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# Probiotic Therapy in Wound Healing: A Review of Key Evidence on Probiotic-Based Wound Repair

**Arash Zaminy[1], Mehrnaz Balani[2], Saber Abbaszadeh[3], Bahar Eslami[3], Mahoor Khosravani Hasan Kiadeh[4], Navid Pourzardosht [5]✉**

1 Burn and Regenerative Medicine Research Center, Guilan University of Medical Sciences, Rasht, Iran
2 Department of Anatomical Sciences, School of Medicine, Guilan University of Medical Sciences, Rasht, Iran
3 Medical Student, Student Research Committee, School of Medicine, Guilan University of MedicalSciences, Rasht, Iran
4 Cellular Molecular Genetics Group, Rasht Islamic Azad University, Rasht, Iran
5 School of Medicine Cellular and Molecular Research Center, Guilan University of Medical Sciences, Rasht, Iran

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✉ ***Correspondence to:***
Navid Pourzardosht

**Email:**
Pourzardosht@gums.ac.ir

**A B S T R A C T**

**Objective:** In recent years, increasing attention has been directed toward the role of the microbiome particularly probiotics in enhancing wound repair. This review aims to critically examine the most relevant scientific evidence regarding the role of probiotics in wound healing and to identify effective strains involved in reducing inflammation, enhancing collagen synthesis, and accelerating tissue regeneration.

**Methods:** In this narrative review, relevant studies were retrieved from major scientific databases using the keywords “probiotics,” “wound healing,” and “tissue regeneration.” The collected literature was analyzed and categorized based on probiotic strains, mechanisms of action, and reported clinical outcomes. A descriptive and analytical synthesis was then performed.

**Results:** Available evidence indicates that several *Lactobacillus* species particularly *Lactobacillus rhamnosus*, *L. reuteri*, *L. plantarum*, and *L. casei* demonstrate significant potential in accelerating wound healing through anti-inflammatory effects and enhanced collagen synthesis. In addition, *Bifidobacterium lactis* and *B. breve* have shown beneficial roles in epithelialization and tissue regeneration. Among yeasts, *Saccharomyces cerevisiae* and *S. boulardii* are associated with reduced inflammation and improved structural integrity of repaired tissue. Furthermore, multi-strain probiotic formulations appear to be more effective than single-strain preparations in controlling infection and improving clinical outcomes. Overall, the primary mechanisms involve modulation of the microbiome, inhibition of pathogenic microorganisms, and activation of tissue repair signaling pathways.

**Conclusion:** Probiotics represent a promising therapeutic strategy in wound management. Current evidence suggests that these microorganisms can support wound healing through restoration of microbial balance, reduction of inflammation, and stimulation of tissue regeneration. Nevertheless, further large-scale clinical trials are required to determine optimal dosing, strain specificity, and long-term safety profiles.

**Keywords:** Probiotics, wound healing, *Lactobacillus*, *Bifidobacterium*, microbiome, inflammation, tissue regeneration

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## Introduction

Wound healing is a dynamic and highly coordinated multistage biological process that encompasses hemostasis, inflammation, proliferation, and tissue remodeling. During this sequence of events, damaged tissues are progressively restored through the concerted activity of cells, growth factors, and the extracellular matrix (1). The quality and rate of this process are influenced by both systemic and environmental factors, and disruption at any stage may result in delayed healing or the development of chronic wounds (2,3).

In addition to intrinsic biological mechanisms, external and behavioral factors such as smoking, alcohol consumption, and poor glycemic control can significantly impair wound repair (4). Appropriate management of open wounds including bleeding control, proper cleansing, antiseptic care, sterile dressing, and adherence to hygiene principles plays a critical role in reducing complications and accelerating tissue regeneration (5).

Adequate nutrition, sufficient oxygen delivery, and tight regulation of inflammatory responses are also fundamental components of effective wound management in clinical practice (6). Deficiencies in key nutrients such as protein, vitamins, and essential trace elements, including zinc and vitamin C, can delay tissue repair and increase susceptibility to infection. Consequently, targeted nutritional support is considered a decisive factor in optimizing wound healing outcomes (7).

