

Review

Topical Probiotics in Dermatology: Microbiological Mechanisms, Delivery Platforms, and Therapeutic Perspectives

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Abstract

The skin microbiome plays a central role in maintaining cutaneous homeostasis, and its disruption has been implicated in a wide range of inflammatory and degenerative skin disorders. This review critically evaluates the current evidence on topical probiotics in dermatology, integrating microbiological mechanisms, formulation strategies, and translational and regulatory challenges within a single framework—an angle that remains insufficiently addressed in previous reviews. A targeted search of PubMed and ScienceDirect (2009–2025) was conducted to identify relevant original studies. The results suggest that topical probiotics may promote skin health through three broad, interconnected axes: (i) modulation of host responses (e.g., inflammation, immune signaling, and oxidative stress); (ii) microbial ecology and pathogen control (e.g., competition, acidification, and antimicrobial metabolite production); and (iii) support of barrier function and tissue repair (e.g., lipid metabolism, re-epithelialization, and extracellular matrix remodeling). Efficacy appears to depend strongly on strain specificity, formulation design, and microbial viability during storage and application. In addition to conventional dosage forms, advanced platforms—hydrogels, microgels, microparticles, and microneedle-based systems—have been investigated to improve stability and local delivery. Promising preclinical and clinical results have been reported for acne, wound healing, skin barrier repair, and anti-aging applications. Nevertheless, major translational challenges remain, including limited standardization, instability of live microorganisms, insufficiently representative experimental models, and regulatory uncertainty. Overall, topical probiotics represent a promising microbiome-based strategy in dermatology, but robust clinical validation and formulation optimization are still needed to support broader clinical implementation.

Keywords: topical probiotics; skin microbiome; dermatology; microbiome modulation; cutaneous dysbiosis; delivery systems; wound healing; acne



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1. Introduction

Probiotics are currently defined as live microorganisms that, when administered in adequate amounts, confer a health benefit on the host [1]. Although the concept has

been historically associated with gastrointestinal health, its roots can be traced to early microbiological thinking on fermentation, host well-being, and the beneficial effects of selected microorganisms [2]. Over time, the field expanded beyond intestinal applications and progressively entered dermatology and cosmetic science, where probiotics began to be explored as topical or systemic interventions capable of influencing skin physiology and disease [3]. Interest in dermatological applications increased further after early clinical evidence suggested that probiotic-based approaches could affect inflammatory skin conditions, including atopic disease [4].

The skin is a complex ecological interface inhabited by diverse microbial communities composed of bacteria, fungi, viruses, and mites. These organisms are not passive colonizers; rather, they actively participate in barrier integrity, immune education, colonization resistance, and tissue homeostasis [5,6]. The structural basis of this defense lies in the epidermal barrier, particularly the stratum corneum, which limits transepidermal water loss and restricts pathogen penetration [7]. Microbial communities further contribute to this protective network by shaping local pH, interacting with keratinocytes and immune cells, and supporting antimicrobial defense [5,6]. Advances in microbiome research have highlighted the site-specific nature of the skin ecosystem, with sebaceous, moist, and dry areas harboring distinct microbial assemblages [8–10].

Evidence from experimental models indicates that commensal microorganisms are functionally linked to skin repair and barrier maintenance. In germ-free settings, delayed epidermal recovery has been observed, whereas recolonization may help restore physiological repair mechanisms through host–microbe signaling pathways [11]. Conversely, cutaneous dysbiosis has been implicated in multiple dermatological disorders. Atopic dermatitis is associated with decreased microbial diversity and overrepresentation of *Staphylococcus aureus* [12], whereas acne appears to be linked not simply to the abundance of *Cutibacterium acnes*, but to shifts in strain composition and ecological imbalance within the pilosebaceous unit [13]. These observations support the concept that targeted modulation of the skin microbiome may represent a relevant therapeutic strategy.

Topical probiotics have therefore emerged as a promising microbiome-based approach in dermatology. By delivering beneficial microorganisms or functionally active microbial systems directly to the skin surface, these interventions may help rebalance dysbiotic communities, reduce inflammation, strengthen barrier function, and support tissue repair [3,14]. However, the development of effective topical probiotic products remains challenging. The cutaneous surface is a harsh environment characterized by low pH, osmotic stress, desiccation, ultraviolet exposure, and fluctuating temperature, all of which may compromise microbial viability and therapeutic consistency [3,14]. As a result, the clinical translation of topical probiotics depends not only on microbiological rationale, but also on formulation design, delivery technology, and regulatory clarity.

