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Probiotic Therapy in Burn Wound Healing: A Concise Review of Preclinical and Clinical Evidence

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A B S T R A C T

Objective: Burns are among the most common forms of skin injury and are frequently associated with high rates of complications, infections, and delayed wound healing. Key factors that impede recovery include disruption of the skin barrier, microbial imbalance (dysbiosis), persistent inflammation, and elevated oxidative stress. In recent years, probiotic therapy has emerged as a novel and complementary strategy to enhance wound repair, primarily through modulation of immune responses and the microbiota of both the skin and gut.

Methods: This concise review systematically examined peer-reviewed literature indexed in reputable databases, including PubMed, Scopus, and Web of Science. Preclinical studies, encompassing cellular and animal models, as well as clinical trials investigating the effects of probiotics on burn wound healing, were analyzed. The review focused on publications from 2010 to 2025, with emphasis on probiotic strains, routes of administration, and wound healing outcomes.

Results: Probiotics, particularly *Lactobacillus plantarum*, have demonstrated notable efficacy in burn wound repair by inhibiting pathogenic microorganisms, reducing inflammation, and accelerating epithelialization, even under infected or diabetic conditions. Other *Lactobacillus* strains, including *L. acidophilus*, *L. rhamnosus*, and *L. casei*, facilitate faster wound recovery by enhancing fibroblast activity and shortening the inflammatory phase. In contrast, *Bifidobacterium* species primarily support burn patients by strengthening mucosal immunity and mitigating systemic infections. Overall, both topical and oral probiotic interventions appear to be safe and effective adjunctive strategies, exerting their effects through modulation of the microbiome and control of inflammation.

Conclusion: Current preclinical and clinical evidence suggests that probiotic therapy can serve as a safe and effective approach to accelerate burn wound healing via modulation of the microbiome and inflammatory responses. Nonetheless, well-designed randomized clinical trials are required to determine the optimal strains, dosages, and routes of administration for maximum therapeutic benefit.

Keywords: Probiotic therapy, Burn wounds, Wound healing, Microbiota, Inflammation, Treatment

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Introduction

Burn injuries rank among the most common and complex forms of skin trauma, affecting millions of individuals worldwide each year and imposing substantial mortality, long-term disability, and significant healthcare costs [1]. Particularly in moderate to severe cases, burn wounds frequently exhibit delayed healing, recurrent infections, pathological scar formation, and reduced quality of life, remaining a major public health challenge [2]. Despite significant advances in supportive care and surgical interventions, effective management of burn wounds continues to represent a formidable clinical challenge [1,2].

Etiologically, burns may result from thermal, chemical, electrical, frictional, or radiative insults, with variable depth and severity of skin damage [3]. Disruption of the skin's physical barrier compromises its protective functions, increases susceptibility to microbial invasion, and impairs local homeostasis [4]. These conditions create a permissive environment for pathogen colonization and both local and systemic infections, which are among the leading causes of delayed wound healing and increased mortality in burn patients [5].

From a pathophysiological perspective, burn wound repair is a dynamic, multi-phase process encompassing inflammation, proliferation, and remodeling, all of which are frequently dysregulated in affected patients [6]. Persistent inflammation, elevated levels of pro-inflammatory cytokines, oxidative stress, impaired fibroblast and keratinocyte function, reduced angiogenesis, and microbial imbalance (dysbiosis) represent critical factors that hinder recovery [7]. These sustained disturbances not only delay wound closure but also increase the risk of hypertrophic and keloid scar formation [8].

Current standard therapies for burn wounds include debridement, topical dressings, antibiotics, anti-inflammatory agents, silver sulfadiazine, skin grafting, and other surgical interventions [9]. While these strategies are effective in controlling infection and preserving patient survival, they are associated with notable limitations and adverse effects [9,10]. Antibiotic resistance, cytotoxicity, delayed epithelialization, allergic reactions, and disruption of the natural skin microbiome are among the unintended consequences of conventional chemical therapies, highlighting the need for safer, complementary approaches [10,11].

