in managing chronic conditions such as diabetic wounds and persistent infections. Enhancing the efficiency and reducing the duration of dermal wound healing is beneficial for patients suffering from wounds,[52] especially chronic wounds.

Beta-glucan is a promising substance for wound healing due to its ability to promote cell growth, nerve regeneration and vasculari sation. This systematic review aimed to evaluate the clinical effects of beta-glucan on wound healing by incorporating various study designs, including randomised controlled trials and retrospective cohort studies while applying rigorous quality assessment. Although the results

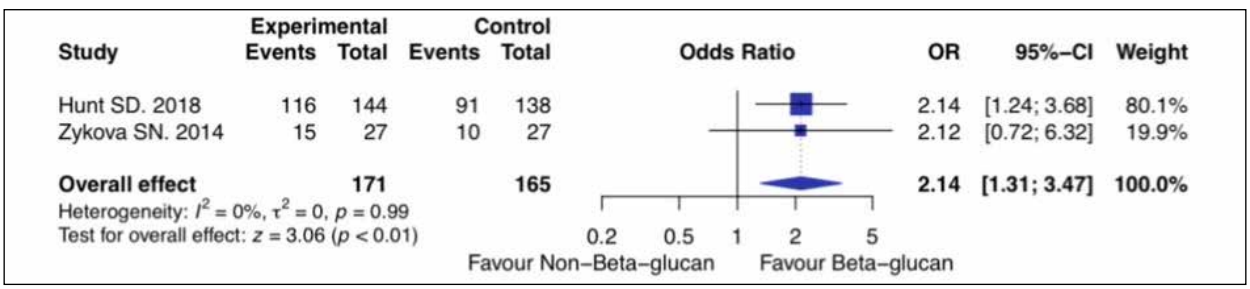

Figure 4. Forest plot of the effect of beta-glucan on wound healing in chronic wounds.

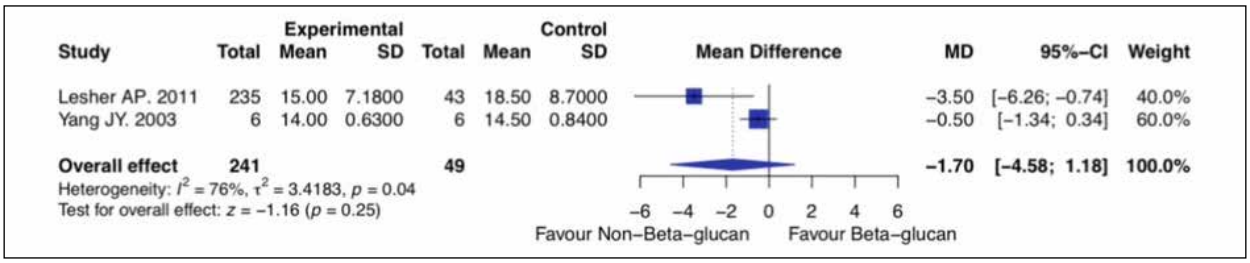

Figure 5. Forest plot of the effect of beta-glucan on wound healing in acute wounds.

from the meta-analysis showed a significant improvement in healing rates for chronic wounds, the evidence supporting the clinical use of beta-glucan remains inconclusive. This is due to the limited number of clinical studies examining its efficacy, the variability in beta-glucan formulations, and the differences in wound types. Furthermore, an attempt was made to evaluate publication bias using the symmetry of the funnel plot. However, due to the limited number of studies, a formal analysis of publication bias could not be conducted (Figure S1). Similarly, an Egger's test could not be performed for the same reason.

