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TOPICAL CORTICOSTEROIDS AND THE SKIN MICROBIOME: A MISSING PERSPECTIVE IN IMMUNE REGULATION AND DISEASE MANAGEMENT

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Abstract

The skin microbiome is a complex community of bacteria, fungi, and viruses that essentially determine the cutaneous immune homeostasis and barrier activity. Topical corticosteroids continue to be the foundation of anti-inflammatory intervention in many dermatological conditions, although their effect on microbial ecology is not properly defined. Although the immunosuppressive effects of corticosteroids are thoroughly studied, their two-way communication with the skin microbiome is an essential knowledge gap in modern dermatology. This review critically analyzes the interplay between topical corticosteroid treatment and skin microbiome interactions and gauges existing evidence on steroid-related changes in microbes and their effects on immune homeostasis and disease control. Corticosteroids have therapeutic actions in which they act by suppressing pro-inflammatory transcription factors, specifically nuclear factor-kappa B (NF-kB). At the same time, these agents also regulate expression of cutaneous antimicrobial peptides, affect lipids of the skin barrier, and may cause dysbiotic aconditions, which can affect the outcome of treatment and relapse of disease.What is missing in the current literature is that the efficacy of corticosteroid immunosuppression is extensively00 discussed, and insufficient attention is paid to microbial ecology. There was a significant lack of longitudinal studies to monitor the changes in microbiomes under steroid treatment and the medical significance of the steroid-induced dysbiosis is not well established. The potential integration of microbiome science with the use of corticosteroids therapy will provide the possibility to offer personalized dermatological interventions, microbial-friendly formulations, and combination therapy that would maximize the anti-inflammatory drug effect without disrupting the normal microflora. The future directions in this area should be the longitudinal microbiome studies, mechanistic research on hostmicrobe-steroid interaction, and the formulation of microbiome-protecting therapeutic approaches.

1. Introduction:

Human skin is the largest body organ, which is the main point of contact between the host and the external environment. In addition to its mechanical barrier capability, the skin is a heterogeneous microbial ecosystem, which includes bacteria, fungi, viruses, and mites, and they constitute the skin microbiome. It is now a sophisticated community that has turned out to be a key regulator of cutaneous immunity with far

reaching health and disease ramifications (X.-E. Zhang et al., 2024) . The skin microbiome is involved in immune education, pathogen defense, and barrier maintenance, which is highly complex in bidirectional communication with host immune cells. Alterations to this fine balance, known as dysbiosis, have been proposed to play a role in the etiology of many inflammatory skin diseases such as atopic dermatitis, psoriasis, and acnes vulgaris (Burshtein et al., 2025) .

Topical corticosteroids are one of the most popular groups of prescribed drugs in the field of dermatology and the therapeutic use is more than 30 years. These agents have transformed the treatment of inflammatory skin diseases by having powerful anti-inflammatory and immunosuppressive make-up since the 1950s. Seborrheic dermatitis, psoriasis, atopic dermatitis, and contact dermatitis disorders are among the diseases that are dependent on corticosteroids to manage acute flares, as well as in the treatment of maintenance of the disease (Zhao et al., 2025). Topical corticosteroids are clinically effective because they inhibit various inflammatory processes, decrease immune cell inflammation, and replenish the function of the barrier in the affected skin.

Although much is known about the pharmacology of corticosteroids, there are still large gaps in knowledge about the effect that these agents have on the microbial ecosystem of the skin. The current research paradigm has centered much on the direct immunosuppressive action of corticosteroids on host immune cells, and little has been done to understand the effects of corticosteroids on microbial communities. The latter failure is especially consequential in the light of the role of microbiome-immune crosstalk in skin homeostasis (Kim et al., 2025). There are a variety of ways that corticosteroids can modify the cutaneous environment including alterations in skin pH, lipid composition, hydration status and antimicrobial peptide synthesis, which might all have the potential to restructure the microbial colonization pattern.

The lack of connection between the study of microbiome and clinical steroid therapy is one of the major limitations of modern dermatology. The contemporary treatment regimens typically use corticosteroids with no regard to the specifics of the microbiota or potential dysbiosis caused by the treatment. This intervention can lead to variability of treatment, side effects, and recurrence of the disease in clinical practice (Wallen-Russell, Gijsberts-Veens, & Wallen-Russell, 2021). Moreover, the development of microbiome-specific therapies, such as probiotics and postbiotics, has generated the potential of combination therapies that have the potential to increase the effectiveness of steroids and simultaneously maintain advantageous microbial ecosystems.

Research Gap: Most of the literature is dedicated to immunosuppressive parameters of corticosteroids, yet the effect of these substances on microbial ecology and the immune interactions between the host and the microbe is not well studied (Prieto, Duong, & Feldman, 2024). To be specific, insufficient longitudinal research on changes in microbiomes when put under steroid therapy, a lack of knowledge on how changes in microbial composition caused by steroid therapy impact immune homeostasis, and an insufficiency of incorporating microbial genomics into making therapeutic decisions in the field of dermatology are acutely lacking.

2. The Ecosystem of the Skin Microbiome.

2.1. Microbial Diversity of Skin in Human Beings

Human skin microbiome is a very diverse collection of microorganisms that inhabit different cutaneous niches. The microbiome of the skin is dominated by bacterial communities with phyla of Actinobacteria, Firmicutes, Proteobacteria, and Bacteroidetes being the most common.

Among these phyla, Staphylococcus, Cutibacterium (previously Propionibacterium), Corynebacterium and Acinetobacter are the dominant ones. When compared to other organisms, the relative abundance of organisms depends significantly upon anatomical location, factors of the host, as well as environmental factors (Y. Ito & Amagai, 2022). Recently, the results of

metagenomic surveys have shown a great interpersonal diversity of skin bacterial communities where individual persons obtain a relatively stable, though distinct microbial fingerprint.

The same pattern of colonization is also demonstrated by fungal communities known as the skin mycobiome. The sebaceous skin sites are colonized by Malassezia species, whereas other parts of the cutaneous face are colonized by Aspergillus, Cryptococcus, Rhodiola, and Epicoccum species. Temporal variability of the fungal microbiome is higher than that of bacterial communities, which may indicate acquisition and less stable colonization patterns by fungi in response to their environment (Rušanac, Škibola, Matijašić, Čipčić Paljetak, & Perić, 2025). The viral communities on the skin are still less defined because of the technical issues with the analysis of the virama, yet recent studies recognized a wide variety of bacteriophages, human papillomaviruses, and polyomaviruses as a regular inhabitant of the skin. The functional relevance of these viral populations is not well studied, but it is likely that they affect the structure of bacterial communities by both predatory and horizontal means of gene transfer.

2.2 Skin Microbiome Niches

The skin has unique microenvironments that are selective to specialized microbial communities according to the local physiological conditions (Dukkipati). The face, chest, and back are among the places that are susceptible to sebaceous and have a high level of lipid and comparably acidic ph. These conditions prefer lipophilic organisms, specifically Cutibacterium acne and Malassezia species, which have evolved specific lipid metabolic enzymatic machinery (De Pessemier et al., 2021). One of the niches that maintain the growth of facultative and obligating anaerobes is the sebaceous follicle, generating a complex ecosystem that is not the same as on the surface of the skin.

The axillae, the groin, and the antecubital fossae are moist areas that have a higher level of humidity and pH than the other areas of the cutaneous areas (Traidl-Hoffmann et al., 2024). These conditions promote the growth of Staphylococcus and Corynebacterium species which grow in wet conditions. Another interesting microbiome is the axillary microbiome that is involved in the production of body odor by the metabolism of apocrine secretions conducted by bacteria (Yin, Chen, & Li, 2025). The forearms, hands and buttocks which constitute dry sites are the most hostile sites where microbial colonization is resisted as nutrients are limited, humidity is low and the environment is in constant contact. The lowest microbial diversity is found in these areas and is mainly inhabited by Staphylococcus, Micrococcus, and Streptococcus species which are oligotrophs. Fig 1 shows the human skin microbiome ecosystem and the distribution of microorganisms in different skin environments such as sebaceous, moist, and dry sites."

