

Review Article

Probiotic Modulation of the Skin Microbiome: Emerging Therapeutic Strategies in Dermatology

Siew Mei Tan¹, Riyanto Teguh Widodo², Yik-Ling Chew³, Siew-Keah Lee⁴, A.B.M. Helal Uddin⁵, Hui Suan Ng^{6*}, Ching Siang Tan^{7*}, Kai Bin Liew^{1*}

Article History

Received: 06 June 2026;

Received in Revised Form:

11 August 2026;

Accepted: 14 August 2026;

Available Online: 12 October 2026

¹Faculty of Pharmacy, University of Cyberjaya, Persiaran Bestari, 63000 Cyberjaya, Selangor, Malaysia; siewmei.tan@cyberjaya.edu.my (SMT)

²Faculty of Pharmacy, Universiti Malaya, 50603 Kuala Lumpur, Wilayah Persekutuan Kuala Lumpur, Malaysia; riyanto@um.edu.my (RTW)

³Faculty of Pharmaceutical Sciences, UCSI University, No 1, Jalan Menara Gading, UCSI Heights, 56000 Cheras, Kuala Lumpur, Malaysia; chewyl@ucsiuniversity.edu.my (YLC)

⁴M. Kandiah Faculty of Medicine and Health Sciences, Universiti Tunku Abdul Rahman, Jalan Sungai Long, Bandar Sungai Long, 43000 Kajang, Selangor, Malaysia; leesiewkeah@utar.edu.my (SKL)

⁵Faculty of Pharmacy, International Islamic University Malaysia, Bandar Indera Mahkota, 25200 Kuantan, Pahang, Malaysia; abmhelal@iiu.edu.my (AMBHU)

⁶Smart Bioresource Recovery and Formulation Laboratory, Department of Chemical Engineering and Materials Science, Yuan Ze University, Chungli, Taoyuan 320, Taiwan

⁷School of Pharmacy, KPJ Healthcare University, Lot PT 17010 Persiaran Seriemas, Kota Seriemas, 71800 Nilai, Negeri Sembilan, Malaysia

*Corresponding authors: Kai Bin Liew; Faculty of Pharmacy, University of Cyberjaya, Persiaran Bestari, 63000 Cyberjaya, Selangor, Malaysia; liewkaibin@cyberjaya.edu.my (KBL), Ching Siang Tan; School of Pharmacy, KPJ Healthcare University, Lot PT 17010 Persiaran Seriemas, Kota Seriemas, 71800 Nilai, Negeri Sembilan, Malaysia; tcsiang@kpju.edu.my (CST); Hui Suan Ng; Smart Bioresource Recovery and Formulation Laboratory, Department of Chemical Engineering and Materials Science, Yuan Ze University, Chungli, Taoyuan 320, Taiwan; grraceng@saturn.yzu.edu.tw (HSN)

Abstract: The skin microbiome is a dynamic microbial ecosystem that plays a fundamental role in maintaining epidermal barrier integrity, regulating immune homeostasis, and protecting against pathogenic colonisation. Dysbiosis of the skin microbiota has been implicated in numerous dermatological disorders, including acne vulgaris, atopic dermatitis, psoriasis, rosacea, and premature skin ageing, highlighting the microbiome as an emerging therapeutic target. In this context, probiotics have attracted increasing attention as microbiome-based interventions owing to their ability to restore microbial equilibrium and modulate host-microbe interactions. This review critically evaluates the current

understanding of probiotics in dermatology, with particular emphasis on the molecular mechanisms underlying their therapeutic effects. Recent studies demonstrate that probiotics exert strain-specific activities through competitive exclusion of pathogens, production of antimicrobial peptides and bioactive metabolites, modulation of Toll-like receptor (TLR)-mediated signalling, regulation of nuclear factor kappa B (NFκB) and mitogen-activated protein kinase (MAPK) pathways, enhancement of tight junction proteins and ceramide synthesis, and modulation of cytokine networks involved in cutaneous immunity. Representative probiotic strains, including *Lactocaseibacillus rhamnosus* GG, *Lactobacillus acidophilus*, *Lactobacillus plantarum*, *Bifidobacterium* species, *Bacillus coagulans*, *Saccharomyces boulardii*, and *Enterococcus faecium*, are discussed with respect to their strain-specific molecular effectors and dermatological applications. Clinical evidence supporting oral and topical probiotic interventions is critically appraised, highlighting both therapeutic potential and the heterogeneity of existing studies. Emerging advances in postbiotics, engineered probiotics, synthetic biology, CRISPR-based microbiome editing, multi-omics technologies, and artificial intelligence-driven precision microbiome medicine are also discussed as future directions. Despite encouraging findings, important challenges remain, including strain standardisation, formulation stability, regulatory harmonisation, and the need for robust multicentre clinical trials. Collectively, current evidence suggests that probiotics represent promising adjunctive strategies for microbiome-targeted dermatological therapy; however, further molecular and translational investigations are required to facilitate their integration into scientifically validated precision dermatology.

Keywords: Probiotics; Gut-skin axis; Postbiotics; Skin microbiome; Microbiome engineering; Dermatology

1. Introduction

The skin is the largest organ of the human body and serves as a dynamic interface between the internal environment and external surroundings ^[1]. Structurally, it consists of three main layers: the epidermis, dermis, and hypodermis, which function collectively to maintain physiological homeostasis and protect the body from physical, chemical, and biological insults ^[2]. The epidermis forms the primary barrier against environmental stressors, while the dermis provides structural support through a complex extracellular matrix containing collagen, elastin, blood vessels, hair follicles, sweat glands, sebaceous glands, and sensory receptors ^[3]. Beneath these layers, the hypodermis or subcutaneous tissue ^[4], serves as an energy reservoir, thermal insulator, and cushioning layer that anchors the skin to underlying muscles and bones ^[5,6]. Beyond its structural functions, the skin plays critical roles in immune surveillance, hydration maintenance, thermoregulation, wound healing, and the synthesis of bioactive molecules essential for overall health ^[7–9]. Figure 1 below shows the cross-sectional representation of the skin structure.

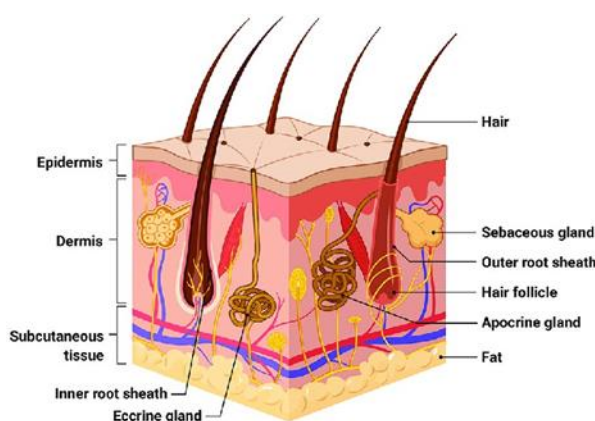


Figure 1. Cross-section of the skin.

Recent advances in microbiome research have revealed that the skin functions as a complex ecological niche inhabited by diverse microorganisms, including bacteria, fungi, viruses, and mites ^[10,11]. These microbial communities are not passive residents but active contributors to skin homeostasis ^[12]. The composition of the skin microbiome varies across anatomical sites in response to local physiological conditions, including moisture content, sebum production, pH, and oxygen availability ^[13]. Through continuous interactions with keratinocytes, sebocytes, and immune cells, commensal microorganisms contribute to barrier maintenance, pathogen exclusion, and immune regulation ^[14]. For example, commensal bacteria can produce antimicrobial peptides and short-chain fatty acids that inhibit pathogen colonisation, while simultaneously promoting regulatory immune responses that prevent excessive inflammation ^[15].

Disruption of the balanced relationship between the host and its resident microbiota, commonly referred to as dysbiosis, has been increasingly recognised as a key factor in the pathogenesis of numerous dermatological disorders ^[16,17]. Alterations in microbial diversity or the overgrowth of opportunistic microorganisms can impair barrier integrity, activate inflammatory signalling pathways, and exacerbate disease progression ^[18]. In acne vulgaris, dysbiosis involving specific strains of *Cutibacterium acnes* may stimulate the production of pro-inflammatory cytokines through Toll-like receptor-mediated pathways ^[19]. Similarly, reduced microbial diversity and increased colonisation by *Staphylococcus aureus* are strongly associated with barrier dysfunction and immune dysregulation in atopic dermatitis ^[20]. These findings highlight the intimate relationship between skin structure, microbial ecology, and cutaneous health.

Conventional dermatological therapies, including antibiotics, corticosteroids, retinoids, antihistamines, and phototherapy, remain the mainstay of dermatological treatment and management ^[21]. While these therapies are generally effective in controlling symptoms, their long-term use may be associated with adverse effects, such as skin irritation, barrier disruption, photosensitivity, and the emergence of antimicrobial resistance ^[22]. Furthermore, most conventional treatments primarily target disease symptoms rather than addressing the underlying microbial imbalance that contributes to disease development and recurrence ^[23]. Consequently, increasing attention has been directed towards microbiome-targeted strategies that aim to restore microbial homeostasis while supporting the skin's natural defence mechanisms.

Among these approaches, probiotics, defined as live microorganisms that confer health benefits when administered in adequate amounts, have emerged as promising candidates for maintaining and restoring skin health ^[24]. Probiotics can exert beneficial effects through multiple mechanisms, including competitive exclusion of pathogens and production of innate and adaptive immune responses ^[25]. These mechanisms directly address several pathways implicated in dysbiosis-associated skin disorders ^[26], making probiotics attractive therapeutic and preventive tools in modern dermatology. As scientific understanding of host-microbiome interactions continues to expand, probiotics and other microbiome-based interventions are increasingly being incorporated into dermatological and skincare applications ^[27].

This review provides a comprehensive overview of the role of probiotics in dermatology and microbiome-based skincare. Specifically, it discusses the mechanisms through which probiotics influence skin health, the major probiotic strains investigated for dermatological applications, formulation and delivery approaches, and their therapeutic potential in common skin disorders. In addition, current challenges, safety considerations, regulatory issues, and future perspectives for probiotic-based skincare products are critically evaluated. This review focuses primarily on probiotic microorganisms and their direct dermatological applications. Detailed discussions of prebiotics, postbiotics, synbiotics, and gut-skin axis interventions, as well as broader cosmetic regulatory frameworks, are beyond the scope of the present review, except where relevant to probiotic function and product development.

2. Review Methodology

To summarise current clinical evidence, published studies investigating probiotic interventions for dermatological conditions were identified through literature searches of

PubMed, Scopus, Web of Science, and Google Scholar. Search terms included combinations of probiotics, skin microbiome, dermatology, acne vulgaris, atopic dermatitis, eczema, psoriasis, skin ageing, topical probiotics, and oral probiotics. Priority was given to randomised controlled trials (RCTs), systematic reviews, meta-analyses, and well-designed clinical studies published in English from 2000 to 2026 to capture both early developments and recent advancements in the field, while relevant landmark studies were included where appropriate. Preclinical studies were incorporated primarily to explain molecular mechanisms when supporting clinical studies was limited. Owing to the heterogeneity of probiotic strains, dosages, treatment durations, and clinical outcome measures, this review is presented as a narrative synthesis rather than a quantitative meta-analysis.

3. The Science Behind Probiotics in Dermatology

Understanding the therapeutic potential of probiotics in dermatology requires an appreciation of the complex interactions between the skin microbiome, host immune system, and microbial metabolites. According to the International Scientific Association for Probiotics and Prebiotics (ISAPP), probiotics are defined as beneficial live microorganisms that confer health benefits to the host when administered in adequate amounts ^[28]. Common probiotic genera include *Escherichia*, *Lactobacillus*, *Bacillus*, *Saccharomyces*, *Bifidobacterium*, *Enterococcus* and *Streptococcus* ^[29]. In dermatological applications, probiotics may be delivered as viable microorganisms, lysates, ferments, or postbiotics, each capable of interacting with host tissues through distinct biological mechanisms ^[30].

3.1. Skin Microbiome and Host-Microbe Interactions

The skin microbiome comprises a diverse ecosystem of bacteria, fungi, viruses, and mites that inhabit the epidermis, sebaceous glands, and hair follicles ^[31]. These microorganisms continuously interact with keratinocytes, sebocytes, dendritic cells, and resident immune cells through pattern recognition receptors (PRRs), which detect conserved microbial-associated molecular patterns (MAMPs) ^[32]. Among these receptors, Toll-like receptors (TLRs), nucleotide-binding oligomerisation domain (NOD)-like receptors, and C-type lectin receptors play essential roles in maintaining immune homeostasis and barrier integrity ^[33]. Under healthy conditions, commensal microorganisms play a crucial role in maintaining skin homeostasis by protecting against pathogenic invasion, modulating immune responses, and supporting skin barrier integrity ^[34]. However, microbial dysbiosis can trigger abnormal PRR activation, excessive inflammation, and disruption of epidermal barrier function, contributing to the development of acne, eczema (atopic dermatitis), psoriasis, and premature skin ageing ^[35].

3.2. Molecular Mechanisms of Probiotic Action

Probiotics exert their dermatological effects through multiple interconnected molecular pathways. One of the primary mechanisms involves modulation of PRR-mediated signalling [36]. Probiotic-derived microbial ligands interact with Toll-like receptor 2 (TLR2), Toll-like receptor 4 (TLR4), and other PRRs expressed on keratinocytes and immune cells, thereby controlling the activation of downstream signalling cascades [37,38]. This interaction can suppress excessive inflammatory responses by inhibiting the activation of nuclear factor kappa B (NF- κ B), a key transcription factor responsible for producing pro-inflammatory mediators such as tumour necrosis factor-alpha (TNF- α), interleukin (IL)-1 β , IL-6, and IL-8 [39].

In addition to regulating NF- κ B signalling, probiotics can modulate mitogen-activated protein kinase (MAPK) pathways, including extracellular signal-regulated kinase (ERK), c-Jun N-terminal kinase (JNK), and cytokinin-specific binding protein (p38 MAPK) [40]. Regulation of these pathways influences cellular proliferation, differentiation, oxidative stress responses, and cytokine production [41]. Through these mechanisms, probiotics help attenuate chronic inflammation while promoting tissue repair and restoration of barrier function [42]. Furthermore, probiotics influence both innate and adaptive immunity by enhancing anti-inflammatory cytokines, such as IL-10 and transforming growth factor-beta (TGF- β), while suppressing pro-inflammatory mediators [43]. Several probiotic strains have also been reported to promote the differentiation of regulatory T cells (Tregs), contributing to immune tolerance and reduced inflammatory responses in chronic skin disorders [43]. The mechanistic figure demonstrating NF- κ B and MAPK pathways is shown in Figure 2.

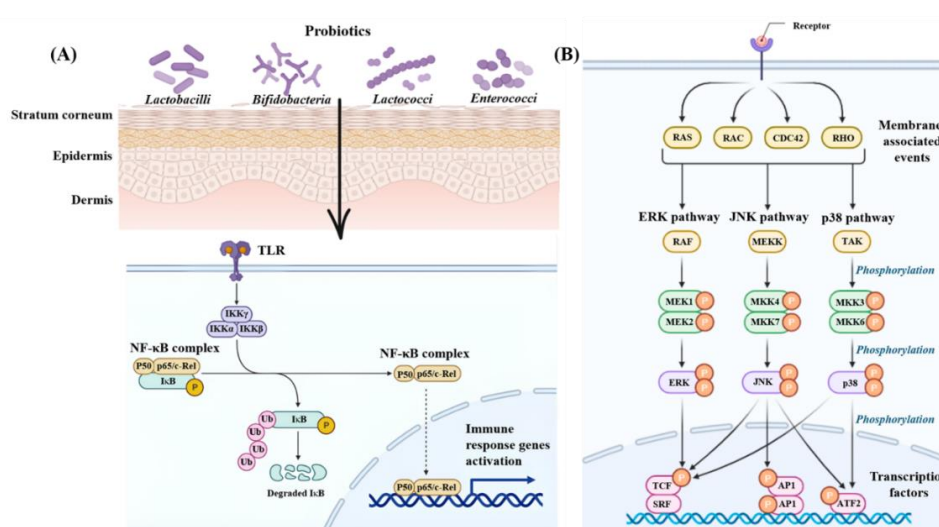


Figure 2. The molecular mechanisms of probiotic action involved in the (A) NF- κ B and (B) MAPK pathways. The icon resources used in this figure were obtained from BioRender software (Toronto, Canada).

3.3. Metabolite-mediated Mechanisms

Beyond direct microbial-host interactions, probiotics produce a variety of bioactive metabolites that contribute to skin health. Among the most extensively studied are short-chain fatty acids (SCFAs), including acetate, propionate, and butyrate ^[44]. SCFAs strengthen epithelial barrier function by enhancing tight-junction protein expression, regulating keratinocyte differentiation, and suppressing inflammatory signalling pathways ^[45]. They also function as histone deacetylase inhibitors by altering DNA transcription ^[46,47], thereby influencing gene expression and immune regulation ^[48].