In this context, growing attention has been directed toward the skin and gut microbiomes due to their roles in modulating immune, inflammatory, and reparative responses, offering new therapeutic avenues for burn wound management [12]. Accumulating evidence indicates that microbial imbalance can exacerbate inflammation, promote pathogen colonization, and impair tissue repair processes [13]. Interventions capable of restoring microbial equilibrium, therefore, hold promise for enhancing wound healing outcomes [12,13].

Probiotics are defined as live microorganisms that, when administered in adequate amounts, confer health benefits on the host [14]. These organisms exert a range of beneficial effects including pathogen inhibition, immune modulation, inflammation reduction, stimulation of growth factors, promotion of angiogenesis, and reinforcement of epithelial barrier function demonstrating significant potential in accelerating skin wound healing, including burn wounds [14,15]. Administration of probiotics, whether orally, topically, or incorporated into advanced bioactive dressings, represents a low-risk, cost-effective strategy that has garnered considerable research interest [15,16].

Given the substantial growth of in vitro, animal, and clinical studies in recent years, a comprehensive synthesis of current evidence regarding the role of probiotic therapy in burn wound healing is warranted [17]. Accordingly, this concise review aims to examine and analyze preclinical (cellular and animal) and clinical studies exploring the effects of probiotics on burn wound repair, elucidate underlying mechanisms of action, and evaluate their potential as an adjunctive therapeutic strategy in clinical practice.

Methods

This study is a concise narrative review of the current scientific evidence regarding the effects of probiotics on burn wound healing, encompassing both preclinical

investigations (cellular and animal models) and human clinical studies. The primary objective of this review was to synthesize and critically analyze available data on the efficacy, safety, and mechanisms of action of probiotics in accelerating burn wound repair and mitigating associated complications.

Data Sources

Relevant studies were identified through comprehensive searches of international databases, including Google Scholar, PubMed, Scopus, and Web of Science, as well as Persian-language repositories such as SID and Magiran.

Search Period

The literature search was limited to publications from 2010 to 2025 to capture both foundational studies and the most recent findings regarding the application of probiotics in burn wound healing.

Keywords and Search Strategy

A combination of primary keywords, MeSH terms, and their equivalents was employed to identify pertinent studies. The main search terms included:

- Probiotics
- Burn wound OR Burns OR Burn injury
- Wound healing
- Skin microbiota OR Gut microbiota
- Lactobacillus OR Bifidobacterium
- Inflammation OR Immune modulation

The search strategy was structured using Boolean operators as follows:

(Probiotics OR "Lactobacillus" OR "Bifidobacterium")
AND ("Burn wound" OR Burns OR "Burn injury")
AND ("Wound healing" OR Inflammation OR "Immune modulation")
AND ("Skin microbiota" OR "Gut microbiota")

Inclusion Criteria

Studies were eligible for inclusion if they met the following criteria:

Original research articles, reviews, experimental studies, clinical trials, and preclinical studies examining the effects of probiotics on burn wound healing.

Investigations conducted in cellular, animal, or human models.

Publications in English or Persian with full-text availability.

Studies reporting outcomes such as wound closure rate, epithelialization, inflammation, infection, collagen synthesis, or underlying molecular mechanisms.

Exclusion Criteria

Studies were excluded based on the following parameters:

Research unrelated to burn wounds or probiotics.

Abstracts, conference proceedings, letters to the editor, or publications lacking full-text access.

Studies with low methodological quality or insufficient data.

Investigations focusing solely on non-burn wounds.

Study Selection Process

Initially, all identified articles were retrieved according to the defined search strategy. A preliminary screening based on titles and abstracts was conducted to remove irrelevant studies. Subsequently, the full texts of remaining articles were meticulously reviewed, and studies meeting the inclusion and exclusion criteria were selected. Key data including study type/model, population or animal/cell model, probiotic type and strain, dosage and duration, main outcomes/effects, and mechanisms of action were extracted and analyzed descriptively.