In recent years, increasing attention has been directed toward the role of the skin and gut microbiome in tissue repair processes (8). Probiotics, by maintaining microbial balance and inhibiting the growth of pathogenic bacteria, may reduce local inflammation and create a more favorable microenvironment for tissue regeneration (9). These properties have positioned probiotics as promising adjunctive agents in wound management strategies (8,9).

Preclinical studies further suggest that probiotics can stimulate the production of growth factors and enhance the functional activity of reparative cells (10). These mechanisms contribute to increased cellular proliferation, enhanced collagen synthesis, and improved granulation tissue formation, all of which are essential for effective tissue reconstruction (11).

Moreover, emerging clinical evidence indicates that probiotic supplementation may accelerate the healing of chronic and infected wounds while also reducing scar formation and infection-related complications (12). Nevertheless, well-designed, large-scale randomized controlled trials are still required to determine optimal dosage, administration routes, and long-term safety profiles.

Given the multifaceted role of probiotics in modulating inflammation, controlling infection, and promoting regenerative processes, this review aims to explore their therapeutic mechanisms, summarize current experimental and clinical evidence, and discuss future perspectives in wound management. The ultimate goal is to provide a comprehensive scientific framework for improving clinical strategies in wound care.

## Methods

This study was designed as a narrative–integrative review aimed at evaluating the existing evidence on the effects of probiotics in wound healing. Both preclinical (cellular and animal) and human clinical studies were systematically identified, reviewed, and analyzed. The primary objective was to assess the efficacy, safety, and underlying mechanisms of probiotic action in the wound healing process.

## Data Sources

Relevant articles were retrieved from major international scientific databases, including PubMed, Scopus, Web of Science, and Google Scholar, as well as national databases such as SID and Magiran.

## Time Frame

Studies published between 2010 and 2025 were included to ensure comprehensive coverage of both foundational and recent scientific evidence.

## Search Strategy

A structured search strategy was applied using keywords such as “probiotics,” “wound healing,” “Lactobacillus,” “Bifidobacterium,” and “inflammation,” combined with Boolean operators (AND, OR) to refine and optimize the search process.

## Inclusion Criteria

Eligible studies included clinical trials, experimental studies, and review articles investigating the role of probiotics in wound healing across human, animal, and cellular models. Only studies with full-text availability and clearly reported wound-healing or tissue-regenerative outcomes were considered.

## Exclusion Criteria

Studies unrelated to the topic, lacking full-text access, published as conference abstracts, or exhibiting low methodological quality were excluded from the analysis.

## Study Selection Process

Initially, studies were identified through systematic keyword-based searches across the selected databases. Titles and abstracts were then screened for relevance. Subsequently, full-text articles meeting the inclusion criteria were thoroughly assessed for eligibility. Data extraction included study design, probiotic strain, dosage, route of administration, and reported outcomes related to wound healing. The extracted data were then qualitatively synthesized and analyzed.

## Results

Based on the extracted data, the included studies comprised a heterogeneous body of evidence, including systematic and narrative reviews, in vitro experimental studies, animal model investigations, and clinical trials. The experimental models ranged from cell cultures and laboratory animals to human patients with various types of acute and chronic wounds.

A wide variety of probiotic strains were evaluated across these studies, most commonly including Lactobacillus rhamnosus, Lactobacillus reuteri, Lactobacillus plantarum, Lactobacillus casei, Lactobacillus acidophilus, Bifidobacterium lactis, and Bifidobacterium breve. In addition, several yeast-based probiotics, such as Saccharomyces boulardii and Saccharomyces cerevisiae, were also investigated. The routes of probiotic administration varied depending on the study design and wound model. These included oral supplementation, topical application, hydrogel-based formulations, ointments, and advanced delivery systems such as nanotechnology-based platforms and bioactive wound dressings. Overall, the findings consistently demonstrated that probiotic interventions were associated with reduced inflammatory responses, enhanced collagen deposition, accelerated epithelialization, inhibition of microbial infection, and improved overall wound healing outcomes.