To critically analyse the limitations observed during data curation and meta-analysis, one of the main concerns is the variability in beta-glucan formulations used across studies. Currently, various formulations of beta-glucan are available on the market, derived from different sources such as mushrooms, yeast, barley and euglena. For instance, a previous study demonstrated that water-insoluble beta-glucan from *Saccharomyces cerevisiae* enhanced venous ulcer healing by increasing epithelial hyperplasia, angiogenesis and fibroblast proliferation.[53] Similarly, a bioactive beta-glucan gel has been shown to effectively manage 'hard-to-heal' wounds by promoting macrophage activation and angiogenesis.[54] Seo et al[18] conducted a comparative study to evaluate the wound-healing effects of various beta-glucans and found that all tested formulations were non-toxic to fibroblasts and effectively promoted keratinocyte migration. Notably, beta-glucan derived from mushrooms demonstrated the most favourable effects on dermal wound healing, emphasising the varying levels of healing properties among different beta-glucan formulations. These findings suggest that the formulation and source of beta-glucan may significantly influence its efficacy in wound healing. High-quality randomised clinical trials are needed to validate this hypothesis in clinical settings.

Regarding different wound types, such as acute and chronic wounds, the results from the meta-analysis indicated that beta-glucan did not significantly promote healing in acute wounds. This finding may be explained by the fundamental differences in the healing mechanisms of acute and chronic wounds. Acute wound healing primarily depends on the rapid resolution of inflammation and epithelial migration—processes that may not require the immunomodulatory effects of beta-glucan[55]. In contrast, beta-glucans ability to enhance macrophage activity and collagen synthesis is likely more relevant to the prolonged inflammatory phase characteristic of chronic wounds.[3, 56]

Nonetheless, this review has certain limitations that should be addressed. First, the meta-analysis included only two studies for each wound type, limiting the robustness of the findings. Among these, one study in each analysis was of low quality based on the risk of bias assessment, while the other was a retrospective study rather than a randomised controlled trial, further reducing the level of evidence. Additionally, the studies included in the acute wound analysis exhibited significant heterogeneity (I^2 = 76%, p = 0.04), raising concerns about the reliability of pooled estimates. These factors significantly constrain the generalisability of the results and necessitate caution in interpreting the findings. Future research should prioritise well-designed randomised controlled trials with larger sample sizes and standardised reporting to strengthen the evidence base.

This distinction emphasises the need for future research to explore beta-glucan formulations tailored to specific wound types. Subsequent studies could also investigate its effects on wound healing across diverse tissue types or its potential applications in regenerative medicine and dentistry. Such investigations may establish beta-glucan as a preferred pharmaceutical option for optimising treatment efficacy and improving patient outcomes, ultimately enhancing the quality of life for individuals with complex wound healing needs.

Conclusions

Topical application of beta-glucan has been shown to significantly increase healing rates at 12 weeks. While these findings suggest that topical beta-glucan may enhance healing responses in chronic wounds, further high-quality randomised clinical trials are needed to confirm its efficacy and identify the most effective formulations for clinical use.

Author contribution

Conceptualisation: T Somboonchokephisal and T Srisuwan
Methodology: S Saokaew
Investigation: T Somboonchokephisal; S Techachan
Data Analysis and Interpretation: T Somboonchokephisal
Writing – Original Draft: T Somboonchokephisal, T Kaokai
Writing – Review and Editing: T Somboonchokephisal, S Kanchanasurakit and T Srisuwan
Supervision: T Srisuwan
Funding Acquisition: T Srisuwan

Conflict of interest

The authors declare no conflict of interest.

Ethics statement

An ethics statement is not applicable.

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References

1. Zhu X, Olsson MM, Bajpai R, Järbrink K, Tang WE, Car J. Health-related quality of life and chronic wound characteristics among patients with chronic wounds treated in primary care: a cross-sectional study in Singapore. *Int Wound J.* 2022;19(5):1121–1132.
2. Singer AJ, Clark RA. Cutaneous Wound Healing. *New Eng J Med.* 1999;341(10):738–746.
3. Wei D, Zhang L, Williams DL, Browder W. Glucan stimulates human dermal fibroblast collagen biosynthesis through a nuclear factor-1 dependent mechanism. *Wound Repair Regen.* 2002;10(3):161–168.