Despite growing interest in microbiome-based dermatology, the current literature on topical probiotics remains highly fragmented. Previous reviews have addressed either skin microbiome biology or selected probiotic applications in isolation, with limited integration of microbiological mechanisms, formulation science, and translational/regulatory considerations. The present review aims to bridge these gaps by (i) combining mechanistic evidence on how topical probiotics interact with the cutaneous ecosystem and host responses; (ii) critically appraising conventional and advanced delivery platforms in light of microbial viability and bioavailability; and (iii) discussing translational and regulatory bottlenecks that currently limit clinical implementation. By addressing this, this review seeks to provide a more integrated framework for the rational development of topical probiotic interventions in dermatology.

2. Literature Search Strategy and Scope of the Review

This narrative review was based on a targeted literature search conducted in PubMed and ScienceDirect to identify studies investigating topical probiotics in dermatology. Original articles published between 2009 and 2025 were prioritized. The search strategy included combinations of the terms “topical probiotics”, “dermatology”, “skin microbiome”, and “delivery systems”. Studies addressing mechanisms of action, formulation strategies, microbial viability, and therapeutic outcomes in dermatological settings were considered relevant. Review articles were also consulted to provide conceptual support and contextual interpretation of the field.

Given the heterogeneity of the available literature—in terms of probiotic strains, formulation platforms, clinical indications, and outcome measures—no quantitative synthesis was attempted. Instead, this review critically integrates the available evidence and highlights the principal microbiological, technological, and translational trends shaping the field.

Throughout the main text and tables, updated post-2020 lactobacilli taxonomy is used whenever possible to ensure consistency, whereas historical names are retained in article titles in the reference list when they reflect the original publication.

3. The Skin Microbiome as a Therapeutic Target in Dermatology

The skin microbiome consists of specialized, site-specific communities shaped by sebum secretion, moisture, pH, host immunity, age, and environmental exposure [5,6,8–10]. Sebaceous regions are typically enriched in lipophilic organisms such as *Cutibacterium* species, moist areas often favor *Staphylococcus* and *Corynebacterium*, and dry regions generally display greater microbial diversity [8–10]. Fungal communities, especially *Malassezia* spp., are also important constituents of the cutaneous ecosystem, particularly in sebaceous areas [10].

Under physiological conditions, these microbial communities contribute to homeostasis through several complementary functions. They can limit pathogen colonization through ecological competition, shape local immune tone, influence keratinocyte behavior, and participate in the maintenance of barrier integrity [5,6,11]. The interaction between commensals and the host is not merely associative; it is increasingly understood as mechanistically relevant. For example, microbiota-dependent signaling through host receptors has been linked to barrier function and wound repair, reinforcing the view that the skin microbiome is a functional component of cutaneous biology rather than a passive bystander [11].

Disruption of this equilibrium, commonly termed dysbiosis, has been associated with inflammatory and chronic dermatological disorders (Table 1) [6,8]. In atopic dermatitis, overgrowth of *Staphylococcus aureus* and reduced microbial diversity are thought to amplify inflammation and barrier dysfunction [12]. In acne, disease-associated alterations appear to involve strain-level imbalance within the *Cutibacterium acnes* population and broader ecological changes within the pilosebaceous microenvironment [13]. Dysbiosis has also been implicated in delayed wound healing and in skin conditions associated with impaired barrier function and chronic low-grade inflammation [6,14].

These findings provide a strong rationale for microbiome-oriented topical interventions. Unlike broad-spectrum antimicrobials, which may indiscriminately reduce both harmful and beneficial microorganisms, topical probiotics aim to restore ecological balance while simultaneously influencing host responses. Their therapeutic rationale lies in local microbiome modulation, pathogen control, immune regulation, and support of tissue integrity [3,14].

Table 1. Comparison of key microbial features in atopic dermatitis and acne vulgaris.

Feature	Atopic Dermatitis	Acne Vulgaris
Dominant dysbiotic taxon	Overgrowth of <i>S. aureus</i>	Strain-level imbalance within <i>C. acnes</i> populations
Microbial diversity	Markedly reduced, especially during flares	Relatively preserved at genus level; altered at strain level
Affected skin compartment	Stratum corneum and superficial epidermis	Pilosebaceous unit
Associated barrier features	Impaired barrier function, increased TEWL, filaggrin deficiency	Follicular hyperkeratinization, altered sebum composition
Inflammatory profile	Th2-skewed inflammation, elevated IL-4, IL-13, IL-31	IL-1 α , IL-6, IL-8 and innate immune activation in the pilosebaceous unit
Commensals reduced/ altered	Coagulase-negative staphylococci (e.g., <i>S. epidermidis</i> , <i>S. hominis</i>)	Shifts in <i>C. acnes</i> phylotype balance; reduced strain-level diversity
Therapeutic rationale for topical probiotics	Restore diversity, suppress <i>S. aureus</i> , reinforce barrier	Rebalance <i>C. acnes</i> populations, attenuate follicular inflammation, modulate sebum

TEWL, transepidermal water loss.