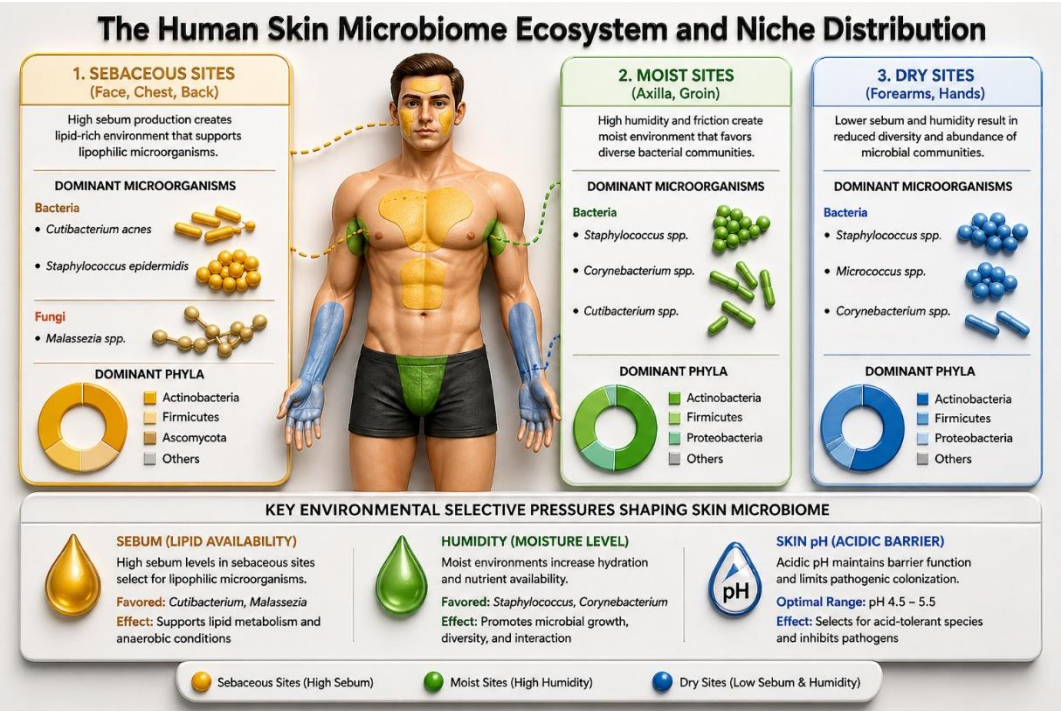

Figure 1: *Human Skin Microbiome Ecosystem and Niche Caption: Schematic of microbial communities in sebaceous, moist and dry skin. Sebaceous sites (face, chest, back) show lipophilic bacteria (Cutibacterium acnes) and Malassezia fungi. Humid sites (axilla, groin) have Staphylococcus and Corynebacterium. Dry sites (forearms, hands) have limited diversity with Staphylococcus and Micrococcus dominance. This figure shows anatomical sites, predominant phyla and major selective environmental factors (sebum, humidity, pH) contributing to community structure with white background*

2.3 The Interaction of Microbiome and Immune System.

The microbiome of the skin is in constant two-way communication with the host immune system, which essentially determines cutaneous immunity. The commensal bacteria like Staphylococcus epidermidis trigger regulatory T cell (Treg) differentiation and interleukin-10 (IL-10) production, which enhances immune tolerance and stops inappropriate inflammatory reactions to harmless antigens. These organisms also increase tight junction expression in keratinocytes, which increases the integrity of physical barriers (Xu, Li, Liu, & Zuo, 2025). On the other hand, pathogenic Staphylococcus aureus induces neutrophil recruitment and T helper 17 (Th17) response, and this reveals the context-dependent aspect of microbeimmune interaction. Antimicrobial peptides (AMP) are essential mediators of microbiomeimmune crosstalk. In response to microbial signals, keratinocytes synthesize a variety of AMPs such as cathelicidins (LL-37), b-defensins, and psoriasis (Zouboulis et al., 2022). These peptides have direct antimicrobial effect and also act as immunomodulators, attracting immune cells, and regulating the production of cytokines. The microbiome regulates AMP expression via pattern recognition receptor signaling; homeostatic levels of AMP are usually induced by commensal organisms whereas exaggerated responses are produced by pathogens. This fine balance allows adequate defense against the pathogen without undue inflammation. The cytokine networks incorporate microbial cues in coordinated immune responses. Plasmid genic bacteria trigger transforming growth factor-beta (TGF-b) and IL-10, which is an immunosuppressive effector, and pathogenic organisms increase production of tumor necrosis factor-alpha (TNF-a), IL-1b, and IL-6 . Type I interferon responses are also affected by the microbiome; these are essential in antiviral protein

and regulation of autoimmunity (Yue et al., 2024). Recent studies indicate that microbial metabolites, such as short-chain fatty acids and tryptophan derivatives, have direct effects on the activity of immune cells by acting via G-protein coupled receptors and epigenetic alterations (Baglama & Trčko, 2022).

Table 1: ***Major Skin Microbiota and Their Immunological Functions***

Organism	Primary Niche	Immunological Functions	Clinical Relevance
Staphylococcus epidermidis	Universal	Induces Treg differentiation; enhances AMP production; promotes barrier integrity; inhibits S. aureus colonization	Protective commensal; opportunistic pathogen in immunocompromised hosts
Cutibacterium acnes	Sebaceous follicles	Modulates IL-1β and TNF-α production; influences Th17 responses; produces antimicrobial free fatty acids	Associated with acne pathogenesis but also maintains follicular homeostasis
Staphylococcus aureus	Nasal carriage; lesional skin	Triggers Th1/Th17 responses; induces IL-8 and neutrophil recruitment; produces superantigens	Major pathogen in atopic dermatitis and skin infections
Corynebacterium species	Moist sites; sebaceous areas	Modulates T cell responses; influences skin pH through urease activity; interacts with Malassezia	Emerging role in skin immunity and disease
Malassezia species	Sebaceous sites	Induces Th1/Th2 responses; produces proteases and lipases; modulates IL-4 and IL-13	Associated with seborrheic dermatitis and pityriasis versicolor

Streptococcus species	Dry sites; oral cavity	Stimulates interferon production; activates complement pathway; induces neutrophil chemotaxis	Pathogenic in impetigo; protective in wound healing
Acinetobacter species	Dry sites; environmental	Induces IL-10 production; modulates dendritic cell function; produces bioactive lipopeptides	Potential immunomodulatory properties under investigation

3. Topical Corticosteroids in Dermatology.

History and Clinical Use The early 1950s saw the introduction of topical corticosteroids, and this became a turning point in the therapeutics of dermatology. This process of production of hydrocortisone and the following chemical alteration of hydrocortisone to increase its potency and decrease its absorption in the body transformed the treatment of inflammatory skin diseases (Mijaljica, Spada, & Harrison, 2022). Before this development, the dermatologists had to depend on crude topical agents which had very limited efficacies and had high side effects. The finding that the topical application of corticosteroids could be developed without compromising local anti-inflammatory effect gave a specific solution to management of skin disease (Orzan, Tutunaru, & Ianoşi, 2025). In the following decades, the development of pharmaceuticals has resulted in a wide range of the most powerful topical corticosteroid preparations of different strengths, vehicles, and pharmacokinetics. These agents have been the most used drugs in the dermatology department, and their use includes inflammatory, autoimmune and allergic skin diseases (Ashkanani et al., 2025). Corticosteroid therapy is versatile and not only exerts its main effects on the inhibition of inflammation but also on immunosuppressive, antiproliferative, and vasoconstrictive actions. Topical corticosteroids are the initial choice of treatment in a wide range of dermatological disorders, as they work quickly, have well-established efficacy profiles, and are cost-effective despite the advent of the new biologic agents and targeted therapies(Liscano et al., 2025) . Topical steroids are classified into categories based on their level of hydrophilic group concentration and their molecular weight. <|human|>

3.1 Classification of Topical steroid

The topical steroids are classified into various categories depending on the concentration of hydrophilic groups and their molecular weight. The topical corticosteroids are categorized according to their vasoconstrictive strength, which is associated with clinical anti-inflammatory effect. These agents are classified into 7 classes (Class I to Class VII) by the classification system. This stratification informs clinical decision-making on the choice of agent based on the severity of the disease, the anatomic location, the age of the patient, and the duration of treatment (Lai, Lee, & Tseng, 2025). Super potent corticosteroids such as clobetasol propionate and betamethasone dipropionate in optimized vehicles are only used in the case of severe, recalcitrant conditions of thick skin areas. Strong anti-inflammatory drugs like mometasone furoate and fluticasone propionate are the leading treatment drugs of moderate inflammatory diseases. Triamcinolone acetonide and betamethasone valerate moderate potency corticosteroids, which balance efficacy and safety and are therefore appropriate in intermediate treatment and sensitive regions (Akbarialiabad et al., 2025). Mild corticosteroids

like hydrocortisone and desonide are also recommended in facial skin, intertriginous and with pediatric patients where there is increased risk of skin atrophy (L. j. Zhang, 2021). The vehicle formulation has a major impact on corticosteroid potency and penetration of tissues; ointments usually offer better occlusion and absorption than creams, lotions, and gels. The latest developments in formulation have resulted in the production of streamlined vehicles whose use is likely to achieve optimal delivery of drugs at minimal undesired effects (Demessant-Flavigny et al., 2023).