4. Champault G, Barrat C. Inguinal hernia repair with beta glucan-coated mesh: Results at two-year follow up. *Hernia.* 2005;9(2):125–130.
5. Berdal M, Appelbom HI, Eikrem JH, Lund Å, Zykova S, Busund LT, et al. Aminated β-1,3-d-Glucan improves wound healing in diabetic db/db Mice. *Wound Repair Regen.* 2007;15(6):825–832.
6. Kwon AH, Qiu Z, Hashimoto M, Yamamoto K, Kimura T. Effects of medicinal mushroom *(Sparassis crispa)* on wound healing in Streptozotocin-induced diabetic rats. *Am J Surg.* 2009;197(4):503–509.
7. Woo YI, Park BJ, Kim HL, Lee MH, Kim J, Yang YI, et al. The biological activities of (1,3)-(1,6)-beta-d-Glucan and porous electrospun PLGA membranes containing beta-glucan in human dermal fibroblasts and adipose tissue-derived stem cells. *Biomedical Materials.* 2010;5(4):044109.
8. Berdal M, Appelbom HI, Eikrem JH, Lund A, Busund LT, Hanes R, et al. Aminated β-1,3-D-glucan has a dose-dependent effect on wound healing in diabetic db/db mice. *Wound Repair Regen.* 2011;19(5):579–587.
9. Hunt SD. A clinical observation evaluation of bioactive soluble beta-glucan gel compared with standard care. *J Wound Care.* 2018;27(9):620–630.
10. Zykova SN, Balandina KA, Vorokhobina NV, Kuznetsova AV, Engstad R, Zykova TA. Macrophage stimulating agent soluble yeast β-1,3/1,6-glucan as a topical treatment of diabetic foot and leg ulcers: a randomized, double blind, placebo-controlled Phase II study. *J Diabetes Investig.* 2014;5(4):392–399.
11. Wang Q, Sheng X, Shi A, Hu H, Yang Y, Liu L, et al. β-Glucans: relationships between modification, conformation and functional activities. *Molecules.* 2017;22(2):257.
12. Ciecierska A, Drywień ME, Hamulka J, Sadkowski T. Nutraceutical Functions of Beta-Glucans in Human Nutrition. *Rocz Panstw Zakl Hig.* 2019;70(4):315–324.
13. Murphy EJ, Rezoagli E, Major I, Rowan NJ, Laffey JG. β-Glucan metabolic and immunomodulatory properties and potential for clinical application. *J Fungi.* 2020;6(4):356.
14. van den Berg LM, Zijlstra-Willems EM, Richters CD, Ulrich MM, Geijtenbeek TB. Dectin-1 activation induces proliferation and migration of human keratinocytes enhancing wound re-epithelialization. *Cellular Immunol.* 2014;289(1-2):49–54.
15. Choi JA, Oh T-H, Choi J-S, Chang D-J, Joo C-K. Impact of β-1, 3-glucan isolated from *Euglena gracilis* on corneal epithelial cell migration and on wound healing in a rat alkali burn model. *Curr Eye Res.* 2013;38(12):1207–1213.
16. Nissola C, Marchioro MLK, de Souza Leite Mello EV, Guidi AC, de Medeiros DC, da Silva CG, et al. Hydrogel Containing (1 → 6)-β-D-Glucan (Lasiodiplodan) effectively promotes dermal wound healing. *Int J Biol Macromol.* 2021;183:316–330.
17. Xin Y, Ji H, Cho E, Roh KB, You J, Park D, et al. Immune-enhancing effect of water-soluble beta-glucan derived from enzymatic hydrolysis of yeast glucan. *Biochem Biophysics Rep.* 2022;30:101256.
18. Seo G, Hyun C, Choi S, Kim YM, Cho M. The Wound Healing Effect of Four Types of Beta-Glucan. Applied Biological Chemistry. 2019;62(1):20.
19. Choi M, Lee SM, Lee JW, Kim I, Pack C-G, Ha CH. Yeast beta-glucan mediates histone deacetylase 5-induced angiogenesis in vascular endothelial cells. *Int J Biol Macromol.* 2022;211:556–567.
20. Lei H, Zhao J, Li H, Fan D. Paramylon hydrogel: A bioactive polysaccharides hydrogel that scavenges ros and promotes angiogenesis for wound repair. *Carbohydrate Polymers.* 2022;289:119467.
