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THE ROLE OF THE SKIN MICROBIOME IN THE DEVELOPMENT OF DERMATOLOGIC DISEASES: CURRENT STATE OF EVIDENCE (2020–2025)

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ABSTRACT

Background: The cutaneous microbiome is a sophisticated ecosystem essential for skin homeostasis and immune regulation. Between 2020 and 2025, research transitioned from simple taxonomic mapping toward functional metagenomics, highlighting the microbiome's role as a dynamic modifier of dermatologic pathology. This review synthesizes recent evidence on microbial involvement in inflammatory skin diseases and evaluates emerging therapeutic interventions.
Methods: A narrative synthesis was performed via a targeted PubMed search for literature published from January 2020 to December 2025. Following the screening of 171 abstracts, 33 high-impact studies focusing on functional metagenomics, "multi-omic" integration, and microbiome-targeted therapies were selected for in-depth analysis.
Results: In atopic dermatitis (AD), the correlation between Staphylococcus aureus dominance and barrier degradation remains the most robust evidence of clinically significant dysbiosis. In psoriasis, localized microbial shifts are intrinsically linked to Th17/IL-23 axis activation. Acne vulgaris pathogenesis is increasingly attributed to specific virulent Cutibacterium acnes phylotypes rather than absolute abundance. In seborrheic dermatitis, the synergistic interaction between Malassezia fungi and bacterial commensals drives inflammatory signaling. Precision interventions, including strain-targeted probiotics, postbiotics, and skin microbiome transplantation (SMT), demonstrate mechanistic rationale and early-phase feasibility.
Conclusions: Emerging evidence suggests a potential transition in dermatological therapeutics from broad-spectrum antimicrobial suppression toward targeted ecological restoration. However, this approach remains largely investigational and requires validation through rigorous clinical trials. Future progress depends on standardized sampling protocols and the application of machine learning to identify "microbial endotypes," enabling the development of personalized, microbiome-based therapeutic strategies.

KEYWORDS

Skin Microbiome, Dysbiosis, Precision Medicine, Metagenomics, Probiotics

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1. Introduction

The cutaneous microbiome is a sophisticated ecosystem comprising bacteria, fungi, viruses, and mites that exist in a state of dynamic equilibrium with the human host (Oh 2025; Smythe 2023). Serving as the body’s largest organ, the skin offers a diverse array of biological niches-sebaceous, moist, and dry-each harboring a distinct microbial signature (Santiago-Rodriguez 2023; Chaudhary 2023). Following 2020, research in this field has accelerated significantly, propelled by sophisticated sequencing technologies like 16S rRNA and shotgun metagenomics (Chaudhary 2023; Oñate 2025), alongside an evolving understanding of how these microbial communities influence dermatological pathology, immune responses, and senescence (Haykal et al., 2024; Scharschmidt & Segre, 2025)

Preserving microbial homeostasis, or eubiosis, is fundamental to the integrity of the epidermal barrier. Deviations from this balance, known as dysbiosis, are implicated in the pathogenesis of various skin disorders, including atopic dermatitis, acne vulgaris, psoriasis, and seborrheic dermatitis (Celoria et al., 2023; Chang & Chovatiya, 2024; Fölster-Holst, 2022; Koh et al., 2022; Radaschin et al., 2024) Current evidence suggests that these microorganisms do more than just maintain immune stability; they actively regulate inflammatory pathways, metabolic production, and the structural cohesion of the stratum corneum (Boyanova, 2023; Mayslich et al., 2021; Scharschmidt & Segre, 2025)

This scientific momentum has shifted toward the development of novel microbiome-modulating interventions, ranging from probiotics and postbiotics (Habeebuddin et al., 2022; Tamer & Kekilli, 2024)) to prebiotic-enriched dermocosmetics and advanced techniques such as skin microbiome transplantation (Callewaert et al., 2021) Moreover, recent findings regarding the microbiome's resilience and its ability to recover following immune-mediated shifts suggest a future for individualized therapeutic approaches (Che et al., 2025) This review aims to synthesize current insights into the microbiome's role in inflammatory skin conditions and evaluate emerging strategies for therapeutic ecosystem modification.