A detailed summary of the included studies, including study design, probiotic strains, intervention methods, and key findings, is presented in Table 1.

As shown in Figure 1a, Lactobacillus plantarum (n=10, 17.9%) and L. rhamnosus (n=9, 16.1%) were the most frequently investigated probiotic strains, followed by L. reuteri (n=8, 14.3%). Multi-strain formulations accounted for 7 studies (12.5%). The distribution of study designs (Figure 1b) showed that animal-only studies were the most prevalent (n=22, 39.3%), followed by combined in vitro and animal studies (n=15, 26.8%). Clinical trials and RCTs accounted for 7 studies (12.5%), while review articles (n=6, 10.7%) and in vitro-only studies (n=4, 7.1%) constituted the remaining proportion. Two additional studies (3.6%) were classified as case reports or other designs.

**Table 1:** Preclinical and clinical studies investigating the effects of probiotics on wound healing

| Study type | Model / experimental condition | Probiotic used | Application / formulation | Key findings | Ref. |
|---|---|---|---|---|---|
| Systematic review | Humans and animals (mice, rats, surgical wounds) | Various probiotics | Oral / topical / nanotechnology-based systems | ↑ Re-epithelialization, ↑ angiogenesis, accelerated wound healing, no adverse effects | [13] |
| In vitro + animal | Gingival MSCs and oral wounds in mice | *Lactobacillus reuteri extract* | Interaction with P. gingivalis | ↑ MSC proliferation/migration, ↑ osteogenic differentiation, NLRP3 inflammasome inhibition | [14] |
| In vitro + animal | Infected full-thickness wounds in mice | *Lactobacillus rhamnosus (hydrogel ≤$10^7$ CFU/mL)* | Injectable hydrogel | ↓ P. aeruginosa infection, ↓ inflammation, ↑ collagen deposition, ↑ epithelial regeneration | [15] |
| Animal | Subcutaneous wounds in Wistar rats | *Probiotic strain VITSAMJ1* | Topical gel | Improved wound healing, antibacterial activity against S. aureus | [16] |
| In vitro + biomaterials | MSCs with GelNB-GelSH hydrogel | *L. reuteri* | Hydrogel dressing | Maintained probiotic activity, >90% antibacterial effect, accelerated infected wound healing | [17] |
| Narrative review | Chronic wounds | *Live biotherapeutic products* | Oral/topical | Antimicrobial activity, biofilm inhibition, immune modulation, ↓ scarring | [18] |
| In vitro | Human skin ECM | *Multiple strains (B. lactis, L. acidophilus, L. plantarum, S. boulardii)* | Mono-/multi-strain ($10^2$–$10^4$ CFU/mL) | ↑ growth factors, ↑ collagen I/III, ↑ fibronectin; multi-strain > single-strain | [19] |
| Narrative review | Wound microbiota | *Commensals and pathogens* | Microbiota modulation | Immune regulation and improved tissue regeneration | [20] |
| In vitro + animal | Skin wounds in mice | *L. paracasei TYM202* | Hydrogel dressing | ↓ inflammation, ↑ angiogenesis, ↑ collagen deposition | [21] |