21. Kang X, Lei J, Yang C, Zhang P, Li X, Zheng S, et al. A hybrid hydrogel composed of chitin and β-glucan for the effective management of wound healing and scarring. *Biomaterials Science.* 2022;10(20):6024–6036.
22. Sen CK. Human wound and its burden: updated 2020 compendium of estimates. *Adv Wound Care (New Rochelle).* 2021;10(5):281–292.
23. Boniakowski AE, Kimball AS, Jacobs BN, Kunkel SL, Gallagher KA. Macrophage-mediated inflammation in normal and diabetic wound healing. *J Immunol.* 2017;199(1):17–24.
24. Wilkinson HN, Hardman MJ. Wound Healing: Cellular mechanisms and pathological outcomes. *Open Biology.* 2020;10(9):200223.
25. Finley PJ, DeClue CE, Sell SA, DeBartolo JM, Shornick LP. Diabetic wounds exhibit decreased Ym1 and arginase expression with increased expression of IL-17 and IL-20. *Adv Wound Care (New Rochelle).* 2016;5(11):486–494.
26. Renke G, Baesso T, Paes R, Renke A. β-Glucan "Trained immunity" immunomodulatory properties potentiate tissue wound management and accelerate fitness recover. *ImmunoTargets Ther.* 2022;11:67–73.
27. Fusté NP, Guasch M, Guillen P, Anerillas C, Cemeli T, Pedraza N, et al. Barley β-glucan accelerates wound healing by favoring migration versus proliferation of human dermal fibroblasts. *Carbohydrate Polymer.* 2019;210:389–398.
28. Xin Y, Ji H, Cho E, Roh KB, You J, Park D, et al. Immune-enhancing effect of water-soluble beta-glucan derived from enzymatic hydrolysis of yeast glucan. *Biochem Biophys Rep.* 2022;30:101256.
29. Mata-Martínez P, Bergón-Gutiérrez M, Del Fresno C. Dectin-1 Signaling update: New perspectives for trained immunity. *Front Immunol.* 2022;13:812148.
30. Son HJ, Bae HC, Kim HJ, Lee DH, Han D-W, Park J-C. Effects of β-Glucan on proliferation and migration of fibroblasts. *Curr Appl Physics.* 2005;5(5):468–471.
31. Lee SM, Lee JW, Cho J, Choi S, Kim I, Pack C-G, et al. Yeast-derived particulate beta-glucan induced angiogenesis via regulating PI3K/Src and ERK1/2 signaling pathway. *Int J Biol Macromol.* 2024;269:131884.
32. Jia Z, Chen L, Gu D, Li X, Wen T, Li W. Lentinan-loaded GelMA hydrogel accelerates diabetic wound healing through enhanced angiogenesis and immune microenvironment modulation. *Int J Biol Macromol.*2024;264(pt 2):130716.
33. Inomata M, Amano S, Abe M, Hayashi T, Sakagami H. Innate immune response of human periodontal ligament fibroblasts via the Dectin-1/Syk pathway. *J Med Microbiol.* 2022;71(12). doi: 10.1099/jmm.0.001627
34. Tamai R, Sugamata M, Kiyoura Y. *Candida albicans* enhances invasion of human gingival epithelial cells and gingival fibroblasts by *Porphyromonas gingivalis*. *Microb Pathog.* 2011;51(4):250–254.
35. Zhang PP, Xin XF, Xu XY, Fang LP, Wu J, Shi Y. Toll-like Receptor 2 and Dectin-1 function as promising biomarker for *Aspergillus fumigatus* infection. *Exp Ther Med.* 2017;14(4):3836–3840.
36. Ha CH, Wang W, Jhun BS, Wong C, Hausser A, Pfizenmaier K, et al. Protein kinase D-dependent phosphorylation and nuclear export of histone deacetylase 5 mediates vascular endothelial growth factor-induced gene expression and angiogenesis. *J Biol Chem.* 2008;283(21):14590-9.
37. Urbich C, Rössig L, Kaluza D, Potente M, Boeckel J-N, Knau A, et al. hdac5 is a repressor of angiogenesis and determines the angiogenic gene expression pattern of endothelial cells. *Blood.* 2009;113(22):5669–5679.