Probiotic microorganisms additionally produce antimicrobial peptides and bacteriocins that inhibit the growth of pathogenic microorganisms, including *Staphylococcus aureus* and pathogenic strains of *Cutibacterium acnes* ^[49]. These antimicrobial compounds help restore microbial balance and reduce pathogen-induced inflammation. Another important class of microbial metabolites comprises tryptophan-derived compounds, including indole derivatives that activate the aryl hydrocarbon receptor (AhR) ^[50]. Activation of AhR regulates epidermal differentiation, immune homeostasis, antioxidant defence mechanisms, and barrier formation ^[51]. Increasing studies suggest that modulation of the AhR pathway shows an important mechanism through which probiotics contribute to skin health and disease prevention ^[52,53].

3.4. The Gut-Skin Axis

The gut-skin axis describes the bidirectional communication network linking the gastrointestinal microbiota and skin through immune, metabolic, endocrine, and neuroendocrine pathways ^[54]. Alterations in gut microbial composition can increase intestinal permeability and promote systemic dissemination of inflammatory mediators, thereby contributing to skin inflammation ^[55]. Conversely, restoration of gut microbial balance through probiotic supplementation may reduce systemic inflammation and improve dermatological outcomes ^[56]. Orally administered probiotics have been shown to modulate circulating cytokine profiles, enhance regulatory immune responses, and increase the production of beneficial microbial metabolites such as SCFAs ^[57]. These systemic effects may influence skin barrier integrity, sebum production, oxidative stress, and inflammatory responses ^[58], providing a mechanistic basis for the beneficial effects observed in conditions such as acne vulgaris and atopic dermatitis.

In this context, probiotics contribute to skin health through several complementary mechanisms. They help restore microbial equilibrium by competing with pathogenic

microorganisms for nutrients and adhesion sites, producing antimicrobial substances, and modulating host immune responses ^[59]. Furthermore, increasing scientific studies support the importance of the gut-skin axis, which describes the bidirectional communication between the gastrointestinal tract and the skin through immune, metabolic, and neuroendocrine pathways ^[60]. This concept suggests that modulation of the gut microbiota through oral probiotics may indirectly improve skin conditions such as acne and atopic dermatitis by reducing systemic inflammation and enhancing immune regulation ^[61].

3.5. Strain-specific Effects of Probiotics

Importantly, probiotic effects are highly strain-dependent, and different probiotic strains exhibit distinct adhesion properties, metabolite production profiles, antimicrobial activities, and immunomodulatory capabilities ^[62]. For example, *Lactobacillus rhamnosus* has been widely associated with enhancing skin barrier function and inducing regulatory immune responses ^[63]. In contrast, *Lacticaseibacillus paracasei* has demonstrated efficacy in reducing skin sensitivity, maintaining hydration, and improving barrier recovery ^[64]. Similarly, *Bifidobacterium lactis* has been reported to enhance skin hydration and reduce inflammatory responses ^[65], while *Lactiplantibacillus plantarum* exhibits strong antioxidant and antimicrobial properties ^[66]. These strain-specific differences highlight the importance of selecting appropriate probiotic strains for targeted dermatological applications and underscore the need for mechanistic studies that link specific microbial functions to clinical outcomes.

4. Molecular Mechanisms of Probiotic Action

The dermatological benefits of probiotics arise from complex molecular interactions involving skin microbiota, epithelial cells, immune cells, and microbial metabolites ^[67]. Rather than acting solely through microbial replacement, probiotics influence microbial ecology, regulate host signalling pathways, reinforce epidermal barrier integrity, and produce bioactive compounds that collectively restore skin homeostasis ^[15]. Importantly, these mechanisms are highly strain-specific and are influenced by probiotic variability, dosage, formulation, and route of administration.

4.1. Molecular Competition Mechanisms

Competitive exclusion is one of the earliest mechanisms through which probiotics suppress pathogen colonisation ^[68]. Probiotic bacteria adhere to keratinocytes and epithelial surfaces via surface adhesions, mucus-binding proteins (MUB), aggregation and promoting factors (APF), lipoteichoic acids, and exopolysaccharides (EPS) ^[69], thereby occupying

ecological niches which would otherwise be available to pathogens. This competition limits the attachment and proliferation of opportunistic microorganisms, including *Staphylococcus aureus* and pathogenic strains of *Cutibacterium acnes* [70].

Beyond simple competition for nutrients and adhesion sites, probiotics regulate microbial ecology through quorum quenching, whereby they interfere with bacterial quorum-sensing molecules such as autoinducing peptides (AIPs) and acyl-homoserine lactones (AHLs) [71]. Disruption of quorum sensing inhibits biofilm formation, virulence factor production, and toxin secretion by pathogenic microorganisms [72]. In addition, several probiotic strains reduce opportunities for horizontal gene transfer, including conjugation and transformation, by destabilising pathogenic biofilms and altering microbial community composition [73].

An emerging area of interest is the role of the skin phageome, which comprises diverse bacteriophages that naturally inhabit the skin and predominantly infect commensal bacteria, such as *Cutibacterium*, *Staphylococcus*, and *Corynebacterium* species [74]. These phages contribute to microbial homeostasis by regulating bacterial population dynamics, facilitating strain-level diversity, and influencing the exchange of bacterial genetic material through transduction [75]. Although direct studies remain limited, probiotics may indirectly modulate phage-bacteria interactions by reshaping the composition and metabolic activity of the skin microbiota, thereby altering the abundance and activity of resident bacteriophages. Such interactions may further enhance microbial stability, suppress the overgrowth of opportunistic pathogens, and contribute to restoration of a healthy skin ecosystem [76]. However, the mechanisms underlying probiotic-phage-host interactions remain incompletely understood and warrant further investigation [76,77].

4.2. Antimicrobial Peptide Production and Regulation

Probiotic microorganisms produce a broad spectrum of antimicrobial compounds that directly inhibit pathogen survival [68]. These include bacteriocins, bacteriocin-like inhibitory substances (BLIS), organic acids, hydrogen peroxide, biosurfactants, and antimicrobial peptides [78]. Bacteriocins permeabilise bacterial membranes or inhibit cell wall biosynthesis, whereas lactic and acetic acids lower local pH, creating an environment that suppresses the growth of *S. aureus*, *C. acnes*, and other opportunistic pathogens [79].

In addition to producing their own antimicrobial molecules, probiotics stimulate keratinocytes to express endogenous antimicrobial peptides, including human β -defensins (hBD-2 and hBD-3), cathelicidin (LL-37), and S100 proteins [80]. Upregulation of these

peptides enhances innate immune defence, restricts pathogen colonisation, and contributes to restoration of microbial homeostasis. Collectively, these mechanisms reduce microbial dysbiosis while preserving beneficial commensal microorganisms ^[81].

4.3. Tight Junction and Ceramide Synthesis Pathways

Management of epidermal barrier integrity is another key mechanism underlying probiotic function. Several probiotic strains regulate genes involved in tight junction assembly, including tight junction protein 1 (TJP1), occludin (OCLN), and claudin-1 (CLDN1) ^[82], thereby reducing transepidermal water loss and strengthening the epidermal barrier ^[83]. Probiotics also promote keratinocyte differentiation by increasing the expression of structural proteins such as filaggrin (FLG) and involucrin, which are essential for maintaining stratum corneum integrity ^[84].

Furthermore, certain probiotic species stimulate epidermal lipid metabolism by enhancing ceramide biosynthesis through activation of sphingomyelinase and ceramide synthases ^[85]. For example, *Streptococcus thermophilus* has been shown to increase endogenous ceramide production, thereby restoring the lipid matrix, improving skin hydration, and reducing barrier dysfunction associated with inflammatory disorders such as atopic dermatitis ^[86].

4.4. TLR-mediated Immune Signalling

Probiotics regulate cutaneous immunity through interactions with pattern recognition receptors (PRRs) expressed on keratinocytes, Langerhans cells, dendritic cells, macrophages, and other immune cells ^[43]. Cell wall components such as lipoteichoic acids, peptidoglycans, and lipoproteins are recognised primarily by TLR2, whereas lipopolysaccharides activate TLR4 ^[87]. Engagement of these receptors initiates intracellular signalling through the myeloid differentiation primary response 88 (MyD88)-dependent pathway, regulating downstream transcription factors including NFκB1 and mitogen-activated protein kinases (MAPKs, ERK, JNK, and p38 MAPK) ^[88].

Unlike pathogenic stimulation, probiotic-mediated activation of TLR signalling generally results in controlled immune responses characterised by reduced activation of NF-κB and suppression of pro-inflammatory genes, including TNF, IL-1β, IL-6, and CXCL8 (IL-8) ^[89]. Simultaneously, probiotics enhance the expression of anti-inflammatory mediators such as IL-10 and TGFB1, promoting differentiation of FoxP3⁺ regulatory T cells (Tregs) and maintaining immune tolerance ^[90]. This balanced modulation of innate and adaptive

immunity contributes to reduced inflammation and improved skin homeostasis, where immune dysregulation plays a central pathological role ^[91].

4.5. Mechanistic Differences between Live Probiotics, Paraprobiotics, and Postbiotics

Although live probiotics remain the most extensively investigated, increasing scientific work indicates that non-viable microbial preparations, often known as paraprobiotics/postbiotics, also possess important biological activities ^[92]. Live probiotics exert their effects through transient colonisation, metabolic activity, production of antimicrobial compounds, and continuous interaction with resident microbiota and host tissues ^[25]. In contrast, paraprobiotics (inactivated microbial cells) retain immunologically active structural components such as peptidoglycans, lipoteichoic acids, and surface proteins that activate PRRs despite the absence of viable cells ^[93]. Postbiotics, comprising microbial metabolites and secreted bioactive molecules, including short-chain fatty acids, bacteriocins, enzymes, extracellular vesicles, and exopolysaccharides, mediate many beneficial effects independently of living microorganisms ^[94]. Owing to their superior stability, safety, and ease of formulation, postbiotics have become increasingly attractive for topical dermatological products.

4.6. Dose-response Relationships and Strain Specificity

The molecular effects of probiotics are highly dependent on strain identity, viable cell concentration, exposure duration, and formulation characteristics. Individual strains differ substantially in adhesion capacity, antimicrobial peptide production, metabolite profiles, and immunomodulatory properties ^[95]. For example, *Lactocaseibacillus rhamnosus* GG enhances barrier integrity primarily by increasing the expression of TJP1, OCLN, and CLDN1 ^[96]. On the other hand, *Lactiplantibacillus plantarum* exhibits stronger antioxidant activity by suppressing reactive oxygen species (ROS) and inhibiting NF- κ B signalling ^[97]. Similarly, *Bifidobacterium lactis* preferentially promotes regulatory immune responses and enhances epidermal hydration by producing SCFAs such as acetate and lactic acid ^[98].

Dose-dependent effects of probiotics have also been reported in dermatological applications ^[99,100]. Moderate probiotic concentrations may support optimal immunomodulatory and skin barrier responses, although increasing the dose does not necessarily produce a proportional increase in therapeutic benefits ^[101]. Importantly, while receptor desensitisation has been suggested as one possible explanation for attenuated responses to high microbial exposure in other biological systems ^[102], direct investigation of this mechanism in the skin remains limited. Therefore, probiotic dose should be optimised

according to the specific strain, formulation, route of administration, and treatment duration to maximise therapeutic efficacy while avoiding unnecessary increases in microbial load.

5. Routes of Administration of Probiotics in Dermatology

The therapeutic efficacy of probiotics in dermatology depends not only on strain selection but also on the route of administration, which determines microbial survival, host interactions, and mechanisms of action [36]. Current probiotic interventions are broadly classified into oral and topical delivery. Oral administration primarily modulates skin health indirectly through the gut-skin axis, whereas topical application delivers microorganisms or their bioactive components directly to the cutaneous microbiome. Both approaches present unique advantages and limitations, and their clinical utility depends on the target dermatological condition, formulation stability, and maintenance of probiotic viability [36,103,104]. Table 1 shows the major comparisons between oral and topical probiotics, particularly in dermatology.

Table 1. Comparison of oral and topical probiotics for dermatological applications.

Feature	Oral Probiotics	Topical Probiotics
Primary target	Gut microbiota	Skin microbiota
Mechanism	Gut-skin axis, systemic immune modulation	Direct microbiome modulation, barrier repair, and local immune regulation
Main pathways	SCFAs, Tregs, cytokine regulation	TLR2/TLR4, AMPs, ceramide synthesis, NF-κB inhibition
Advantages	Whole-body immune effects; suitable for chronic inflammatory disorders	Localised action; avoids gastrointestinal degradation; direct modulation of skin microbiota
Limitations	Gastric acid, bile salts, viability loss, variable colonisation	Limited shelf-life for live probiotics; formulation stability; transient skin colonisation
Clinical evidence grading basis	Moderate quality (GRADE) (Supported by multiple double-blinded RCTs for acne and AD)	Low to moderate quality (GRADE) (Supported by small-scale RCTs, pilot studies, and cell lysates/postbiotics)
Suitable conditions	Acne, atopic dermatitis, psoriasis, rosacea	Acne, atopic dermatitis, wound healing, skin ageing
Major challenge	Survival through the gastrointestinal tract	Preservation of viability on the skin and during storage

Clinical evidence grading basis: The clinical evidence is rated using the grading of recommendations assessment, development and evaluation (GRADE) framework, where:

- (i) moderate quality – Further research is likely to have an important impact on confidence in the estimate of effect. Supported by multiple double-blinded, placebo-controlled randomised clinical trials (RCTs);
- (ii) low quality – Further research is very likely to have an important impact on confidence in the estimate of effect. Supported primarily by small-scale RCTs, open-label trials, or studies utilising bacterial lysates/postbiotics rather than live strains.

5.1. Oral Administration

Oral probiotics exert their effects principally through modulation of the intestinal microbiota and the gut-skin axis^[105]. By restoring intestinal microbial balance, strengthening gut barrier integrity, and reducing systemic inflammation, orally administered probiotics indirectly influence cutaneous immune responses and skin barrier function^[106]. Clinical studies have demonstrated beneficial effects of oral probiotic supplementation in inflammatory skin disorders, particularly acne vulgaris and atopic dermatitis^[107], where reductions in disease severity have been associated with decreased circulating pro-inflammatory cytokines and improved immune regulation^[103,108].

Oral formulations are available as powders, tablets, capsules, liquids, and fermented foods^[109]. Although advances in delivery technologies have improved probiotic survival during gastrointestinal transit^[110–112], upholding bacterial viability remains a major challenge because exposure to gastric acid, bile salts, oxygen, moisture, and temperature fluctuations can substantially reduce viable cell numbers before intestinal colonisation occurs^[113]. Therefore, the clinical efficacy of oral probiotics depends not only on the selected strain but also on adequate viable counts at the time of administration and throughout the product shelf life.

Despite encouraging clinical findings, considerable variability exists among published studies owing to differences in probiotic strains, dosages, treatment duration, and formulation characteristics^[114,115]. Furthermore, many commercially available probiotic products provide limited data regarding strain variability at the point of consumption, making direct comparison between studies more difficult^[116].

5.2. Topical Administration

Topical probiotic formulations are designed to modulate the skin microbiome directly by restoring microbial balance, suppressing pathogenic microorganisms, reinforcing epidermal barrier function, and regulating local immune responses^[59]. Unlike oral administration, topical delivery enables direct interaction between probiotics and resident skin microorganisms, keratinocytes, and immune cells, thereby facilitating local modulation of microbial ecology and inflammatory signalling pathways^[117].

Current topical formulations include creams, lotions, gels, serums, sprays, and masks containing live probiotics, paraprobiotics, bacterial lysates, or postbiotics^[118]. Increasing research suggests that non-viable preparations may offer comparable biological activity while overcoming numerous stability challenges associated with live microorganisms^[119,120].

Postbiotics and bacterial lysates retain immunomodulatory and antimicrobial properties despite the absence of viable cells, making them particularly attractive for dermatological formulations requiring prolonged storage and consistent product quality ^[121].

Clinical studies supporting topical probiotics are growing, particularly for acne vulgaris and atopic dermatitis ^[122,123]. Several studies have reported reductions in *Staphylococcus aureus* colonisation, decreased inflammatory lesions, and improved epidermal barrier function following topical probiotic treatment ^[124,125]. However, many investigations remain limited by small sample sizes, heterogeneous study designs, and short follow-up periods. Thus, additional well-designed clinical trials are required before widespread clinical recommendations can be established.

