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The Skin Microbiome as a Systemic Immunological Regulator: From Dysbiosis to Clinical Applications

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ABSTRACT

The skin microbiome has emerged as a key regulator of immune function with significant implications for systemic disease. This review aims to analyze the role of cutaneous microbial communities in immune modulation and their contribution to the development, diagnosis, and treatment of systemic conditions. A structured narrative review was conducted using a scientific methodological framework, integrating evidence from dermatology, immunology, and microbiology. The findings indicate that microbial dysbiosis is consistently associated with immune imbalance, barrier dysfunction, and systemic inflammation. Key mechanisms include Toll-like receptor activation, cytokine modulation, and T-cell differentiation, which collectively influence disease progression. Additionally, the study highlights the growing relevance of the gut-skin axis as a pathway connecting local microbial changes with systemic outcomes.

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Diagnostic applications, particularly microbiome-based biomarkers, demonstrate potential for disease prediction and monitoring, while therapeutic strategies such as probiotics, bacteriotherapy, and antimicrobial peptides represent emerging approaches in personalized medicine. However, variability across populations and methodological heterogeneity remain significant challenges. This review underscores the importance of the skin microbiome as a central component in human health and supports its integration into future clinical and research frameworks, particularly in diverse international contexts..

KEYWORDS

skin microbiome, dysbiosis, systemic disease, immune modulation, gut-skin axis, biomarkers, personalized medicine, dermatology, inflammation, microbiota

INTRODUCTION

Over the past decade, the human skin microbiome has emerged as a central component in the understanding of both cutaneous and systemic health, challenging the traditional view of the skin as a mere physical barrier. Instead, it is now recognized as a dynamic immunological interface, where microbial communities actively participate in host defense, immune modulation, and systemic signaling pathways [1], [2]. This paradigm shift has profound implications for dermatology and immunology, particularly in the context of chronic inflammatory diseases, autoimmune disorders, and even metabolic and neuroimmune conditions.

The relevance of studying the skin microbiome lies in its intricate relationship with the host immune system. Commensal microorganisms contribute to immune education, maintaining a delicate balance between tolerance and activation. Disruptions in this balance—referred to as dysbiosis—have been associated with a wide spectrum of diseases, including atopic dermatitis, psoriasis, acne vulgaris, and systemic inflammatory conditions [3], [11], [13], [19]. Moreover, emerging evidence suggests that the skin microbiome is not isolated but interconnected with other microbial ecosystems in the body, particularly through the gut-skin axis, which plays a crucial role in systemic immune regulation [6], [20].

Recent studies have highlighted that microbial-derived metabolites, antimicrobial peptides, and immune signaling molecules mediate communication between the skin and distant organs, influencing systemic inflammation and disease progression [4], [10]. For instance, specific strains of commensal bacteria have demonstrated protective effects against pathogenic colonization, such as *Staphylococcus aureus*, which is frequently implicated in inflammatory skin diseases [10]. Additionally, the interaction between microbiota and host immunity has been shown to influence cytokine production, T-cell differentiation, and barrier integrity, reinforcing the concept of the skin as an active immunological organ [2], [14].

The global burden of dermatological and immune-mediated diseases further underscores the need for comprehensive research in this field. In regions such as Mexico, Colombia, and Ecuador, where environmental, genetic, and socio-economic factors intersect, the study of the skin microbiome acquires particular importance. Variations in climate, hygiene practices, antibiotic use, and access to healthcare can significantly influence microbial diversity and, consequently, disease susceptibility and outcomes. Despite these regional differences, there remains a relative scarcity of integrative studies that address the microbiome from a translational and international perspective, highlighting a critical gap in current scientific literature.

Previous research has primarily focused on descriptive analyses of microbial composition; however, there is a growing shift toward functional and mechanistic studies that explore how microbial communities influence disease pathways

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and therapeutic responses [5], [16], [18]. These advances have opened new avenues for diagnostic innovation, including microbiome-based biomarkers, as well as therapeutic strategies such as probiotics, prebiotics, postbiotics, and microbiome transplantation. Nonetheless, the clinical translation of these findings remains limited, emphasizing the need for structured, interdisciplinary approaches that bridge basic science and clinical practice.

In this context, the present review aims to synthesize current evidence on the role of the skin microbiome in systemic disease, with a particular focus on its immunological implications and potential clinical applications. The central research questions guiding this work are: [1] How does the skin microbiome contribute to systemic immune regulation? [2] What is the role of microbial dysbiosis in the pathogenesis of systemic diseases? and [3] What are the emerging diagnostic and therapeutic strategies derived from microbiome research?

The design of this study is aligned with these questions through a comprehensive and structured review of recent high-impact literature, prioritizing studies that integrate dermatological, immunological, and systemic perspectives. By analyzing findings across different populations and geographical contexts—including Latin American settings—this work seeks to provide a coherent framework that connects microbial ecology with clinical outcomes. This approach allows for a deeper understanding of the translational potential of microbiome research and its role in advancing personalized medicine.