38. Secchiero P, Gonelli A, Carnevale E, Milani D, Pandolfi A, Zella D, et al. TRAIL promotes the survival and proliferation of primary human vascular endothelial cells by activating the Akt and ERK pathways. *Circulation.* 2003;107(17):2250-2256.
39. Hsu AY-H, Hsieh S-T. Role of Dectin-1 in peripheral nerve injury. *Front Cell Neurosci.* 2022;16. doi: 10.3389/fncel.2022.810647
40. Kaokai T, Ittichaicharoen J, Srisuwan T. Beta-glucan promotes dental pulp healing by enhancing cell proliferation, migration, and mineralization. *J Dent Sci.* 2024.
41. Hasan A, Roome T, Wahid M, Ansari SA, Akhtar H, Jilani SNA, et al. Gene expression analysis of toll like Receptor 2 and 4, Dectin-1, qsteopontin and inflammatory cytokines in human dental pulp ex-vivo. *BMC Oral Health.* 2022;22(1):563.
42. King B, Barrett S, Cutting KF. Clinical evaluation of a bioactive beta-glucan gel in the treatment of 'hard-to-heal' wounds. *J Wound Care.* 2017;26(2):58–63.
43. Hajialyani M, Tewari D, Sobarzo-Sánchez E, Nabavi SM, Farzaei MH, Abdollahi M. Natural product-based nanomedicines for wound healing purposes: therapeutic targets and drug delivery systems. *Int J Nanomed.* 2018;13:5023–5043.
44. Elg F, Posnett J, Hunt S. Cost-effectiveness of soluble beta-glucan gel in hard-to-heal wounds: an evaluation. *J Wound Care.* 2019;28(7):454–460.
45. Cutting KF. The cost-effectiveness of a novel soluble beta-glucan gel. *J Wound Care.* 2017;26(5):228–234.
46. Karaaslan O, Kankaya Y, Sungur N, Kocer U, Sedat Cuzdan S, Sahin B, et al. Case series of topical and orally administered β-Glucan for the treatment of diabetic wounds: clinical study. *J Cutan Med Surg.* 2012;16(3):180–186.
47. Grip J, Engstad RE, Skjæveland I, Škalko-Basnet N, Isaksson J, Basnet P, et al. Beta-glucan-loaded nanofiber dressing improves wound healing in diabetic mice. *Eur J Pharm Sci.* 2018;121:269–280.
48. Lesher AP, Curry RH, Evans J, Smith VA, Fitzgerald MT, Cina RA, et al. Effectiveness of biobrane for treatment of partial-thickness burns in children. *J Pediat Surg.* 2011;46(9):1759–1763.
49. Yang JY, Chuang SS, Yang WG, Tsay PK. Egg membrane as a new biological dressing in split-thickness skin graft donor sites: a preliminary clinical evaluation. *Chang Gung Med J.* 2003;26(3):153–159.
50. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ.* 2021;372:n71.
51. Wan X, Wang W, Liu J, Tong T. Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range. *BMC Medl Res Methodol.* 2014;14(1):135.
52. Vogt TN, Koller FJ, Santos PND, Lenhani BE, Guimarães PRB, Kalinke LP. Quality of life assessment in chronic wound patients using the Wound-QoL and FLQA-Wk Instruments. *Invest Educ Enferm.* 2020;38(3):e11.
53. Medeiros SDV, Cordeiro SL, Cavalcanti JEC, Melchuna KM, Lima A, Filho IA, et al. Effects of purified *Saccharomyces cerevisiae* (1→3)-β-Glucan on venous ulcer healing. *Int J Mol Sci.* 2012;13(7):8142–8158.
54. King B, Barrett S, Cutting KF. Clinical evaluation of a bioactive beta-glucan gel in the treatment of 'hard-to-heal' wounds. *J Wound Care.* 2017;26(2):58–63.
55. Li J, Chen J, Kirsner R. Pathophysiology of acute wound healing. *Clin Dermatol.* 2007;25(1):9–18.
56. Son HJ, Han D-W, Baek HS, Lim HR, Lee MH, et al. Stimulated TNF-α release in macrophage and enhanced migration of dermal fibroblast by β-Glucan. *Curr Appl Phys*. 2007;7:e33–e36.