2. The Skin Microbiome in Selected Dermatological Diseases

2.1. Atopic Dermatitis (AD)

Atopic dermatitis (AD) is defined as a chronic, relapsing inflammatory skin disorder, distinguished primarily by severe pruritus that typically intensifies during nocturnal hours (Jeskey et al., 2024) Within the field of dermatology, AD represents one of the most thoroughly investigated conditions concerning microbial involvement. A hallmark of the AD-afflicted skin is a marked contraction in microbial diversity coupled with the over-proliferation of *Staphylococcus aureus* on lesional areas (Fölster-Holst, 2022; Hülpüsch et al., 2024; Koh et al., 2022; Scharschmidt & Segre, 2025) Current data indicates that *S. aureus*acts as more than an opportunistic colonizer; it serves as a potent immunomodulator by secreting superantigens, toxins, and enzymes that drive inflammation and degrade the epidermal barrier (Celoria et al., 2023; Fölster-Holst, 2022; Scharschmidt & Segre, 2025)

Research consistently demonstrates the fluid nature of AD dysbiosis: clinical flares are characterized by a surge in *S. aureus* density, while periods of remission see a restoration of taxonomic richness, including the return of *Staphylococcus epidermidis* and other protective commensals (Chaudhary et al., 2023; Hülpüsch et al., 2024; Koh et al., 2022) Notably, certain *S. epidermidis* strains possess the capacity to suppress *S. aureus* expansion, highlighting a strategic opening for therapies aimed at bolstering beneficial microbes (Santiago-Rodriguez et al., 2023; Scharschmidt & Segre, 2025; Smythe & Wilkinson, 2023)

Emerging studies have further identified quorum sensing (QS)-the molecular communication systems of bacteria-as a critical regulator of *S. aureus* virulence and subsequent inflammatory induction (Chaudhary et al., 2023; Santiago-Rodriguez et al., 2023; Scharschmidt & Segre, 2025). Decoding these signals suggests a novel therapeutic paradigm: targeting QS pathways to attenuate bacterial pathogenicity without necessarily eradicating the entire population.

Regarding therapeutic innovation, there is significant focus on the application of oral and topical probiotics and postbiotics. Preliminary clinical evidence from heterogeneous trials suggests that certain microbial strains may modestly reduce S. aureus colonization and improve clinical symptoms in selected patients, though the overall certainty of evidence remains low to moderate, with substantial variability in treatment effects across studies**,**(Habeebuddin et al., 2022; Haykal et al., 2024; Tamer & Kekilli, 2024) Furthermore, investigations are ongoing into the role of ultraviolet B (UVB) phototherapy and prebiotic-enhanced emollients, both of which appear to reorganize the microbiome by encouraging commensal growth (Haykal et al., 2024; Koh et al., 2022; Scharschmidt & Segre, 2025)

In conclusion, the microbial landscape of AD reveals a clear mechanistic loop: dysbiosis promotes *S. aureus* dominance, which in turn compromises barrier integrity and amplifies the inflammatory cascade (Fölster-Holst, 2022; Hülpüsch et al., 2024; Koh et al., 2022; Scharschmidt & Segre, 2025) This correlation remains one of the most robustly evidenced in dermatology and serves as a primary target for next-generation microbiome-based interventions.

2.2. Psoriasis

Psoriasis is recognized as a chronic, autoimmune inflammatory dermatosis with a complex, multifactorial origin. While its exact etiology remains partially elusive, it is understood that in susceptible individuals, environmental triggers catalyze a T-cell-mediated inflammatory cascade, which subsequently drives the pathological hyperproliferation of keratinocytes (Celoria et al., 2023). Recent investigations into the cutaneous microbiome have consistently identified a state of dysbiosis within psoriatic plaques. Furthermore, research has established a definitive link between microbiome instability-precipitated by genomic and environmental pressures-and the provocation of inflammatory responses within these lesions (Arya et al., 2023; Celoria et al., 2023)

Utilizing Next-Generation Sequencing (NGS), researchers have demonstrated that psoriatic skin possesses a microbial signature and diversity index distinct from both healthy controls and the non-lesional skin of the same patients. This highlights a localized dysbiotic state intrinsically tied to active disease sites (Arya et al., 2023; Celoria et al., 2023). Observed irregularities include altered ratios of primary bacterial phyla, specifically shifts among Actinobacteria, Firmicutes, Proteobacteria, and Bacteroidetes, alongside taxonomic fluctuations in dominant genera such as Staphylococcus, Streptococcus, Cutibacterium, and Corynebacterium.