4. Microbiological Mechanisms Underlying Topical Probiotic Activity

4.1. Modulation of Cutaneous Inflammation

One of the most consistently proposed mechanisms of topical probiotics is the modulation of cutaneous inflammation. Certain probiotic strains appear capable of reducing the production of pro-inflammatory mediators by keratinocytes, sebocytes, and other skin-associated cells. This effect may involve attenuation of signaling pathways associated with innate immune activation, including pathways converging on NF- κ B and downstream cytokine production [15,16]. In acne-related models, topical *Lactiplantibacillus plantarum* preparations have been associated with marked reductions in IL-1 α , IL-6, and IL-8, suggesting that selected strains may help limit inflammatory amplification within the pilosebaceous unit [16]. Similar anti-inflammatory trends have been reported in wound-healing models, in which probiotic treatment was associated with lower expression of inflammatory mediators and reduced inflammatory cell infiltration [17,18].

It is also important to note that excessive or non-selective weakening of cutaneous immune responses could theoretically compromise antimicrobial defense and immune surveillance, particularly in patients with impaired barrier function or immunosuppression. This reinforces the need for strain- and context-specific characterization of immunomodulatory effects, rather than a generalized anti-inflammatory framing of topical probiotics.

Nevertheless, these anti-inflammatory effects should be interpreted cautiously. The magnitude of the response is likely to be strain-specific, context-dependent, and influenced by the formulation matrix and local microenvironment. Accordingly, probiotic-mediated immunomodulation should be viewed as a promising but still incompletely standardized mechanism.

4.2. Rebalancing of the Cutaneous Microbiota

A second major mechanism relates to the ability of probiotics to rebalance the cutaneous microbiota through ecological competition and antimicrobial activity. Proposed processes include competition for adhesion sites and nutrients, acidification of the local environment, and secretion of bioactive metabolites such as organic acids, bacteriocin-like

compounds, or other inhibitory molecules [15,19,20]. This mechanism is especially relevant in conditions associated with dysbiosis such as acne and infected wounds.

These findings discriminate between two related but conceptually distinct outcomes: the “reduction in pathogen load” is typically demonstrated by quantitative decreases in target microorganisms such as *C. acnes* or *S. aureus* following probiotic application [16,19] and the “ecological rebalancing of the cutaneous microbiota” implies broader shifts in community composition, diversity, or strain-level structure, beyond the suppression of a single pathogen [19]. While many studies report pathogen reduction, fewer provide robust microbiome-level evidence of ecological restoration. This distinction is relevant both mechanistically and clinically, as durable therapeutic benefit is more likely to depend on genuine ecological rebalancing rather than transient antimicrobial effects.

4.3. Reinforcement of Skin Barrier Function

Barrier reinforcement is another key mechanism underlying the potential benefits of topical probiotics. Impaired barrier function is a hallmark of several inflammatory and degenerative skin conditions, and improving barrier integrity may help interrupt cycles of irritation, water loss, inflammation, and microbial imbalance. Experimental evidence suggests that specific skin-associated commensals and probiotic candidates may contribute to barrier homeostasis by affecting lipid metabolism and structural organization [6,11].

A notable example is provided by *Staphylococcus epidermidis*, which has been shown to generate protective ceramides through sphingomyelinase activity, thereby contributing to skin barrier homeostasis [21]. Enhancement of ceramide-associated pathways may reduce transepidermal water loss and improve the resilience of the epidermal barrier [21]. Additional preclinical work using topical probiotic systems has reported improved tissue cohesion and reduced water loss, supporting the broader concept that microbial interventions can positively influence barrier-related parameters [22].

Importantly, the commensal–pathogen frontier is not absolute. Although *S. epidermidis* generally contributes to barrier homeostasis and antimicrobial defense, certain strains can behave as opportunistic pathogens under conditions of barrier disruption, indwelling device colonization, or immune dysregulation, contributing to biofilm formation and nosocomial infection. This duality demonstrates that the therapeutic potential of skin commensals is strain- and context-dependent, and reinforces the importance of precise strain characterization in topical probiotic development.

4.4. Sebum Regulation and Follicular Homeostasis

In acne-prone skin, probiotics may also interfere with sebaceous activity and follicular inflammatory signaling. This is clinically relevant because excessive sebum production, altered lipid composition, and follicular dysbiosis are major contributors to acne pathophysiology. Experimental and preliminary clinical data suggest that some topical probiotic strains can reduce lipid production in sebocytes and modulate inflammatory mediators linked to acne lesion formation [16]. Clinical observations have also suggested improvements in oiliness and acne-related symptoms following the application of probiotic serums [23]. Although these findings remain preliminary, they support the possibility that probiotics may exert combined microbiological and metabolic effects within the pilosebaceous environment.