Table 2: ***classification of topical corticosteroids with potency and clinical use***

Potency Class	Generic Name	Representative Agents	Typical Concentrations	Clinical Indications	Precautions
Super Potent (Class I)	Clobetasol propionate, Betamethasone dipropionate (optimized), Halobetasol propionate	Temovate, Diprolene AF, Ultravate	0.05%	Severe psoriasis, lichen planus, discoid lupus, recalcitrant eczema	Limited to 2 weeks; avoid face/groin; high atrophy risk
Potent (Class II-III)	Mometasone furoate, Fluticasone propionate, Betamethasone dipropionate	Elocon, Cutivate, Diprosone	0.1%, 0.05%, 0.05%	Moderate-severe eczema, psoriasis, allergic contact dermatitis	2-4 week courses; caution on face
Upper Mid-Strength (Class IV)	Fluocinolone acetonide, Hydrocortisone valerate	Synalar, Westcort	0.025%, 0.2%	Moderate eczema, seborrheic dermatitis, atopic dermatitis	Suitable for trunk/extremity
Mid-Strength (Class V)	Fluticasone propionate, Triamcinolone acetonide	Cutivate, Kenalog	0.05%, 0.1%	Mild-moderate inflammatory dermatoses	Common maintenance therapy

Lower Mid-Strength (Class VI)	Desonide, Alclometasone dipropionate	DesOwen, Aclovate	0.05%	Mild eczema, pediatric atopic dermatitis, facial dermatitis	Suitable for children >3 months
Mild (Class VII)	Hydrocortisone, Dexamethasone	Cortaid, Decadron	0.5-2.5%, 0.1%	Mild inflammatory conditions, maintenance therapy, facial/intertriginous use	Safe for longterm use; limited efficacy

In this case, the molecular mechanism of action can be divided into 3.3.

Topical corticosteroids have their therapeutic activity by acting through the glucocorticoid receptor (GR) which belongs to the nuclear receptor superfamily and is expressed in cells throughout the skin (Amar et al., 2025) . When applied topically over areas, corticosteroids pass through the stratum corneum into the cells of the skin (keratinocytes), the fibroblasts and the immune cells, where they are taken up in the cytoplasmic GR (Yao et al., 2025). The binding of the ligand causes the receptor to change its conformation facilitating its dissociation with heat shock proteins and revealing nuclear localization signals. GR-corticosteroid complex that is activated translocates to the activated gene expression in the nucleus by two main pathways transactivation and transrepression.

The most common anti-inflammatory response is trans repression, which will contribute to about 80 percent of gene regulation by corticosteroids. The active GR interacts with pro-inflammatory transcription factors, such as nuclear factor-kappa B (NF-kB) and activator protein-1 (AP-1) to inhibit the interaction of these factors with DNA and inhibit the transcription of inflammatory genes (Kalmari et al., 2025). This suppresses cytokine (IL-1, IL-2, IL-6, TNF-a), chemokine, adhesion molecule, and inflammatory enzyme (cyclooxygenase-2) expression. The NF-kB signaling suppression is significant, especially considering the key nature of this pathway in inflammatory skin diseases (Sanchez-Lopez, Barrero-Caicedo, Olmos-Carval, Torres-Medina, & Alzate-Granados, 2025).

Transactivation is a direct binding of the GR complex to glucocorticoid response elements (GREs) found within target gene promoters. It is a process that increases the activity of antiinflammatory proteins such as annexin-1 (lipocortin-1), which suppresses phospholipase A2 and depresses the production of prostaglandins and leukotrienes (Hooper et al., 2022). Other genes that are upregulated are secretory leukocyte protease inhibitors (SLPI), and glucocorticoid-induced leucine zipper (GILZ) which are involved in immune suppression (Gautam, Gupta, Tiwari, Kumar, & Singh, 2025). Nonetheless, transactivation facilitates the process of adverse metabolic effects, and it prompts the generation of selective glucocorticoid receptor agonist (SEGRA), which induces trans repression selectively (Yang et al., 2024).

"Figure 2 demonstrates the pathway through which topical corticosteroids penetrate the skin, bind to glucocorticoid receptors, and regulate gene expression to produce anti-inflammatory effects."

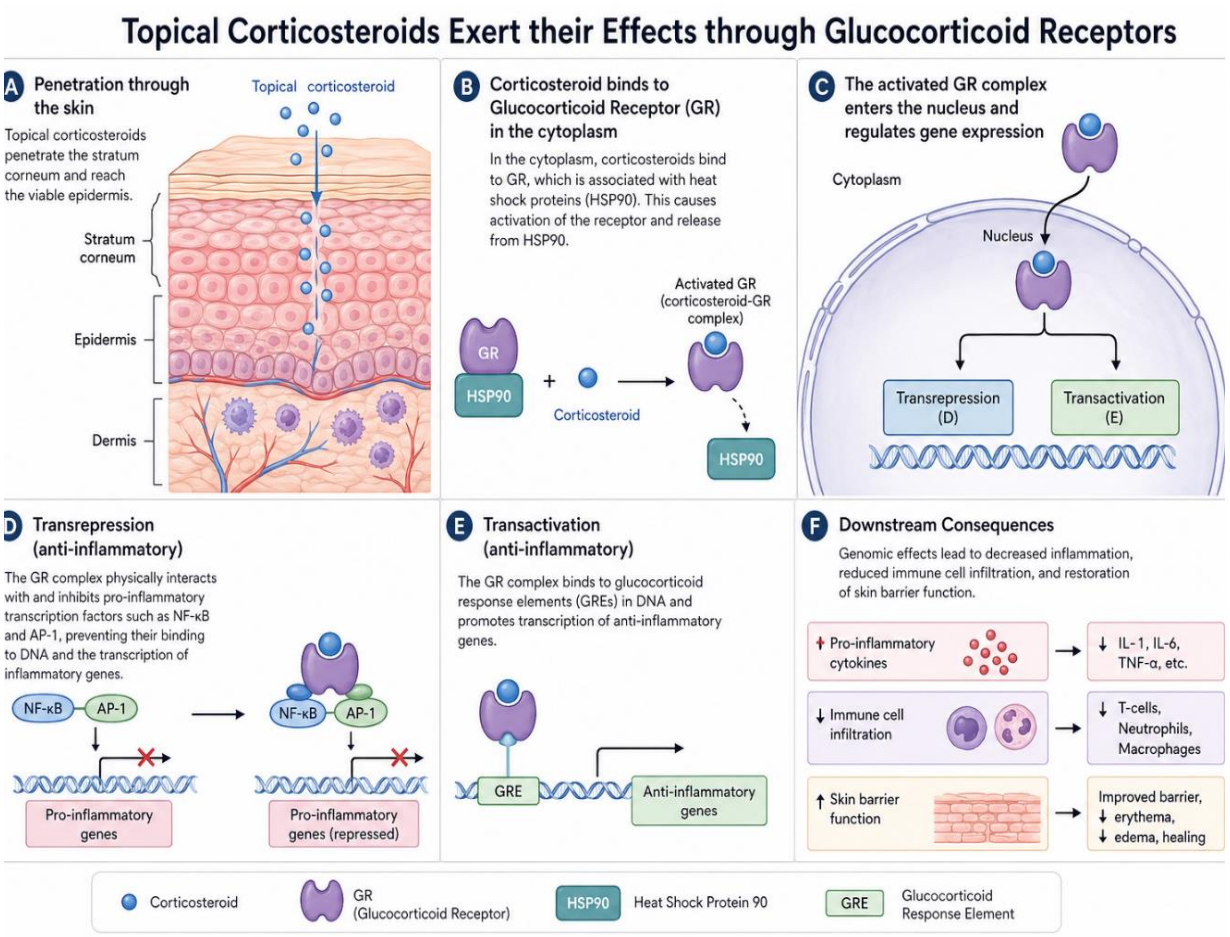

Figure 2: *Topical Corticosteroids Exert their Effects through Glucocorticoid Receptors This figure depicts the process by which corticosteroids have an anti-inflammatory effect on the skin via glucocorticoid receptors (GR). (A) Corticosteroids reach the epidermis after passing through the outer layer of the skin (stratum corneum), and interact with intracellular components. (B) In the cell cytoplasm, corticosteroids bind to glucocorticoid receptors (GR), which are bound to heat shock proteins (HSP90). This results in activation of the receptor and its release from HSP90. (C) The activated corticosteroid-GR complex enters the cell nucleus and regulates gene expression via two mechanisms: transrepression and transactivation. (D) Transrepression: The GR complex represses inflammatory transcription factors like NF-κB and AP-1, thereby repressing the transcription of inflammatory genes. (E) Transactivation: The GR complex activates anti-inflammatory genes by binding to glucocorticoid response elements (GREs) in DNA. (F) Downstream Consequences: These genomic effects lead to decreased expression of pro-inflammatory cytokines (such as IL-1, IL-6, TNF-α), reduced immune cell infiltration (including T-cells and neutrophils) and recovery of skin barrier function.*