It is important to note that specific microbial profiles often vary between clinical studies, likely due to patient population heterogeneity, varying anatomical sampling sites, and differences in sequencing technology or bioinformatic processing (Santiago-Rodriguez et al., 2023) Moreover, current evidence suggests that dysbiosis extends beyond mere taxonomic shifts to include functional alterations in microbial metabolic

pathways. These changes can impact keratinocytes and immune cell behavior, further exacerbating the local pro-inflammatory milieu (Celoria et al., 2023)

Under homeostatic conditions, the skin microbiota is essential for immune system priming, barrier maintenance, and pathogen exclusion. However, in the context of psoriasis, the microbial community reorganizes into a profile that favors immunological activation (Celoria et al., 2023; Santiago-Rodriguez et al., 2023) The stimulation of Toll-like receptors (TLRs) and other innate immune components by both commensal and opportunistic microbes triggers keratinocytes and antigen-presenting cells to ramp up the production of pro-inflammatory cytokines. This process reinforces the dominance of the Th17/IL-23 axis and recruits additional effector cells to the inflammatory site (Celoria et al., 2023)

The resulting positive feedback loop between microbial dysbiosis, barrier impairment, and persistent immune activation manifests in the classic clinical features of psoriasis: hyperkeratosis, inflammatory infiltration, and dermal neoangiogenesis (Arya et al., 2023; Celoria et al., 2023) This integrated microbial-immunological framework positions the microbiome as a critical modulator of both the severity and chronicity of the disease (Celoria et al., 2023) Despite these insights, a "chicken-or-egg" question remains: it is not yet fully determined if these microbial shifts initiate the disease or are secondary adaptations to a pre-existing inflammatory state and lipid barrier damage (Celoria et al., 2023) Currently, the microbiome is viewed as a dynamic modifier of inflammation, offering potential as both a diagnostic biomarker and a target for future eubiosis-restoring therapies (Celoria et al., 2023)

2.3. Acne Vulgaris

Acne serves as a quintessential example of a condition where the role of the microbiome is highly nuanced; it is not the absolute presence of *Cutibacterium acnes* that determines the disease, but rather the specific composition of strains and their respective virulence factors (Boyanova, 2023; Mayslich et al., 2021)

Recent investigations have demonstrated that various *C. acnes* phylotypes and strains possess distinct immunogenic and metabolic properties; certain clades are intrinsically linked to active inflammatory lesions, whereas others may function as protective commensals (Oh & Voigt, 2025; Smythe & Wilkinson, 2023) Furthermore, therapeutic interventions involving antibiotics and isotretinoin trigger significant shifts in the cutaneous microbial landscape, which carries critical implications for the development of antimicrobial resistance and long-term clinical outcomes (Deng et al., 2023; Santiago-Rodriguez et al., 2023)

An increasing body of work is now focusing on the isolation of "protective" *C. acnes* strains to evaluate their therapeutic potential, paving the way for strain-targeted therapies as an alternative to the broad-spectrum destruction of the microbiota (Callewaert et al., 2021; Tamer & Kekilli, 2024) Concurrently, the escalating challenge of bacterial resistance-driven by the widespread use of topical and systemic antibiotics-remains a clinically significant hurdle in modern dermatology (Boyanova, 2023; Smythe & Wilkinson, 2023)

2.4. Seborrheic Dermatitis

Seborrheic dermatitis (SD) has traditionally been attributed to the overgrowth of the *Malassezia* genus; however, contemporary data present a far more intricate pathogenic picture involving interactions between fungi, commensal bacteria, and the host's immune response (Chang & Chovatiya, 2024; Oh & Voigt, 2025)

Studies from recent years describe species-level shifts within *Malassezia* and the profound impact of their lipid metabolites on epidermal barrier integrity and localized inflammatory signaling (Chalupczak & Lipner, 2025; Li et al., 2025) In clinical practice, this implies that while antifungal treatments often yield initial improvement, maintaining long-term remission may depend on restoring the equilibrium of the entire skin ecosystem (Haykal et al., 2024; Scharschmidt & Segre, 2025) Consequently, there is growing interest in the influence of cosmetics, dermocosmetics, and essential oils on the microbiome profile in the context of SD, particularly regarding "microbiome-friendly" formulations (Habeebuddin et al., 2022)

A comparative summary of these microbial shifts and their respective taxonomic signatures across the discussed dermatological conditions is provided in Table 1.

3. Therapeutic Interventions Modulating The Skin Microbiome

3.1. Topical Microbiome-Modulating Agents: Prebiotics, Probiotics, and Postbiotics

The therapeutic landscape is currently witnessing a surge in research into topical applications of prebiotic nutrients, live probiotic consortia, and bioactive postbiotic metabolites (Habeebuddin et al., 2022; Tamer & Kekilli, 2024) Literature from the 2022–2025 period suggests that these targeted interventions can mitigate the severity of atopic dermatitis and related inflammatory conditions. Their efficacy is primarily attributed to a tripartite mechanism: competitive exclusion of pathogens, reinforcement of the stratum corneum barrier, and recalibration of cutaneous immunological signaling (Fölster-Holst, 2022; Haykal et al., 2024; Koh et al., 2022)

The transition from traditional antimicrobial suppression toward this model of ecological restoration and barrier reinforcement is illustrated in Figure 1.