Overall, although the rationale for sebum regulation by topical probiotics is biologically plausible, the available clinical evidence remains preliminary, derived mostly from small or exploratory studies with heterogeneous designs. More importantly, well-controlled clinical trials with standardized sebum quantification are needed before secure conclusions can be drawn.

4.5. Promotion of Wound Healing and Skin Regeneration

Topical probiotics have shown particular promise in wound healing, where their effects may extend beyond antimicrobial action (Box 1). In preclinical studies, probiotic treatment has been associated with improved re-epithelialization, increased angiogenesis, enhanced collagen organization, and faster wound closure [17,18,22,24–27]. These benefits are likely mediated by a combination of reduced pathogen burden, attenuation of excessive inflammation, and support of regenerative signaling pathways.

For example, strain-specific effects have been reported in excisional wound models, where *Lactiplantibacillus plantarum* primarily reduced inflammation, whereas *Lacticaseibacillus rhamnosus* and *Bifidobacterium longum* were associated with enhanced tissue repair and angiogenesis [17]. In burn wounds, topical *L. plantarum* has been linked to improved bacterial clearance and reduced hypertrophic scarring [24,26]. In diabetic wound models, probiotic hydrogels and oleogels have been associated with accelerated closure and improved oxidative and inflammatory profiles [18,25]. These observations position topical probiotics as promising adjuncts in chronic and infected wound management.

Box 1. Integrated mechanistic model of topical probiotic activity in wound healing.

Topical probiotics appear to support wound repair through three interconnected mechanistic axes:

- 1. Modulation of inflammation**—attenuation of NF- κ B-associated signaling, reduction in pro-inflammatory cytokines (e.g., IL-1 α , IL-6, IL-8, TNF- α), and decreased inflammatory cell infiltration.
- 2. Promotion of angiogenesis**—stimulation of pro-angiogenic signaling and increased vascularization of the wound bed, with strain-specific effects (e.g., *L. rhamnosus*, *B. longum*).
- 3. Extracellular matrix (ECM) remodeling and re-epithelialization**—enhanced collagen deposition and organization, improved tissue cohesion, and accelerated epithelial closure.

These axes are reinforced by complementary effects on pathogen burden and oxidative stress, which together shape a wound microenvironment more conducive to regeneration.

4.6. Antioxidant Activity and Indirect Immunomodulatory Effects

Oxidative stress is increasingly recognized as a relevant component of chronic inflammation, impaired healing, and skin aging. Several topical probiotic systems have been reported to reduce reactive oxygen species or favor redox conditions compatible with tissue repair [18,25]. In a diabetic wound model, a probiotic gel promoted healing while reducing local glucose levels and oxidative stress markers, suggesting that metabolic and antioxidant effects may contribute to its therapeutic activity [18]. Related formulations have also been associated with decreased inflammatory signaling and improved tissue microenvironment [25]. It is important to note that antioxidant and metabolic effects appear to be strain-specific rather than a generalizable characteristic of topical probiotics. For instance, glucose-consuming and ROS-modulating activities have been documented for specific *L. reuteri* and strains in diabetic wound models [18,25], whereas other strains in the same studies showed limited or no effect [25]. Accordingly, claims of antioxidant or metabolic activity should be linked to characterized strains and not directly extrapolated to topical probiotics as a class.

In addition to direct anti-inflammatory actions, probiotics may exert indirect immunomodulatory effects by shaping epithelial responses and promoting balanced host–microbe communication [15]. This broader immunoregulatory role may be particularly relevant in chronic inflammatory states, where excessive immune activation coexists with impaired tissue repair. However, mechanistic interpretation should remain cautious, since many available data derive from preclinical systems and are not yet supported by large-scale human studies.

5. Topical Delivery Systems and Microbial Viability

5.1. Conventional Formulations

The formulation platform is a major determinant of the feasibility and performance of topical probiotics. Conventional systems such as creams, ointments, gels, serums, and saline-based preparations are attractive because of their accessibility, patient acceptability, and relative ease of manufacturing [3,14]. These vehicles have been used in a range of dermatological contexts, including acne, burns, anti-aging applications, and general skin care [16,19,23,24,26,28,29].

Despite their practical advantages, conventional formulations present important limitations. Most were not originally designed to carry live microorganisms and may provide suboptimal protection against desiccation, oxidation, ultraviolet exposure, or thermal instability [3,14]. In addition, most conventional topical products rely on antimicrobial preservatives (e.g., parabens, phenoxyethanol, organic acids) to ensure microbiological safety and shelf-life, but these agents can be incompatible with live microorganisms and compromise their viability. Moreover, they often offer limited control over microbial release kinetics and retention at the target site. Consequently, the success of conventional probiotic formulations may vary substantially depending on the specific strain, excipients, and storage conditions.