Results

The findings indicate that probiotics can play a significant role in enhancing burn wound healing. Preclinical evidence demonstrates that various probiotics including Lactobacillus spp., Bifidobacterium spp., kefir, and Saccharomyces cerevisiae accelerate wound repair by reducing inflammation, inhibiting pathogenic microorganisms, and promoting fibroblast proliferation and collagen synthesis. These effects are primarily mediated through modulation of the microbiome,

downregulation of pro-inflammatory cytokines, and upregulation of growth factors such as bFGF and TGF-β1 (Table 1).

In contaminated or diabetic animal models, strains such as Lactobacillus plantarum, L. rhamnosus, L. casei, and Enterococcus mundtii have been shown to reduce infection and scar formation, enhance epithelialization, and improve tissue mechanical strength, thereby facilitating wound repair. These benefits are achieved through antimicrobial activity, activation of immune pathways, and maintenance of probiotic viability (Table 1).

Clinical studies involving patients with severe and deep burns report that oral administration or topical application (e.g., sprays) of probiotics such as Lactobacillus plantarum and Bifidobacterium infantis reduces graft loss, improves wound healing quality, enhances immune responses, and restores microbiome balance. Furthermore, these interventions are associated with shorter hospital stays and lower infection rates (Table 1).

Systematic reviews and narrative articles consistently support the safety and efficacy of probiotics particularly Lactobacillus spp. and Bifidobacterium spp. in burn wound healing. Topical application or incorporation into dressings and hydrogels may further enhance reparative effects while reducing the risk of sepsis and infection (Table 1).

Detailed results, categorized according to study type, model, probiotic strain, and observed outcomes, are summarized in Table 1.

Table 1: Preclinical and clinical studies evaluating the effects of probiotics on burn wound healing

Study Type / Population / Model	Probiotic Strain(s)	Dose & Duration	Main Outcomes / Effects	Mechanism / Notes	Ref.
In vitro & in vivo, Cellular and animal burn models	*Lactobacillus* spp., *Bifidobacterium* spp.	10^6–10^9 CFU/day, 7–21 days	Reduced inflammation, inhibited pathogens, enhanced fibroblast proliferation, improved epidermal regeneration	Delivered via hydrogel; complex wound healing mechanisms	[18]
Narrative review, Preclinical and laboratory studies	Topical probiotics	—	Infection control, inflammation modulation, improved tissue repair	Targeting skin microbiome	[19]
Animal study, Burn model in rats	*Saccharomyces cerevisiae* (hydrogel–collagen scaffold)	12–22 days	Reduced inflammation, increased epithelialization, collagen deposition, improved tissue strength, reduced scarring	Combined with biphasic bioactive dressing	[20]
Experimental in vivo	—	Encapsulated *Lactiplantibacillus plantarum*; viability ≥82%, initial swelling ~2000%	Accelerated wound closure, infection clearance, modulation of inflammatory and oxidative stress responses	Stabilized formulation using cationic–anionic polymer	[21]
Experimental in vivo	—	Immobilized probiotics in sodium alginate–chloride film + Aloe vera gel; daily	Reduced microbial load, shorter healing time, improved repair indices	Probiotic stabilization with Aloe vera	[22]
Review, Recent studies	Probiotics	—	Reduced inflammation, pathogen inhibition, biofilm prevention, accelerated tissue repair	Combined with nanoparticles or phage therapy	[23]
Animal study, Burn sepsis model in mice	*Lactobacillus plantarum*	—	Reduced mortality, prevented sepsis, inhibited systemic pathogen spread, decreased inflammatory cytokines	Preventive topical application	[24]