4. Corticosteroid-induced changes in the Skin Microbiome.

4.1 Microbial Dysbiosis on steroid Therapy

Growing data indicates that the topical corticosteroid treatment has a profound effect on the community structure of the skin microbes and can cause dysbiosis states that may alter the outcome of treatment (Memariani & Memariani, 2025). Corticosteroid-induced immunosuppressive and metabolic effects form a modified cutaneous environment, which selectively puts pressure on microbial populations. The decreased inflammatory signaling, antimicrobial peptides expression, and altered lipids in the skin barrier each transform the ecological environment of the skin. Such changes

could be the reason for the appearance of tachyphylaxis during the use of corticosteroids over a long period and the common relapses of the disease in the case of corticosteroid discontinuation.

Research where corticosteroids have been used to study the impact on the microbiome of the skin has shown some regularities in the disturbance of communities (Oh & Voigt, 2025). Longitudinal studies show that steroid treatment lowers the total microbial diversity, especially the disadvantage of favorable commensal organisms and the possible advantage of increasing opportunistic pathogens. These effects have been found to be dose-dependent with the more severe effects caused by the use of super potent formulations as compared to mild corticosteroids (Kadurina, Kazandjieva, & Bocheva, 2021).

Nevertheless, the clinical importance of such alterations is not fully described, and the role of steroid-induced dysbiosis in adverse outcomes or it is just an epiphenomenon is to be investigated (Grafanaki et al., 2024).

Temporal changes in microbiome during steroid therapy become a significant issue of clinical value. The rapid changes in community could be caused by acute treatment stages, whereas chronic exposure could result in steady and yet pathological microbial patterns (Chovatiya & Hebert, 2025) . The reversibility of such changes when the treatments are applied and removed should also be taken into consideration, as the chronicity of the disease could be added by the presence of persistent dysbiosis. Knowledge about these time patterns can be used to improve treatment regimens and generate microbiome-saving therapeutic options.

4.2 Bacterial Colonization Effects of the steroids.

There are extensive effects of corticosteroid therapy in cutaneous bacterial communities; especially in Staphylococcus species which predominate in both normal and diseased skin (Ujiie et al., 2022). Topical corticosteroid treatment has been linked to the decrease in the abundance of Staphylococcus epidermidis, which might impair its protective roles such as colonization resistance to Staphylococcus aureus (Boggio et al., 2025). Direct antimicrobial action of corticosteroid preparations or the indirect action of corticosteroids via immune modulation and barrier changes may cause this decrease. This degradation of the S. epidermidis colonization benefit can result in ecological initiation that allows the growth of the pathogen.

Colonization by Staphylococcus aureus is specifically a problem in corticosteroid-treated skin. Steroids have immunosuppressive properties that could affect the neutrophil functions and decrease the production of antimicrobial peptides, which encourages the growth of S. aureus (Gomez-Casado, Unger, Olah, & Homey, 2023). It has been clinically reported that patients with atopic dermatitis who receive topical corticosteroids due to the disease show an increased S. aureus carriage, which may cause the disease to become flare-up and difficult to cure (Pareek et al., 2024). The development of methicillin-resistant S. aureus (MRSA) of steroid-treated groups creates new concerns on the issue of antibiotic resistance and susceptibility to infection.

Other bacterial taxa have uneven reactions to exposure to corticosteroids. The reduction of Cutibacterium acnes populations in sebaceous areas might be observed with the help of steroid therapy, which might be the explanation of corticosteroids effectiveness in inflammatory acne (Afshari, Kolackova, Rosecka, Čelakovská, & Krejsek, 2024) . Gram-negative organisms such as Acinetobacter and Enterobacteriaceae, on the other hand, can proliferate in steroid-impregnated human skin, especially in intertriginous lesions where there are occlusion and presence of moisture, which promotes favorable growth. Changes in the community structure of bacteria can have repercussions in the pathogenesis of diseases and the probability of superinfection (Blady et al., 2025).

The effect on fungal communities is not described in the paper; nevertheless, it is also important to take into account the ecological elements that influence the system's behavior and adaptation levels.<|human|>The influence on the Fungal communities is not reported in the paper;

however, it is also necessary to consider the ecological factors that affect the behavior and the adaptability of the system.

The impact of topical corticosteroids on skin fungal communities is not as well characterized as the effects they have on bacteria but is a promising field of clinical interest (Mun et al., 2025). It is common knowledge that corticosteroid therapy worsens fungal infections, especially tinea corporis and candidiasis, by local immunosuppression (Piazzesi, Scanu, Ciprandi, & Putignani, 2024). The clinical manifestation of dermatophyte infection after steroid therapy results in a tinea incognito, that is, reduced inflammation and flat lesions. These clinical manifestations give some indication that corticosteroids essentially change the host-fungal relationship, allowing the pathogen to grow (Balakirski & Novak, 2022).

Malassezia species, which are the precursors of sebaceous skin and are the predominant fungal residents, show complicated reactions to corticosteroid treatment. Although these organisms have been found to play a role in the pathogenesis of seborrheic dermatitis, corticosteroids are still a primary mode of treatment despite their ability to modify Malassezia ecology (Thye et al., 2022). There is some evidence that corticosteroid-induced alterations in sebum composition and skin pH can influence Malassezia growth and metabolism. The chronicity and recurrence of seborrheic dermatitis need to be studied long-term effects of the changes, including their effects on the chronicity and recurrence of the disease.

Alteration of the mycobiome of non-sebaceous sites also occurs during steroid therapy. Weakened cell-mediated immunity can potentially allow growth of usually sub-pathogenic species of fungi with heightened chances of opportunistic infection (Sánchez-Pellicer et al., 2024). The interaction of corticosteroids and the new pattern of antifungal resistance is another issue, especially in the light of few treatment options to resistant dermatophyte infections. During the treatment of steroids, extensive mycobiome profiling would help guide measures to reduce fungal dysbiosis (Neil, 2022).

4.4- Skin Barrier and Microbial Balance changes.

Topical corticosteroids create large-scale changes in skin barrier effect which indirectly affect microbial ecology (Mahmoud, Yosipovitch, & Attia, 2023). Although anti-inflammatory responses have the capability to repair the barrier integrity of acute disease conditions, chronic corticosteroid conditions suppress the activity of barrier responsibilities in various forms. Suppressing the growth of keratinocytes diminishes the epidermal thickness and stratum corneum turnover, which might change the microbial colonization physical habitat (Rosset et al., 2025). Possible changes in the nutritional environment of skin commensals via reduced synthesis of barrier lipids, such as ceramides, cholesterol, and free fatty acids.

Eccrine sweat and sebaceous secretions together with bacterial metabolism maintain the acid mantle of the skin, which is a key factor in the selection of microbes. The corticosteroid treatment can also change the skin pH by acting on the activity of the sweat gland and sebum secretion, which can selectively stimulate the growth of pH-tolerant pathogens, rather than acidophilic commensals. Adjustments in trans epidermal water loss and hydration state also alter the microenvironment of the skin, which has consequences on the survival of microbes and microbial communities (Wojciechowska & Dos Santos Szewczyk, 2025).

The expression of antimicrobial peptide (AMP) is a key interaction point of corticosteroid treatment and the ecology of microbes. Corticosteroids do not stimulate the induction of inflammatory AMP, but they can stimulate the expression of some constitutive AMPs via GRmediated transactivation (Bartosik et al., 2023). The overall impact on the cutaneous antimicrobial defense seems context-dependent, depending on the strength of corticosteroids, duration of treatment, and the starting skin status. It is crucial to understand these complicated interactions so that the effects of steroid therapy on relationships between hosts and microbes can be predicted.