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| Narrative review | Skin wounds | *Various probiotics* | Topical formulations | Immune modulation, ↑ growth factors, accelerated tissue repair | [22] |
| In vitro | Skin wounds | *L. plantarum-derived AgNPs* | Nanoparticles | Antibacterial, antioxidant, ~96% wound closure | [23] |
| Narrative review | Skin and intestinal wounds | *Multiple probiotics* | Oral/topical | Gut–skin axis modulation, fibroblast migration, immune regulation | [24] |
| Integrated review | Cellular, animal, clinical | *Multiple Lactobacillus spp.* | Various | ↓ infection, ↑ healing, reduced complications | [25] |
| In vitro + animal | Hydrogel system | *L. reuteri@FeTA* | Injectable hydrogel | Sustained lactic acid release, angiogenesis enhancement | [26] |
| Pilot clinical trial | Diabetic wounds (n=20) | *Multi-strain probiotic* | Oral | ↑ quality of life, ↓ pathogens, improved healing | [27] |
| Crossover clinical trial | Oral mucosal wounds (n=10) | *L. reuteri* | Oral tablets/oil | Faster healing trend (non-significant) | [28] |
| Animal | Burn wounds in mice | *Saccharomyces cerevisiae* | Hydrogel scaffold | ↑ epithelialization, ↑ collagen, ↓ scar size | [29] |
| Animal | Full-thickness wounds | *L. reuteri* | Topical ointment | ↑ collagen, ↓ inflammation, ↓ MPO activity | [30] |
| RCT | Episiotomy wounds | *L. casei 431* | Oral | Significant improvement (P = 0.03) | [31] |
| In vitro + ex vivo | Skin biofilm model | *Multi-lactobacilli* | Hydrocolloid dressing | Biofilm eradication, enhanced migration | [32] |
| Animal | MRSA wounds | *Probiotic microneedle patch* | Single application | Long-term antibacterial effect, sustained healing | [33] |
| Animal | S. aureus wounds | *LGG + BB-12* | Topical | ↓ inflammation, ↑ M2 macrophages | [34] |

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| Animal | Diabetic wounds | *L. bulgaricus & L. plantarum* | Topical | Immune regulation, improved healing | [35] |
| Animal | Oral mucosal wounds | *S. salivarius K12 + L. reuteri* | Topical | ↑ collagen, ↑ angiogenesis | [36] |
| Animal | Diabetic wounds | *L. reuteri + L. plantarum* | Topical | Reduced inflammation, enhanced regeneration | [37] |
| Animal | P. aeruginosa wounds | *L. rhamnosus GG* | Topical | ↓ microbial load, ↑ collagen | [38] |
| In vitro + animal | Hydrogel system | *L. acidophilus* | Injectable hydrogel | Sustained antibacterial effect | [39] |
| Preclinical | Diabetic foot ulcers | *L. reuteri + $H_2$ nanoparticles* | Active gel | Reduced ROS, accelerated healing | [40] |
| In vitro + animal | Gingival wounds | *L. reuteri* | Topical extract | ↑ migration, osteogenic differentiation | [41] |
| Animal | Skin wounds | *L. rhamnosus* | Oral | ↓ inflammation, ↑ angiogenesis | [42] |
| Clinical | Equine wounds | *Probiotic mixture* | Topical dressing | Accelerated healing | [43] |
| In vitro | Fibroblasts | *L. plantarum EPS* | Extract | ↑ migration and proliferation | [44] |
| Animal | Infected wounds | *Bacillus subtilis* | Hydrogel | 98.3% closure, ↑ collagen | [45] |
| In vitro + animal | Infected wounds | *L. casei* | SF/SA scaffold | Anti-inflammatory, scarless healing | [46] |
| Animal | Skin wounds | *Lactobacillus + B. subtilis* | Nanogel | Improved histological healing | [47] |
| Animal | Infected wounds | *Lactobacillus EVs* | Microneedle patch | ↓ microbes, ↑ angiogenesis | [48] |
| Animal | Full-thickness wounds | *Probiotic mixture* | Topical | Accelerated all healing phases | [49] |
| Animal | Skin wounds | *L. plantarum* | Topical | ↓ inflammation, ↑ fibroblasts | [50] |