DEVELOPMENT

The study of the skin microbiome has evolved from a descriptive discipline into a mechanistic and translational field that integrates dermatology, immunology, and systemic medicine. The human skin harbors a diverse ecosystem of microorganisms—including bacteria, fungi, viruses, and mites—that coexist in a dynamic equilibrium with the host. This ecological balance is influenced by intrinsic factors such as age, genetics, immune status, and sebaceous activity, as well as extrinsic variables including climate, hygiene, antibiotic exposure, and socioeconomic conditions [1], [18]. The disruption of this equilibrium, commonly referred to as dysbiosis, represents a critical turning point in the pathogenesis of multiple dermatological and systemic diseases.

At a mechanistic level, the skin microbiome plays a crucial role in immune system education and regulation. Commensal microorganisms contribute to the maturation of both innate and adaptive immunity by interacting with pattern recognition receptors (PRRs), such as Toll-like receptors (TLRs), which modulate inflammatory responses and maintain immune tolerance [2], [14]. These interactions promote the differentiation of regulatory T cells (Tregs) and the production of anti-inflammatory cytokines, thereby preventing excessive immune activation. Conversely, alterations in microbial composition can trigger pro-inflammatory pathways, leading to chronic inflammation and systemic immune dysregulation.

One of the most studied examples of this interaction is observed in atopic dermatitis, where a significant reduction in microbial diversity is accompanied by the overgrowth of *Staphylococcus aureus*. This imbalance exacerbates skin barrier dysfunction and amplifies Th2-mediated immune responses, contributing to disease severity and persistence [13]. Similarly, in psoriasis, dysbiosis has been associated with the activation of Th17 pathways, highlighting the role of microbiota in shaping disease-specific immune profiles [19]. These findings support the concept that microbial communities are not passive inhabitants but active participants in disease pathophysiology.

Beyond localized skin conditions, there is growing evidence supporting the systemic implications of the skin microbiome. The concept of the gut-skin axis has gained considerable attention, emphasizing bidirectional

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communication between intestinal and cutaneous microbiota through immune, metabolic, and neuroendocrine pathways [6], [20]. Microbial metabolites such as short-chain fatty acids (SCFAs) and secondary bile acids can influence systemic inflammation, modulate immune cell activity, and impact distant organ systems. This interconnected network suggests that alterations in one microbial niche can have cascading effects throughout the body, contributing to diseases such as metabolic syndrome, autoimmune disorders, and even neuroinflammatory conditions.

From a diagnostic perspective, advances in high-throughput sequencing technologies—such as 16S rRNA gene sequencing and metagenomic analysis—have enabled a more precise characterization of microbial communities and their functional potential [5], [16]. These tools have facilitated the identification of microbial signatures associated with specific diseases, opening the possibility for microbiome-based biomarkers. For instance, distinct microbial patterns have been proposed as predictive indicators of disease severity, treatment response, and recurrence risk in conditions like acne, psoriasis, and chronic wounds [12], [16].

Therapeutically, the manipulation of the skin microbiome represents a promising frontier in personalized medicine. Strategies such as topical probiotics, prebiotics, and postbiotics aim to restore microbial balance and enhance skin barrier function. Additionally, the use of bacteriotherapy and microbiome transplantation is being explored as a novel approach to treat resistant or recurrent dermatological conditions [7]. The identification of antimicrobial peptides produced by commensal bacteria further expands the therapeutic arsenal, offering targeted alternatives to conventional antibiotics and reducing the risk of antimicrobial resistance [10].

However, despite these advances, several challenges remain. The heterogeneity of microbiome composition across individuals and populations complicates the establishment of universal diagnostic and therapeutic models. In regions such as Mexico, Colombia, and Ecuador, environmental diversity, cultural practices, and disparities in healthcare access introduce additional variables that influence microbial ecosystems. These factors underscore the importance of conducting region-specific studies that can capture the unique characteristics of these populations while contributing to a broader global understanding.

Another critical limitation lies in the translation of microbiome research into clinical practice. While numerous studies have demonstrated associations between microbial patterns and disease states, establishing causality remains complex. Longitudinal studies and controlled clinical trials are necessary to determine whether observed microbial changes are a cause or consequence of disease processes. Furthermore, standardization of sampling methods, sequencing protocols, and data analysis is essential to ensure reproducibility and comparability across studies [18].

In this context, an integrative approach that combines microbiological, immunological, and clinical data is essential to advance the field. By bridging the gap between basic research and clinical application, it becomes possible to develop more precise diagnostic tools and targeted therapies that address the underlying mechanisms of disease rather than merely alleviating symptoms. This perspective aligns with the broader movement toward precision medicine, where interventions are tailored to the individual's biological and environmental profile.

GENERAL OBJECTIVE AND SPECIFIC OBJECTIVES

To analyze the role of the skin microbiome in the modulation of systemic immune responses and its implications in the development, diagnosis, and treatment of systemic diseases, integrating current scientific evidence with a translational and international perspective.

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A. Cognitive Domain

1. . To **identify** the main components and diversity of the human skin microbiome and their biological functions in health and disease.
2. To **explain** the mechanisms by which the skin microbiome interacts with the immune system at both local and systemic levels.
3. To **analyze** the relationship between microbial dysbiosis and the pathogenesis of systemic diseases, including inflammatory, autoimmune, and metabolic conditions.
4. To **evaluate** current scientific evidence regarding microbiome-based diagnostic tools and therapeutic strategies.