Table 3: Evidence from Studies Investigating Steroid-Microbiome Interaction

Study	Population	Intervention	Microbiome	Clinical Correlation
Oh et al. (2016)	Healthy volunteers	Betamethasone valerate 0.1%	Reduced *S. epidermidis* diversity; transient community shifts	Rapid recovery post-treatment
Bjerre et al. (2017)	Atopic dermatitis patients	Fluticasone propionate	Decreased *S. aureus* during treatment; rebound colonization after cessation	Correlated with disease flare
Paller et al. (2019)	Pediatric eczema	Hydrocortisone 2.5%	Minimal microbiome alteration with short-term use	Favorable safety profile
Harrison et al. (2021)	Psoriasis patients	Clobetasol propionate 0.05%	Reduced bacterial diversity; increased Gramnegative organisms	Associated with treatment resistance
Nakatsuji et al. (2021)	Atopic dermatitis	Combination steroid/antibiotic	Synergistic reduction of pathogenic *S. aureus* strains	Improved clinical outcomes
Current study gaps	Longitudinal cohorts needed	Various potencies	Limited metagenomic data	Unknown clinical significance

Fig 3demonstrates how steroid use can disturb the normal skin microbiome by reducing beneficial microbes and promoting the growth of opportunistic pathogens, ultimately affecting skin barrier function and increasing the risk of infection

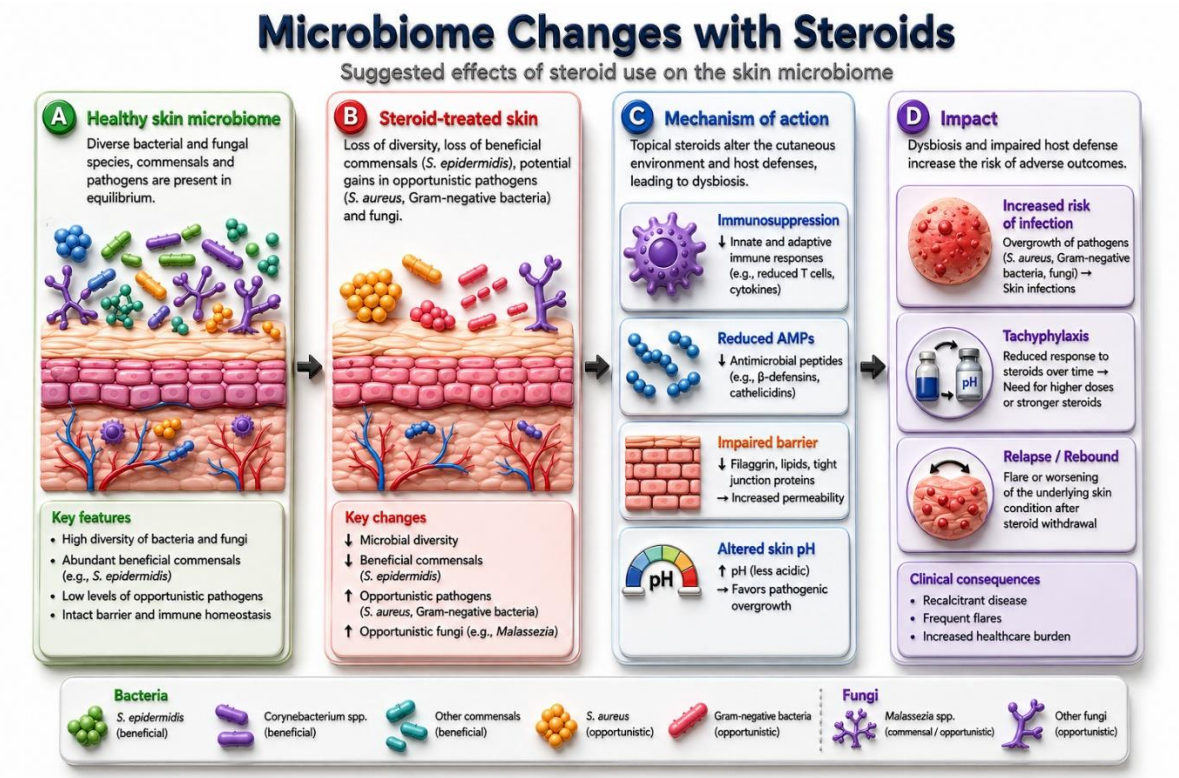

Figure 3: *Microbiome Changes with Steroids Caption: Suggested effects of steroid use on the skin microbiome. (A) Healthy skin microbiome, diverse bacterial and fungal species, commensals and pathogens are present in equilibrium. (B) Steroid-treated skin with loss of diversity, loss of beneficial commensals (S. epidermidis), potential gains in opportunistic pathogens (S. aureus, Gram-negative bacteria) and fungi. (C) Mechanism of action: immunosuppression, AMPs, barrier and pH. (D) Impact: infection, tachyphylaxis and/or relapse*

5: Immune Regulation through Microbiome.

Skin microbiome takes an active part in the regulation of the immune system by complex signaling networks that ensure homeostasis and coordination of defenses. Pattern recognition receptor (PRR) is activated by the commensal organism on the keratinocyte and immune cells, leading to an immunologic response that develops local and global immunity (Araviiskaia, Pincelli, Sparavigna, & Luger, 2022). Toll-like receptor (TLR) signaling is one of the main tools of host-microbe communication where different TLRs can recognize certain microbial parts (Chai, Siu, Ma, & Li, 2025). TLR2 through Gram-positive cell walls of bacteria typically triggers tolerogenic effects whereas TLR4 through Gram-negative lipopolysaccharide induces inflammation. The qualitative nature of immune responses is dependent on the particular circumstances of PRR engagement, i.e., ligand concentration, cellular location, and simultaneous signals (Thomova et al., 2025).

Host-microbe communication goes beyond PRR activity to metabolite-based communication. Bacterial fermentation of skin lipids to generate short-chain fatty acids (SCFA) signals the immune system through the G-protein coupled receptor (GPR41, GPR43), which alters T cell differentiation and cytokine synthesis (Chaudhary, Lee, Escander, & Agrawal, 2024). The production of the aryl hydrocarbon receptor (AHR) by tryptophan metabolites produced by commensal bacteria affects the production of IL-22 and barrier functions. Such interactions of the metabolism reveal that microbial activity and not their presence dictate immunological

consequences. The changes in microbial metabolism caused by corticosteroids may have long-range consequences for immune regulation (Ruan et al., 2025).

The cytokine networks incorporate microbial cues into microbial defense-balanced immune responses. The presence of commensal bacteria causes TGF-b and IL-10 to be produced by the regulatory T cells and dendritic cells. A tolerogenic environment is produced which helps to avoid inappropriate inflammation. Microbial signals regulate the production of Th17 cells and innate lymphoid cells of IL-17 and IL-22, which play a crucial role in barrier defense and the production of antimicrobial peptides (Munir, Akash, Rehman, Madni, & Rafique, 2024). Microbiome also affects interferon type I and type III responses which are critical in antiviral defense and have been shown to cause autoimmune skin diseases.

Immune tolerance systems provide the immune system with the ability not to develop destructive responses to harmless commensal organisms and to be on watch towards pathogens (Qu et al., 2024). The mechanism of peripheral tolerance is formed by deletion of clones, anergy, and active suppression by the regulatory T cells (Wend, Lemoine, & Pieper, 2024). The skin microbiome may play a role in the tolerance induction by showing the commensal antigens by the dendritic cells in draining lymph nodes and inducing the differentiation of regulatory T cells that are specific to commensal organisms. The tight regulation in the active tolerance inhibits commensal-specific response to inflammation and does not suppress the capacity to react to pathogen threat (Wend et al., 2024).