5.3. Challenges and Future Perspectives

A critical challenge affecting both oral and topical probiotic formulations is the preservation of microbial viability throughout manufacturing, storage, distribution, and administration ^[126]. Exposure to gastric acid and bile salts following oral administration, as well as oxygen, moisture, ultraviolet radiation, temperature fluctuations, and formulation excipients during processing and storage, can substantially reduce the number of viable microorganisms before they reach their intended site of action. Importantly, many commercially available probiotic products report viable cell counts only at the time of manufacture rather than guaranteed potency at the end of shelf life, which is an issue compounded by regulatory frameworks that often lack stringent requirements for end-of-shelf-life viability testing ^[127,128]. Furthermore, independent market analyses and product-testing studies have confirmed that numerous commercial formulations fail to meet their stated viable counts near or at expiry ^[129,130]. Consequently, the actual dose of viable microorganisms delivered to consumers may differ considerably from the labelled content ^[131], potentially contributing to inconsistent therapeutic outcomes and variability among clinical studies. Furthermore, the absence of standardised methods for assessing probiotic viability complicates comparisons across products and limits reproducibility. Addressing these gaps requires harmonised quality-control standards, standardised viability testing, and stricter regulatory mandates for end-of-shelf-life reporting.

Another important consideration is that probiotic efficacy is highly strain-specific and dose-dependent ^[116]. Differences in microbial adhesion, metabolite production, immunomodulatory activity, and environmental tolerance contribute to substantial variability among clinical studies. Therefore, future research should prioritise the standardisation of probiotic formulations, strain identification, viability assessment throughout shelf life, and

clinical trial methodology to facilitate comparison between studies and support dermatological applications.

6. Probiotic Strains in Dermatology: Strain-Specific Properties and Clinical Evidence

The therapeutic potential of probiotics in dermatology is increasingly recognised due to their ability to influence skin homeostasis through multiple mechanisms, including modulation of immune responses, enhancement of epithelial barrier integrity, regulation of microbial balance, and attenuation of inflammatory pathways [105]. However, probiotic activity is highly dependent on strain-specific characteristics, and the beneficial effects observed for one strain cannot be directly extrapolated to other strains within the same species or genus. Differences in genomic composition, adhesion capacity, metabolite production, antimicrobial activity, and interaction with host immune pathways contribute to variations in biological efficacy. Therefore, understanding the strain-specific properties of probiotics is essential for evaluating their potential applications in dermatological conditions. Table 2 summarises the key probiotic strains in dermatological applications.

Table 2. Summary of key probiotic strains in dermatology.

Probiotic strain	Evidence level	Major molecular effectors	Proposed mechanism	Main dermatological indications	Ref
<i>Lactobacillus acidophilus</i>	RCTs, clinical studies, <i>in vitro</i>	Lactic acid, bacteriocins	↓ TNF- α , ↑ IL-10, barrier repair	Acne vulgaris, atopic dermatitis, skin ageing	[132–134]
<i>Lactocaseibacillus rhamnosus</i> GG	Multiple RCTs, <i>in vivo</i>	p40, p75 proteins	↑ TJP1, ↑ OCLN, ↓ NF- κ B	Atopic dermatitis, eczema	[135,136]
<i>Lactiplantibacillus plantarum</i>	RCTs, <i>in vitro</i>	Plantaricins	↓ ROS, ↑ ceramide synthesis	Acne, wound healing	[137,138]
<i>Limosilactobacillus fermentum</i>	<i>In vivo</i> , <i>in vitro</i>	Fermenticin, SCFAs	Antioxidant, immune modulation	Photoaging, eczema	[139,140]
<i>Bifidobacterium infantis</i>	RCTs, clinical studies	SCFAs	↑ IL-10, ↑ filaggrin	Psoriasis, atopic dermatitis	[141,142]
<i>Bifidobacterium longum</i>	RCTs	Acetate	↓ skin sensitivity	Sensitive skin, eczema	[143,144]
<i>Saccharomyces boulardii</i>	RCTs	Secreted proteases	Anti-inflammatory	Dermatitis	[145,146]
<i>Bacillus coagulans</i>	RCTs, clinical studies	Lactic acid, bacteriocins	Gut-skin modulation	Acne	[147,148]
<i>Enterococcus faecium</i>	RCTs, clinical studies	Enterocins	Competitive exclusion	Acne	[149]
<i>Akkermansia muciniphila</i>	<i>In vivo</i>	Amuc_1100 proteins	Barrier integrity	Emerging	[150]
<i>Faecalibacterium prausnitzii</i>	<i>In vivo</i>	Butyrate, MAM proteins	↓ NF- κ B	Emerging	[151]

Abbreviations & terminology – RCTs: Randomised controlled trials; SCFAs: Short-chain fatty acids; TJP1: Tight junction protein 1; OCLN: Occludin; MAM: Microbial anti-inflammatory molecule; ROS: Reactive oxygen species.

Evidence level definitions – (i) Randomised controlled trials (RCTs): Human clinical trials utilising randomised, controlled (placebo or active comparator) designs (including double-blinded or single-blinded protocols); (ii) Clinical studies: Human clinical evaluations that are not double-blinded RCTs, including open-label trials, non-randomised prospective cohort studies, or single-arm pilot intervention trials; (iii) *In vivo*: Preclinical experimental studies conducted within intact living organisms (e.g., animal models of dermatitis or skin ageing); and (iv) *In vitro*: Preclinical experimental studies conducted using isolated cellular cultures, tissue constructs, or cell-free assays outside a living organism. The evidence levels indicate the types of experimental or clinical study designs reported in the literature and do not constitute a formal methodological quality grading.

6.1. Strain-specific determinants of probiotic efficacy

Several functional characteristics, including survival capacity, colonisation ability, production of bioactive metabolites, and immunomodulatory effects, influence the effectiveness of probiotics in skin health. Probiotic strains with strong epithelial adhesion properties may improve microbial interactions with the host and contribute to the restoration of microbial balance^[62]. In addition, the production of organic acids, bacteriocins, and other antimicrobial compounds may inhibit the growth of pathogenic microorganisms associated with skin dysbiosis^[79]. Many probiotic strains also exhibit anti-inflammatory and antioxidant properties by regulating cytokine production, suppressing excessive immune activation, and reducing oxidative stress^[152]. Through the gut-skin axis, probiotics may further influence dermatological health by modulating the composition of the intestinal microbiota and systemic immune responses.

6.1.1. *Lactobacillus* species

Lactobacillus species are the most extensively studied group of probiotics due to their established safety profile and diverse biological functions^[36]. Their potential dermatological benefits have been associated with the maintenance of microbial equilibrium, the regulation of inflammation, the enhancement of barrier function, and the modulation of host immunity^[15]. However, the therapeutic profile of individual *Lactobacillus* strains is heavily dictated by distinct and strain-specific molecular effectors, including unique bacteriocin classes, surface proteins, and secreted enzymes.

One of the most notable strains is *Lactobacillus acidophilus* (*L. acidophilus*), a Gram-positive lactic acid bacterium that naturally inhabits the human gastrointestinal tract, oral cavity, and vaginal microbiota. *L. acidophilus* produces specific Class II non-lanthionine-containing bacteriocins (such as Acidocin A, B, and LF221) alongside surface-

layer proteins (SlpA) ^[153,154]. Acidocins act predominantly by inducing pore formation and dissipation of the proton motive force in membrane-targeted pathogens. In contrast, *Lactobacillus plantarum* secretes a structurally distinct arsenal of two-peptide Class IIb plantaricins (e.g., Plantaricin EF and JK) and the peptide signal Plantaricin A, which disrupt target cell membranes via cooperative dual-peptide insertion ^[155]. Furthermore, *L. plantarum* produces broad-spectrum non-peptide metabolites such as phenyllactic acid (PLA), giving it enhanced antifungal and broad antimicrobial activity compared to the narrower activity spectrum of *L. acidophilus* ^[156]. At the skin interface, while *L. acidophilus* relies significantly on SlpA-mediated TLR2 binding to regulate inflammatory responses ^[157], *L. plantarum* leverages high-molecular-weight exopolysaccharides (EPS) to quench reactive oxygen species (ROS) and accelerate cutaneous wound healing ^[158].

Lacticaseibacillus rhamnosus GG (LGG) further illustrates these effector-level distinctions. Unlike *L. acidophilus* or *L. plantarum*, which primarily execute antimicrobial action via bacteriocin secretion, LGG's mucosal and cutaneous activities are largely driven by specialised SpaCBA pili adhesins and secreted functional proteins, notably p40 and p75 ^[159]. These soluble endopeptidases directly transactivate the epidermal growth factor receptor (EGFR) and inhibit p38 MAPK-mediated apoptosis, preserving epithelial junctional integrity independently of bacteriocin-mediated lysis ^[160].

Similarly, *Lactobacillus fermentum* relies on specialised antioxidant enzymes (e.g., manganese superoxide dismutase) and short-chain fatty acids (SCFAs) to neutralise oxidative stress and suppress pro-inflammatory cytokines, complementing the membrane-active mechanisms of other lactobacilli ^[161]. Optimising probiotic therapy thus requires selecting strains based on these explicit molecular signatures rather than broad species-level assumptions.

6.1.2. *Bifidobacterium* species

Bifidobacterium species are important members of the human microbiota and have received increasing attention due to their role in immune regulation and maintenance of intestinal homeostasis ^[42]. Through the gut-skin axis, *Bifidobacterium* strains, including *Bifidobacterium infantis* and *Bifidobacterium longum*, may influence dermatological outcomes by regulating systemic inflammation, improving barrier function, and modulating immune tolerance ^[26,162,163].

Among these species, *Bifidobacterium infantis* has attracted considerable attention due to its potent immunoregulatory properties, particularly through modulation of

inflammatory responses and promotion of immune balance ^[141]. Its ability to reduce excessive immune activation may be beneficial in inflammatory skin conditions where immune dysregulation plays a central role ^[164]. Furthermore, its contribution to microbiome stability may indirectly support skin health. For instance, oral supplementation with *Bifidobacterium infantis* has been shown to reduce systemic inflammation, as indicated by decreased levels of C-reactive protein (CRP) and increased production of anti-inflammatory cytokines such as interleukin-10 (IL-10) ^[162].

Bifidobacterium longum (*B. longum*) is another clinically relevant strain with emerging evidence in dermatological applications ^[165]. It has been investigated for its ability to improve skin sensitivity, regulate inflammatory responses, and enhance barrier-related functions ^[166]. The beneficial effects of *B. longum* are linked to its capacity to influence immune pathways, reduce oxidative stress, and maintain microbial equilibrium, highlighting its potential role in managing skin conditions associated with inflammation and barrier dysfunction ^[167].

6.2. Other Clinically Relevant Probiotics

Beyond *Lactobacillus* and *Bifidobacterium*, several other probiotic microorganisms have demonstrated potential relevance in dermatology. *Saccharomyces boulardii*, a probiotic yeast, differs from bacterial probiotics but has gained recognition due to its ability to modulate intestinal microbiota and immune responses ^[146]. Although direct clinical data in dermatological applications remains limited, its influence on gut microbial balance and inflammatory regulation suggests potential relevance through the gut-skin axis.

Bacillus coagulans is another promising probiotic due to its spore-forming ability, which provides enhanced stability and survival under environmental stress ^[168]. Its potential benefits are associated with immune modulation, antioxidant activity, and regulation of microbial communities ^[148]. These characteristics make *B. coagulans* an attractive candidate for functional formulations targeting systemic and skin health.

Enterococcus faecium has been explored as a probiotic due to its antimicrobial properties and ability to influence microbial communities ^[149]. However, its application requires careful consideration because certain strains may pose safety concerns, including antimicrobial resistance ^[169]. Therefore, strain selection and comprehensive safety evaluation remain essential before clinical application.

6.3. Next-Generation Probiotics

The emergence of next-generation probiotics marks a shift towards the utilisation of beneficial commensal microorganisms that naturally inhabit the human microbiome ^[170]. These organisms offer new opportunities for targeted microbiome-based interventions due to their specialised biological functions. The next-generation probiotics, such as *Akkermansia muciniphila* and *Faecalibacterium prausnitzii* ^[171], are discussed as follows.

Akkermansia muciniphila (*A. muciniphila*) is a promising next-generation probiotic that contributes to intestinal barrier maintenance through the regulation of mucin metabolism and epithelial integrity ^[172]. By suppressing gut permeability and lipopolysaccharide (LPS) translocation, *A. muciniphila* exerts well-documented systemic anti-inflammatory and metabolic regulatory effects that may indirectly influence skin homeostasis through the gut-skin axis (e.g., attenuation of gut permeability and endotoxemia) ^[173,174]. However, while its oral administration shows potential for modulating systemic inflammatory skin disorders, direct dermatological or topical applications of *A. muciniphila* remain highly speculative and currently lack robust experimental or clinical validation, largely owing to its strict anaerobic nature, as well as formulation hurdles ^[175].

Faecalibacterium prausnitzii (*F. prausnitzii*) is another emerging probiotic candidate recognised as a major butyrate-producing bacterium with potent anti-inflammatory properties ^[176]. Through the production of short-chain fatty acids and the regulation of immune responses, *F. prausnitzii* may contribute to the restoration of microbial balance and suppression of inflammatory pathways ^[151]. Although clinical studies in dermatology remain limited, its role in maintaining intestinal and immune homeostasis highlights its potential for future microbiome-based dermatological therapies.

In short, probiotic research in dermatology has progressed from the general classification of probiotic organisms towards a more precise understanding of strain-specific functions. Future developments should focus on identifying clinically validated strains, elucidating mechanisms of action, and establishing scientifically validated applications of probiotic interventions in skin health and disease management.

7. Benefits & Clinical Efficacy of Probiotics in Dermatology

The skin is not merely a passive physical barrier, but a dynamic ecosystem inhabited by a diverse community of microorganisms collectively known as the skin microbiome ^[31]. This complex microbial environment plays a vital role in maintaining skin homeostasis,

regulating immune responses, and protecting against pathogenic invasion. Disruptions in microbial balance have been linked to various dermatological disorders, including acne vulgaris, atopic dermatitis (eczema), and premature skin ageing [10]. As understanding of the skin microbiome continues to expand, probiotics have emerged as promising therapeutic agents for promoting skin health and managing dermatological conditions. Table 3 shows several clinical studies associated with the efficacy of probiotics, particularly in dermatological applications.

Table 3. Clinical studies on the efficacy of probiotics in dermatological disorders.

Study	Design	Sample size (N)	Probiotic strain	Route	Duration	Main outcome	Main findings (Effect size)	Major limitations	Ref
Acne vulgaris	RCT	45	<i>Lactobacillus acidophilus</i> , <i>Lactobacillus delbrueckii bulgaricus</i> & <i>Bifidobacterium bifidum</i>	Oral	12 weeks	Acne lesion count	Inflammatory lesions ↓ 67% versus baseline (p < 0.01)	Small sample size; single-centre study	[177]
Acne vulgaris	Double-blind RCT	20	<i>Lactobacillus rhamnosus</i> SP1	Oral	12 weeks	Lesion count	Non-inflammatory lesions ↓ 32% (p < 0.001)	Young adults only	[178]
Acne vulgaris	Double-blind RCT	30	<i>Lactobacillus plantarum</i> CJLP55	Oral	12 weeks	Acne severity; skin hydration	Acne grade ↓ 29.33% (p = 0.03); skin hydration ↑ 14.52% (p = 0.003)	Small sample size	[138]
Acne vulgaris	Double-blind RCT	70	<i>Enterococcus faecalis</i> SL-5	Topical	8 weeks	Pustule count	Inflammatory lesion (pustule) count ↓ > 60% versus placebo (p < 0.05)	Limited follow-up	[179]
Acne vulgaris	RCT	104	<i>Lactobacillus paracasei</i> MSMC 39-1	Topical	4 weeks	Acne lesion counts & erythema index	Inflammatory acne lesion counts & erythema index significantly ↓ (p < 0.001)	Short intervention period	[180]
Atopic dermatitis	Double-blind RCT	22	<i>Lactobacillus plantarum</i> IS-10506	Oral	12 weeks	SCORAD	SCORAD score of probiotic group (18.53 ± 14.2) significantly ↓ than placebo (22.04 ± 8.8) (p = 0.044)	Single-country study	[181]
Atopic dermatitis	Double-blind RCT	50	<i>Bifidobacterium lactis</i> CECT 8145, <i>Bifidobacterium longum</i> CECT 7347, and <i>Lactobacillus casei</i> CECT 9104	Oral	12 weeks	SCORAD	SCORAD score ↓ 8.3 points versus placebo (MD = -2.4, p < 0.001)	Heterogeneous disease severity	[182]
Atopic dermatitis	Double-blind RCT	75	<i>Vitreoscilla filiformis</i> lysate	Topical	30 days	SCORAD	SCORAD score of probiotic group (15.1) significantly ↓ than placebo (24.9) (p = 0.004)	Short intervention period	[183]

Study	Design	Sample size (N)	Probiotic strain	Route	Duration	Main outcome	Main findings (Effect size)	Major limitations	Ref
Skin ageing	Double-blind RCT	110	<i>Lactobacillus plantarum</i> HY7714	Oral	12 weeks	Skin elasticity	Hydration ↑ 21.73%; versus placebo (p < 0.01) Skin sensitivity ↓ significantly (p = 0.0024), with TEWL ≥ 15 g/cm ² /h	Healthy women only	[184]
Sensitive skin	Double-blind RCT	66	<i>Bifidobacterium longum</i> lysate	Topical	2 months	Skin sensitivity		Female volunteers only	[99]

RCT: Randomised controlled trial; SCORAD: Scoring atopic dermatitis; ICF-1: Insulin-like growth factor 1; TEWL: Transepidermal water loss; MD: Mean difference; ↓: Statistically significant decrease; ↑: Statistically significant increase

*Sample size (N): Values represent the total number of evaluable/randomised human participants enrolled in the study (analysed across active treatment and placebo/control groups).