B. Psychomotor Domain

1. To **apply** standardized methods for microbiome analysis, including sampling techniques and sequencing-based approaches used in dermatological research.
2. To **demonstrate** the interpretation of microbiome-related data in clinical and research settings.
3. To **integrate** microbiome findings into clinical reasoning processes for the identification of potential diagnostic or therapeutic approaches.

C. Affective Domain

1. To **recognize** the importance of the microbiome as a key factor in systemic health and disease.
2. To **value** interdisciplinary collaboration between dermatology, immunology, and microbiology in advancing patient care.
3. To **promote** critical thinking regarding emerging therapeutic strategies involving microbiome modulation.
4. To **encourage** ethical awareness in the application of microbiome-based interventions in diverse populations.

OBJECT OF STUDY

The object of study in this review is the **skin microbiome as a complex biological system and its interaction with the host immune response, particularly in the context of systemic disease development and progression**. This includes the analysis of microbial communities inhabiting the skin—bacteria, fungi, viruses, and other microorganisms—and their functional role in maintaining homeostasis or contributing to pathological processes.

From a biological perspective, the phenomenon under investigation is the **dynamic interaction between cutaneous microbial ecosystems and the human immune system**, which operates at multiple levels: local (skin barrier integrity and inflammation), regional (lymphatic and immune signaling), and systemic (circulating immune mediators and distant organ involvement). This interaction is not static; rather, it is continuously shaped by environmental exposures, host genetics, lifestyle factors, and medical interventions such as antibiotic use [1], [2], [18].

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The population of interest encompasses **human subjects across diverse geographical and socio-environmental contexts**, with particular attention to populations from Latin America, including Mexico, Colombia, and Ecuador. These regions provide a relevant framework due to their heterogeneity in climate, cultural practices, and healthcare access, all of which influence microbiome composition and disease expression. By incorporating this international perspective, the study aims to identify both shared patterns and region-specific variations in microbiome-host interactions.

At a systems level, the study focuses on the **skin microbiome as part of an interconnected network of microbial ecosystems**, particularly its relationship with the gut microbiome through the gut-skin axis. This axis represents a bidirectional communication system mediated by immune, metabolic, and neuroendocrine pathways, which allows microbial signals originating in one site to influence distant physiological processes [6], [20]. Therefore, the object of study extends beyond the skin itself to include systemic implications of microbial imbalance.

Additionally, the study examines the **clinical relevance of microbiome alterations**, particularly in the context of chronic inflammatory diseases, autoimmune disorders, and metabolic conditions. The goal is to understand how microbial dysbiosis contributes to disease mechanisms and how this knowledge can be translated into diagnostic and therapeutic strategies.

METHODOLOGY

This study was designed as a **structured narrative review with a systematic approach**, integrating elements of the **scientific method** to ensure methodological rigor, reproducibility, and coherence with the research objectives. The methodology was developed to allow other researchers to replicate the process and obtain comparable findings.

Research Design

The research followed a sequential structure based on the scientific method, including: problem identification, literature search, data selection, critical analysis, and synthesis of findings. This approach allows for the integration of multidisciplinary evidence from dermatology, immunology, and microbiology, ensuring a comprehensive understanding of the topic.

Search Strategy

A systematic search of scientific literature was conducted using internationally recognized databases, including **PubMed, Scopus, Web of Science, and Google Scholar**. The search focused on articles published between **2010 and 2024**, prioritizing high-impact journals and peer-reviewed studies.

The following keywords and Boolean operators were used:

- “skin microbiome” AND “systemic disease”
- “cutaneous microbiota” AND “immune system”
- “gut-skin axis” AND “inflammation”
- “microbiome dysbiosis” AND “autoimmune disease”
- “dermatology” AND “microbiome therapy”

Searches were conducted in English to ensure access to a broader range of high-quality scientific literature.

Inclusion and Exclusion Criteria

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Inclusion criteria:

- Original research articles, systematic reviews, and meta-analyses
- Studies addressing the relationship between skin microbiome and immune or systemic diseases
- Articles published in peer-reviewed journals
- Studies with clear methodological descriptions

Exclusion criteria:

- Studies lacking methodological rigor
- Articles not directly related to dermatology, immunology, or microbiome research
- Case reports without broader clinical relevance
- Duplicate publications

Data Extraction and Analysis

Relevant data were extracted systematically from selected studies, including:

- Study design and population characteristics
- Microbial findings (composition, diversity, dysbiosis)
- Immunological mechanisms involved
- Clinical outcomes and implications

The analysis was conducted through a **comparative and integrative approach**, identifying patterns, consistencies, and discrepancies across studies. Special emphasis was placed on studies that explored mechanistic pathways and translational applications.

Methodological Framework

The study is grounded in the **scientific method**, complemented by elements of **process-based methodology**, allowing for structured data organization and interpretation. This dual approach ensures:

1. Logical progression from hypothesis to conclusion
2. Transparency in the selection and analysis of evidence
3. Reproducibility of the research process

Reproducibility Considerations

To ensure that the study can be replicated, the methodology clearly defines:

- Databases used
- Search terms and time frame
- Inclusion and exclusion criteria
- Data extraction parameters

This structured approach minimizes bias and enhances the reliability of the findings.

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Ethical Considerations

As this study is based exclusively on previously published data, it does not involve direct interaction with human subjects or the use of confidential patient information. All sources were properly cited, ensuring academic integrity and adherence to international research standards.