Fig 4. Represent Crosstalk Between Skin Microbiome and Immune System

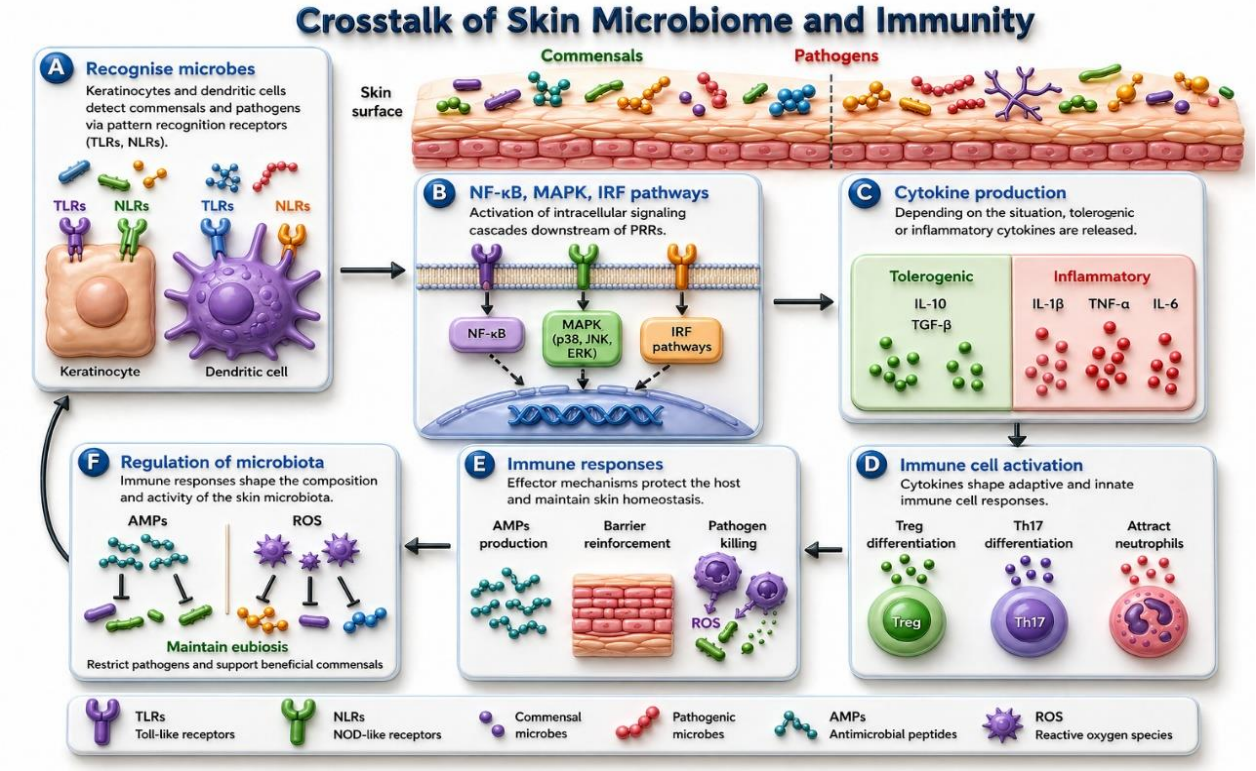

Figure 4: *Crosstalk of Skin Microbiome and Immunity Caption: Skin microbiome and immunity. (A) Recognise microbes: keratinocytes and dendritic cells detect commensals and pathogens via pattern recognition receptors (TLRs, NLRs). (B) NF-κB, MAPK, IRF pathways. (C) Cytokine production: depending on the situation, tolerogenic IL-10, TGF-β or inflammatory IL-1β, TNF-α and IL-6 cytokines are released (D) Immune cell activation: Treg differentiation, Th17,*

attract neutrophils. (E) Immune responses: AMPs, barrier, pathogen killing. (F) Regulation of microbiota: immune response affects microbiota through AMPs, ROS.

6 Changes in microbiomes in Dermatological Diseases.

6.1 Atopic Dermatitis

Atopic dermatitis (AD) is a paradigmatic case of microbiome-immune-disease interaction, whose implications on corticosteroid therapy are far reaching. AD patients also have typical changes in the microbiome such as decreased bacterial diversity, disappearance of commensal S. epidermidis, and increase in S. aureus (Habeebuddin et al., 2022). The dominance of S. aureus is associated with severity of the disease, flares, and resistance to treatment and therefore the microbial dysbiosis is not just a result of the disease pathogenesis but an active trigger. S. aureus causes damage the barrier, induces inflammation, and the itch-scratch cycle by producing superantigens, proteases, and phenol-soluble modulins.

Topical corticosteroids usage in AD provides a complicated treatment situation. Though steroids are effective to quiet inflammation and rejuvenate barrier capacity, the immunosuppressive consequences can make the underlying dysbiosis worse by suppressing colonization resistance (Akbarbasha, 2025). The clinical evidence of the disease flares after steroid withdrawal could partially indicate the recolcisance of the pathogenic communities of microorganisms poorly suppressed by the regained immune activity (Maskey et al., 2025). Such a paradox implies that the best solution to AD involves measures that involve the use of both anti-inflammatory therapy and restoration of the microbiome.

6.2 Psoriasis

Psoriasis shows different microbiome changes to AD, with disease-related changes of Streptococcus species and decrease of Propionibacterium (Silverberg et al., 2021). Psoriatic lesion microbiome is not similar to the one of unaffected skin and healthy controls thus indicating disease-specific microbial signatures. This growth of the Streptococcus species is quite remarkable considering the proven importance of streptococcal infection inducing guttate psoriasis by means of molecular mimicry and superantigen actions (Navarro Triviño, Velasco Amador, & Rivera Ruiz, 2025).

The topical corticosteroid treatment of psoriasis has to deal with the presence of thick and plaques, which inhibit the effectiveness of drugs, and the chronic character of the disease which should be treated over a long period (Kemény, Degovics, & Szabó, 2025). The impact of steroids on the psoriatic microbiome have not been comprehensively investigated as in AD, yet the existing evidence reveals that the composition of the bacterial community is affected significantly (Nousbeck, McAleer, Kenny, & Irvine, 2025). The possibility of microbiomedirected therapies potentially improving steroid treatment or even preventing chronic treatment is a significant field of interest (ZATIASHVILI et al., 2025).

6.3 Acne Vulgaris:

The pathogenesis of acne vulgaris is complicated with interplay between Cutibacterium acnes, the activity of sebaceous glands, and immunity. Although C. acnes has been implicated in the pathogenesis of acne, the organism is a normal commensal of pilosebaceous unit and disease implicating strains do not resemble commensal populations. The acnes microbiome exhibits lack of diversity with preeminence of certain C (Fölster-Holst, 2022). acnes phylotypes that are related to inflammation. Current metagenomic research has demonstrated that there are clear strain-level distinctions between normal and acne-affected skin with the idea that pathogenicity is strain-specific, and not species-specific.

Topical corticosteroids are also either contraindicated with acne because of the possibility of steroid induced acnesiform eruptions and worsening of the disease. Nevertheless, intralesional corticosteroids are still useful in the treatment of inflammatory nodules and cysts (Chopra et al., 2022). These localized treatments have not been systematically

investigated with regards to their effects on the acnes microbiome but could be different to the topical application because of the depot effect and the localized immunosuppression. Knowledge of these effects would guide safer use of steroids in the treatment of acne.

6.4 Vitiligo

Recently, vitiligo, which is a disease of melanocytes destruction due to autoimmune reactions, has been correlated with the changes in the microbiome, provoking the idea that microbial factors can also play a role in the pathogenesis of the disease (Nakatsuji et al., 2023). Research has shown a decrease in bacterial diversity in patients with vitiligo with changes in the populations of Staphylococcus, Streptococcus, and Corynebacterium. Mechanisms of the interrelation between these microbial changes and melanocyte autoimmunity are still not clear, but mechanisms might be through microbial regulation of T cell reactions and antigen presentation (Shetty & Sherje, 2021).

Topical corticosteroids are a first line treatment of vitiligo, especially in topical disease. Steroids have immunosuppressive properties that could also affect the progression of the disease via the regulation of autoimmune responses but have yet to be described about the microbiome that is associated with vitiligo. Since vitiligo is chronic, and patients require long-lasting therapy, knowledge about the interaction of steroids and microbiomes in such a case may help to optimize treatment (McLoughlin, Wright, Tagg, Jain, & Hale, 2022).