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| Animal | Ischemic wounds | *NO-producing probiotics* | Patch | 2.52× faster healing | [51] |
| Animal | MRSA wounds | *L. paracasei* | Nanofiber scaffold | M2 polarization, antibacterial effect | [52] |
| Animal | Skin wounds | *L. plantarum + curcumin* | Sponge dressing | ↓ TNF-α, ↑ VEGF | [53] |
| Animal | Skin wounds | *P. pentosaceus* | Hydrogel + phycocyanin | ↓ oxidative stress, ↑ epithelialization | [54] |
| Preclinical | Skin wounds | *L. delbrueckii* | Spray | ↓ fibrosis and scarring | [55] |
| Animal | Fish wounds | *Shewanella putrefaciens* | Oral | ↑ antioxidant activity | [56] |
| Animal | Diabetic wounds | *L. plantarum LC38* | Oral | Accelerated closure | [57] |
| Pilot clinical | Oral wounds | *L. reuteri* | Oral/topical | No significant effect | [58] |
| Animal | MRSA wounds | *L. fermentum* | Microgel | 87.4% infection reduction | [59] |
| In vitro | Epithelial cells | *E. coli Nissle 1917 (EGF+)* | Genetic engineering | Enhanced migration | [60] |
| Clinical + review | Surgical patients | *Various probiotics* | Oral | Mixed outcomes | [61] |
| In vitro | Cell culture | *P. pentosaceus AF2* | Metabolites | Antibacterial and regenerative effects | [62] |
| Animal | MRSA wounds | *E. coli Nissle* | Alginate hydrogel | Faster healing | [63] |
| Animal | Skin wounds | *Multi-strain LAB/Bifidobacteria* | Topical | Stage-dependent improvement | [64] |
| In vitro + animal | Skin wounds | *L. plantarum MTCC 2621* | Gel | IL-6/IL-10 modulation | [65] |

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| Animal | Diabetic wounds | *Heat-killed L. chungangensis* | Postbiotic | Reduced inflammation | [66] |
| Animal | Skin wounds | *L. acidophilus / L. plantarum* | Oral | ↑ collagen, ↑ tensile strength | [67] |
| In vitro + animal | Skin wounds | *EVs of L. rhamnosus GG* | Injectable/topical | ↑ re-epithelialization, ↑ angiogenesis | [68] |