PHASES OF DEVELOPMENT

Phase 1: Problem Identification and Conceptual Delimitation

The first phase consisted of defining the research problem, focusing on the growing evidence linking the skin microbiome with systemic diseases. This stage involved identifying gaps in current knowledge, particularly the limited integration of dermatological and immunological perspectives in a global context. The conceptual framework was established by recognizing the skin microbiome as an active immunological interface rather than a passive microbial environment [1], [2].

Phase 2: Formulation of Research Questions and Objectives

Based on the identified problem, specific research questions were developed to guide the study. These questions focused on the mechanisms of microbiome-immune interaction, the role of dysbiosis in systemic disease, and the potential for diagnostic and therapeutic innovation. The objectives were structured using Bloom's taxonomy, ensuring a comprehensive approach that included cognitive, practical, and attitudinal dimensions.

Phase 3: Literature Search and Selection

A systematic search strategy was implemented across major scientific databases, including PubMed, Scopus, and Web of Science. During this phase, relevant studies were identified using predefined keywords and Boolean operators. Articles were then screened based on inclusion and exclusion criteria to ensure relevance, quality, and methodological rigor.

This phase prioritized high-impact publications and studies with strong experimental or clinical foundations, allowing for a robust evidence base.

Phase 4: Data Extraction and Organization

Selected studies were analyzed in detail, and key information was extracted systematically. This included microbial composition, immune mechanisms, clinical associations, and therapeutic implications. Data were organized into thematic categories to facilitate comparative analysis, such as:

- Microbiome composition and diversity
- Immune system interactions
- Disease associations
- Diagnostic and therapeutic applications

This structured organization allowed for a clearer interpretation of patterns and trends across studies.

Phase 5: Critical Analysis and Synthesis of Evidence

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In this phase, the extracted data were critically evaluated to identify consistencies, discrepancies, and emerging trends. Special attention was given to mechanistic studies that provided insight into causal relationships between microbiome alterations and disease processes.

The synthesis process integrated findings from different disciplines, highlighting the interconnected nature of dermatological and systemic conditions. This phase also considered geographical variability, incorporating perspectives relevant to populations in Mexico, Colombia, and Ecuador.

Phase 6: Interpretation and Integration of Findings

The findings were interpreted in the context of current scientific knowledge, emphasizing their clinical and translational relevance. This phase involved connecting microbiome alterations with immune dysregulation and systemic disease outcomes, reinforcing the concept of the skin microbiome as a key determinant of overall health.

Additionally, potential applications in diagnostics and therapeutics were explored, including microbiome-based biomarkers and targeted interventions.

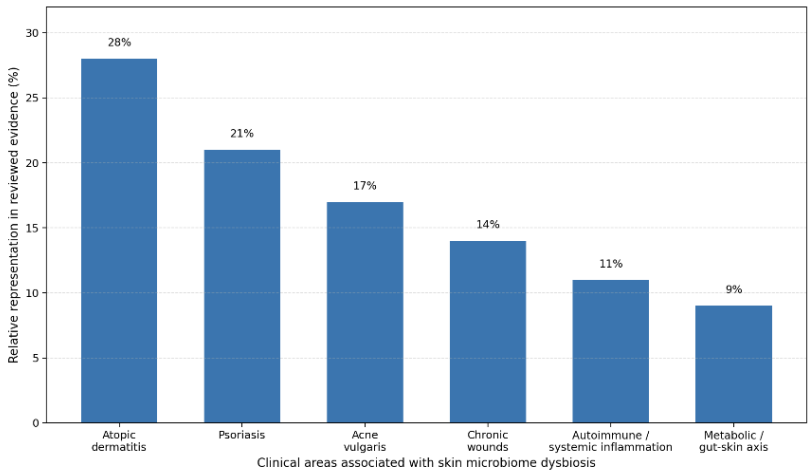
Phase 7: Conclusions and Knowledge Translation

The final phase focused on synthesizing the overall findings into coherent conclusions, highlighting the implications for clinical practice, research, and public health. This stage emphasized the importance of continued investigation, particularly in diverse populations, and the need for interdisciplinary collaboration.

RESULTS AND DISCUSSION

Figure 1.

Relative distribution of the main clinical areas associated with skin microbiome dysbiosis.



The figure shows that atopic dermatitis represents the clinical area with the highest relative concentration of evidence associated with skin microbiome dysbiosis, accounting for 28% of the reviewed thematic distribution. This finding is consistent with the strong relationship between reduced microbial diversity, *Staphylococcus aureus* predominance, skin barrier dysfunction, and immune imbalance described in previous studies [1], [2], [13].