5.2. Hydrogels, Microgels, and Microparticulate Systems

To address these challenges, advanced delivery systems have been developed to better preserve viability and improve local bioactivity. Hydrogels are particularly attractive for wound care because they provide a moist microenvironment, facilitate contact with the wound bed, and may support sustained release of viable microorganisms or microbial products [18]. In diabetic wound models, probiotic-containing hydrogels have been associated with improved healing and reduced oxidative stress, supporting their potential as multifunctional delivery systems [18].

Microgels and related compartmentalized matrices provide additional opportunities to enhance stability and local retention. A cationic microgel system carrying human-derived probiotics and deferoxamine showed activity against multidrug-resistant pathogens while promoting tissue regeneration, illustrating how advanced formulations can integrate antimicrobial, adhesive, and regenerative functions within a single platform [27].

Microparticulate systems, including polymer-based encapsulation strategies, may also protect microorganisms from environmental stress and prolong their delivery. *Bacillus subtilis* incorporated into poly(vinyl alcohol) microparticles demonstrated antibacterial activity and enhanced wound healing in vivo, highlighting the usefulness of polymeric carriers in open wound applications [22]. More broadly, encapsulation approaches may improve probiotic shelf-life and facilitate controlled release, although their translational scalability remains to be fully established [14].

5.3. Microneedle-Based Delivery

Microneedle-based systems represent one of the most innovative strategies in the field because they can overcome the superficial barrier of the stratum corneum and deliver probiotics or probiotic-derived systems directly into deeper tissue layers. This approach may be especially useful in infected or chronic wounds, where deeper local delivery can be advantageous. Living microneedles loaded with *L. reuteri* have shown antibacterial, anti-inflammatory, and pro-regenerative effects in infected wound models, together with favorable biocompatibility [20]. Such platforms illustrate how delivery technology can shape not only formulation stability, but also the therapeutic scope of topical probiotics.

Each of these advanced delivery platforms offers distinct advantages and limitations relevant to topical probiotic applications. Hydrogels provide a hydrated microenvironment particularly suited to wound healing, but may offer limited long-term protection of microbial viability under ambient storage. Microgels allow finer control over local retention, sustained release, and co-delivery of bioactive agents, though scalability and reproducibility of manufacturing remain challenging. Microparticulate systems, including polymer-based encapsulation, can substantially improve shelf-life and protect microorganisms from environmental stress, but may require additional steps for release activation and uniform distribution at the application site. Microneedle-based systems offer the unique ability to bypass the stratum corneum and deliver probiotics into deeper tissue compartments, which is particularly valuable in chronic or infected wounds, although manufacturing complexity, sterility assurance, and regulatory pathways are more demanding. A summary comparison is provided in Table 2.

Table 2. Comparative overview of advanced delivery platforms for topical probiotics.

Platform	Main Advantages	Main Limitations	Most Suited Applications
Hydrogels	Moist microenvironment, biocompatibility, sustained release	Limited long-term viability under ambient storage; mechanical fragility	Wound care, diabetic wounds
Microgels	Localized retention, co-delivery of bioactives, antimicrobial reinforcement	Manufacturing complexity, scalability	Infected wounds, multidrug-resistant infections
Microparticles (e.g., PVA)	Improved shelf-life, protection against environmental stress	Release activation may be required; uniform distribution challenges	Open wounds, controlled-release applications
Microneedle patches	Penetration beyond stratum corneum, targeted deep delivery	Manufacturing complexity, sterility, regulatory hurdles	Chronic/infected wounds, deep tissue targets

5.4. Key Formulation Challenges

Although delivery technologies have advanced substantially, several unresolved issues remain. These include maintaining adequate microbial viability during manufacturing and storage, ensuring compatibility between microorganisms and excipients, preserving functional activity after application, and defining the optimal role of live probiotics, inactivated bacteria, lysates, or postbiotic fractions [3,14]. Moreover, the performance of a delivery system should not be judged solely by microbiological survival; it must also support clinically relevant bioavailability, safety, and reproducibility. For this reason, future development of topical probiotic formulations should integrate microbiological viability data with dermatological efficacy endpoints.

6. Therapeutic Applications in Dermatology

6.1. Acne Vulgaris

Acne vulgaris is one of the most intensively explored indications for topical probiotics. The rationale for their use lies in the interaction between follicular dysbiosis, inflammatory signaling, and sebaceous dysfunction [13,16,19]. Rather than indiscriminately suppressing the skin microbiota, probiotic strategies seek to rebalance microbial communities, reduce inflammatory mediators, and potentially regulate sebum production.