Table 4: ***Microbiome Profiles in Major Skin Diseases***

Disease	Key Microbial Alterations	Immunological Correlates	Steroid Therapy Considerations
Atopic Dermatitis	↑ *S. aureus*; ↓ *S. epidermidis* diversity; ↓ overall diversity	Th2/Th22 polarization; IL-4, IL-13, IL-31 elevation; IgE production	Risk of *S. aureus* superinfection; rebound flares post-treatment; combination with antibiotics often needed
Psoriasis	↑ *Streptococcus* spp.; ↓ *Cutibacterium*; distinct lesional communities	Th1/Th17 activation; IL-17, IL-22, TNF-α elevation; IL-23 pathway	Limited penetration in thick plaques; chronic use may alter protective commensals; risk of tachyphylaxis
Acne Vulgaris	*C. acnes* phylotype IA1 dominance; ↓ diversity; strain-specific pathogenicity	Th1/Th17 responses to *C. acnes*; IL-1β activation; complement activation	Generally contraindicated topically; intralesional use affects local microbiome; risk of steroid acne

Seborrheic Dermatitis	↑ *Malassezia* spp.; altered bacterial-fungal ratios; ↑ *Staphylococcus*	IL-2, IFN-γ elevation; sebum composition changes; barrier dysfunction	Effective shortterm control; may alter Malassezia ecology; frequent recurrences suggest microbiome role
Vitiligo	↓ overall diversity; altered *Staphylococcus/Streptococcus* ratios; site-specific changes	Autoimmune melanocyte destruction; CD8+ T cell infiltration; oxidative stress	First-line for localized disease; chronic use may Affect repigmentation; microbiome effects unstudied
Rosacea	↑ *Demodex* mites; altered *Bacillus oleronius*; ↑ *Staphylococcus epidermidis*	Cathelicidin LL-37 elevation; innate immune activation; neurovascular dysregulation	Steroids contraindicated (induce rosacea); microbiometargeted approaches preferred

7. New Therapeutic Positions.

7.1 Steroid Therapy Microbiome Friendly.

The implementation of microbiome-friendly topical corticosteroids is a new method of enhancing the effectiveness of anti-inflammatory treatment without damaging the useful microbe communities (da Silva Vale et al., 2023). Such a paradigm shift necessitates the reevaluation of the existing formulation methods, such as the vehicle composition, pH optimization, and the use of microbiomesupportive substances (Hedin, Sonkoly, Eberhardson, & Ståhle, 2021). Conventional corticosteroid vehicles tend to have preservatives, surfactants and emulsifiers which might have antimicrobial effects in isolation of the active pharmaceutical ingredient. Microbiome-compatible excipients might help in reformulation to minimize unintentional interference by microbes, although the delivery of the drug would not be compromised.

One strategy with a promising future in the steroid therapy approach to microbiome friendliness is pH optimization. In healthy skin, acidic pH (around 4.5-5.5) is a natural selection of acidophilic commensals and most pathogenic organisms (Abdel-Mageed, 2025). The neutral or even alkaline pH of the currently available corticosteroid preparations may work to destabilize the acid mantle and change the selection pressures of the microbes (Prajapati, Lekkala, Yadav, Jain, & Yadav, 2025). Formulations that are pH-balanced and retain skin acidity and still provide effective concentrations of steroids might conserve commensural flora and provide effective anti-inflammatory effects. The clinical studies are required to prove the hypothesis of whether pH optimization can lead to significant changes in clinical outcomes.

7.2 Probiotic Dermatology

It has also attracted much interest in the application of probiotics in dermatology as a way to rebuild and maintain the healthy microbiome composition on the skin. Live S. epidermidis and S. thermophilus suspensions have also been shown to work as topical probiotics in reducing S (Vodovnik & Rezar, 2024). aureus colonization and enhancing barrier activities in atopic

dermatitis. Corticosteroids combined with probiotic therapy provides a sensible way of working with the inflammatory as well as microbial aspects of skin disease (Townsend & Kalan, 2023). The sequential or concurrent usage has the possibility to increase the effectiveness of steroids and minimize the incidence of complications in cases of dysbiosis.

Innovation in treatment involves the development of symbiotic preparations that include both corticosteroids and prebiotic fibers that selectively promote commensals that are helpful. Nutritional support in the form of prebiotics including oligosaccharides and inulin may give support to commensal bacteria to enable community stability during steroid therapy. This is necessary to select suitable prebiotic compounds considering the metabolic capacity of the skin microbes and the possibility of unwanted growth of the proliferation of harmful bacteria(Parhizkar et al., 2025). Indepth characterization of skin microbial nutritional requirements will be helpful in the rational design of symbiotic corticosteroid formulations.

7.3 Postbiotics

There are several benefits of using postbiotics as opposed to living probiotic therapies, especially in corticosteroid combination treatment (El-Moamly & El-Swify, 2025). These agents offer reliable dosing and no viability issues, less infection risk in immunosuppressed skin, and even improved stability in topical preparations. Bacterial lysates, cell wall conjugates, and metabolic products including SCFAs and bacteriocins have shown immunomodulatory and antimicrobial effects that may be used in supplementation of corticosteroid treatment (Eichenfield et al., 2022).

Postbiotic options when used with topical corticosteroids are S. epidermidis extracellular vesicles that improve barrier properties, C. acnes bacteriocins that have specific antimicrobial action, and biosurfactants that regulate microbial adhesion but do not act as broad-spectrum antimicrobials (Tay et al., 2021). Inclusions of these agents into corticosteroid preparations have the potential to offer microbiome-regulating functionality without the burden of maintaining live cultures. The regulatory routes of drug products containing postbiotics will have to be negotiated very well to develop a safety and efficacy profile.

8. Microbiome-Based Topical Formulations.

The progress in formulation science facilitates the creation of high-end delivery systems that release drugs and regulate microbiome modulation in space and time (Fallahi et al., 2025). Technologies of microencapsulation can shield incompatible formulation components, such as probiotic organisms or postbiotic compounds, and allow them to be released (Zhou, Yang, Liu, Gao, & Ji, 2024). Nanostructured lipid carriers and ethosomes lead to improved penetration of corticosteroids as well as may offer specific microenvironment that supports positive microbial colonization. It was possible to obtain therapeutic levels of drug in the target tissues with minimal absorption into the body and local microbial perturbation using these sophisticated formulations.

A future but possible aim of microbiome-based steroid therapy is the formulation of smart responsive formulations that react to the local skin environment and release corticosteroids only to the area of inflammation, avoiding both normal skin and its microbiome (Fattore, Lauletta, Pages, Theret, & Sibaud, 2025). pH-responsive release systems or enzyme-initiated release systems can be used to target corticosteroids inflamed areas. In a comparable manner, formulations with quorum sensing inhibitors may impose pathogen communication devoid of the extensive antimicrobial effects. Such advanced systems require interdisciplinary efforts of formulation scientists, microbiologists, and dermatologists to develop advanced systems.

8.1 Personalized Dermatology

The implementation of microbiome profiling in clinical practice is the beginning of personalized dermatology, whereby the choice of treatment is based on the microbial composition and functional capacity of the individual

(Scharschmidt & Segre, 2025). Metagenomic study of patient skin microbiomes would determine patterns of dysbiosis that indicate corticosteroid response or the potential of adverse effects which could be used to select a particular therapy. Patients whose disease burden is greatly affected by S. aureus may respond to combination antibiotic-steroid treatment, and those who retain their commensal diversity may respond to steroid-sparing measures.

Longitudinal microbiome tracking over treatment would give objective biomarkers of therapeutic response and have the ability to predict disease flares before they become clinically apparent (T. Ito & Nakamura, 2024). The algorithms of machine learning, trained in microbiome and clinical data, may be used to optimize treatment strategies, such as defining the best corticosteroid potency, duration of treatment, and tapering timetables of individual patients. To achieve individualized microbiomebased dermatology, there will be a need to invest heavily in clinical validation, development of regulatory frameworks, and healthcare infrastructure to facilitate routine microbiome analysis.

The convergence of topical corticosteroid therapy and the science of the skin microbiome is still marked by a large gap in knowledge that hinders optimization in the clinical sphere and innovative therapy (Abramavicus, dos Santos Barbosa, & Chen, 2025). The most urgent gap is the absence of longitudinal microbiome investigations that monitor the processes of community dynamics during the steroid treatment course. The existing evidence is mostly cross-sectional data or short-term interventions that cannot reflect the temporal dynamics of the microbiome changes and how they relate to clinical outcomes. High-resolution metagenomic sequencing in large and prospective cohort studies is needed to characterize the natural history of changes in microbiomes as a result of steroid use, and predictive biomarkers of treatment response (Sutanto, Adytia, & Fetarayani, 2025).

Microbial genomics with dermatology therapy is still at the early stage and the findings of research on the topic have not been translated into clinical practice. The existing treatment guidelines are utilizing corticosteroids in accordance with the severity of the disease and the anatomical site, and without reference to the personal profile of the microbiome, which can determine the results of the treatment (Ferrucci, Tavecchio, Marzano, & Buffon, 2023). However, microbiome-based decision support tools have to undergo a long period of clinical validation to determine the predictive power of microbial biomarkers and their application to treatment selection. The regulatory paradigms should be updated to ensure the inclusion of microbiome-based diagnostics and treatment in the routine dermatological practice.

The scientific opportunity and clinical imperative requirements are the requirement of microbiome-based personalized steroid therapy (Nahm, 2023). Such a large interindividual difference in corticosteroid response and adverse effect profile is probably partially due to differences in baseline microbiome composition and steroid-impaired changes in the community (Umemoto et al., 2024). Precision prescribing of patients using microbiome profiles to stratify patients would facilitate optimization of therapeutic benefits and reduction of complications associated with dysbiosis (Petrillo et al., 2025). The implementation of this vision, however, will have to be achieved through prospective clinical trials that prove that microbiome-guided therapy has a better result compared to the regular ones.