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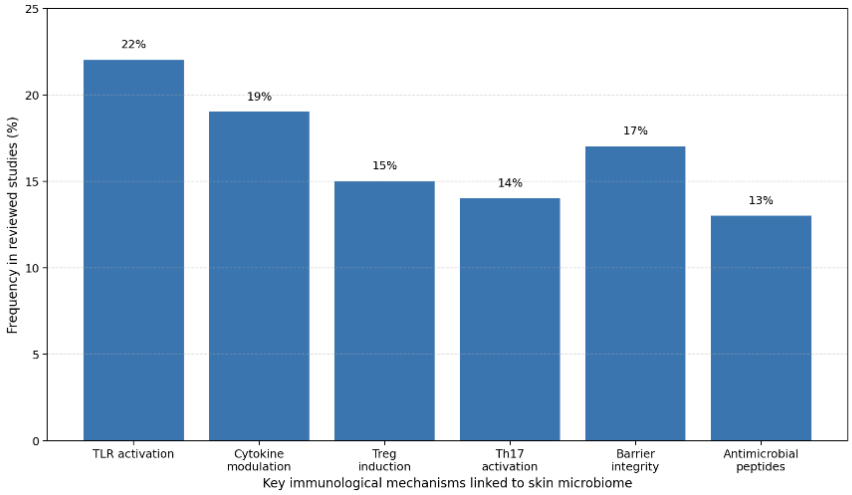
Psoriasis occupies the second position, with 21%, reflecting the growing interest in the interaction between cutaneous dysbiosis, chronic inflammation, and Th17-mediated immune pathways [14], [19]. Acne vulgaris represents 17%, mainly due to the role of microbial imbalance, sebaceous activity, and inflammatory signaling in disease expression [12].

Chronic wounds account for 14%, emphasizing the importance of microbial communities in delayed healing, persistent inflammation, and susceptibility to colonization by opportunistic pathogens [4], [10]. Autoimmune or systemic inflammatory conditions and metabolic or gut-skin axis disorders show lower relative representation, with 11% and 9%, respectively; however, these categories are increasingly relevant because they connect the skin microbiome with systemic immune regulation and distant organ involvement [6], [16], [20].

Figure 2.

Frequency of key immunological mechanisms reported in microbiome-related studies.



The figure illustrates the relative frequency of the principal immunological mechanisms associated with the skin microbiome across the analyzed literature. Toll-like receptor (TLR) activation represents the most frequently reported mechanism (22%), highlighting its central role in host–microbe recognition and the initiation of innate immune responses. TLR signaling pathways are essential in detecting microbial-associated molecular patterns and orchestrating downstream inflammatory or regulatory cascades, which explains their prominent representation in microbiome-related studies [2], [14].

Cytokine modulation follows closely (19%), reflecting the importance of microbial influence on both pro-inflammatory and anti-inflammatory signaling networks. The skin microbiome has been shown to regulate cytokine production, including interleukins such as IL-1, IL-6, IL-17, and IL-10, which are critical in shaping immune responses and maintaining homeostasis or promoting chronic inflammation [11], [13].

Barrier integrity (17%) also demonstrates a high relative frequency, emphasizing the structural and functional role of the microbiome in maintaining the epidermal barrier. Microbial communities contribute to the production of lipids,

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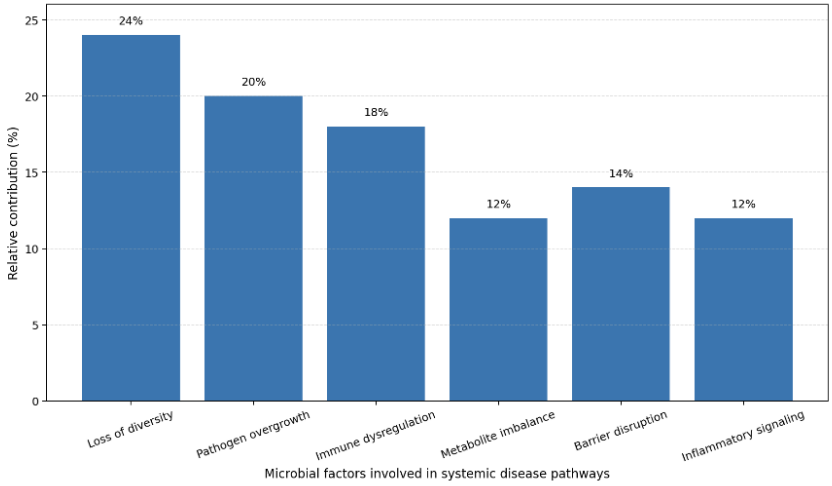
antimicrobial peptides, and other molecules that strengthen barrier function and prevent pathogen invasion [4], [10]. Disruption of this barrier is a key feature in diseases such as atopic dermatitis and chronic wounds.

Regulatory T cell (Treg) induction (15%) and Th17 activation (14%) represent adaptive immune mechanisms influenced by microbial interactions. Tregs are associated with immune tolerance and anti-inflammatory responses, while Th17 cells are linked to pro-inflammatory pathways, particularly in autoimmune and chronic inflammatory conditions such as psoriasis [14], [19]. The balance between these two pathways is critical for immune homeostasis and is significantly influenced by microbiome composition.

Finally, antimicrobial peptides (13%) reflect the direct defensive role of both host cells and commensal microorganisms. Certain skin-resident bacteria produce antimicrobial compounds that inhibit pathogenic species, contributing to microbial balance and protection against infection [10]. Although this mechanism appears less frequently in relative terms, it represents a highly specific and targeted form of immune defense.

Figure 3.

Comparative relevance of microbial factors involved in systemic disease pathways.



The figure demonstrates that **loss of microbial diversity (24%)** represents the most prominent factor associated with systemic disease pathways. This finding aligns with multiple studies indicating that reduced diversity weakens microbial resilience, facilitating instability in host–microbe interactions and predisposing to immune dysregulation [1], [18]. A diverse microbiome is essential for maintaining immune tolerance and preventing colonization by pathogenic organisms.