Clinical and translational studies have yielded encouraging results. A topical *L. plantarum* serum has been reported to reduce inflammatory cytokines and sebocyte lipid production in acne-related models, suggesting a mechanistic basis for anti-acne activity [16]. A cream containing live lactobacilli reduced inflammatory lesions and favorably altered skin

microbiota composition, with effects that persisted beyond the active treatment phase [19]. In a more cosmetically oriented setting, a serum containing *Micrococcus luteus* Q24 was associated with improvements in oiliness, redness, and overall skin quality [23]. Although the available evidence remains limited in scale and heterogeneous in methodology, these findings collectively support further investigation of topical probiotics as adjunctive or alternative interventions for acne management.

6.2. Wound Healing, Burns, and Diabetic Wounds

Wound healing represents one of the strongest translational domains for topical probiotics. In this context, probiotics may offer a combination of antimicrobial, anti-inflammatory, antioxidant, and regenerative effects, all of which are highly relevant to the pathophysiology of chronic, infected, and burn-related wounds [14,17,18,24–27]. Importantly, strain specificity appears to matter. Some strains seem to exert primarily anti-inflammatory effects, whereas others may more strongly promote angiogenesis, collagen deposition, or tissue remodeling [17].

Clinical and preclinical studies support this therapeutic potential. In burn wounds, topical *L. plantarum* has shown efficacy comparable to silver sulfadiazine in some settings and may be particularly useful in infected burns [24]. Additional animal data suggest that the same organism can reduce hypertrophic scar formation and improve collagen organization after burn injury [26]. In diabetic wound models, probiotic oleogels and hydrogels have accelerated wound closure while improving the local oxidative and inflammatory milieu [18,25]. Advanced systems such as microgels and microneedle-based platforms have further expanded this field by demonstrating activity against multidrug-resistant pathogens and promoting regeneration in infected wounds [20,27]. Taken together, these findings indicate that wound-directed applications may currently represent the most advanced area of topical probiotic research in dermatology.

6.3. Skin Barrier Repair and Anti-Aging Applications

Topical probiotics have also been explored in relation to skin aging, barrier repair, and overall skin quality. These applications are supported by the ability of selected strains to influence hydration, elasticity, transepidermal water loss, and structural proteins relevant to the dermal matrix [21,22,28,29]. However, the evidence in this area spans a spectrum from mechanistic preclinical work to exploratory clinical studies, and not all reported benefits should be interpreted as equivalent in clinical significance.

In reconstructed human skin, topical delivery of living, quiescent *L. plantarum* Lp90 stimulated elastin expression, suggesting a potential link between probiotics and support of the dermal matrix [28]. In an exploratory clinical study, an ointment containing *L. plantarum* LB244R was associated with improvements in wrinkles, hydration, elasticity, firmness, and other age-related skin parameters [29]. In parallel, evidence that the commensal *S. epidermidis* can generate protective ceramides provides a mechanistic basis for barrier-oriented applications [21]. Additional data from polymer-based probiotic systems have also suggested reductions in transepidermal water loss and improved tissue cohesion [22]. Collectively, these findings indicate that topical probiotics may have a role in barrier repair and skin-aging strategies, although stronger clinical trials are still needed to distinguish cosmetic benefits from robust therapeutic effects.

Representative studies evaluating topical probiotics in dermatology, including formulation platforms, clinical targets, and major outcomes, are summarized in Table 3.

Table 3. Representative studies evaluating topical probiotics in dermatology, with emphasis on formulation platform, clinical target, and major outcomes.