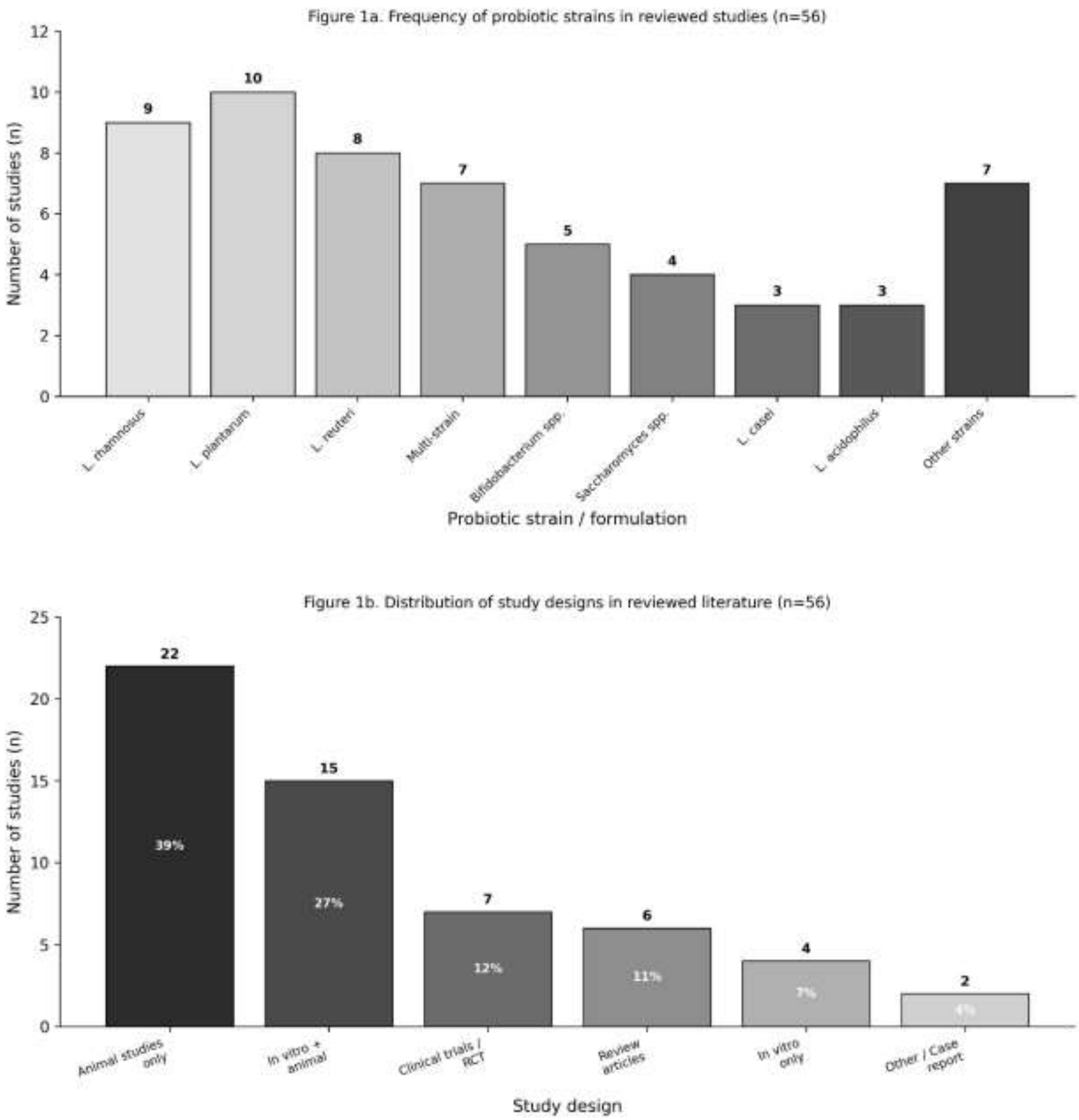


Figure 1: Probiotic strains and study designs in the reviewed literature (n=56 studies). a, Frequency of probiotic strains across included studies. L. plantarum (n=10), L. rhamnosus (n=9), and L. reuteri (n=8) were the most frequently investigated. b, Distribution of study designs. Animal-only studies (n=22, 39.3%) and in vitro/animal combined studies (n=15, 26.8%) dominated the evidence base

**Table 1:** Summary of probiotic strains identified in 56 reviewed studies. Values indicate number of studies (percentage). Lactobacillus species were most frequent (58.9%). See main text for detailed reference list.

| Strain/Formulation | Studies (n) | Percentage | Reference numbers (from table 1) |
|---|---|---|---|
| *L. Plantarum* | 10 | 17.9% | 19,35,37,44,50,53,57,65+2 others |
| *L.rhamnosus* | 9 | 16.1% | 15,17,34,38,42,48,64, 68,+1 other |
| *L.reuteri* | 8 | 14.3% | 14,17,26,28,30,36,41,58 |
| *Multi-Strain* | 7 | 12.5% | 19,27,34,49,64 + 2 others |
| *Bifidobacterium spp.* | 5 | 8.9% | 19,34,64 +2 others |
| *Saccharomyces spp.* | 4 | 7.1% | 19,29 + 2 others |
| *L. casei* | 3 | 5.4% | 31,46 + 1 other |
| *L. acidophilus* | 3 | 5.4% | 19,39,67 |
| Other strains | 7 | 12.5% | Various (single appearance) |
| TOTAL | 56 | 100% | - |

Table 1 Frequency of probiotic strains and formulations in the reviewed literature (n=56 studies). The table presents the number and percentage of studies investigating each probiotic strain or multi-strain formulation, along with corresponding reference numbers from the included publications. Lactobacillus species collectively accounted for 33 studies (58.9%), with L. plantarum (n=10, 17.9%), L. rhamnosus (n=9, 16.1%), and L. reuteri (n=8, 14.3%) being the most prevalent. Multi-strain formulations were evaluated in 7 studies (12.5%). "Other strains" includes L. casei, L. acidophilus, P. pentosaceus, B. subtilis, E. coli Nissle 1917, L. bulgaricus, L. paracasei, L. fermentum, L. delbrueckii, and L. chungangensis, each appearing once.

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## Discussion

The findings of this review indicate that probiotics represent a promising and multifaceted therapeutic strategy in wound management. Evidence synthesized from in vitro studies, animal models, and clinical trials suggests that these microorganisms can accelerate wound repair through multiple complementary mechanisms, including modulation of inflammatory responses, inhibition of pathogenic microbial growth, enhancement of epithelial barrier integrity, and stimulation of tissue regeneration. Collectively, these effects reflect a complex and dynamic interaction between probiotics, the host immune system, and the wound microbiome, ultimately contributing to improved healing outcomes (69).