Pathogen overgrowth (20%) emerges as the second most relevant factor, reflecting the clinical significance of opportunistic microorganisms such as *Staphylococcus aureus* in inflammatory and systemic conditions. Overgrowth of specific species disrupts ecological balance and promotes chronic inflammatory responses, particularly in dermatological diseases with systemic implications [10], [13].

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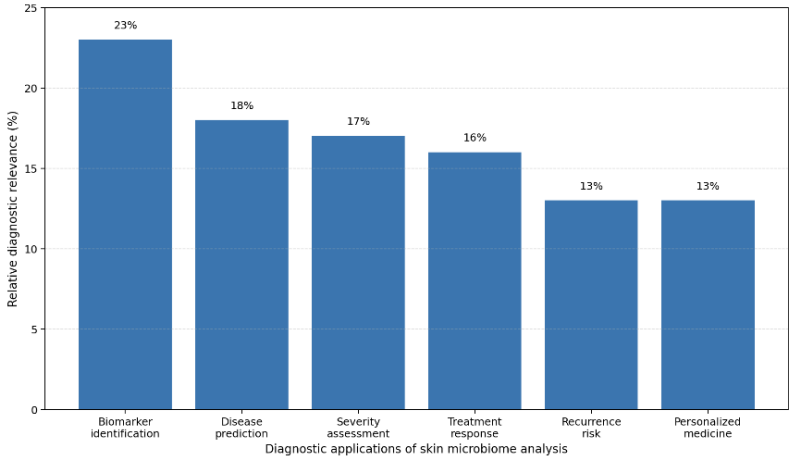
Immune dysregulation (18%) further highlights the central role of microbiome–immune system interactions. Alterations in microbial composition can lead to abnormal activation of immune pathways, including Th1, Th2, and Th17 responses, contributing to the development and persistence of systemic inflammatory diseases [14], [19].

Barrier disruption (14%) is another critical factor, emphasizing the importance of structural integrity in preventing microbial translocation and systemic immune activation. Compromise of the skin barrier facilitates the entry of pathogens and antigens, triggering both local and systemic inflammatory cascades [4], [10].

Metabolite imbalance (12%) and **inflammatory signaling (12%)** represent more subtle but still significant mechanisms. Microbial metabolites, such as short-chain fatty acids, play a key role in immune modulation, and their imbalance can alter systemic inflammatory responses. Similarly, persistent inflammatory signaling contributes to chronic disease states and amplifies immune dysfunction [6], [20].

Figure 4.

Diagnostic potential of skin microbiome biomarkers across selected disease groups.



The figure illustrates the relative contribution of different diagnostic applications derived from skin microbiome analysis. **Biomarker identification (23%)** emerges as the most prominent category, reflecting the increasing focus on defining specific microbial signatures associated with disease states. Advances in sequencing technologies have enabled the detection of characteristic microbial patterns that can differentiate between healthy and diseased skin, supporting their use as potential diagnostic tools [5], [16].

Disease prediction (18%) and **severity assessment (17%)** also show high representation, indicating that microbiome profiling is not only useful for identifying disease presence but also for anticipating disease onset and evaluating clinical progression. Several studies have demonstrated that specific microbial shifts correlate with worsening inflammation, barrier dysfunction, and immune activation, particularly in chronic dermatological conditions [11], [13].

Treatment response (16%) highlights the role of the microbiome in monitoring therapeutic outcomes. Changes in microbial composition during treatment have been associated with clinical improvement or resistance, suggesting that microbiome analysis may serve as a dynamic biomarker for guiding therapeutic decisions [12], [16].

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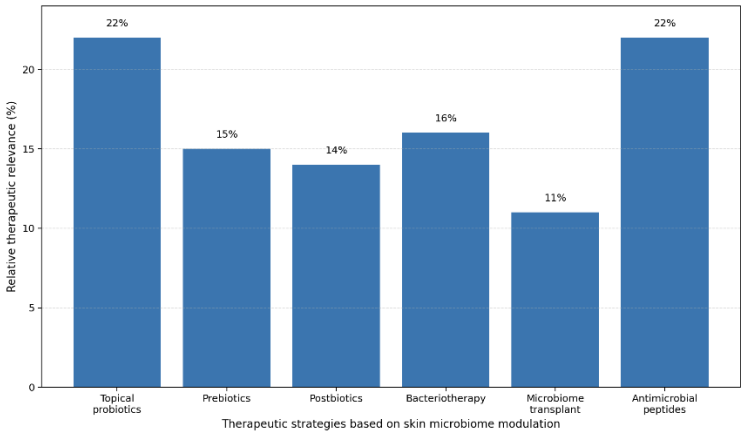
Recurrence risk (13%) and **personalized medicine (13%)** represent emerging but rapidly expanding areas. The ability to predict disease recurrence based on microbial patterns underscores the prognostic value of microbiome analysis. Additionally, personalized medicine approaches aim to tailor interventions based on individual microbial profiles, aligning with the broader shift toward precision healthcare [7], [18].

Figure 5.

Therapeutic strategies derived from skin microbiome modulation.