Delivery System	Probiotic	Application	Type of Study	Main Outcomes	References
Cream	<i>L. plantarum</i> Lp90	Stimulation of elastin expression	Preclinical (<i>in vitro</i>)	Topical application of a reconstituted cream containing <i>L. plantarum</i> Lp90 significantly upregulated elastin expression in reconstructed human skin in a dose-dependent manner. No effects were observed on type I collagen filaggrin, or hyaluronic acid.	[28]
Ointment	<i>L. plantarum</i> LB244R	Skin aging	Clinical	After 56 days of topical application statistically significant improvements were observed in multiple skin aging parameters. Reductions were reported in SLEB thickness, TEWL, and crow's feet wrinkles, whereas increases were noted in dermal density, elasticity, hydration, skin firmness, and clinical scores for smoothness, pigmentation, and radiance.	[29]
Cream	<i>L. rhamnosus</i> GG, <i>L. plantarum</i> WCFS1, <i>L. pentosus</i> KCA1	Acne vulgaris	Randomized controlled trial	Topical application of encapsulated live lactobacilli for 8 weeks significantly reduced inflammatory acne lesions with effects persisting for 4 weeks after treatment. This was associated with an increase in skin lactobacilli and a reduced staphylococci. No adverse events were reported.	[19]
Serum	<i>Micrococcus luteus</i> Q24	Skin health	Clinical observational study	The study involved 96 participants, after 28 days of topical application of the serum containing <i>M. luteus</i> Q24, an improvement in skin parameters was observed. No adverse effects were reported.	[23]
Not specified	<i>S. epidermidis</i> 1457 and <i>S. epidermidis</i> S25	Skin barrier homeostasis	Preclinical (<i>in vivo</i>)	In murine and cellular models, <i>S. epidermidis</i> was shown to strengthen the skin barrier through sphingomyelinase production. No adverse effects, cytotoxicity, or biofilm induction were observed.	[21]
Serum	<i>L. plantarum</i> LP01	Anti acne	<i>Ex vivo</i> study with healthy-volunteer validation	SkinDuo™ containing <i>L. plantarum</i> , maintained viability on skin and significantly reduced <i>C. acnes</i> and <i>S. epidermidis</i> viability, sebocyte lipid production, and inflammatory markers in <i>ex vivo</i> acne related models.	[16]
Ointment	<i>L. plantarum</i> UBLP-40, <i>L. rhamnosus</i> UBLR-58 and <i>B. longum</i> UBBL-64	Wound healing	Preclinical (<i>in vivo</i>)	Topical probiotics demonstrated strain-specific effects in a rat excisional wound model. <i>L. plantarum</i> primarily exerted anti-inflammatory effects, whereas <i>L. rhamnosus</i> and <i>B. longum</i> more strongly promoted healing and angiogenesis-related factors.	[17]
Saline solution	<i>L. plantarum</i> ATCC 10241	Burn wound healing	Clinical comparative study	In a clinical study of 80 burn patients, topical application of a saline solution containing <i>L. plantarum</i> showed efficacy comparable to SD-Ag in second degree and non-infected third-degree burns, and superior outcomes in infected third-degree burns, with improved healing, bacterial clearance, and graft uptake.	[24]

Table 3. Cont.

Delivery System	Probiotic	Application	Type of Study	Main Outcomes	References
Oleogel	<i>L. rhamnosus</i> IBRC-M 11409, <i>L. casei</i> IRBC-M 10711, <i>L. fermentum</i> IRBC-M 10816, and <i>L. acidophilus</i> IRBC-M 10815	Diabetic ulcer	Preclinical (<i>in vivo</i>)	Topical application of <i>L. acidophilus</i> IBRC-M 10815 and <i>L. rhamnosus</i> IBRC-M 11409 significantly accelerated diabetic wound healing. <i>L. casei</i> IBRC-M 10711 showed no significant effect compared with the untreated group.	[25]
Ointment	<i>L. plantarum</i> ATCC 10241	Burn wound healing	Preclinical (<i>in vivo</i>)	Probiotic treatment significantly reduced hypertrophic scarring, decreased inflammatory cell infiltration, and improved collagen organization. These findings suggest that probiotic application can modulate both inflammation and tissue modelling during burn wound healing.	[26]
Hydrogel	<i>L. reuteri</i> BNCC192190	Diabetic wound healing	Preclinical (<i>in vivo</i>)	A hydrogel based on <i>L. reuteri</i> accelerated diabetic wound healing in mice, enhanced antioxidant enzyme activity, reduced local glucose and ROS levels, and modulated inflammation-related gene expression. No adverse effects or toxicity were reported.	[18]
Microgel	<i>L. fermentum</i>	Wound healing	Preclinical (<i>in vivo</i>)	In murine model of MRSA-infected wounds a cationic microgel containing <i>L. fermentum</i> and DFO provided adhesion, bacterial protection, and sustained release, resulting in antimicrobial activity and enhanced tissue regeneration.	[27]
Microneedle patch	<i>L. reuteri</i> ATCC 53608	Wound healing	Preclinical (<i>in vivo</i>)	The study demonstrated the therapeutic potential of microneedle patch containing <i>L. reuteri</i> for infected wounds, with antibacterial, anti-inflammatory, and pro-regenerative effects together with good biocompatibility.	[20]
PVA microparticles	<i>Bacillus subtilis</i> 3610	Treatment of open wounds	Preclinical (<i>in vivo</i>)	<i>Bacillus subtilis</i> loaded PVA microparticles exhibited strong antibacterial activity against MRSA and <i>S. aureus</i> and accelerated wound healing in mice. No adverse effects were reported.	[22]

Abbreviations: DFO, deferoxamine; MRSA, methicillin-resistant *Staphylococcus aureus*; PVA, poly(vinyl alcohol); ROS, reactive oxygen species, SD-Ag, silver sulfadiazine; SLEB, sub-epidermal low-echogenic band; TEWL, transepidermal water loss.