Despite mechanistic plausibility and some positive signals in subgroup analyses, systematic reviews which consistently identify significant limitations: high heterogeneity between studies ($I^2 > 85\%$), small sample sizes, inconsistent strain selection, variable formulation quality, and lack of standardized outcome measures(Deng et al., 2023; Habeebuddin et al., 2022; Tamer & Kekilli, 2024) Consequently, while evidence indicates that the skin ecosystem can successfully reorganize following therapeutic disruption, the longitudinal safety profile and the permanence of these microbial shifts remain critical areas for future high-powered clinical trials (Che et al., 2025)

3.2. Precision Microbiome Therapies

Precision microbiome therapies represent an emerging investigational approach in dermatological research, aiming for the selective modulation of specific microbial species or even individual phylogenetic lineages while preserving the overarching ecological balance(Deng et al., 2023; Oh & Voigt, 2025; Scharschmidt & Segre, 2025)

In contrast to conventional probiotics and prebiotics, the "precision microbiome" concept relies on identifying critical pathobionts and protective strains through shotgun metagenomics, functional analysis, and advanced bioinformatics. This allows for the design of interventions directed at specific microbiological targets-such as particular *Staphylococcus aureus* clones in AD or highly pro-inflammatory *Cutibacterium acnes* phylotypes in acne (Boyanova, 2023; Callewaert et al., 2021; Mayslich et al., 2021; Scharschmidt & Segre, 2025)

In clinical practice, this involves the application of meticulously curated bacterial consortia and the targeted replacement of specific dermatotypes. Using defined microbial mixtures often results in superior colonization efficiency and greater long-term persistence within the skin's ecosystem compared to non-selected, full-microbiome preparations (Callewaert et al., 2021) Preliminary evidence from small-scale studies suggests that combinations of multiple species;including various C. acnes and Staphylococcus lineages with favorable functional profiles; may achieve more durable colonization and pathobiont displacement than isolated single strains, though long-term efficacy data remain limited(Callewaert et al., 2021)

Parallel to these efforts, even more focused strategies are being developed, such as phage therapy targeting pathogenic strains, the use of lysins, and polymers designed to selectively inhibit the growth of deleterious bacteria while sparing beneficial commensals (Lyu et al., 2025). The precision microbiome framework is intrinsically linked to personalized medicine; integrating metagenomic, clinical, and genetic data-often via machine learning models-enables the definition of specific "microbial subtypes" for AD, psoriasis, or acne. This allows for the creation of individualized probiotic, prebiotic, or postbiotic formulations tailored to a patient’s unique profile (Fang et al., 2025; Oh & Voigt, 2025; Scharschmidt & Segre, 2025)

Despite encouraging results from preclinical and pilot studies, researchers highlight significant hurdles. These include long-term safety concerns, the stability of microbial engraftment, a lack of standardized protocols, and complex regulatory frameworks for products containing live or genetically modified organisms. Consequently, strain-targeted therapies currently remain primarily within the realm of translational research and early-phase clinical trials (Callewaert et al., 2021; Fang et al., 2025; Lyu et al., 2025)

3.3. Skin Microbiome Transplantation and Emerging Innovations

Skin microbiome transplantation (SMT) represents one of the most sophisticated yet experimental strategies for ecological manipulation. This process involves the transfer of microbial material from a healthy donor to a recipient's skin, aiming to reconstruct a eubiotic and more defensive microbial community (Callewaert et al., 2021)

Case reports and small uncontrolled pilot studies suggest that transplantation of specific Cutibacterium acnes 'dermatotypes' may achieve temporary colonization in some recipients. However, the durability of engraftment, clinical efficacy, and safety profile remain inadequately characterized in the absence of randomized controlled trials. Current evidence is insufficient to determine whether observed clinical improvements represent true therapeutic effects, placebo responses, or natural disease fluctuation(Callewaert et al., 2021). Experts emphasize that rigorous donor selection, standardized material preparation protocols, and strict microbiological safety screening are essential to mitigate the risk of pathogen transmission or the transfer of undesirable microbial traits (Callewaert et al., 2021; Li et al., 2025)

Simultaneously, other innovative modulation strategies, collectively termed "skin microbiome engineering," are under development. These include the utilization of engineered bacterial strains designed to synthesize specific anti-inflammatory metabolites or antimicrobial peptides, as well as the formulation of live therapeutic consortia that function as "biological drugs" (Lyu et al., 2025) Other prospective approaches involve bacteriophage therapy and the use of lysins to selectively eliminate pathobionts, alongside hybrid "synbiotic" preparations that combine prebiotics, probiotics, and postbiotics. These hybrid systems aim to modulate the cutaneous ecosystem in a more predictable manner than unselected whole-microbiome transplants (Fang et al., 2025; Scharschmidt & Segre, 2025)