Animal study, Second-degree burn in Wistar rats	*Lactobacillus acidophilus*	Daily, 14 days	Increased wound closure percentage, reduced inflammation, infection prevention, accelerated re-epithelialization	Oserin-based formulation	[25]
Systematic review, In vitro, animal, RCT	Probiotics & postbiotics	Topical, oral, systemic	Accelerated burn healing, immune modulation, increased keratinocyte & fibroblast proliferation, collagen synthesis, angiogenesis, biofilm inhibition	Restoration of microbiome balance	[26]
Clinical study, 64 patients, deep burns	Oral probiotics	Full hospitalization period	Reduced graft loss percentage, improved graft quality	—	[27]
Animal study, Rabbit	*Lactobacillus plantarum*	Topical	Reduced infection severity & duration, decreased hypertrophic scarring	Decreased collagen I mRNA and protein deposition	[28]
Animal study, Burn-infected mice	*Lactobacillus plantarum* (cells & supernatant)	14 days	Reduced wound size, increased healing percentage, eradicated *Pseudomonas aeruginosa*	Accelerated healing in infected wounds; effective antibiotic alternative	[29]
Clinical study, Children with acute burns	Daily probiotics	—	Safe, shortened wound healing time, no increased infection risk	—	[30]
Systematic review & meta-analysis, 3 RCTs + 2 cohort studies, 341 patients	Probiotics	Completion of adjunct therapy	Significantly reduced sepsis risk, lower infection rates, improved CRP & IgA, enhanced wound healing indices	Safe and effective	[31]
Case review, 2 RCTs	Probiotics	—	Reduced systemic inflammation, enhanced immune function, decreased hs-CRP, increased IgA, accelerated wound healing	Adjunct therapy	[32]
Preclinical, In vitro & burn model in rats	Kefir	3.12–12.5 µL/mL	Enhanced fibroblast proliferation & migration, decreased IL-1β & TGF-β1,	Combined with silver sulfadiazine	[33]

			increased bFGF, improved angiogenesis & connective tissue formation		
Preclinical, In vitro & mouse wound model	*Lactiplantibacillus plantarum*	—	Inhibited *P. aeruginosa* & *S. aureus*, accelerated wound healing	Antimicrobial factor secretion, co-aggregation with pathogens	[34]
Double-blind clinical trial, 40 children, 20–50% BSA burns	Oral probiotics	—	Improved wound healing indices, shorter hospitalization, reduced diarrhea & graft requirement	—	[35]
Clinical case study, 20 patients, deep second-degree burns	*Lactobacillus plantarum* supernatant	—	Reduced infection, improved healing, 66.7% bacteria-free wounds	—	[36]
Preclinical, BALB/c mice, second-degree burns	*Enterococcus mundtii* QAUEM2808	—	Enhanced epithelialization, collagen deposition, hair follicle formation, inhibited harmful bacteria	Electrospun nanocomposite	[37]
Clinical study, 16 burn patients	*Bifidobacterium infantis* 35624	14 days	Increased SIgA, improved gut immunity	Single-strain, enhanced mucosal immune response	[38]
Preclinical, Burn animal model	*Lactiplantibacillus plantarum* microparticles	—	Enhanced wound healing, inhibited *P. aeruginosa*, maintained probiotic viability	High moisture-absorbing polymer, spray-drying	[39]
Experimental, Male diabetic rats, burn wounds	*Lactobacillus plantarum* gel	—	Reduced wound size, increased TGF-β, shortened inflammatory phase, enhanced wound mechanical strength	Compared with SSD	[40]
Narrative review, Preclinical & clinical	*Lactobacillus* spp., *Bifidobacterium* spp.	—	Cytokine profile modulation, increased IgA, epithelial regeneration, up to 75% reduction in infection-related mortality	IL-10 & Th1 pathway activation, accelerated healing in diabetic/surgical conditions	[41]