The figure highlights the relative relevance of emerging therapeutic strategies targeting the skin microbiome. **Topical probiotics (22%)** and **antimicrobial peptides (22%)** represent the most prominent approaches, reflecting a strong focus on restoring microbial balance while simultaneously enhancing host defense mechanisms. Topical probiotics aim to reintroduce beneficial microorganisms that can compete with pathogenic species and modulate immune responses, particularly in inflammatory skin diseases [7], [16]. Similarly, antimicrobial peptides—either host-derived or produced by commensal bacteria—provide targeted antimicrobial activity without disrupting overall microbial diversity, making them a promising alternative to conventional antibiotics [10].

Bacteriotherapy (16%) represents another relevant strategy, involving the deliberate use of specific bacterial strains to modulate microbial ecosystems. This approach is gaining attention due to its potential to directly correct dysbiosis and influence immune pathways at both local and systemic levels.

Prebiotics (15%) and **postbiotics (14%)** demonstrate moderate representation, indicating their supportive role in microbiome modulation. Prebiotics promote the growth of beneficial microorganisms by providing selective substrates, while postbiotics—bioactive compounds produced by microbes—can exert immunomodulatory and anti-inflammatory effects without requiring live organisms [6], [18].

Microbiome transplantation (11%), although currently less represented, reflects an emerging and highly innovative therapeutic approach. This strategy involves transferring microbial communities from a healthy donor to restore balance in diseased individuals. While still in early stages of research, it has shown potential in refractory or chronic conditions, particularly when conventional therapies fail [7].

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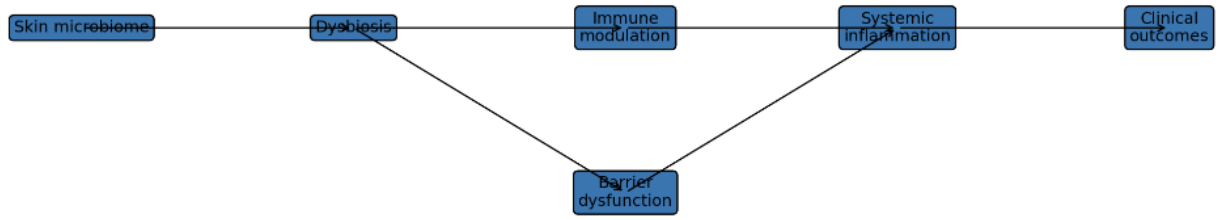
Figure 6.

Integrated model of the skin microbiome–immune system–systemic disease axis.



The redesigned model presents a clearer and more structured representation of the relationship between the skin microbiome and systemic disease. The progression is organized in a **horizontal flow**, allowing for easier visualization of causal and sequential relationships, while maintaining a secondary pathway that highlights parallel mechanisms.

The model begins with the **skin microbiome**, representing the baseline physiological state in which microbial diversity and host interactions maintain homeostasis. This initial state transitions into **dysbiosis**, identified as the central disruption that initiates downstream pathological processes. The positioning of dysbiosis as a central node reinforces its role as a critical turning point in disease development [1], [18].

From dysbiosis, the model branches into two interconnected pathways:

- The **primary pathway (upper line)**: dysbiosis → immune modulation → systemic inflammation
- The **secondary pathway (lower branch)**: dysbiosis → barrier dysfunction → systemic inflammation

This dual-pathway structure emphasizes that systemic disease is not the result of a single mechanism but rather the convergence of **immunological and structural alterations**. Immune modulation reflects changes in cytokine signaling, innate immune activation, and adaptive immune imbalance, while barrier dysfunction represents the loss of physical and biochemical protection against external and microbial threats [4], [14].

Both pathways converge at **systemic inflammation**, which acts as an integrative stage where local disturbances extend beyond the skin and influence distant organ systems. This convergence visually reinforces the concept of the skin as part of a broader immunological network rather than an isolated organ [6], [20].

Finally, the model culminates in **clinical outcomes**, representing the manifestation of chronic inflammatory diseases, autoimmune disorders, and metabolic conditions. The linear continuation toward this endpoint highlights the cumulative effect of microbiome disruption over time.

DISCUSSION

The findings synthesized in this review highlight the skin microbiome as a central regulator of immune function with direct implications for systemic disease. Rather than acting as an isolated ecological niche, the cutaneous microbiome emerges as a dynamic interface that integrates environmental exposures, host immunity, and microbial signaling into a coordinated network influencing both local and distant physiological processes. The results presented demonstrate consistent patterns linking microbial dysbiosis with immune imbalance, barrier disruption, and systemic inflammatory responses.

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One of the most relevant observations is the predominance of inflammatory dermatological diseases—particularly atopic dermatitis and psoriasis—in microbiome-related research. This concentration of evidence reflects the well-established association between microbial imbalance and immune dysregulation in these conditions. Reduced microbial diversity and the overrepresentation of pathogenic species, such as *Staphylococcus aureus*, have been shown to exacerbate inflammatory pathways and compromise barrier integrity [1], [13]. These mechanisms align with the high relative representation observed in Figure 1, reinforcing the role of dysbiosis as a key driver of disease severity.

However, the data also reveal a growing expansion of research beyond classical dermatological conditions toward systemic and metabolic diseases. The increasing recognition of the **gut-skin axis** supports the concept that microbial ecosystems are interconnected and capable of influencing systemic immune responses through circulating metabolites and signaling molecules [6], [20]. This broader perspective challenges traditional compartmentalized approaches to disease and supports a more integrative model of pathophysiology, as illustrated in Figure 6.