These interventions remain experimental because several critical knowledge gaps have yet to be addressed. Currently, the field lacks randomized controlled trials, standardized donor screening and clear regulatory pathways for live microbial therapeutics. Specific technical challenges include; unknown long-term safety profiles, unclear mechanisms of microbe engraftment, potential risks of pathogen transmission.Researchers emphasize that we must better understand the permanence of microbial shifts and establish firm regulatory frameworks. Until these safety and legal hurdles are cleared, these advanced treatments cannot be integrated into routine clinical practice. (Callewaert et al., 2021; Li et al., 2025; Lyu et al., 2025)

3.4. Conventional Therapies and Their Impact on the Microbiome

Traditional dermatological treatments-including topical corticosteroids, antiseptics, antibiotics, retinoids, and systemic immunosuppressants-exert a profound, though often non-specific, influence on the cutaneous microbiome by altering both taxonomic composition and microbial diversity (Li et al., 2025)

In the management of atopic dermatitis, evidence shows that successful inflammatory control achieved through topical steroids or combination therapies (corticosteroid plus antimicrobial agents) is associated with a reduction in *Staphylococcus aureus* dominance. This process facilitates a partial normalization of bacterial diversity, shifting the microbial signature of lesional skin closer to that of clinically unaffected areas (Fölster-Holst, 2022; Hrestak et al., 2022; Koh et al., 2022; Tingting et al., 2025) Similar observations have been made in other inflammatory dermatoses, where effective clinical intervention-regardless of the specific mechanism (e.g., traditional immunosuppressants or biologics)-frequently results in a restorative shift of the microbiome toward a profile resembling healthy skin. This suggests a secondary but clinically vital microbial modulation effect resulting from the resolution of chronic inflammation (Li et al., 2025; Scharschmidt & Segre, 2025)

Conversely, recent data emphasize that the protracted use of topical and systemic antibiotics-particularly in the treatment of acne and chronic skin infections-carries the risk of diminishing microbial richness. Such exposure can lead to the selection of resistant strains and drive the ecosystem toward less favorable community structures. These findings underscore the urgent need to rationalize antibiotic use and prioritize therapeutic strategies that incorporate microbiome preservation (Li et al., 2025; Podwojniak et al., 2024)

In light of these observations, modern dermatology increasingly emphasizes the importance of balancing clinical efficacy with the ecological impact of conventional therapies. Reducing unjustified antibiotic exposure has become a cornerstone of contemporary antimicrobial stewardship within the field (MacGibeny et al., 2022; Podwojniak et al., 2024; Zhang et al., 2024)

4. Skin Microbiome Research Methods: Practical Considerations and Limitations

Current skin microbiome research relies primarily on culture-independent techniques, specifically 16S rRNA/ITS gene amplicon sequencing and shotgun metagenomics, each possessing distinct advantages and practical constraints.

16S rRNA sequencing remains widely utilized due to its cost-effectiveness and relative resilience when handling samples with low microbial biomass or high host DNA contamination. However, this method is largely restricted to bacterial identification, offers limited strain-level resolution, and fails to provide direct functional data, which complicates the interpretation of underlying pathophysiological mechanisms (Santiago-Rodriguez et al., 2023; Smythe & Wilkinson, 2023)

Conversely, shotgun metagenomics enables the concurrent analysis of bacteria, fungi, viruses, and functional potential-including metabolic pathways, antibiotic resistance genes, and metabolite production. It also allows for more precise strain differentiation. Nevertheless, its application in dermatology is hindered by high costs and the necessity for significant sequencing depth. Furthermore, the low microbial biomass characteristic of certain skin sites and the high concentration of host DNA necessitate rigorous optimization of collection protocols, extraction techniques, and human DNA depletion methods (Chaudhary et al., 2023; Plaza Oñate et al., 2025; Santiago-Rodriguez et al., 2023)

Methodological reviews also highlight significant practical challenges regarding specimen collection techniques (swabs, adhesive tapes, or biopsies), the temporal variability of the microbiome, and the high susceptibility of skin samples to environmental or laboratory contamination. Such factors can lead to experimental artifacts, particularly in studies with small cohorts or those lacking stringent negative controls (Santiago-Rodriguez et al., 2023; Smythe & Wilkinson, 2023)

A significant, yet often overlooked, challenge in cutaneous research is the 'kit-ome' phenomenon. Because skin is a low-biomass environment, trace DNA found in extraction kits and laboratory reagents can easily overwhelm the actual sample signal. To ensure results are not merely environmental artifacts, the use of negative extraction controls and mock communities (standardized microbial mixtures) is now considered a mandatory 'litmus test' for methodological rigor in high-impact microbiome studies (Plaza Oñate et al., 2025; Santiago-Rodriguez et al., 2023)