7. Current Limitations, Regulatory Challenges, and Translational Barriers

Despite encouraging findings, the field of topical probiotics remains constrained by major scientific and translational limitations. First, probiotic activity is highly strain-specific, making broad claims about “topical probiotics” scientifically problematic when precise taxonomic and functional characterization is lacking [1,3,14]. Second, the maintenance of viable microorganisms in topical formulations remains technically challenging, especially under non-refrigerated storage conditions and in products intended for real-world clinical or commercial use [3,14]. These stability issues affect not only shelf-life, but also reproducibility of dosing and biological activity.

Another important limitation is the lack of standardization across studies. The published literature includes marked differences in strain selection, formulation vehicle, dose, treatment duration, comparator groups, and outcome measures [14,16–20,23–29]. Such vari-

ability complicates cross-study comparison and makes it difficult to define best-performing strains or platforms for specific dermatological indications. In addition, many studies remain preclinical or exploratory, with relatively small sample sizes and limited long-term follow-up, especially in acne and anti-aging applications [16,23,28,29].

Model validity also remains an unresolved issue. Although animal models, reconstructed skin systems, and ex vivo assays provide valuable mechanistic insight, they do not fully reproduce the complexity of the human skin microbiome or its dynamic interaction with host immunity and environmental exposure [8,11,14]. This gap limits direct clinical extrapolation and highlights the need for more robust translational designs.

Regulatory uncertainty constitutes a further barrier to the clinical translation of topical probiotics. Depending on the jurisdiction, intended use, and claims made, the same probiotic-based product may fall ambiguously between cosmetic, pharmaceutical, medical device, and live biotherapeutic product (LBP) categories [3]. A concrete illustration of this divergence is the contrast between the European Union and the United States. In the EU, most currently marketed topical probiotic preparations are framed as *“cosmetic products”* under Regulation (EC) No 1223/2009, with emphasis on safety assessment and, in practice, limited claims regarding therapeutic activity; live microorganisms in cosmetics also raise specific microbiological safety considerations. In the United States, by contrast, products containing live microorganisms intended to prevent or treat disease are typically regulated by the FDA as biological products and may fall under the LBP framework, which imposes substantially more stringent requirements regarding strain characterization, manufacturing quality, preclinical safety, and clinical evidence.

This regulatory ambiguity is further compounded by the conceptual heterogeneity of the products themselves. Probiotics (live microorganisms conferring a health benefit), postbiotics (preparations of inanimate microorganisms and/or their components that confer a health benefit), bacterial lysates, and LBPs are not interchangeable categories. They differ in composition, mechanism, stability, and—critically—in the regulatory and evidentiary pathways that apply. Clearer harmonization across jurisdictions, together with explicit guidance on quality control, strain identity, viability assessment, and claim substantiation, will be essential for the maturation of the field.

8. Conclusions and Future Directions

Topical probiotics represent a promising microbiome-based strategy for the management of selected dermatological conditions. Current evidence suggests that these interventions may influence cutaneous homeostasis through multiple interconnected mechanisms, including modulation of microbial communities, attenuation of inflammation, reinforcement of barrier function, regulation of sebaceous activity, and support of tissue regeneration [16–18,21,24–29]. These properties make topical probiotics particularly attractive for wound healing, acne management, and barrier-oriented interventions.

At the same time, the field remains in an early translational phase. Much of the available evidence is heterogeneous, strain-dependent, and frequently derived from small clinical studies or preclinical models. Future research should prioritize rigorous strain characterization, mechanistic validation in clinically relevant systems, robust randomized trials, and formulation strategies capable of preserving stability and reproducible bioactivity [3,14,18,20,27]. In this sense, trials should adopt a standardized minimum reporting framework, including precise strain identification (e.g., down to strain-level genomic characterization), quantification of viable microorganisms at the time of application (e.g., CFU/g or CFU/cm²), full disclosure of the formulation vehicle and excipients, and predefined dermatological endpoints validated for the indication studied (e.g., lesion counts and IGA (Investigator Global Assessment) scores for acne; TEWL,

SCORAD (SCORing Atopic Dermatitis), and EASI (Eczema Area and Severity Index) for barrier and atopic conditions; PUSH (Pressure Ulcer Scale for Healing) or wound area closure for wound healing). In addition, future studies need to include longitudinal microbiome profiling before, during, and after treatment, in order to distinguish transient pathogen suppression from durable ecological rebalancing, and to assess the persistence of effects after treatment discontinuation. The integration of these design elements with adequately powered randomized controlled designs and appropriate arms, e.g., placebo, standard of care, or heat-inactivated probiotic controls, would significantly strengthen the evidence base necessary for clinical translation and regulatory recognition.

Ultimately, progress in this area will depend on closer integration among microbiology, dermatology, pharmaceutical technology, and regulatory science. With improved standardization and stronger clinical evidence, topical probiotics may evolve from promising experimental tools into reliable components of next-generation dermatological therapy [30].

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