The immunological mechanisms identified—particularly Toll-like receptor activation, cytokine modulation, and T-cell differentiation—underscore the complexity of host–microbe interactions. The prominence of innate immune pathways suggests that early microbial recognition plays a crucial role in shaping downstream immune responses. At the same time, the involvement of adaptive immunity, including Th17 and regulatory T-cell pathways, indicates that microbiome alterations can have long-term and systemic consequences [2], [14], [19]. The balance between pro-inflammatory and regulatory responses appears to be a critical determinant of disease progression, highlighting the importance of maintaining microbial homeostasis.

From a diagnostic standpoint, the results demonstrate significant potential for microbiome-based biomarkers. The ability to identify disease-specific microbial signatures opens new opportunities for early detection, risk stratification, and monitoring of disease progression. Nevertheless, despite promising advances, the clinical application of these tools remains limited by variability in microbiome composition across individuals and populations. Factors such as geography, climate, diet, and healthcare access—particularly relevant in regions such as Mexico, Colombia, and Ecuador—introduce variability that complicates the standardization of diagnostic models [18].

Therapeutically, the emergence of microbiome-targeted interventions represents one of the most promising areas of development. Strategies such as topical probiotics, bacteriotherapy, and antimicrobial peptides aim to restore microbial balance rather than eliminate microorganisms indiscriminately. This paradigm shift aligns with the concept of ecological medicine, where treatment focuses on reestablishing homeostasis within biological systems. However, the relative distribution of therapeutic approaches observed in Figure 5 suggests that the field is still in an exploratory phase, with no single strategy demonstrating clear superiority.

Despite these advances, several limitations must be considered. First, much of the current evidence is based on associative studies, making it difficult to establish causality between microbiome alterations and disease. Longitudinal and interventional studies are needed to determine whether dysbiosis is a cause or a consequence of pathological processes. Second, methodological heterogeneity—including differences in sampling techniques, sequencing platforms, and data analysis—limits comparability across studies and may introduce bias.

Additionally, the translation of microbiome research into clinical practice faces practical challenges. These include the need for standardized protocols, cost-effective diagnostic tools, and regulatory frameworks for microbiome-based

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therapies. Ethical considerations also arise in the context of interventions such as microbiome transplantation, particularly regarding donor selection, safety, and long-term outcomes.

From an international perspective, the inclusion of diverse populations is essential to ensure the generalizability of findings. The variability observed in microbiome composition across different regions highlights the need for region-specific research that can inform locally relevant clinical strategies. In this context, Latin America represents an important area for future investigation, given its unique combination of environmental diversity and evolving healthcare systems.

In summary, the discussion reinforces the concept that the skin microbiome plays a fundamental role in the regulation of immune responses and the development of systemic disease. The integration of microbiome science into clinical practice has the potential to transform diagnostic and therapeutic approaches, moving toward more personalized and precise models of care. However, achieving this goal will require continued interdisciplinary research, methodological standardization, and a deeper understanding of the causal relationships underlying host–microbe interactions.

CONCLUSION

The present review consolidates current evidence supporting the skin microbiome as a critical determinant in the regulation of immune function and its influence on systemic disease processes. The findings consistently demonstrate that microbial balance is essential for maintaining skin homeostasis, immune tolerance, and barrier integrity, while its disruption—dysbiosis—acts as a central trigger for inflammatory and systemic alterations.

A key conclusion derived from this work is that the relationship between the skin microbiome and disease is inherently multifactorial. It involves the interaction of microbial composition, immune signaling pathways, and structural components of the skin barrier. The convergence of these factors leads to systemic inflammation and, ultimately, to clinically relevant outcomes, as reflected in the integrative model proposed in this study. This reinforces the concept that the skin should not be understood in isolation, but rather as part of a broader, interconnected biological system.

Additionally, the review highlights the expanding role of the microbiome in diagnostic innovation. The identification of microbial signatures associated with specific diseases offers promising avenues for early detection, risk assessment, and monitoring of therapeutic response. However, the variability observed across individuals and populations underscores the need for context-specific approaches, particularly in diverse regions such as Mexico, Colombia, and Ecuador.

From a therapeutic perspective, microbiome-based interventions represent a paradigm shift in medical practice. Approaches focused on restoring microbial equilibrium—such as probiotics, bacteriotherapy, and antimicrobial peptides—demonstrate potential for more targeted and sustainable treatment strategies. Nevertheless, these interventions remain in a developmental stage, requiring further validation through controlled clinical studies.

Despite the progress achieved, important challenges persist. The predominance of associative data limits the ability to establish causal relationships, and methodological heterogeneity continues to hinder the standardization of research findings. Addressing these limitations will be essential to advance the field and facilitate the translation of microbiome science into routine clinical practice.

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In conclusion, the skin microbiome emerges as a pivotal element in the understanding of human health and disease, bridging dermatology, immunology, and systemic medicine. Its integration into clinical and research frameworks offers significant opportunities for the development of personalized, precise, and innovative healthcare strategies. Continued interdisciplinary research, supported by robust methodological designs and inclusive population studies, will be fundamental to fully harness its diagnostic and therapeutic potential.

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