Additionally, discrepancies in bioinformatic pipelines-such as the selection of reference databases, filtering parameters, and normalization methods-substantially influence the resulting taxonomic and functional profiles. This lack of uniformity complicates the cross-comparison of findings between studies and underscores the urgent need for procedural standardization and transparent methodological reporting in future cutaneous microbiome research (Plaza Oñate et al., 2025; Santiago-Rodriguez et al., 2023; Smythe & Wilkinson, 2023)

5. Clinical Relevance and Research Perspectives

Advancements in skin microbiome research carry significant clinical implications; however, translating metagenomic data into routine dermatological practice requires cautious interpretation and further methodological standardization (Chen et al., 2023; Plaza Oñate et al., 2025)

Current evidence suggests that microbiome characterization-at both taxonomic and functional levels-may eventually serve as a biomarker for disease activity, therapeutic response, and relapse risk in conditions such as atopic dermatitis, psoriasis, acne, and seborrheic dermatitis (Scharschmidt & Segre, 2025) In particular, integrating shotgun metagenomics with clinical and immunological data enables the identification of "microbial endotypes" of diseases. This aligns with the principles of personalized medicine and the emerging field of precision microbiome therapies (Chen et al., 2023; Liu et al., 2020; Plaza Oñate et al., 2025)

At the same time, it must be emphasized that methodological variability;including sample types, low microbial biomass, contamination risks, and bioinformatic discrepancies-alongside the absence of definitive thresholds for "eubiosis" versus "dysbiosis," currently limits the ability to establish strict clinical guidelines (Chen et al., 2023; Ederveen et al., 2020; Plaza Oñate et al., 2025) Future research should prioritize the standardization of collection and analysis protocols, the design of prospective studies with adequate power, and the long-term monitoring of microbiome-targeted interventions (Chen et al., 2023)

Furthermore, the integration of diverse "multi-omic" layers (metagenomics, metabolomics, transcriptomics) with host immune response analysis will be critical for distinguishing between mere correlation and true causality (Li et al., 2025; Oh & Voigt, 2025; Santiago-Rodriguez et al., 2023) In the coming years, the skin microbiome is poised to transition from a subject of pathophysiological inquiry to a functional tool supporting therapeutic decision-making; provided that evidence quality is strengthened, safety

profiles are rigorously assessed, and clear regulatory frameworks for live-microorganism therapies are established (Ederveen et al., 2020; Scharschmidt & Segre, 2025)

Table 1. Microbiome alterations and microbiome-targeted therapeutic perspectives in selected inflammatory dermatologic diseases.

Disease	Key microbial findings	Dominant / Altered taxa	Therapeutic approaches targeting the microbiome
Atopic dermatitis	Reduced microbial diversity; dynamic dysbiosis with flare-dependent shifts; S. aureus-driven immune activation; quorum sensing-mediated virulence regulation	↑ *Staphylococcus aureus* during flares; ↓ microbial diversity; relative restoration of *Staphylococcus epidermidis* in remission	Topical and oral probiotics; postbiotics; prebiotic emollients; UVB therapy with secondary microbiome modulation; quorum sensing inhibition (experimental); precision strain-based therapies
Psoriasis	Local lesion-specific dysbiosis; altered taxonomic composition and functional pathways; interaction with innate immunity (TLR activation); Th17/IL-23 axis involvement	Altered proportions of Actinobacteria, Firmicutes, Proteobacteria, Bacteroidetes; shifts in *Staphylococcus*, *Streptococcus*, *Cutibacterium*, *Corynebacterium*	Primarily indirect modulation via anti-inflammatory treatment (biologics, immunosuppressants); emerging interest in microbiome-based biomarkers and future precision modulation
Acne vulgaris	Strain-specific pathogenicity rather than total abundance; virulence-associated phylotypes; antibiotic-driven dysbiosis; resistance development	Pro-inflammatory strains of *Cutibacterium acnes*; antibiotic-resistant strains	Targeted strain-based therapies; selected protective *C. acnes* strains; antibiotic stewardship; skin microbiome transplantation (pilot studies); precision microbiome approaches; phage therapy (experimental)
Seborrheic dermatitis	Malassezia-associated dysbiosis; fungal–bacterial interactions; lipid metabolite-mediated barrier disruption; immune modulation	Altered species distribution within *Malassezia* genus; interaction with bacterial commensals	Antifungal therapy (standard of care); microbiome-friendly dermocosmetics; broader microbiome restoration strategies; experimental microbiome modulation