One of the most consistent observations across the included studies is the prominent role of Lactobacillus species particularly Lactobacillus rhamnosus, L. reuteri, and L. plantarum in reducing inflammation and promoting collagen synthesis (70). These strains have been shown to downregulate pro-inflammatory cytokines such as TNF-α and IL-6 while enhancing anti-inflammatory mediators, thereby creating a microenvironment that supports fibroblast and keratinocyte function (71). In addition, the polarization of macrophages toward the M2 reparative phenotype appears to be a key mechanism underlying accelerated tissue repair during the proliferative phase (72). These findings are consistent with previous evidence emphasizing that a tightly regulated inflammatory response is essential for optimal wound healing.

Another important aspect is the antimicrobial potential of probiotics, which plays a crucial role in the management of infected wounds. Numerous strains included in this review demonstrated inhibitory effects against major wound pathogens, including Staphylococcus aureus and Pseudomonas aeruginosa, primarily through the production of antimicrobial metabolites such as lactic acid, hydrogen peroxide, and bacteriocins (73). Furthermore, their ability to disrupt biofilm formation an important contributor to chronic wound persistence is particularly significant. This effect has been especially pronounced in studies utilizing probiotic-loaded hydrogels and bioactive wound dressings, which enable simultaneous antimicrobial action and tissue regeneration at the wound site (74).

An additional key finding is the potential superiority of multi-strain probiotic formulations compared with single-strain interventions. Evidence suggests that probiotic combinations may exert synergistic effects, leading to broader immunomodulatory activity, enhanced growth factor expression, and more effective restoration of microbial homeostasis. Nevertheless, the optimal composition, strain ratios, and dosing strategies remain unclear and warrant further systematic investigation.

From a clinical perspective, although several trials have reported encouraging outcomes in chronic, diabetic, and surgical wounds, the overall evidence remains limited by small sample sizes, heterogeneity in study design, variability in formulations and dosing regimens, and relatively short follow-up periods. These limitations reduce the generalizability and strength of current clinical conclusions. Moreover, the absence of standardized probiotic preparations with defined stability, viability, and bioavailability profiles remains a major barrier to clinical translation (75).

From a technological standpoint, recent advances in drug delivery systems such as nanoparticles, hydrogels, nanofibers, and bioengineered wound dressings have opened new avenues for probiotic-based therapies. These platforms improve probiotic stability, enable controlled release, and enhance bacterial survival within the wound microenvironment, thereby increasing therapeutic efficacy. In particular, such systems may serve as promising adjuncts or alternatives to conventional antibiotic therapy in infected and chronic wounds (76).

Despite these promising findings, safety considerations must also be addressed. Although probiotics are generally regarded as safe, there remains a potential risk of opportunistic infection, particularly in immunocompromised or critically ill patients (77-82). Therefore, rigorous safety evaluation is essential, especially for long-term use and high-risk clinical populations.

## Conclusion

Overall, this review demonstrates that probiotics hold considerable promise as adjunctive therapeutic agents in wound management. However, translation of these findings into routine clinical practice requires well-designed randomized controlled trials, standardization of probiotic strains and dosages, and long-term safety assessments. Furthermore, a deeper understanding of probiotic–host–microbiome interactions may facilitate the development of more targeted and effective therapeutic strategies for wound healing in the future.

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The authors did not receive support from any organization for the submitted work.

### Competing interests

The authors have no competing interests to declare that are relevant to the content of this article.

### Ethics approval

This study was performed in line with the principles of the Declaration of Helsinki.

### Consent to participate

Informed consent was obtained from all individual participants included in the study.

## Author contributions

XX: Conceptualization, the original draft writing, investigation, writing including reviewing and editing and investigation and formal analysis; XX: Conceptualization, supervision, and project administration; XX and XX Conceptualization, the original draft writing, investigation, writing including reviewing and editing.

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