7.1. Acne Vulgaris

Acne vulgaris is among the most extensively investigated dermatological conditions for probiotic therapy owing to the recognised involvement of microbial dysbiosis, particularly the overgrowth of *Cutibacterium acnes*, together with excessive sebum production and chronic inflammation [185]. Both oral and topical probiotics have demonstrated the capacity to reduce inflammatory lesions by suppressing pathogenic microorganisms, enhancing skin barrier function, and modulating innate immune responses [30,36,186]. Several randomised controlled trials have reported significant improvements in lesion counts following supplementation with *Lactocaseibacillus rhamnosus*, *Lactiplantibacillus plantarum*, and combinations of *L. acidophilus*, *L. bulgaricus*, and *Bifidobacterium bifidum* [138,186,187]. However, reported treatment effects vary considerably among studies attributed to the differences in probiotic strains, viable cell concentrations, treatment duration, concurrent therapies, and outcome measures. Although reductions in inflammatory lesion counts ranging from approximately 20–70% have been reported [188,189], these findings should be interpreted cautiously because many studies involve relatively small sample sizes, short intervention periods, or lack long-term follow-up. Consequently, larger multicentre randomised controlled trials are required to establish optimal probiotic regimens and confirm sustained clinical efficacy.

7.2. Atopic Dermatitis (Eczema)

Among inflammatory skin disorders, atopic dermatitis possesses the strongest clinical data supporting probiotic intervention [190], particularly during early childhood. Multiple randomised controlled trials and meta-analyses have demonstrated reductions in scoring atopic dermatitis (SCORAD) scores following supplementation with strains such as

Lactocaseibacillus rhamnosus GG, *Lactiplantibacillus plantarum*, and *Bifidobacterium* species [135,191,192]. These improvements are thought to result from the restoration of microbial diversity, reduced *Staphylococcus aureus* colonisation, enhancement of epidermal barrier function, and increased regulatory T-cell activity [91]. However, clinical outcomes remain inconsistent. Several trials have failed to demonstrate significant improvements, particularly in adults, and treatment efficacy appears to depend on patient age, disease severity, probiotic strain, and duration of supplementation [67,193]. Therefore, although probiotics are promising adjunctive therapy, current clinical studies have yet to support universal recommendations for all patients with atopic dermatitis.

7.3. Skin Ageing

Increasing scientific studies suggest that probiotics may attenuate cutaneous ageing through multiple molecular pathways associated with oxidative stress, chronic inflammation, and extracellular matrix degradation [105,194]. Ultraviolet (UV) radiation stimulates reactive oxygen species (ROS) production, activating MAPK and NF- κ B signalling pathways that subsequently increase the expression of matrix metalloproteinases (MMP-1 (collagenase), MMP-3 (stromelysin), and MMP-9 (gelatinase)) [195]. These enzymes degrade collagen and elastin fibres, resulting in the formation of wrinkles and loss of skin elasticity [36]. Several probiotic strains, including *Lactiplantibacillus plantarum* and *Bifidobacterium longum*, have demonstrated the ability to suppress ROS accumulation, reduce MMP expression, enhance antioxidant enzyme activity (i.e. superoxide dismutase and catalase), and activate the nuclear factor erythroid 2-related factor 2 (NRF2) antioxidant pathway [196–198]. Additional studies have reported increased collagen synthesis, improved epidermal hydration, and enhanced barrier function following probiotic supplementation [199,200]. However, clinical work remains limited compared with acne vulgaris and atopic dermatitis, with most studies involving relatively small cohorts and short treatment durations.

7.4. Critical Appraisal of Current Clinical Work

Although numerous studies have reported beneficial effects of probiotics in dermatology, interpretation of the available data should be undertaken cautiously. Considerable heterogeneity exists among published work with respect to probiotic strain selection, viable cell concentration, formulation, treatment duration, patient characteristics, disease severity, and clinical outcome measures. These differences complicate direct comparisons between studies and limit the ability to establish standardised treatment recommendations.

Publication bias is also an important consideration because studies reporting positive outcomes are generally more likely to be published than studies demonstrating neutral or negative findings. This bias can inflate pooled effect sizes in literature syntheses and mask true clinical variability. Indeed, while several rigorous randomised controlled trials evaluating *Lactobacillus* and *Bifidobacterium* strains have demonstrated no statistically significant superiority over placebo in reducing SCORAD scores or preventing eczema flare-ups [193,201], selective reporting and the under-reporting of such non-significant results remain widespread. To rigorously identify and account for publication bias in future synthesis, systematic reviews should routinely employ quantitative diagnostic tools, including funnel plot asymmetry assessments, Egger's linear regression test, and Duval and Tweedie's trim-and-fill method to estimate bias-adjusted effect sizes [202–204]. Furthermore, many existing studies involve relatively small sample sizes and limited follow-up, making long-term efficacy and safety difficult to assess. Future multicentre randomised controlled trials using standardised probiotic strains, dosage regimens, and validated clinical outcome measures are thus essential to strengthen the evidence base.

7.5. Dose-Response Relationships and Treatment Duration

Probiotic efficacy appears to be influenced by both the administered dose and the duration of treatment. Most clinical studies have employed daily doses ranging from approximately 10^8 to 10^{11} colony-forming units (CFUs), although the optimal therapeutic dose has not yet been established [186,205]. Clinical improvements are generally observed after 8–12 weeks of continuous supplementation, whereas shorter treatment periods often produce limited effects [206]. Moreover, increasing probiotic dosage does not necessarily result in greater clinical benefit because therapeutic responses are highly strain-specific and depend on microbial viability, host microbiome composition, and disease characteristics [207]. Future dose-finding clinical trials are required to define minimum effective doses and optimal treatment duration for individual dermatological conditions.

8. Complementary and Integrative Approaches: Probiotics in Modern Dermatological Therapy

Although conventional pharmacological therapies remain the cornerstone of dermatological management, increasing scientific studies suggest that probiotics may serve as valuable complementary interventions rather than direct therapeutic substitutes [208]. Unlike antibiotics, corticosteroids, or retinoids, which primarily target specific pathological processes, probiotics act by restoring microbial homeostasis, strengthening the epidermal barrier, and modulating host immune responses [209]. These distinct mechanisms provide

opportunities for integration with conventional therapies to improve treatment outcomes while potentially reducing treatment-related adverse effects.

8.1. Probiotics as Adjunctive Therapy

For acne vulgaris, topical and systemic antibiotics remain highly effective in rapidly reducing *Cutibacterium acnes* proliferation and inflammation. However, prolonged antibiotic therapy may disrupt commensal microbial communities and contribute to antimicrobial resistance. Probiotics offer a complementary microbiome-centred approach by suppressing pathogenic microorganisms through competitive exclusion, bacteriocin production, and immune modulation while preserving microbial diversity [30]. Consequently, probiotics are increasingly investigated as adjuncts to antibiotic therapy rather than replacements, particularly for reducing recurrence and supporting restoration of microbial balance following antimicrobial treatment [180].

Similarly, topical corticosteroids remain the first-line treatment for inflammatory disorders such as atopic dermatitis because of their rapid anti-inflammatory activity. However, long-term corticosteroid use may result in skin atrophy, impaired barrier function, and local adverse effects. Probiotic supplementation may complement corticosteroid therapy by enhancing epidermal barrier integrity, promoting regulatory T-cell responses, increasing expression of barrier-associated proteins, and reducing *Staphylococcus aureus* colonisation [193]. Such complementary mechanisms may facilitate maintenance therapy and potentially reduce corticosteroid requirements in selected patients, although robust clinical studies remain limited [182].

Retinoids continue to be the gold standard for photoageing and acne owing to their ability to regulate keratinocyte differentiation and stimulate collagen synthesis. In contrast, probiotics exert anti-ageing effects primarily by reducing oxidative stress, suppressing matrix metalloproteinase (MMP) expression, enhancing skin hydration, and improving barrier function [197,198]. Although these mechanisms do not replace the pharmacological potency of retinoids, probiotic formulations may improve treatment tolerability and reduce irritation when incorporated into comprehensive skincare regimens [83].

8.2. Combination and Sequential Therapeutic Strategies

The complementary mechanisms of probiotics have generated increasing interest in combination therapies. Several clinical studies suggest that concurrent administration of oral probiotics with systemic antibiotics may reduce gastrointestinal dysbiosis while supporting restoration of beneficial microbial communities [210,211]. In acne management, probiotics

administered alongside antibiotics have been associated with improved lesion reduction, decreased treatment-related gastrointestinal adverse effects, and enhanced patient adherence compared with antibiotic therapy alone ^[177].

Sequential treatment strategies have also been proposed. Administration of probiotics following completion of antibiotic therapy may facilitate recolonisation of beneficial microorganisms, restore microbial diversity, and reduce the likelihood of recurrent dysbiosis ^[212]. Similarly, combining probiotics with topical retinoids or corticosteroids may improve epidermal barrier recovery and alleviate treatment-induced irritation without compromising therapeutic efficacy ^[213]. Although these integrative approaches are biologically plausible and supported by preliminary clinical studies, larger randomised controlled trials are required to determine optimal treatment sequencing, duration, and probiotic strain selection.

8.3. Safety, Accessibility, and Regulatory Considerations

Overall, probiotics demonstrate favourable safety profiles and are generally well tolerated in healthy individuals, with mild gastrointestinal discomfort indicating the most frequently reported adverse event following oral administration. Topical formulations similarly exhibit low incidences of irritation and allergic reactions compared with many conventional dermatological therapies. However, the administration of live probiotics requires careful consideration in immunocompromised individuals, critically ill patients, or those with implanted medical devices, as rare cases of opportunistic bacteraemia and fungaemia have been reported ^[214]. Equally critical is the requirement for rigorous, strain-level safety evaluations, where safety profiles cannot be generalised across a species as individual strains may harbour strain-specific virulence factors or antimicrobial resistance (AMR) genes capable of horizontal gene transfer ^[215,216]. In vulnerable populations or when safety risks are present, non-viable alternatives such as paraprobiotics and postbiotics may provide safer therapeutic options while retaining many beneficial biological activities ^[217].

From an economic perspective, probiotics may reduce long-term dependence on anti-inflammatory medications and antibiotics, potentially lowering healthcare costs associated with chronic dermatological diseases. However, product accessibility and affordability vary considerably among regions, and many commercially available formulations lack independent verification of strain identity, viability, and clinical efficacy. Furthermore, regulatory requirements differ substantially between countries, with probiotic products frequently marketed as foods, dietary supplements, cosmetics, or therapeutic agents under distinct regulatory frameworks ^[218]. Harmonisation of quality standards, strain identification,

viability assessment, genomic screening for resistance genes, and clinical data requirements will therefore be essential to support wider clinical implementation.

Taken together, current literature indicates that probiotics should be regarded as complementary components of integrated dermatological management rather than direct replacements for established pharmacological therapies. Their greatest clinical value is likely to be achieved through personalised treatment strategies that combine microbiome modulation with conventional interventions according to disease severity, patient characteristics, and therapeutic objectives. Table 4 outlines the comparison of probiotics and conventional dermatological therapies in terms of mechanisms of action, clinical applications, safety, and evidence level [36,189,219].

Table 4. Comparison of probiotics and conventional therapeutic approaches in dermatology.

Parameter	Probiotics	Antibiotics	Corticosteroids	Retinoids
Primary mechanism	Microbiome modulation, immune regulation, barrier repair	Antibacterial	Anti-inflammatory	Keratinocyte differentiation synthesis
Onset of action	Variable (slow to moderate; days to weeks)	Rapid (hours to days)	Rapid (hours to days)	Moderate to slow (weeks to months)
Best indication	Adjunctive therapy	Acute bacterial acne	Acute inflammatory dermatoses	Acne, photoageing
Common adverse effects	Mild gastrointestinal symptoms (oral); occasional local irritation (topical)	Antimicrobial resistance, gastrointestinal disturbance	Skin atrophy, hypothalamic-pituitary-adrenal axis suppression with prolonged use	Irritation, erythema, photosensitivity
Suitability for long-term use	Generally favourable (strain-dependent)	Limited by antimicrobial resistance	Limited by cumulative adverse effects	Requires monitoring for tolerability
Evidence level	Moderate; strain-specific	High	High	High
Regulatory status	Foods, dietary supplements, cosmetics, or therapeutics, depending on jurisdiction	Prescription medicines	Prescription medicines	Prescription and over-the-counter formulations, depending on concentration
Approximate relative cost	Low to moderate	Moderate	Low to moderate	Moderate

(i) Onset of action: The therapeutic onset of probiotics varies considerably by administration route, formulation type, and clinical endpoint. Fast-acting topical formulations (such as cell lysates or postbiotics targeting skin barrier hydration) can demonstrate local physiological effects within days, whereas oral live probiotics targeting

systemic immune modulation or gut-skin axis remodelling typically require several weeks (4-12 weeks) of continuous administration to manifest meaningful clinical responses.

(ii) Approximate relative cost: Costs are approximate and vary substantially across geographic regions, jurisdictions, and product classifications (e.g., over-the-counter dietary supplements/cosmetics versus prescription-grade pharmaceuticals). High-potency topical retinoids and specialised medical-grade or multi-strain probiotic formulations may incur significantly higher out-of-pocket costs in certain markets.

9. Challenges, Emerging Technologies, and Future Perspectives

Despite the growing body of research supporting probiotics in dermatology, several scientific, technological, regulatory, and translational challenges remain before microbiome-based interventions can be routinely incorporated into clinical practice. Addressing these limitations will require multidisciplinary collaboration among microbiologists, dermatologists, formulation scientists, bioinformaticians, and regulatory agencies to ensure that probiotic products are safe, effective, reproducible, and clinically validated.

9.1. Strain Identification and Characterisation Standards

One of the major challenges in probiotic research is the lack of standardised approaches for strain identification and functional characterisation. Since probiotic activity is highly strain-specific, taxonomic identification at the species level alone is insufficient to predict therapeutic efficacy ^[36]. Whole-genome sequencing, multilocus sequence typing (MLST), comparative genomics, and metabolomic profiling are increasingly employed to characterise probiotic strains, identify functional genes, and ensure batch-to-batch consistency ^[220]. Future studies should integrate genomic, transcriptomic, proteomic, and metabolomic analyses to establish molecular signatures associated with specific dermatological benefits and facilitate the development of standardised probiotic reference strains ^[189].

9.2. Advanced Molecular Tools for Microbiome Engineering

Rapid advances in synthetic biology have opened new opportunities for engineering probiotics with enhanced therapeutic functions. Genetically modified probiotic strains can be designed to secrete anti-inflammatory cytokines, antimicrobial peptides, antioxidants, or growth factors directly at the site of inflammation, thereby improving therapeutic specificity while minimising systemic adverse effects ^[213]. Clustered regularly interspaced short palindromic repeats-associated protein (CRISPR-Cas) genome editing further enables precise modification of probiotic genomes, allowing optimisation of metabolic pathways, bacteriocin production, and host-microbe interactions ^[221]. In parallel, CRISPR-based antimicrobials and engineered bacteriophages emerge as innovative approaches for

selectively eliminating pathogenic microorganisms such as *Cutibacterium acnes* and *Staphylococcus aureus* while preserving beneficial members of skin microbiota. However, translating CRISPR-based editing to the skin microbiome in situ faces substantial technical hurdles. Key challenges include overcoming the physical barrier of the stratum corneum, penetrating dense cutaneous biofilms, and achieving efficient, targeted vector delivery (such as via engineered phages, lipid nanoparticles, or bacterial conjugation) to specific bacterial targets in an open, harsh microenvironment [222–224]. While these technologies show promising next-generation microbiome therapeutics, overcoming delivery limitations alongside evaluating biosafety, genetic stability, and ecological impact will be essential before clinical implementation.

9.3. Postbiotics as Next-Generation Therapeutics

An important future direction involves the transition from live probiotics toward postbiotics and paraprobiotics. Unlike viable microorganisms, postbiotics consist of bioactive metabolites, cell-wall components, enzymes, extracellular vesicles, and other microbial products that retain biological activity without requiring bacterial survival [219]. These preparations offer several practical advantages, including improved physicochemical stability, simplified manufacturing, longer shelf life, reduced risk of microbial contamination, and enhanced safety for immunocompromised individuals. Furthermore, postbiotics may facilitate regulatory approval because they eliminate concerns regarding microbial viability during storage and administration. Continued characterisation of their molecular mechanisms and active components will be essential for expanding their clinical applications in dermatology.