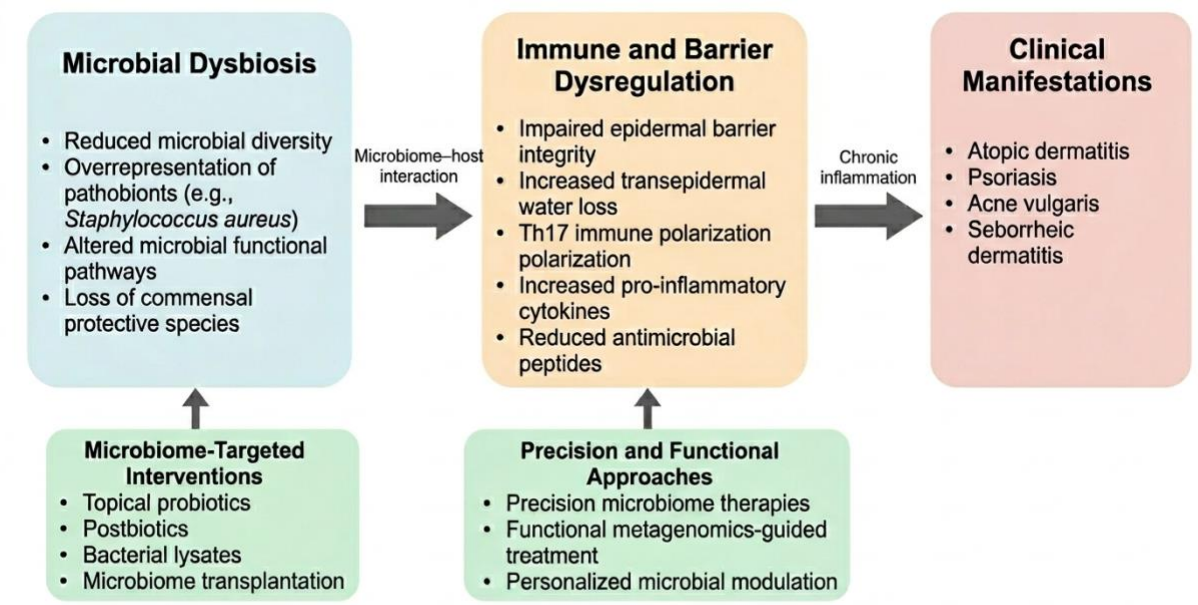

Figure 1. Conceptual model of microbiome-driven inflammatory pathways and emerging microbiome-targeted therapeutic strategies in inflammatory dermatologic diseases.

6. Methods

This narrative review was based on a targeted literature search conducted in the PubMed database to identify relevant publications addressing the role of the human skin microbiome in inflammatory dermatologic diseases. It was conducted in December 2025. The search focused on articles published between January 2020 and December 2025. Search terms included combinations of "skin microbiome," "skin microbiota," "cutaneous microbiome," and "cutaneous microbiota," along with disease-specific terms such as "atopic dermatitis," "psoriasis," "acne," and "seborrheic dermatitis." Additional keywords related to methodology and therapeutic approaches, including "16S sequencing," "shotgun metagenomics," "topical probiotics," "postbiotics," "microbiome transplantation," and "precision microbiome," were also explored.

Studies were selected based on their scientific relevance, methodological rigor, and contribution to understanding microbiome-host interactions and emerging microbiome-targeted interventions. Of the 171 abstracts screened, 33 high-impact studies were selected for in-depth synthesis based on their contribution to functional metagenomics. Priority was given to original research articles, systematic reviews, and clinically relevant translational studies. Reference lists of selected publications were additionally screened to identify further pertinent articles. Exclusion criteria included case reports, and studies not published in English. In the initial phase, two authors (FW and WW) conducted a screening of titles and abstracts. Subsequently, they assessed full-text articles to confirm their alignment with the specified inclusion criteria. In case of uncertainty, a supervising author, JG, was consulted to reach a consensus.

This review was conducted as a narrative synthesis and does not represent a fully systematic analysis of all available literature.

7. Limitations

This review has several limitations inherent to its narrative design. Although efforts were made to include representative and high-quality studies, the selection process was not conducted using a predefined systematic protocol and may therefore be subject to selection bias. Additionally, heterogeneity in sampling techniques, sequencing methodologies, and study populations across the included publications limits direct comparability of findings. Finally, the rapidly evolving nature of microbiome research means that emerging data may further refine current interpretations.