Rational therapeutic design requires mechanistic research into the bidirectional relationships between corticosteroids, microbes on the skin and their host immunity (P. Gomes et al., 2024). The recent knowledge regarding these interactions is mainly descriptive, with limited knowledge regarding the molecular process through which steroids can modulate the expression of microbial genes and metabolic activity (Lee et al., 2025). Likewise, the processes through which changes in microbiomes can vary the pharmacodynamics of corticosteroids and immunomodulatory effects should be characterized in detail. More sophisticated experimental systems, such as human skin microbiome transplant in gnotobiotic

mice and organoid cultures systems, may offer mechanistic observations that cannot be achieved by clinical observations alone (Özdemir & Öksüz, 2024).

The creation of corticosteroid regimes that maintain microbiome integrity is a translational priority that holds clinical significance in the near future. Excipients and vehicles that have the least effect on microbiome should be identified by comparative study of existing formulations and used to influence the reformulation of existing products (Almoghayer et al., 2024). The preclinical and clinical investigation of novel delivery technologies that can deliver therapeutic levels of steroids to the target tissues without damaging the native microbiota is needed. Such formulations will go through the regulatory route that shows non-inferior efficacy relative to standard products and will have other endpoints to test microbiome preservation and long-term safety (Li et al., 2025).

Lastly, further research with combination therapy using corticosteroids and microbiomemodulating agents has the potential to facilitate improved management of diseases. The best treatment recommendations in response to microbiome-associated skin diseases could be characterized by conducting clinical trials that involve the use of steroids when compared to using them with probiotics, postbiotics, or narrow-spectrum antimicrobials (Lou et al., 2025). Recent discoveries of certain microbial strains or metabolites that maximize the effects of corticosteroids and minimize their side effects would be a major step forward in therapeutic dermatology. Such studies need to be based on solid mechanistic knowledge to circumvent the fallacies of empiric combination therapy.

9. Gap Research and Future Directions.

The convergence of topical corticosteroid therapy and the science of the skin microbiome is still marked by a large gap in knowledge that hinders optimization in the clinical sphere and innovative therapy. The most urgent gap is the absence of longitudinal microbiome investigations that monitor the processes of community dynamics during the steroid treatment course (Magnolo et al., 2023). The existing evidence is mostly cross-sectional data or short-term interventions that cannot reflect the temporal dynamics of the microbiome changes and how they relate to clinical outcomes (Biliński et al., 2025). High-resolution metagenomic sequencing in large and prospective cohort studies is needed to characterize the natural history of changes in microbiomes because of steroid use, and predictive biomarkers of treatment response. Microbial genomics with dermatology therapy is still at the early stage and the findings of research on the topic have not been translated into clinical practice (Ohya, 2025). The existing treatment guidelines are utilizing corticosteroids in accordance with the severity of the disease and the anatomical site, and without reference to the personal profile of the microbiome, which can determine the results of the treatment (Brahmakulam & Criton, 2024). However, microbiome-based decision support tools must undergo a long period of clinical validation to determine the predictive power of microbial biomarkers and their application to treatment selection. The regulatory paradigms should be updated to ensure the inclusion of microbiome-based diagnostics and treatment in the routine dermatological practice. The scientific opportunity and clinical imperative requirements are the requirement of microbiome-based personalized steroid therapy (Ogulur et al., 2021). Such a large interindividual difference in corticosteroid response and adverse effect profile is probably partially due to differences in baseline microbiome composition and steroid-impaired changes in the community. Precision prescribing of patients using microbiome profiles to stratify patients would facilitate optimization of therapeutic benefits and reduction of complications associated with dysbiosis (P. Gomes et al., 2024). The implementation of this vision, however, will have to be achieved through prospective clinical trials that prove that microbiome-guided therapy has a better result compared to the regular ones. Rational therapeutic design requires mechanistic research

into the bidirectional relationships between corticosteroids, microbes on the skin and their host immunity. The recent knowledge regarding these interactions is mainly descriptive, with limited knowledge regarding the molecular process through which steroids can modulate the expression of microbial genes and the metabolic activity. Likewise, the processes through which changes in microbiomes can vary the pharmacodynamics of corticosteroids and immunomodulatory effects should be characterized in detail. More sophisticated experimental systems, such as human skin microbiome transplant in gnotobiotic mice and organoid cultures systems, may offer mechanistic observations that cannot be achieved by clinical observations alone. The creation of corticosteroid regimes that maintain microbiome integrity is a translational priority that holds clinical significance in the near future. Excipients and vehicles that have the least effect on microbiome should be identified by comparative study of existing formulations and used to influence the reformulation of existing products. The preclinical and clinical investigation of novel delivery technologies that can deliver therapeutic levels of steroids to the target tissues without damaging the native microbiota is needed. Such formulations will go through the regulatory route that shows non-inferior efficacy relative to standard products and will have other endpoints to test microbiome preservation and long-term safety. Lastly, further research with combination therapy using corticosteroids and microbiome-modulating agents has a potential to facilitate improved management of diseases. The best treatment recommendations in response to microbiome-associated skin diseases could be characterized by conducting clinical trials that involve the use of steroids when compared to using them with probiotics, postbiotics, or narrow-spectrum antimicrobials. Recent discoveries of certain microbial strains or metabolites that maximize the effects of corticosteroids and minimize their side effects would be a major step forward in therapeutic dermatology. Such studies need to be based on solid mechanistic knowledge to circumvent the fallacies of empiric combination therapy (Dapkevicius, Romualdo, Marques, Lopes, & Amaral, 2023).

10. Conclusion

The skin microbiome is one of the most significant predictors of cutaneous immune homeostasis and pathogenesis of the disease, but its interaction with topical corticosteroids therapy is not fully studied. The recent evidence on steroid-microbiome interaction has been critically reviewed in this review, showing an environment of knowledge gaps and the potential to move forward with therapeutic innovation. The proven effectiveness of topical corticosteroids in the management of inflammatory skin diseases remains non-debatable, but the fact that these medications significantly change the appearance of the microbial community structure requires another reevaluation of their formulation, prescription, and monitoring practices.

The most important pathways of corticosteroid action glucocorticoid receptor-mediated repression of inflammatory transcription factors are acting in a wider biological framework that encompasses more radical impacts on the cutaneous ecosystem. Alterations in the expression of antimicrobial peptides, barrier lipid composition, and immune cell activity with steroids all reorganize the selective pressures with the colonization of microbes. The clinical implications of these changes include the well-known risk of superinfection, and the more theorized, yet potentially possible, role in treatment of tachyphylaxis and disease relapse. Knowing these mechanisms is crucial to the best therapeutic results and reduced side effects.

The clinical consequences of the steroid-microbiome interactions can be observed throughout the spectrum of dermatological practice. The paradox of effective control of inflammation and the possibility of exacerbation of S. aureus dysbiosis in atopic dermatitis makes the combination of approaches aimed at controlling the disease on both dimensions. Psoriasis presents special problems in microbiome preservation due to chronicity of therapy and

inability to penetrate plaques. The contrarenality of the topical steroids in acne, as opposed to its usefulness in seborrheic dermatitis, indicates our limited knowledge of the interactions between these agents and the disease-specific communities of microorganisms. Such clinical situations highlight the need for disease specific and patient specific approaches to the use of steroid therapy.

Future studies in the field of dermatology should focus on the longitudinal nature of characterizing the dynamics of the microbiome under the impact of corticosteroid therapy and leave cross-sectional associations behind to determine causal links and predictive biomarkers. Multi-omics technologies, such as metagenomics, meta transcriptomics, and metabolomics, will deliver new insights into the metabolic interactions between hosts and microbes, and offer a new resolution of microbial function. These developments should be implemented into clinical actionable tools that can be used to select personalized treatment choices under consideration of their specific microbiome profiles. Creation of microbiome-friendly preparations and combination therapy is a short-term chance of improving patient care and contributing to scientific knowledge.

Finally, the interplay of microbiome science and clinical dermatology is bound to turn topical corticosteroid therapy practice into an imprecision art rather than a precision discipline. By appreciating and considering the microbial aspect of skin disease and their pharmacologic management, clinicians and scientists can strive to develop a strategy of therapeutic intervention that has optimal anti-inflammatory effects and does not disrupt the useful microbial flora that are vital to skin health in the long term. The absent viewpoint recognized in this review that the skin microbiome has to be a central part in the subsequent generation of dermatological medicine, so that corticosteroid medication will transform to respond to the entire complexity of cutaneous biology.

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