9.4. Regulatory and Commercialisation Challenges

The global regulatory landscape for probiotic dermatological products remains fragmented. At an international level, the Food and Agriculture Organisation and World Health Organisation (FAO/WHO) established joint guidelines offering a foundational framework for probiotic characterisation, strain-level identification, safety testing, and health-claim validation [225]. However, adoption and enforcement of these WHO guidelines vary widely, and global regulatory pathways continue to depend heavily on a product's intended classification. In the United States, classification falls under Food and Drug Administration (FDA) as a cosmetic, dietary supplement, biologic, or drug depending on intended use. Within the European Union, probiotic cosmetics and therapeutics are regulated under the European Medicines Agency (EMA) framework, while oral probiotic health claims are evaluated by the European Food Safety Authority (EFSA). Across Asia, regulatory

requirements vary considerably among countries, with Japan, South Korea, China, and Singapore adopting distinct national frameworks for functional foods, cosmetics, and microbiome-based therapeutics. These global inconsistencies create significant challenges for international commercialisation, product standardisation, and clinical translation ^[218,226].

Commercialisation is further complicated by intellectual property considerations. Naturally occurring probiotic strains are often difficult to patent, leading developers to focus on proprietary formulations, engineered strains, novel delivery platforms, postbiotic compositions, or manufacturing technologies ^[227]. Consequently, balancing innovation with accessibility remains an important challenge for both academia and industry.

9.5. Artificial Intelligence and Precision Dermatology

Artificial intelligence (AI) and machine learning are expected to transform personalised probiotic therapy by integrating multi-omics datasets, including metagenomics, host genomics, transcriptomics, and metabolomics profiles, with clinical endpoints and environmental factors ^[228]. In microbiome analysis, machine learning algorithms are already accelerating strain identification and functional profiling, whereby deep learning frameworks (such as deep neural networks and random forest classifiers) enable high-resolution strain-level taxonomy and functional gene annotation directly from complex metagenomic sequencing data ^[229]. Furthermore, supervised learning models, such as gradient-boosted trees (e.g., XGBoost) and support vector machines, have been successfully applied to predict patient-specific treatment responses and microbiome compositional shifts prior to therapy ^[230,231]. In precision dermatology, such predictive modelling can facilitate the identification of optimal probiotic strains, individualised dosage regimens, and targeted treatment durations tailored to a patient's unique microbiome signature, ultimately advancing data-driven therapeutic decision-making ^[232].

9.6. Future Research Priorities

Although considerable progress has been achieved, several fundamental questions remain unresolved. Future research should prioritise:

- Standardisation of probiotic strain identification, genomic characterisation, and quality-control procedures.
- Elucidation of strain-specific molecular mechanisms through integrated multi-omics approaches.
- Optimisation of probiotic dosage, formulation, treatment duration, and delivery systems for different dermatological conditions.

- Comparative evaluation of live probiotics, paraprobiotics, postbiotics, and synbiotics in randomised controlled clinical trials.
- Investigation of long-term safety, microbiome stability, and host-microbe interactions following prolonged probiotic administration.
- Development of engineered probiotics and CRISPR-based microbiome editing strategies with demonstrated biosafety.
- Establishment of internationally harmonised regulatory frameworks for probiotic skincare products.
- Validation of AI-assisted precision microbiome platforms for individualised probiotic selection.
- Identification of predictive biomarkers associated with clinical response and treatment resistance.
- Evaluation of the economic feasibility, patient acceptance, and real-world effectiveness of microbiome-based dermatological therapies.

Collectively, these multidisciplinary research directions are expected to accelerate the translation of microbiome science into safe, evidence-based, and personalised dermatological interventions.

10. Conclusion

Probiotics have emerged as promising microbiome-based interventions for dermatological applications through their multifaceted ability to modulate microbial homeostasis, epidermal barrier function, immune responses, and host-microbe interactions. Increasing mechanistic and clinical studies indicate that specific probiotic strains, together with postbiotics and other microbiome-derived therapeutics, may complement conventional management strategies for acne vulgaris, atopic dermatitis, skin ageing, and other inflammatory skin disorders. However, their therapeutic efficacy remains highly strain-dependent, with outcomes influenced by formulation, dosage, treatment duration, route of administration, and host-specific factors. Therefore, probiotics should be considered as targeted, rather than universally applicable interventions.

Despite encouraging findings, translation into routine dermatological practice remains constrained by substantial heterogeneity in strains, formulations, dosing regimens, study populations, and outcome measures. Most of the current research is derived from *in vitro* studies, animal models, or small clinical trials, while long-term safety, optimal treatment protocols, and strain-specific mechanisms remain incompletely defined. Standardised approaches to strain characterisation, viability assessment, formulation, clinical

trial design, and outcome evaluation are therefore needed to improve reproducibility and enable meaningful comparison across studies.

Future research should prioritise the integration of molecular microbiology, multi-omics, formulation science, bioengineering, and clinical dermatology to identify strain-specific determinants of efficacy and develop more precise microbiome-based interventions. Greater emphasis on well-designed, adequately powered clinical trials and rigorous quality-control and regulatory frameworks will be essential to establish clinical efficacy and safety. Collectively, these efforts can help advance probiotics and related microbiome-based therapeutics from promising adjunctive approaches toward precision-oriented strategies in dermatological care.

Author Contributions: Conceptualization: HSN and KBL. Writing – original draft preparation: SMT, RTW, YLC, SKL. Writing – review and editing: ABMHU, HSN, CST and KBL. Validation: KBL and CST. Supervision: KBL. Funding acquisition: CST and KBL.

Funding: This work was supported by University of Cyberjaya Research Grant Scheme (Grant no: UOC/DVC(R&I)/RMU/URGS_APPROVAL_08/2023)

Acknowledgements: The authors acknowledge University of Cyberjaya for providing literature search database and facility to complete the review article.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Hani Yousef, Mandy Alhaji, Sandeep Sharma. Anatomy, Skin (Integument), Epidermis - StatPearls - NCBI Bookshelf. StatPearls Publishing, Treasure Island (FL). 2024. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK470464/>.
2. Lotfollahi Z. The anatomy, physiology and function of all skin layers and the impact of ageing on the skin. Wound Practice and Research 2024;32(1):6. doi:10.33235/wpr.32.1.6-10.
3. Thomas M. Brown, Karthik Krishnamurthy. Histology, Dermis - StatPearls - NCBI Bookshelf. StatPearls Publishing, Treasure Island (FL). 2022. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK535346/>.
4. Seliem AO, Mahmoud AAE, Ezzat KM, *et al.* An Overview on Histology of the skin. International Journal of Multiphysics 2024;18(3):2932. Available from: <https://themultiphysicsjournal.com/index.php/ijm/article/view/1910>.
5. Stecco C, Hammer W, Vleeming A, *et al.* Subcutaneous Tissue and Superficial Fascia. In: Functional Atlas of the Human Fascial System. Elsevier Ltd. China 2015:21-49. doi:10.1016/b978-0-7020-4430-4.00002-6.
6. Prohic A. Skin Structure and Functions of the Skin. In: Dermatovenerology Textbook. Cham: Springer Nature Switzerland 2024:3-15. doi:10.1007/978-3-031-66131-0_1.

7. Trivedi NR, Cong Z, Nelson AM, *et al.* Peroxisome proliferator-activated receptors increase human sebum production. *Journal of Investigative Dermatology* 2006;126(9):2002. doi:10.1038/sj.jid.5700336.
8. Romanovsky AA. Skin temperature: Its role in thermoregulation. *Acta Physiologica* 2014;210(3):498. doi:10.1111/apha.12231.
9. Verdier-Sévrain S, Bonté F. Skin hydration: A review on its molecular mechanisms. *Journal of Cosmetic Dermatology* 2007;6(2):75. doi:10.1111/j.1473-2165.2007.00300.x.
10. Hong JY, Kwon D, Park KY. Microbiome-Based Interventions for Skin Aging and Barrier Function: A Comprehensive Review. *Annals of Dermatology* 2025;37(5):259. doi:10.5021/ad.25.009.
11. Suri H, Suri H, Nagda N, *et al.* Current perspectives on the human skin microbiome: Functional insights and strategies for therapeutic modulation. *Biomedicine and Pharmacotherapy* 2025;193:118655. doi:10.1016/j.biopha.2025.118655.
12. Sanabani SS. The skin microbiome: from historical ecology to therapeutic frontiers. *Anais Brasileiros de Dermatologia* 2026;101(4):501393. doi:10.1016/j.abd.2026.501393.
13. Nicholas-Haizelden K, Murphy B, Hoptroff M, *et al.* Bioprospecting the Skin Microbiome: Advances in Therapeutics and Personal Care Products. *Microorganisms* 2023;11(8):1899. doi:10.3390/microorganisms11081899.
14. Coates M, Blanchard S, MacLeod AS. Innate antimicrobial immunity in the skin: A protective barrier against bacteria, viruses, and fungi. *PLoS Pathogens* 2018;14(12):e1007353. doi:10.1371/journal.ppat.1007353.
15. Li Z, Zhang J, Zhang Y, *et al.* Skin Microbiome in Health and Disease: Mechanisms and Emerging Therapeutic Strategies. *Clinical, Cosmetic and Investigational Dermatology* 2025;18:3443. doi:10.2147/CCID.S571984.
16. Hawkins B, Montgomery M, Bokota G, *et al.* Gut microbiota dysbiosis at the interface of neuropsychiatric disorders and their dermatological comorbidities. *Gut Microbes* 2025;17(1):2574934. doi:10.1080/19490976.2025.2574934.
17. Alagiakrishnan K, Morgadinho J, Halverson T. Approach to the diagnosis and management of dysbiosis. *Frontiers in Nutrition* 2024;11:1330903. doi:10.3389/fnut.2024.1330903.
18. Toydemir S, Merey G. Biochemistry of Human Gut Microbiota: Related Diseases and Dietary Interactions. *Molecules* 2026;31(8):1369. doi:10.3390/molecules31081369.
19. Mayslich C, Grange PA, Dupin N. *Cutibacterium acnes* as an opportunistic pathogen: An update of its virulence-associated factors. *Microorganisms* 2021;9(2):303. doi:10.3390/microorganisms9020303.
20. Okamoto H, Nakamura Y. Dysbiosis in the Pathogenesis of Atopic Dermatitis. *The Journal of Dermatology* 2026;53(3):388. doi:10.1111/1346-8138.70191.

21. Aravinda Kumar B. Dermatological Pharmacology. In: Introduction to Basics of Pharmacology and Toxicology: Volume 2: Essentials of Systemic Pharmacology: From Principles to Practice 2021. doi:10.1007/978-981-33-6009-9_67.
22. Pancu DF, Scurtu A, Macasoi IG, *et al.* Antibiotics: Conventional therapy and natural compounds with antibacterial activity-a pharmaco-toxicological screening. *Antibiotics* 2021;10(4):401. doi:10.3390/antibiotics10040401.
23. Kamel M, Aleya S, Alsubih M, *et al.* Microbiome Dynamics: A Paradigm Shift in Combatting Infectious Diseases. *Journal of Personalized Medicine* 2024;14(2):217. doi:10.3390/jpm14020217.
24. Puebla-Barragan S, Reid G. Probiotics in cosmetic and personal care products: Trends and challenges. *Molecules* 2021;26(5):1249. doi:10.3390/molecules26051249.
25. Tukaram KS, Sopanrao SR, Kacharu LO. Unveiling The Therapeutic Potential of Probiotics: A Review. *Journal of Future Foods* 2025;13(6):e70364. doi:10.1016/j.jfutfo.2025.09.011.
26. Renuka SR, Ashok Kumar N, Manoharan D, *et al.* Probiotics: A Review on Microbiome That Helps for Better Health – A Dermatologist’s Perspective. *Journal of Pharmacology and Pharmacotherapeutics* 2023;14(1):5. doi:10.1177/0976500X231175225.
27. The Skin Microbiome Revolution: The Science and Challenges of Prebiotics, Probiotics, and Postbiotics in Skincare. *Cosmetics* 2026;13(1):43. doi:10.3390/cosmetics13010043.
28. Gibson GR, Hutkins R, Sanders ME, *et al.* Expert consensus document: The International Scientific Association for Probiotics and Prebiotics (ISAPP) consensus statement on the definition and scope of prebiotics. *Nature Reviews Gastroenterology and Hepatology* 2017;14:491. doi:10.1038/nrgastro.2017.75.
29. Kezer G, Paramithiotis S, Khwaldia K, *et al.* A comprehensive overview of the effects of probiotics, prebiotics and synbiotics on the gut-brain axis. *Frontiers in Microbiology* 2025;16:1651965. doi:10.3389/fmicb.2025.1651965.
30. De Almeida CV, Antiga E, Lulli M. Oral and Topical Probiotics and Postbiotics in Skincare and Dermatological Therapy: A Concise Review. *Microorganisms* 2023;11(6):1420. doi:10.3390/microorganisms11061420.
31. Chen H, Zhao Q, Zhong Q, *et al.* Skin Microbiome, Metabolome and Skin Phenome, from the Perspectives of Skin as an Ecosystem. *Phenomics* 2022;2(6):363. doi:10.1007/s43657-022-00073-y.
32. Lunjani N, Ahearn-Ford S, Dube FS, *et al.* Mechanisms of microbe-immune system dialogue within the skin. *Genes and Immunity* 2021;22:276. doi:10.1038/s41435-021-00133-9.
33. Li D, Wu M. Pattern recognition receptors in health and diseases. *Signal Transduction and Targeted Therapy* 2021;6(1):291. doi:10.1038/s41392-021-00687-0.
34. Byrd AL, Belkaid Y, Segre JA. The human skin microbiome. *Nature Reviews Microbiology* 2018;16:143. doi:10.1038/nrmicro.2017.157.

35. Borrego-Ruiz A, Borrego JJ. Microbial Dysbiosis in the Skin Microbiome and Its Psychological Consequences. *Microorganisms* 2024;12(9):1908. doi:10.3390/microorganisms12091908.
36. Gowda V, Sarkar R, Verma D, *et al.* Probiotics in Dermatology: An Evidence-based Approach. *Indian Dermatology Online Journal* 2024;15(4):571. doi:10.4103/idoj.idoj_614_23.
37. Paveljšek D, Ivičak-Kocjan K, Treven P, *et al.* Distinctive probiotic features share common TLR2-dependent signalling in intestinal epithelial cells. *Cellular Microbiology* 2021;23(1):e13264. doi:10.1111/cmi.13264.
38. Coutinho-Wolino KS, Almeida PP, Mafra D, *et al.* Bioactive compounds modulating Toll-like 4 receptor (TLR4)-mediated inflammation: pathways involved and future perspectives. *Nutrition Research* 2022;107:96. doi:10.1016/j.nutres.2022.09.001.
39. Qian C, Cao X, Hoffmann JA. Toll-like receptors in innate immunity and inflammation: from fundamental biology to clinic insights. *Immunity & Inflammation* 2026;2(1):22. doi:10.1007/s44466-026-00040-6.
40. Vincenzi A, Goettert MI, Volken de Souza CF. An evaluation of the effects of probiotics on tumoral necrosis factor (TNF- α) signaling and gene expression. *Cytokine and Growth Factor Reviews*. 2021;57:27. doi:10.1016/j.cytogfr.2020.10.004.
41. Kubatka P, Bojkova B, Nosalova N, *et al.* Targeting the MAPK signaling pathway: implications and prospects of flavonoids in 3P medicine as modulators of cancer cell plasticity and therapeutic resistance in breast cancer patients. *EPMA Journal* 2025;16(2):437. doi:10.1007/s13167-025-00407-6.
42. You Y, Kim TR, Sohn M, *et al.* Protective Effects of a Bifidobacterium-Based Probiotic Mixture on Gut Inflammation and Barrier Function. *Microbiology Research* 2025;16(8):168. doi:10.3390/microbiolres16080168.
43. Mazziotta C, Tognon M, Martini F, *et al.* Probiotics Mechanism of Action on Immune Cells and Beneficial Effects on Human Health. *Cells* 2023;12(1):184. doi:10.3390/cells12010184.
44. Lange O, Proczko-Stepaniak M, Mika A. Short-Chain Fatty Acids—A Product of the Microbiome and Its Participation in Two-Way Communication on the Microbiome-Host Mammal Line. *Current Obesity Reports* 2023;12(2):108. doi:10.1007/s13679-023-00503-6.
45. Xiao X, Hu X, Yao J, *et al.* The role of short-chain fatty acids in inflammatory skin diseases. *Frontiers in Microbiology* 2023;13:1083432. doi:10.3389/fmicb.2022.1083432.
46. Licciardi P V., Ververis K, Karagiannis TC. Histone Deacetylase Inhibition and Dietary Short-Chain Fatty Acids. *ISRN Allergy* 2011;2011:869647. doi:10.5402/2011/869647.
47. Thomas SP, Denu JM. Short-chain fatty acids activate acetyltransferase p300. *Elife* 2021;10;10:e72171. doi:10.7554/eLife.72171.