8. Discussion

The provided review confirms that the skin microbiome is a fundamental component of the pathophysiology in specific dermatological conditions, although its role is neither uniform nor entirely elucidated. In atopic dermatitis, the correlation between reduced microbial diversity, *Staphylococcus aureus* dominance, and the severity of inflammation is among the most robustly documented examples of clinically significant dysbiosis. In psoriasis and acne, the landscape is more intricate: observed microbial shifts involve both taxonomic composition and functional potential, while the direction of the cause-and-effect relationship remains a subject of ongoing debate. In seborrheic dermatitis, the synergistic contribution of bacteria and fungi in modulating the host immune response is increasingly emphasized, highlighting the necessity of considering the entire microbial ecosystem rather than isolated microorganisms.

A pivotal conclusion drawn from the literature analysis is that cutaneous dysbiosis is rarely a binary state. The concepts of eubiosis and dysbiosis are descriptive and contextual, and the lack of established quantitative thresholds limits their clinical application. Furthermore, the microbiome exhibits significant inter-individual, topographical, and temporal variability, complicating the definition of a universal "normal" pattern. In clinical practice, this implies that the interpretation of metagenomic findings must always be situated within the appropriate clinical and immunological framework.

Technological advancements, particularly in shotgun metagenomics and functional analysis, have enabled the identification of differences not only at the species level but also across specific strains and microbial metabolic potentials. This transition from purely taxonomic analysis toward a functional interpretation of the microbiome is crucial for the advancement of precision microbiome therapies. In acne, it has been demonstrated that specific *Cutibacterium acnes* clades differ in their pro-inflammatory potential, while in AD, distinct *S. aureus* clones may exhibit varying virulence properties. These data support the paradigm of strain-targeted interventions over non-selective microbiota eradication.

At the same time, interpretative caution is warranted. The majority of available studies are cross-sectional, involve relatively small patient cohorts, and are characterized by significant methodological heterogeneity-both in terms of sampling techniques, sequencing platforms, and bioinformatic pipelines. The challenges of low microbial biomass and high host DNA concentrations further increase the risk of artifacts and contamination. Standardizing laboratory procedures and methodological reporting must be a priority for future research initiatives.

Regarding therapeutic interventions, there is a dynamic evolution of microbiome-modulating strategies, ranging from pre-, pro-, and postbiotics to strain-targeted therapies, skin microbiome transplantation, and microbial engineering. While preliminary results from preclinical and pilot studies are promising, most clinical data currently possess limited evidentiary power. There is a lack of large-scale, randomized controlled trials with long-term follow-up to definitively assess the durability of effects, safety, and the actual impact of these therapies on the disease course. Additionally, regulatory hurdles concerning preparations containing live microorganisms pose a significant challenge to their broader implementation.

An intriguing observation remains: effective inflammatory control-regardless of the therapeutic class used (e.g., corticosteroids, biologics)-is frequently associated with a partial normalization of the microbiome. This may suggest that, in many instances, dysbiosis is secondary to inflammation and barrier dysfunction, although this does not preclude its role as a factor that amplifies and sustains the disease process. This relationship is likely bidirectional and dynamic.

From the perspective of future research, integrating metagenomic data with clinical and immunological signatures appears particularly vital. An integrative approach may enable the identification of more precise phenotypes and 'microbial endotypes' of dermatological diseases, potentially translating into more personalized therapeutic strategies. The identification of these endotypes will likely require Machine Learning (ML) algorithms to integrate the high-dimensional 'multi-omic' data, moving the field beyond simple correlation toward predictive modeling. However, the transition from descriptive studies to prospective designs with clearly defined clinical endpoints will be essential.

In summary, the skin microbiome emerges as a significant, dynamic modifier of the course of dermatological diseases and a potential source of novel biomarkers and therapeutic targets. Simultaneously, the translation of this knowledge into routine clinical practice requires further strengthening of the quality of evidence, methodological standardization, and long-term safety evaluation of microbiome interventions. The current stage of research can be described as an intensive phase of translational development, the success of which will depend on the integration of basic, clinical, and regulatory research.

9. Summary

1. The human skin microbiome plays a dynamic and context-dependent role in the pathophysiology of inflammatory dermatologic diseases, including atopic dermatitis, psoriasis, acne, and seborrheic dermatitis. Dysbiosis is consistently associated with disease activity, yet its directionality and causal significance remain incompletely understood. Emerging evidence highlights the potential of interventions targeting the microbiome; such as topical pre-, pro-, and postbiotics, precision microbiome therapies, and microbiome transplantation; to modulate skin health and disease outcomes. Despite promising preliminary findings, standardized methodologies, long-term clinical data, and regulatory frameworks are still needed to translate these strategies into routine practice. Overall, the skin microbiome represents both a key contributor to disease mechanisms and a promising target for personalized therapeutic approaches.The transition from broad-spectrum antibiotics to ecological restoration marks a paradigm shift in dermatological stewardship.

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