Supplementary Information

The effect of beta-glucan on duration of wound healing: A systematic review and meta-analysis

Publication bias assessment

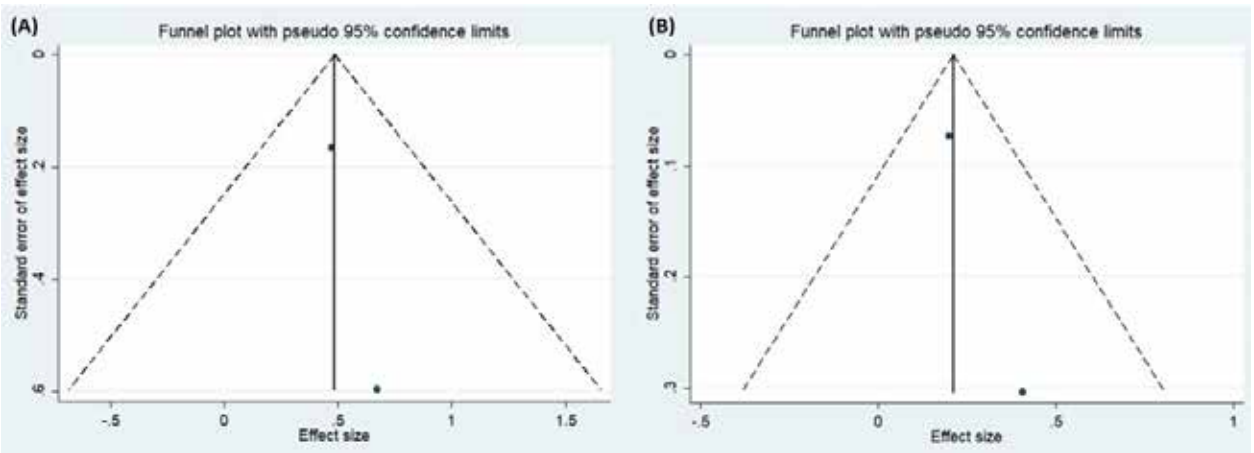

Figure S1. Funnel plot of the result of the effect of beta-glucan on the healing rate of acute (A) and chronic wounds (B).

Quality assessment of included studies

Table S1. Quality assessment of the two randomised controlled trials.

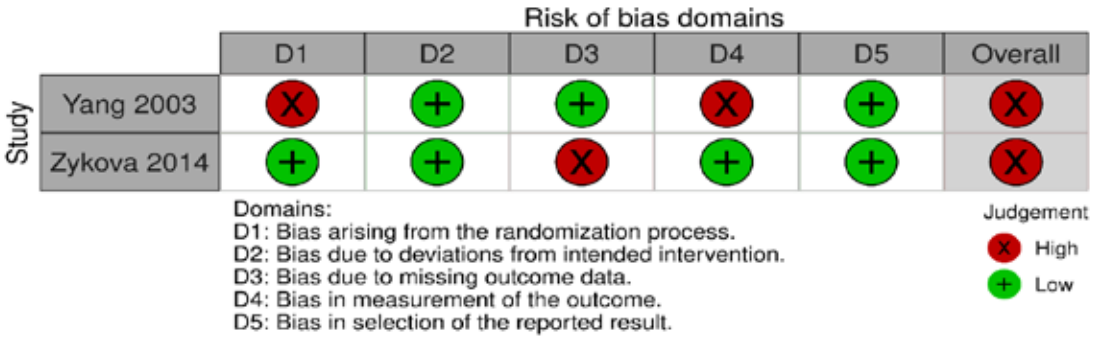

Table S2. Quality assessment of cohort studies included.

First author, year	Selection (4)			
	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study
Lesher, 2011	*	*	*	0
Hunt, 2018	*	*	*	0

Table S2. Quality assessment of cohort studies included continued.

First author, year	Comparability (2)		Outcome (3)			Total (9)
	Comparability of cohorts on the basis of the design or analysis		Assessment of outcome	Was follow-up long enough for outcomes to occur	Adequacy of follow-up of cohorts	
	Main factor	Additional factor				
Lesher, 2011	*	0	*	*	*	7/9
Hunt, 2018	*	0	0	*	*	6/9