48. Magrin GL, Strauss FJ, Benfatti CAM, *et al.* Effects of short-chain fatty acids on human oral epithelial cells and the potential impact on periodontal disease: A systematic review of in vitro studies. *International Journal of Molecular Sciences* 2020;21(14):4895. doi:10.3390/ijms21144895.
49. Fournière M, Latire T, Souak D, *et al.* Staphylococcus epidermidis and cutibacterium acnes: Two major sentinels of skin microbiota and the influence of cosmetics. *Microorganisms* 2020;8(11):1752. doi:10.3390/microorganisms8111752.
50. Hezaveh K, Shinde RS, Klötgen A, *et al.* Tryptophan-derived microbial metabolites activate the aryl hydrocarbon receptor in tumor-associated macrophages to suppress anti-tumor immunity. *Immunity* 2022;55(2):324. doi:10.1016/j.immuni.2022.01.006.
51. Yang J, Qiao P, Wang G, *et al.* The Role of Aryl Hydrocarbon Receptor in Skin Homeostasis: Implications for Therapeutic Strategies in Skin Disorders. *Cell Biochemistry and Function* 2025;43(2):e70047. doi:10.1002/cbf.70047.
52. Qiu X, Wu L, Jiang F, *et al.* Engineered probiotic-derived indole-3-propionic acid inhibits ubiquitination via AHR signaling to treat postmenopausal osteoporosis. *Gut Microbes* 2026;18(1):2612620. doi:10.1080/19490976.2025.2612620.
53. Ahn YM, Shin S, Jang J hye, *et al.* Bojungikgi-tang improves skin barrier function and immune response in atopic dermatitis mice fed a low aryl hydrocarbon receptor ligand diet. *Chinese Medicine* 2023;18(1):100. doi:10.1186/s13020-023-00806-9.
54. Munteanu C, Turti S, Marza SM. Unraveling the Gut–Skin Axis: The Role of Microbiota in Skin Health and Disease. *Cosmetics* 2025;12(4):167. doi:10.3390/cosmetics12040167.
55. Andrzejczak K, Kucharczyk E, Sternak A, *et al.* Gut Dysbiosis and the Molecular Landscape of the Gut–Skin Axis: Comparative Insights and Therapeutic Implications for Atopic Dermatitis and Psoriasis. *Cells* 2026;15(7):594. doi:10.3390/cells15070594.
56. Mahmud MR, Akter S, Tamanna SK, *et al.* Impact of gut microbiome on skin health: gut-skin axis observed through the lenses of therapeutics and skin diseases. *Gut Microbes* 2022;14(1):2096995. doi:10.1080/19490976.2022.2096995.
57. Raheem A, Liang L, Zhang G, *et al.* Modulatory Effects of Probiotics During Pathogenic Infections With Emphasis on Immune Regulation. *Frontiers in Immunology* 2021;12:616713. doi:10.3389/fimmu.2021.616713.
58. Nami Y, Shaghaghi Ranjbar M, Modarres Aval M, *et al.* Harnessing Lactobacillus-derived SCFAs for food and health: Pathways, genes, and functional implications. *Current Research in Microbial Sciences* 2025;9:100496. doi:10.1016/j.crmicr.2025.100496.
59. Habeebuddin M, Karnati RK, Shiroorkar PN, *et al.* Topical Probiotics: More Than a Skin Deep. *Pharmaceutics* 2022;14(3):557. doi:10.3390/pharmaceutics14030557.
60. Salem I, Ramser A, Isham N, *et al.* The gut microbiome as a major regulator of the gut-skin axis. *Frontiers in Microbiology* 2018;9:1459. doi:10.3389/fmicb.2018.01459.

61. Lee LH. Probiotics in Depression Management: Efficacy, Mechanisms and Future Directions. *Progress in Microbes and Molecular Biology* 2025;8(1):a0000459. doi:10.36877/pmmmb.a0000459.
62. Bubnov R V., Babenko LP, Lazarenko LM, *et al.* Specific properties of probiotic strains: relevance and benefits for the host. *EPMA Journal* 2018;9(2):205. doi:10.1007/s13167-018-0132-z.
63. Jung YO, Jeong H, Cho Y, *et al.* Lysates of a probiotic, *Lactobacillus rhamnosus*, can improve skin barrier function in a reconstructed human epidermis model. *International Journal of Molecular Science* 2019;20(17):4289. doi:10.3390/ijms20174289.
64. Lee S, Lee EJ, Ahn CW, *et al.* Beneficial Effects of *Lactocaseibacillus paracasei* subsp. *paracasei* ABF21013 on Skin Health by Regulating MMPs Production and EGFR Signal Pathway. *Journal of Microbiology and Biotechnology* 2026;36:e2601006. doi:10.4014/jmb.2601.01006.
65. Kimoto-Nira H. New lactic acid bacteria for skin health via oral intake of heat-killed or live cells. *Animal Science Journal* 2018;89(6):835. doi:10.1111/asj.13017.
66. Tenea GN, Pircalabioru GG, Cifuentes V, *et al.* Metabolomic and functional profiling of *Lactiplantibacillus plantarum* strains reveals distinct probiotic, immunomodulatory, and antimicrobial signatures. *Applied Microbiology and Biotechnology* 2026;110(1):24. doi:10.1007/s00253-026-13706-3.
67. McLoughlin IJ, Wright EM, Tagg JR, *et al.* Skin Microbiome—The Next Frontier for Probiotic Intervention. *Probiotics and Antimicrobial Proteins* 2022;14(4):630. doi:10.1007/s12602-021-09824-1.
68. Alshatari SS, Ziarno M. Probiotic-Driven Competitive Exclusion in the Human Gut: A Meta-Analysis of Microbial Diversity and Pathogen Suppression. *Nutrients* 2026;18(5):796. doi:10.3390/nu18050796.
69. Javanshir N, Hosseini GNG, Sadeghi M, *et al.* Evaluation of the Function of Probiotics, Emphasizing the Role of their Binding to the Intestinal Epithelium in the Stability and their Effects on the Immune System. *Biological Procedures Online* 2021; 23(1):23. doi:10.1186/s12575-021-00160-w.
70. Khalfallah G, Gartzén R, Möller M, *et al.* A New Approach to Harness Probiotics Against Common Bacterial Skin Pathogens: Towards Living Antimicrobials. *Probiotics and Antimicrobial Proteins* 2021;13(6):1557. doi:10.1007/s12602-021-09783-7.
71. Salman MK, Abuqwider J, Mauriello G. Anti-Quorum Sensing Activity of Probiotics: The Mechanism and Role in Food and Gut Health. *Microorganisms* 2023;11(3):793. doi:10.3390/microorganisms11030793.
72. Zhang X, Zhang D, Zhou D, *et al.* A comprehensive review of the pathogenic mechanisms of *Pseudomonas aeruginosa*: synergistic effects of virulence factors, quorum sensing, and biofilm formation. *Frontiers in Microbiology* 2025;16:1619626. doi:10.3389/fmicb.2025.1619626.
73. Barzegari A, Kheyrolahzadeh K, Mahdi S, *et al.* The battle of probiotics and their derivatives against biofilms. *Infection and Drug Resistance* 2020;13:659. doi:10.2147/IDR.S232982.

74. Alsaadi SE, Lu H, Zhang M, *et al.* Bacteriophages from human skin infecting coagulase-negative Staphylococcus: diversity, novelty and host resistance. *Scientific Reports* 2024;14(1):8245. doi:10.1038/s41598-024-59065-9.
75. Skowron K, Bauza-kaszewska J, Kraszewska Z, *et al.* Human skin microbiome: Impact of intrinsic and extrinsic factors on skin microbiota. *Microorganisms* 2021;9(3):543. doi:10.3390/microorganisms9030543.
76. Federici S, Nobs SP, Elinav E. Phages and their potential to modulate the microbiome and immunity. *Cellular and Molecular Immunology* 2021;18:889. doi:10.1038/s41423-020-00532-4.
77. Rybicka I, Kaźmierczak Z. The human phageome: niche-specific distribution of bacteriophages and their clinical implications. *Applied and Environmental Microbiology* 2025;91(6):e01788. doi:10.1128/aem.01788-24.
78. Hefzy EM, Khalil MAF, Ibrahim Amin AA, *et al.* Bacteriocin-like inhibitory substances from probiotics as therapeutic agents for candida vulvovaginitis. *Antibiotics* 2021;10(3):306. doi:10.3390/antibiotics10030306.
79. Cesa-Luna C, Alatorre-Cruz JM, Carreño-López R, *et al.* Emerging applications of bacteriocins as antimicrobials, anticancer drugs, and modulators of the gastrointestinal microbiota. *Polish Journal of Microbiology* 2021;70(2):143. doi:10.33073/PJM-2021-020.
80. Wang G. Human antimicrobial peptides and proteins. *Pharmaceuticals* 2014;7(5):545. doi:10.3390/ph7050545.
81. Aggarwal N, Kitano S, Puah GRY, *et al.* Microbiome and Human Health: Current Understanding, Engineering, and Enabling Technologies. *Chemical Reviews* 2022;123(1):31. doi:10.1021/acs.chemrev.2c00431.
82. Zhang S, Zhang G, Xu J, *et al.* Roles of Tight Junction Proteins in Intestinal Barrier Function and Health of Weaned Piglets: A Review. *Veterinary Sciences* 2026;13(2):131. doi:10.3390/vetsci13020131.
83. Kober MM, Bowe WP. The effect of probiotics on immune regulation, acne, and photoaging. *International Journal of Women's Dermatology* 2015;1(2):85. doi:10.1016/j.ijwd.2015.02.001.
84. Fang Z, Li L, Zhang H, *et al.* Gut Microbiota, Probiotics, and Their Interactions in Prevention and Treatment of Atopic Dermatitis: A Review. *Frontiers in Immunology* 2021;12:720393. doi:10.3389/fimmu.2021.720393.
85. Kim MS, Lee M, Oh H, *et al.* Enhanced ceramides production by *Lactobacillus rhamnosus* IDCC 3201 and its proposed mechanism. *Applied Biological Chemistry* 2021;64(1):50. doi:10.1186/s13765-021-00620-7.
86. Otsuka A, Moriguchi C, Shigematsu Y, *et al.* Fermented Cosmetics and Metabolites of Skin Microbiota—A New Approach to Skin Health. *Fermentation* 2022;8(12):703. doi:10.3390/fermentation8120703.

87. Mukherjee S, Karmakar S, Babu SPS. TLR2 and TLR4 mediated host immune responses in major infectious diseases: A review. *Brazilian Journal of Infectious Diseases* 2016;20(2):193. doi:10.1016/j.bjid.2015.10.011.
88. Ahmed H, Khan MA, Kahlert UD, *et al.* Role of adaptor protein myeloid differentiation 88 (Myd88) in post-subarachnoid hemorrhage inflammation: A systematic review. *International Journal of Molecular Sciences* 2021;22(8):4185. doi:10.3390/ijms22084185.
89. Kreouzi M, Theodorakis N, Nikolaou M, *et al.* Skin Microbiota: Mediator of Interactions Between Metabolic Disorders and Cutaneous Health and Disease. *Microorganisms* 2025;13(1):161. doi:10.3390/microorganisms13010161.
90. Guo N, Lv L lu. Mechanistic insights into the role of probiotics in modulating immune cells in ulcerative colitis. *Immunity, Inflammation and Disease* 2023;11(10):e1045. doi:10.1002/iid3.1045.
91. Rather IA, Bajpai VK, Kumar S, *et al.* Probiotics and atopic dermatitis: An overview. *Frontiers in Microbiology* 2016;7:507. doi:10.3389/fmicb.2016.00507.
92. Akter S, Park JH, Jung HK. Potential Health-promoting benefits of paraprobiotics, inactivated probiotic cells. *Journal of Microbiology and Biotechnology* 2020;30(4):477. doi:10.4014/JMB.1911.11019.
93. Lee N -K, Park YS, Kang DK, *et al.* Paraprobiotics: definition, manufacturing methods, and functionality. *Food Science and Biotechnology* 2023;32(14):1981. doi:10.1007/s10068-023-01378-y.
94. Prajapati N, Patel J, Singh S, *et al.* Postbiotic production: harnessing the power of microbial metabolites for health applications. *Frontiers in Microbiology* 2023;14:1306192. doi:10.3389/fmicb.2023.1306192.
95. Dhakephalkar T, Pisu V, Margale P, *et al.* Strain-Dependent Adhesion Variations of *Shouchella clausii* Isolated from Healthy Human Volunteers: A Study on Cell Surface Properties and Potential Probiotic Benefits. *Microorganisms* 2024;12(9):1771. doi:10.3390/microorganisms12091771.
96. Suntornsaratoon P, Antonio JM, Flores J, *et al.* *Lactobacillus rhamnosus* GG Stimulates Dietary Tryptophan-Dependent Production of Barrier-Protecting Methylnicotinamide. *Cellular and Molecular Gastroenterology and Hepatology* 2024;18(2):101346. doi:10.1016/j.jcmgh.2024.04.003.
97. Falholt Elvebakken H, Bruntse AB, Vedel C, *et al.* Topical *Lactiplantibacillus plantarum* LB244R® ointment alleviates skin aging: An exploratory trial. *Journal of Cosmetic Dermatology* 2023;22(6):1911. doi:10.1111/jocd.15657.
98. Du H, Cai Y, Shen L, Zheng Y, Zhao L, Hu R, *et al.* *Bifidobacterium animalis* subsp. *lactis* modulates early-life immune response and gut metabolism. *Animal Models and Experimental Medicine* 2025;8(6):965. doi:10.1002/ame2.70034.
99. Guéniche A, Bastien P, Ovigne JM, *et al.* *Bifidobacterium longum* lysate, a new ingredient for reactive skin. *Experimental Dermatology* 2010;19(8):e1. doi:10.1111/j.1600-0625.2009.00932.x.

100. Gueniche A, Liboutet M, Cheilian S, *et al.* Vitreoscilla filiformis Extract for Topical Skin Care: A Review. *Frontiers in Cellular and Infection Microbiology* 2021;11:747663. doi:10.3389/fcimb.2021.747663.
101. Aponte M, Murru N, Shoukat M. Therapeutic, Prophylactic, and Functional Use of Probiotics: A Current Perspective. *Frontiers in Microbiology* 2020;11:562048. doi:10.3389/fmicb.2020.562048.
102. Otte JM, Cario E, Podolsky DK. Mechanisms of Cross Hyporesponsiveness to Toll-Like Receptor Bacterial Ligands in Intestinal Epithelial Cells. *Gastroenterology*. 2004;126(4):1054. doi:10.1053/j.gastro.2004.01.007.
103. Latif A, Shehzad A, Niazi S, *et al.* Probiotics: mechanism of action, health benefits and their application in food industries. *Frontiers in Microbiology* 2023;14:1216674. doi:10.3389/fmicb.2023.1216674.
104. Deng K, Fan X, Yuan Z, *et al.* Probiotic effects on skin health: comprehensive visual analysis and perspectives. *Frontiers in Microbiology* 2024;15:1453755. doi:10.3389/fmicb.2024.1453755.
105. Gao T, Wang X, Li Y, *et al.* The Role of Probiotics in Skin Health and Related Gut–Skin Axis: A Review. *Nutrients* 2023;15(14):3123. doi:10.3390/nu15143123.
106. Mishra S, Rath S, Mohanty N. Probiotics—A complete oral healthcare package. *Journal of Integrative Medicine* 2020;18(6):462. doi:10.1016/j.joim.2020.08.005.
107. Tay TY, Wong MYZ, Wee AS, *et al.* Clinical Applications of Probiotics in Atopic Dermatitis. *Progress in Microbes and Molecular Biology* 2025;8(1):a0000473. doi:10.36877/pmmb.a0000473.
108. Jin Z, Wang Y. Recent Progress in Probiotic Encapsulation: Techniques, Characterization and Food Industry Prospects. *Foods* 2026;15(3):431. doi:10.3390/foods15030431.
109. Wang G, Chen Y, Xia Y, *et al.* Characteristics of Probiotic Preparations and Their Applications. *Foods* 2022;11(16):2472. doi:10.3390/foods11162472.
110. Baral KC, Bajracharya R, Lee SH, *et al.* Advancements in the pharmaceutical applications of probiotics: Dosage forms and formulation technology. *International Journal of Nanomedicine* 2021;16:7535. doi:10.2147/IJN.S337427.
111. Allahverdi M, Dadmehr M. Probiotic innovation: From next-generation strains and advanced encapsulation strategies to probiotic engineering. *Journal of Food Composition and Analysis* 2026;153:108917. doi:10.1016/j.jfca.2026.108917.
112. Jin Z, Wang Y. Recent Progress in Probiotic Encapsulation: Techniques, Characterization and Food Industry Prospects. *Foods* 2026;15(3):431. doi:10.3390/foods15030431.
113. Goderska K, Agudo Pena S. An in vitro gastrointestinal model to evaluate the tolerance of encapsulated Lactobacillus and Lactococcus strains with synbiotic containing lactobionic acid via lyophilization technique to harsh gastric conditions during storage time. *European Journal of Pharmaceutics and Biopharmaceutics* 2024;197:114147. doi:10.1016/j.ejpb.2023.11.012.