Controlled clinical trial, 28 patients, second-degree burns	Probiotic spray 10^9 CFU/mL	Twice daily, 28 days	90% wound size reduction, decreased infection & inflammation, improved epithelialization & microbiome balance	—	[42]
Animal study, Sprague-Dawley rats, second-degree burns	*Lactobacillus rhamnosus* ATCC 7469 ointment	Days 1, 3, 7, 14	Increased wound closure percentage, anti-inflammatory effect, enhanced fibroblast migration, epithelial regeneration	—	[43]
Animal study, Wistar rats, infected wounds	*Lactobacillus casei* supernatant	Daily	Reduced inflammation, increased fibroblast activity, enhanced re-epithelialization, increased epidermal & dermal thickness	Lactic, acetic, citric, succinic acids	[44]
Animal study, Wistar rats, infected wounds	*Lactobacillus plantarum* 299v (cells & supernatant)	7 days	Reduced wound size, decreased inflammation, improved skin repair parameters; cell pellet more effective than imipenem	—	[45]

Discussion

Current preclinical and clinical evidence indicates that probiotic therapy may play a significant role in accelerating burn wound healing. Findings from cellular and animal models demonstrate that probiotics particularly strains such as *Lactobacillus plantarum*, *L. acidophilus*, *L. rhamnosus*, and *L. casei* can expedite wound repair by modulating immune responses, reducing inflammation, enhancing fibroblast proliferation, and promoting epithelialization. These mechanisms are primarily mediated through pathogen inhibition, decreased production of pro-inflammatory cytokines, upregulation of growth factors (bFGF, TGF-β1), stimulation of angiogenesis, and maintenance of skin and gut microbiome homeostasis [18–45].

In infected or diabetic animal models, probiotic administration was associated with reduced microbial load, prevention of sepsis, decreased scarring, and improved tissue mechanical strength [21,24,29,40]. The incorporation of probiotics into hydrogels, bioactive dressings, or nanocomposites enhanced microbial stability and viability, thereby potentiating their reparative effects [20,22,37,39]. These findings underscore the importance of innovative delivery systems and advanced drug delivery technologies in optimizing probiotic efficacy.

Clinical studies involving both pediatric and adult patients with moderate to severe burns demonstrated that oral or topical probiotics can reduce graft loss, shorten hospitalization, attenuate systemic inflammation, enhance mucosal immune responses (IgA, SIgA), and lower infection incidence [27,30,31,36,38,42]. These results suggest that probiotics not only accelerate wound healing but also serve as a safe, low-risk adjunctive therapy for improving immune function and mitigating complications associated with burn injuries [30,31].

Furthermore, systematic and case reviews indicate that probiotics can restore microbiome balance and activate anti-inflammatory pathways, including IL-10 and Th1 signaling, thereby reducing infection-related mortality and preventing hypertrophic scar formation [41]. Topical application or combination with hydrogels and bioactive dressings may further enhance wound repair, highlighting the complementary role of probiotics in therapeutic strategies [19,23].

Despite these promising findings, heterogeneity across studies in terms of probiotic strains, dosages, routes of administration, and study design poses limitations. Consequently, well-designed randomized clinical trials with adequate sample sizes are necessary to determine the optimal strain, dose, and administration route for maximal therapeutic benefit [26,31].

The therapeutic potential of probiotics in burn wound management is further reinforced by mechanistic evidence demonstrating their ability to promote skin repair and modulate the gut microbiome. Collectively, the integration of preclinical and clinical data supports the use of probiotics as a safe and effective adjunctive intervention to accelerate burn wound repair, reduce infection, modulate immune responses, and improve the quality of regenerated tissue [18–49]. These findings provide valuable guidance for developing innovative and clinically applicable strategies for burn wound management, reinforcing the complementary role of probiotics.

Conclusion

Preclinical and clinical evidence supports probiotic therapy as a safe and effective strategy for accelerating burn wound healing. Probiotics facilitate wound repair by modulating inflammatory responses, promoting epidermal regeneration, enhancing fibroblast proliferation, and inhibiting pathogenic microorganisms. Combining probiotics with bioactive dressings, hydrogels, or nanocomposites further amplifies their reparative effects while reducing the risk of infection and scarring. Oral or topical administration of probiotics in burn patients not only accelerates wound healing but also enhances mucosal immunity and shortens hospitalization. Nevertheless, determining the optimal probiotic strain, dosage, and administration route requires rigorously designed randomized clinical trials.

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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.

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