114. Berenice LE, Rigoberto B, Abraham C, *et al.* Encapsulation and Functional Activity of *Lactobacillus reuteri* Strains: Advances, Challenges, and Perspectives. *Comprehensive Reviews in Food Science and Food Safety* 2026;25(2):e70412. doi:10.1111/1541-4337.70412.
115. Abolhassani A, Esmaili H, Rahati S, *et al.* The Role of Lactobacillus Strain Probiotics in Breast Cancer: Strain-Specific Mechanisms and Therapeutic Potential Beyond Probiotics. *Probiotics and Antimicrobial Proteins* 2026;18(3):3535. doi:10.1007/s12602-025-10741-w.
116. McFarland L V., Evans CT, Goldstein EJC. Strain-specificity and disease-specificity of probiotic efficacy: A systematic review and meta-analysis. *Frontiers in Medicine* 2018;5:124. doi:10.3389/fmed.2018.00124.
117. Nowicka D, Kucharczyk E, Pawłuszkiewicz K, *et al.* Topical Probiotics as a Novel Approach in the Treatment of Chronic Dermatoses Associated with Skin Dysbiosis: A Narrative Review. *International Journal of Molecular Sciences* 2025;26(20):10195. doi:10.3390/ijms262010195.
118. Taléns-Visconti R, Diez-Sales O, Nácher A. Cosmetic Interventions for Skin Microbiome Modulation: Current Strategies and Future Directions. *Skin Research and Technology* 2026;32(4):e70352. doi:10.1111/srt.70352.
119. Pihurov M, Cotârleț M, Borda D, *et al.* The Effects of Non-Viable Probiotic *Lactobacillus paracasei* on the Biotechnological Properties of *Saccharomyces cerevisiae*. *Applied Sciences* 2025;15(16):9221. doi:10.3390/app15169221.
120. Sibanda T, Marole TA, Thomashoff UL, *et al.* Bifidobacterium species viability in dairy-based probiotic foods: challenges and innovative approaches for accurate viability determination and monitoring of probiotic functionality. *Frontiers in Microbiology* 2024;15:1327010. doi:10.3389/fmicb.2024.1327010.
121. Hashemi SS, Rafati A, Roohinejad S, *et al.* Postbiotics as Emerging Therapeutics for Skin Wound Healing and Dermatological Care: Clinical Trends and Mechanistic Insights. *International Wound Journal* 2025;22(12):e70799. doi:10.1111/iwj.70799.
122. Ho HH, Chen CW, Yi TH, *et al.* Novel application of a Co-Fermented postbiotics of TYCA06/AP-32/CP-9/collagen in the improvement of acne vulgaris—A randomized clinical study of efficacy evaluation. *Journal of Cosmetic Dermatology* 2022;21(11):6249. doi:10.1111/jocd.15228.
123. Lebeer S, Oerlemans EFM, Claes I, *et al.* Selective targeting of skin pathobionts and inflammation with topically applied lactobacilli. *Cell Reports Medicine* 2022;3(2):100521. doi:10.1016/j.xcrm.2022.100521.
124. Lizardo M, Magalhães RM, Tavaría FK. Probiotic Adhesion to Skin Keratinocytes and Underlying Mechanisms. *Biology (Basel)* 2022;11(9):1372. doi:10.3390/biology11091372.
125. Rosignoli C, Thibaut de Ménonville S, Orfila D, *et al.* A topical treatment containing heat-treated *Lactobacillus johnsonii* NCC 533 reduces *Staphylococcus aureus* adhesion and induces antimicrobial

- peptide expression in an in vitro reconstructed human epidermis model. *Experimental Dermatology* 2018;27(4):358. doi:10.1111/exd.13504.
126. Kieps J, Dembczyński R. Current Trends in the Production of Probiotic Formulations. *Foods* 2022;11(15):2330. doi:10.3390/foods11152330.
 127. Jackson SA, Schoeni JL, Vegge C, *et al.* Improving end-user trust in the quality of commercial probiotic products. *Frontiers in Microbiology* 2019;10:739. doi:10.3389/fmicb.2019.00739.
 128. Zawistowska-Rojek A, Rybak J, Smoleń P, *et al.* Evaluating the Quality of Selected Commercial Probiotic Products, Both Dietary Supplements and Foods for Special Medical Purposes. *Foods* 2026;15(2):373. doi:10.3390/foods15020373.
 129. Wilcox H, Carr C, Seney S, *et al.* Expired probiotics: what is really in your cabinet? *FEMS Microbes* 2020;1(1):xtaa007. doi:10.1093/femsmc/xtaa007.
 130. Ullah M, Raza A, Ye L, *et al.* Viability and composition validation of commercial probiotic products by selective culturing combined with next-generation sequencing. *Microorganisms* 2019;7(7):188. doi:10.3390/microorganisms7070188.
 131. Čuljak N, Repić I, Čanak I, *et al.* Label accuracy of commercial probiotics—CFU enumeration and microbial composition. *Annals of Microbiology* 2026;76(1):26. doi:10.1186/s13213-026-01854-w.
 132. Zhao W, Liu Y, Kwok LY, *et al.* The immune regulatory role of *Lactobacillus acidophilus*: An updated meta-analysis of randomized controlled trials. *Food Bioscience* 2020;36:100656. doi:10.1016/j.fbio.2020.100656.
 133. Goktas NT, Guven S, Dinleyici EC. The combination of *Lactobacillus acidophilus* DSMZ 26280 and *Limosilactobacillus reuteri* DSMZ 25441 has an impact on clinical course and gut microbiota of children with acute infectious diarrhea. *Frontiers in Microbiology* 2026;17:1792126. doi:10.3389/fmicb.2026.1792126.
 134. Abd Elmacksood A, Basha O, Talat D, *et al.* In Vitro evaluation of antimicrobial activity of *Lactobacillus acidophilus* against some pathogens. *Damanhour Journal of Veterinary Sciences* 2021;6(1):21. doi:10.21608/djvs.2021.81934.1042.
 135. Cukrowska B, Ceregra A, Maciorkowska E, *et al.* The effectiveness of probiotic *Lactobacillus rhamnosus* and *Lactobacillus casei* strains in children with atopic dermatitis and cow's milk protein allergy: A multicenter, randomized, double blind, placebo controlled study. *Nutrients* 2021;13(4):1169. doi:10.3390/nu13041169.
 136. Xie L, Li X, Liu L, *et al.* Oral administration of *Lactobacillus rhamnosus* HM126 alleviates DNFB-induced atopic dermatitis in BALB/c mice by modulating immunity, gut microbiota, and metabolites. *Frontiers in Immunology* 2025;16:1739967. doi:10.3389/fimmu.2025.1739967.
 137. Wang X, Li X, Liu J, *et al.* *Lactobacillus Plantarum* Promotes Wound Healing by Inhibiting the NLRP3 Inflammasome and Pyroptosis Activation in Diabetic Foot Wounds. *Journal of Inflammation Research* 2024;17:1707. doi:10.2147/JIR.S449565.

138. Kim MJ, Kim KP, Choi E, *et al.* Effects of lactobacillus plantarum cjlp55 on clinical improvement, skin condition and urine bacterial extracellular vesicles in patients with acne vulgaris: A randomized, double-blind, placebo-controlled study. *Nutrients* 2021;13(4):1368. doi:10.3390/nu13041368.
139. Park JY, Lee JY, Hong S, *et al.* Limosilactobacillus fermentum MG5368 and Lactiplantibacillus plantarum MG989 Regulates Skin Health in UVB-Induced HaCaT Cells and Hairless Mice Model. *Nutrients* 2024;16(23):4083. doi:10.3390/nu16234083.
140. Choi H, Kwak MJ, Choi Y, *et al.* Extracellular vesicles of Limosilactobacillus fermentum SLAM216 ameliorate skin symptoms of atopic dermatitis by regulating gut microbiome on serotonin metabolism. *Gut Microbes* 2025;17(1):2474256. doi:10.1080/19490976.2025.2474256.
141. Uma Mageswary M, Li P, Richmond RV, *et al.* Clinical benefits of Bifidobacterium infantis YLGB-1496 in modulating gut microbiota and immunity in young children. *Frontiers in Nutrition* 2026;12:1713135. doi:10.3389/fnut.2025.1713135.
142. Arai S, Hiraku A, Nakata S, *et al.* Effects of Bifidobacterium infantis M-63 on gut environment and bowel function during weaning: RCT. *Pediatric Research* 2026;1. doi:10.1038/s41390-026-04960-2.
143. Cardoso A, Naghibi M, Climent E, *et al.* Effects of Live and Heat-Treated Bifidobacterium longum CECT 7347 in Adults With Allergic Rhinitis: A Randomised, Double-Blind, Placebo-Controlled Trial. *Allergy* 2026. doi:10.1111/all.70360.
144. Srivastava S, Basak U, Naghibi M, *et al.* A randomized double-blind, placebo-controlled trial to evaluate the safety and efficacy of live Bifidobacterium longum CECT 7347 (ES1) and heat-treated Bifidobacterium longum CECT 7347 (HT-ES1) in participants with diarrhea-predominant irritable bowel syndrome. *Gut Microbes* 2024;16(1):2338322. doi:10.1080/19490976.2024.2338322.
145. Sharma AK, Puri N, Mathur M, *et al.* A Randomized Controll Trial to Compare The Efficacy of Saccharomyces Boulardii, Bacillus Clausii, and Lactobacillus Rhamnosus GG Preparation in The Treatment of Acute Diarrhea in Children. *Asian Journal of Pharmaceutical and Clinical Research* 2022;15(4):63. doi:10.22159/ajpcr.2022.v15i4.44199.
146. Ehrhardt S, Guo N, Hinz R, *et al.* Saccharomyces boulardii to prevent antibiotic-associated diarrhea: A randomized, double-masked, placebo-controlled trial. *Open Forum Infectious Diseases* 2016;3(1):ofw011. doi:10.1093/ofid/ofw011.
147. Gupta AK, Maity C. Efficacy and safety of Bacillus coagulans LBSC in irritable bowel syndrome: A prospective, interventional, randomized, double-blind, placebo-controlled clinical study [CONSORT Compliant]. *Medicine (Baltimore)* 2021;100(3):e23641. doi:10.1097/MD.00000000000023641.
148. Abhari K, Saadati S, Yari Z, *et al.* The effects of Bacillus coagulans supplementation in patients with non-alcoholic fatty liver disease: A randomized, placebo-controlled, clinical trial. *Clinical Nutrition ESPEN*. 2020;39:53. doi:10.1016/j.clnesp.2020.06.020.

149. Greuter T, Michel MC, Thomann D, *et al.* Randomized, Placebo-Controlled, Double-Blind and Open-Label Studies in the Treatment and Prevention of Acute Diarrhea With *Enterococcus faecium* SF68. *Frontiers in Medicine* 2020;7:276. doi:10.3389/fmed.2020.00276.
150. Huang B, Xian Y, Xue W, *et al.* Probiotic attributes and safety profile of AKM Lab-01: a novel *Akkermansia muciniphila* strain combating obesity and metabolic disorders in diet-induced obese mice. *Frontiers in Microbiology* 2026;16:1627870. doi:10.3389/fmicb.2025.1627870.
151. Guo X, Chen W, Zhang Y, *et al.* Microbial Anti-Inflammatory Molecule (MAM) secreted by *Faecalibacterium prausnitzii* ameliorates colitis through autophagy and gut microbiota modulation. *Journal of Translational Medicine* 2025;24(1):149. doi:10.1186/s12967-025-07493-0.
152. Caliman-Sturdza OA, Vaz JA, Lupaescu AV, *et al.* Antioxidant and Anti-Inflammatory Activities of Probiotic Strains. *International Journal of Molecular Sciences* 2026;27(2):1079. doi:10.3390/ijms27021079.
153. Ahmed Z, Wang Y, Cheng Q, *et al.* *Lactobacillus acidophilus* bacteriocin, from production to their application: An overview. *African Journal of Biotechnology* 2010;9(20):2843. doi:10.5897/AJB2010.000-3111.
154. Johnson B, Selle K, O'Flaherty S, *et al.* Identification of extracellular surface-layer associated proteins in *Lactobacillus acidophilus* NCFM. *Microbiology (Reading)* 2013;159(Pt 11):2269. doi:10.1099/mic.0.070755-0.
155. Diep DB, Straume D, Kjos M, *et al.* An overview of the mosaic bacteriocin *pln* loci from *Lactobacillus plantarum*. *Peptides* 2009;30(8):1562. doi:10.1016/j.peptides.2009.05.014.
156. Sehar N, Pino R, Pellegrino M, *et al.* Lactic Acid Bacteria for Fungal Control and Shelf-Life Extension in Fresh Pasta: Mechanistic Insights and Clean-Label Strategies. *Molecules* 2026;31(2):389. doi:10.3390/molecules31020389.
157. Sagmeister T, Gubensäk N, Buhlheller C, *et al.* The molecular architecture of *Lactobacillus* S-layer: Assembly and attachment to teichoic acids. *The Proceedings of the National Academy of Sciences* 2024;121(24):e2401686121. doi:10.1073/pnas.2401686121.
158. Demir A, Aslim B. Investigation of multifaceted wound healing effect of exopolysaccharide (EPS) produced from probiotic strain *Lactiplantibacillus plantarum* GD2 as in vitro and in ovo. *Scientific Reports* 2025;15(1):36512. doi:10.1038/s41598-025-90682-0.
159. Leser T, Baker A. Molecular Mechanisms of *Lactocaseibacillus rhamnosus*, LGG® Probiotic Function. *Microorganisms* 2024;12(4), 794. doi:10.3390/microorganisms12040794.
160. Yan F, Liu L, Dempsey PJ, *et al.* A *Lactobacillus rhamnosus* GG-derived soluble protein, p40, stimulates ligand release from intestinal epithelial cells to transactivate epidermal growth factor receptor. *Journal of Biological Chemistry* 2013;288(42):30742. doi:10.1074/jbc.M113.492397.
161. Mikelsaar M, Zilmer M. *Lactobacillus fermentum* ME-3 - An antimicrobial and antioxidative probiotic. *Microbial Ecology in Health and Disease* 2009;21(1):1. doi:10.1080/08910600902815561.

162. Quigley E, Groeger D, O'Mahony L, *et al.* Oral Administration of the Probiotic Bifidobacterium Infantis 35624 to Humans Induces Immunoregulatory Responses In Vivo. *American Journal of Gastroenterology* 2011;106:p S463. doi:10.14309/00000434-201110002-01228.
163. Mills S, Yang B, Smith GJ, *et al.* Efficacy of Bifidobacterium longum alone or in multi-strain probiotic formulations during early life and beyond. *Gut Microbes* 2023;15(1):2186098. doi:10.1080/19490976.2023.2186098.
164. Ma X, Pan Y, Zhao W, *et al.* Bifidobacterium infantis strain YLGB-1496 possesses excellent antioxidant and skin barrier-enhancing efficacy in vitro. *Experimental Dermatology* 2022;31(7):1089. doi:10.1111/exd.14583.
165. Marras L, Caputo M, Bisicchia S, *et al.* The role of bifidobacteria in predictive and preventive medicine: A focus on eczema and hypercholesterolemia. *Microorganisms* 2021;9(4):836. doi:10.3390/microorganisms9040836.
166. Gao T, Li Y, Wang X, *et al.* Bifidobacterium longum 68S mediated gut-skin axis homeostasis improved skin barrier damage in aging mice. *Phytomedicine* 2023;120:155051. doi:10.1016/j.phymed.2023.155051.
167. Kim S, Han SY, Lee J, *et al.* Bifidobacterium longum and Galactooligosaccharide Improve Skin Barrier Dysfunction and Atopic Dermatitis-like Skin. *Allergy, Asthma and Immunology Research* 2022;14(5):549. doi:10.4168/aair.2022.14.5.549.
168. Cao J, Yu Z, Liu W, *et al.* Probiotic characteristics of Bacillus coagulans and associated implications for human health and diseases. *Journal of Functional Foods* 2020;64:103643. doi:10.1016/j.jff.2019.103643.
169. Huang C, Moradi S, Sholeh M, *et al.* Global trends in antimicrobial resistance of Enterococcus faecium: a systematic review and meta-analysis of clinical isolates. *Frontiers in Pharmacology* 2025;16:1505674. doi:10.3389/fphar.2025.1505674.
170. Jan T, Negi R, Sharma B, *et al.* Next generation probiotics for human health: An emerging perspective. *Heliyon* 2024;10(16):e35980. doi:10.1016/j.heliyon.2024.e35980.
171. Loo KY, Thong JYH, Tan LTH, Letchumanan V, Chan KG, Lee LH, *et al.* A Current Overview of Next-Generation Probiotics and Their Prospects in Health and Disease Management. *Progress in Microbes and Molecular Biology* 2024;7(1):a0000457. doi:10.36877/pmmb.a0000457.
172. Xue C, Li G, Gu X, *et al.* Health and Disease: Akkermansia muciniphila , the Shining Star of the Gut Flora. *Research* 2023;6:0107. doi:10.34133/research.0107.
173. Derrien M, Belzer C, de Vos WM. Akkermansia muciniphila and its role in regulating host functions. *Microbial Pathogenesis* 2017;106:171. doi:10.1016/j.micpath.2016.02.005.
174. Effendi RMRA, Anshory M, Kalim H, *et al.* Akkermansia muciniphila and Faecalibacterium prausnitzii in Immune-Related Diseases. *Microorganisms* 2022;10(12):2382. doi:10.3390/microorganisms10122382.

175. Cani PD, de Vos WM. Next-generation beneficial microbes: The case of *Akkermansia muciniphila*. *Frontiers in Microbiology* 2017;8:01765. doi:10.3389/fmicb.2017.01765.
176. Dikeocha IJ, Al-Kabsi AM, Chiu HT, *et al.* *Faecalibacterium prausnitzii* Ameliorates Colorectal Tumorigenesis and Suppresses Proliferation of HCT116 Colorectal Cancer Cells. *Biomedicines* 2022;10(5):1128. doi:10.3390/biomedicines10051128.
177. Jung GW, Tse JE, Guiha I, *et al.* Prospective, randomized, open-label trial comparing the safety, efficacy, and tolerability of an acne treatment regimen with and without a probiotic supplement and minocycline in subjects with mild to moderate acne. *Journal of Cutaneous Medicine and Surgery* 2013;17(2):114. doi:10.2310/7750.2012.12026.
178. Fabbrocini G, Bertona M, Picazo, *et al.* Supplementation with *Lactobacillus rhamnosus* SP1 normalises skin expression of genes implicated in insulin signalling and improves adult acne. *Beneficial Microbes* 2016;7(5):625. doi:10.3920/BM2016.0089.
179. Kang BS, Seo JG, Lee GS, *et al.* Antimicrobial activity of enterocins from *Enterococcus faecalis* SL-5 against *Propionibacterium acnes*, the causative agent in acne vulgaris, and its therapeutic effect. *Journal of Microbiology* 2009;47(1):101. doi:10.1007/s12275-008-0179-y.
180. Sathikulpakdee S, Kanokrungrsee S, Vitheejongjaroen P, *et al.* Efficacy of probiotic-derived lotion from *Lactobacillus paracasei* MSMC 39-1 in mild to moderate acne vulgaris, randomized controlled trial. *Journal of Cosmetic Dermatology* 2022;21(10):5092. doi:10.1111/jocd.14971.
181. Prakoeswa CRS, Herwanto N, Prameswari R, *et al.* *Lactobacillus plantarum* IS-10506 supplementation reduced SCORAD in children with atopic dermatitis. *Beneficial Microbes* 2017;8(5):833. doi:10.3920/bm2017.0011.
182. Navarro-Lopez V, Ramirez-Bosca A, Ramon-Vidal D, *et al.* Effect of oral administration of a mixture of probiotic strains on SCORAD index and use of topical steroids in young patients with moderate atopic dermatitis a randomized clinical trial. *JAMA Dermatology* 2018;154(1):37. doi:10.1001/jamadermatol.2017.3647.
183. Gueniche A, Knaudt B, Schuck E, *et al.* Effects of nonpathogenic gram-negative bacterium *Vitreoscilla filiformis* lysate on atopic dermatitis: A prospective, randomized, double-blind, placebo-controlled clinical study. *British Journal of Dermatology* 2008;159(6):1357. doi:10.1111/j.1365-2133.2008.08836.x.
184. Lee DE, Huh CS, Ra J, *et al.* Clinical evidence of effects of *Lactobacillus plantarum* HY7714 on skin aging: A randomized, double blind, placebo-controlled study. *Journal of Microbiology and Biotechnology* 2015;25(12):2160. doi:10.4014/jmb.1509.09021.
185. Dapkevicius I, Romualdo V, Marques AC, *et al.* Acne Vulgaris Topical Therapies: Application of Probiotics as a New Prevention Strategy. *Cosmetics* 2023;10(3):77. doi:10.3390/cosmetics10030077.
186. Navarro-lópez V, Núñez-delegido E, Ruzafa-costas B, *et al.* Probiotics in the therapeutic arsenal of dermatologists. *Microorganisms* 2021;9(7):1513. doi:10.3390/microorganisms9071513.

187. Lao J, Chen M, Yan S, *et al.* Lacticaseibacillus rhamnosus G7 alleviates DSS-induced ulcerative colitis by regulating the intestinal microbiota. *BMC Microbiology* 2025;25(1):168. doi:10.1186/s12866-025-03904-w.
188. Eguren C, Navarro-Blasco A, Corral-Forteza M, *et al.* A Randomized Clinical Trial to Evaluate the Efficacy of an Oral Probiotic in Acne Vulgaris. *Acta Dermato-Venereologica* 2024;104:adv33206. doi:10.2340/actadv.v104.33206.
189. Sutema IAMP, Latarissa IR, Widowati IGAR, *et al.* Efficacy of Probiotic Supplements and Topical Applications in the Treatment of Acne: A Scoping Review of Current Results. *Journal of Experimental Pharmacology* 2025;17:1. doi:10.2147/JEP.S498769.
190. Umborowati MA, Damayanti D, Anggraeni S, *et al.* The role of probiotics in the treatment of adult atopic dermatitis: a meta-analysis of randomized controlled trials. *Journal of Health, Population and Nutrition* 2022;41(1):37. doi: 10.1186/s41043-022-00318-6.
191. Prakoeswa CRS, Bonita L, Karim A, *et al.* Beneficial effect of Lactobacillus plantarum IS-10506 supplementation in adults with atopic dermatitis: a randomized controlled trial. *Journal of Dermatological Treatment* 2022;33(3):1491. doi:10.1080/09546634.2020.1836310.
192. Depner M, Taft DH, Peschel S, *et al.* The Janus face of Bifidobacterium in the development of atopic eczema: A role for compositional maturation. *Pediatric Allergy and Immunology* 2025;36(2):e70041. doi:10.1111/pai.70041.
193. Arif MI, Dai Q, Ru L. Probiotics for pediatric atopic dermatitis: A systematic review and meta-analysis of randomized controlled trials. *Journal of Allergy and Clinical Immunology: Global* 2026;5(2):100649. doi:10.1016/j.jacig.2026.100649.
194. Jwo JY, Chang YT, Huang YC. Effects of probiotics supplementation on skin photoaging and skin barrier function: A systematic review and meta-analysis. *Photodermatology, Photoimmunology, and Photomedicine* 2023;39(2):122. doi:10.1111/phpp.12861.
195. Tang X, Yang T, Yu D, *et al.* Current insights and future perspectives of ultraviolet radiation (UV) exposure: Friends and foes to the skin and beyond the skin. *Environment International* 2024;185:108535. doi:10.1016/j.envint.2024.108535.
196. Feng T, Wang J. Oxidative stress tolerance and antioxidant capacity of lactic acid bacteria as probiotic: a systematic review. *Gut Microbes* 2020;12(1):1801944. doi:10.1080/19490976.2020.1801944.
197. Zou S, Wu Q, Li Z, *et al.* Lactiplantibacillus plantarum A72, a Strain with Antioxidant Properties, Obtained through ARTP Mutagenesis, Affects Caenorhabditis elegans Anti-Aging. *Foods* 2024;13(6):924. doi:10.3390/foods13060924.
198. Xia C, Cao X, Cui L, *et al.* Anti-aging effect of the combination of Bifidobacterium longum and B. animalis in a D-galactose-treated mice. *Journal of Functional Foods* 2020;69:103938. doi:10.1016/j.jff.2020.103938.

199. Lee K, Kim HJ, Kim SA, *et al.* Exopolysaccharide from *Lactobacillus plantarum* HY7714 protects against skin aging through skin–gut axis communication. *Molecules*. 2021;26(6):1651. doi:10.3390/molecules26061651.
200. Gao T, Li Y, Wang X, *et al.* *Bifidobacterium longum* 68S mediated gut-skin axis homeostasis improved skin barrier damage in aging mice. *Phytomedicine* 2023;120:155051. doi:10.1016/j.phymed.2023.155051.
201. Gaikwad R, Kondle S, Chang S, *et al.* Impact of Probiotics on Atopic Dermatitis in Pediatric Patients: A Systematic Review and Meta-Analysis. *Medicina* 2025;61(12):2090. doi:10.3390/medicina61122090.
202. Duval S, Tweedie R. A Nonparametric “Trim and Fill” Method of Accounting for Publication Bias in Meta-Analysis. *Journal of the American Statistical Association* 2000;95(449):89. doi:10.1080/01621459.2000.10473905.
203. Sterne JAC, Harbord RM. Funnel Plots in Meta-analysis. *The Stata Journal: Promoting communications on statistics and Stata* 2004;4(2):127. doi:10.1177/1536867x0400400204.
204. Park S, Beretvas SN, Smith TE. Extending Egger’s Regression: Detecting Outcome Reporting Bias in Meta-Analysis on Dependent Multiple Outcomes. *The Journal of Experimental Education* 2025;94(4):1066. doi:10.1080/00220973.2025.2477720.
205. Boyte ME, Benkowski A, Pane M, *et al.* Probiotic and postbiotic analytical methods: a perspective of available enumeration techniques. *Frontiers in Microbiology* 2023;14:1304621. doi:10.3389/fmicb.2023.1304621.
206. Fanfaret I, Boda D, Ion L, *et al.* Probiotics and prebiotics in atopic dermatitis: Pros and cons (Review). *Experimental and Therapeutic Medicine* 2021;22(6):1376. doi:10.3892/etm.2021.10811.
207. Li Y, Zhang B, Guo J, *et al.* The efficacy of probiotics supplementation for the treatment of atopic dermatitis in adults: a systematic review and meta-analysis. *Journal of Dermatological Treatment* 2022;33(6):2800. doi:10.1080/09546634.2022.2080170.
208. Suellen Ferro de Oliveira C, Kekhasharú Tavaría F. The impact of bioactive textiles on human skin microbiota. *European Journal of Pharmaceutics and Biopharmaceutics* 2023;188:66. doi:10.1016/j.ejpb.2023.05.004.
209. Navarro Triviño FJ, Velasco Amador JP, Rivera Ruiz I. Seborrheic Dermatitis Revisited: Pathophysiology, Diagnosis, and Emerging Therapies—A Narrative Review. *Biomedicine* 2025;13(10):2458. doi:10.3390/biomedicine13102458.
210. Éliás AJ, Barna V, Patoni C, *et al.* Probiotic supplementation during antibiotic treatment is unjustified in maintaining the gut microbiome diversity: a systematic review and meta-analysis. *BMC Medicine* 2023;21(1):262. doi:10.1186/s12916-023-02961-0.

211. Dahiya D, Nigam PS. Antibiotic-Therapy-Induced Gut Dysbiosis Affecting Gut Microbiota—Brain Axis and Cognition: Restoration by Intake of Probiotics and Synbiotics. *International Journal of Molecular Sciences* 2023;24(4):3074. doi:10.3390/ijms24043074.
212. Thompson KG, Rainer BM, Antonescu C, *et al.* Minocycline and its impact on microbial dysbiosis in the skin and gastrointestinal tract of acne patients. *Annals of Dermatology* 2020;32(1):21. doi:10.5021/ad.2020.32.1.21.
213. Lebeer S, Oerlemans EFM, Claes I, *et al.* Selective targeting of skin pathobionts and inflammation with topically applied lactobacilli. *Cell Reports Medicine* 2022;3(2):100521. doi:10.1016/j.xcrm.2022.100521.
214. Xu R, Yu Y, Chen T. Exploring the dark side of probiotics to pursue light: Intrinsic and extrinsic risks to be opportunistic pathogens. *Current Research in Food Science* 2025;10:101044. doi:10.1016/j.crfs.2025.101044.
215. Sanders ME, Akkermans LMA, Haller D, *et al.* Safety assessment of probiotics for human use. *Gut Microbes* 2010;1(3):164. doi:10.4161/gmic.1.3.12127.
216. Rychen G, Aquilina G, Azimonti G, *et al.* Guidance on the characterisation of microorganisms used as feed additives or as production organisms. *EFSA Journal* 2018;16(3):e05206. doi:10.2903/j.efsa.2018.5206.
217. Monteiro SS, Schnorr CE, Pasquali MA de B. Paraprobiotics and Postbiotics—Current State of Scientific Research and Future Trends toward the Development of Functional Foods. *Foods* 2023;12(12):2394. doi:10.3390/foods12122394.
218. Spacova I, Binda S, ter Haar JA, *et al.* Comparing technology and regulatory landscape of probiotics as food, dietary supplements and live biotherapeutics. *Frontiers in Microbiology* 2023;14:1272754. doi:10.3389/fmicb.2023.1272754.
219. França K. Topical Probiotics in Dermatological Therapy and Skincare: A Concise Review. *Dermatology and Therapy* 2021;11(1):71. doi:10.1007/s13555-020-00476-7.
220. Watthanasakphuban N, Abibi H, Nitayapat N, *et al.* Genome-Driven Insights into *Lactococcus* sp. KTH0-1S Highlights Its Biotechnological Potential as a Cell Factory. *Biology* 2025;14(10):1323. doi:10.3390/biology14101323.
221. Wang P, Yi Y, Lü X. CRISPR/Cas9-Based Genome Editing Platform for *Companilactobacillus crustorum* to Reveal the Molecular Mechanism of Its Probiotic Properties. *Journal of Agricultural and Food Chemistry* 2021;69(50):15279. doi:10.1021/acs.jafc.1c05389.
222. Selle K, Barrangou R. Harnessing CRISPR-Cas systems for bacterial genome editing. *Trends in Microbiology* 2015;23(4):225. doi:10.1016/j.tim.2015.01.008.
223. Thakur N, Thakur S, Singh YP, *et al.* A Current Review on Transdermal Delivery of Protein and Peptides: Possibilities and Challenges. *Letters in Drug Design and Discovery* 2025;21(19):4597. doi:10.2174/0115701808357267250102054810.

224. Bhoir S, Singh S, Phalak S. Innovations in Transdermal Drug Delivery: Challenges, Approaches and Future Perspectives. *International Journal of Pharmaceutical Sciences* 2025;3(4):57. doi:10.5281/zenodo.15118663.
225. WHO. Health and Nutritional Properties of Probiotics in Food including Powder Milk with Live Lactic Acid Bacteria. FAO & WHO 2001. doi:10.1201/9781420009613.ch16.
226. Zovi A, Vitiello A, Sabbatucci M, *et al.* Food Supplements Marketed Worldwide: A Comparative Analysis Between the European and the U.S. Regulatory Frameworks. *Journal of Dietary Supplements* 2025;22(1):25. doi:10.1080/19390211.2024.2389397.
227. Haffner FB, Diab R, Pasc A. Encapsulation of probiotics: Insights into academic and industrial approaches. *AIMS Materials Science* 2016;3(1):114. doi:10.3934/matricsci.2016.1.114.
228. Sagastume-Canova R, Fernández-Guarino M. Emerging Trends in Facial Cosmetics: Innovation, Science, and Sustainable Beauty. *Cosmetics* 2026;13(2):58. doi:10.3390/cosmetics13020058.
229. Oh M, Zhang L. DeepMicro: deep representation learning for disease prediction based on microbiome data. *Scientific Reports* 2020;10(1):6026. doi:10.1038/s41598-020-63159-5.
230. Topçuoğlu BD, Lesniak NA, Ruffin MT, *et al.* A framework for effective application of machine learning to microbiome-based classification problems. *mBio* 2020;11(3):e00434. doi:10.1128/mBio.00434-20.
231. Baruch EN, Youngster I, Ben-Betzalel G, *et al.* Fecal microbiota transplant promotes response in immunotherapy-refractory melanoma patients. *Science* (1979) 2021;371(6529):602. doi:10.1126/science.abb5920.
232. Hou Y, Chen C, Chen X. Advancing precision immuno-oncology in melanoma: the synergistic convergence of personalized neoantigen vaccines and multi-omics biomarker profiling. *Frontiers in Immunology* 2026;17:1831047. doi:10.3389/fimmu.2026.1831047.



Author(s) shall retain the copyright of their work and grant the Journal/Publisher right for the first publication with the work simultaneously licensed under:

Creative Commons Attribution-NonCommercial 4.0 International (CC BY-NC 4.0). This license allows for the copying, distribution and transmission of the work, provided the correct attribution of the original creator is stated. Adaptation and remixing are also permitted.