Indian Journal of
Nutrition

Open Science Publications

Volume 12, Issue 2 - 2025

www.opensciencepublications.com

The Gut Skin Connection in Acne and Rosacea: Therapeutic Roles of Probiotics and Prebiotics

Review Article

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Article Information: **Submission:** 29/05/2025; **Accepted:** 20/06/2025; **Published:** 24/06/2025

Abstract

Acne and rosacea are chronic inflammatory skin disorders increasingly linked to disturbances in the gut-skin axis. This review explores how probiotics and prebiotics modulate immune responses, enhance epithelial barrier function, and influence gut and skin microbiota to improve dermatological outcomes. Clinical and mechanistic evidence shows that specific strains and fibers reduce inflammatory markers, lesion counts, and symptoms such as erythema and sensitivity. Oral and topical formulations demonstrate promise as adjunctive therapies. Despite encouraging findings, standardized clinical trials and personalized approaches are needed to fully integrate microbiome-targeted strategies into dermatology for the effective management of acne and rosacea.

Keywords: Probiotics; Prebiotics; Acne; Rosacea; Gut-Skin Axis; Inflammation

Introduction

Acne and rosacea are chronic inflammatory skin disorders with distinct clinical presentations but overlapping pathogenic mechanisms. Acne is primarily linked to the over colonization of Cutibacterium acnes in the pilosebaceous unit, triggering an immune response characterized by the release of inflammatory cytokines such as IL-1β and TNF-α [1]. Conversely, rosacea manifests with persistent erythema, papules, and pustules, with its pathogenesis closely associated with abnormal vascular reactivity and the inflammatory response mediated by triggers including Demodex folliculorum mites and ultraviolet radiation [2]. Emerging evidence implicates the gut-skin axis as a significant contributor to both conditions. Dysbiosis in the intestinal microbiota may disrupt systemic immune homeostasis and promote cutaneous inflammation via pro-inflammatory mediators [3]. Several studies have demonstrated that interventions with probiotics and prebiotics can restore microbial balance and modulate inflammatory pathways, thereby improving clinical outcomes in both acne and rosacea [4].

Future research is warranted to explore the specific strains and prebiotic formulations that effectively target the inflammatory cascades implicated in these disorders [5]. Enhanced understanding of these underlying mechanisms may facilitate the development of comprehensive microbiome-based therapies for inflammatory skin conditions [6]. Moreover, ongoing clinical trials are evaluating optimal dosages and formulations, paving the way for personalized dermatological interventions [7].

Role of Probiotics in Skin Health

Mechanisms of Action

Probiotics influence skin health through immunomodulatory, antimicrobial, and barrier-reinforcing effects. They downregulate pro-inflammatory cytokines such as IL-8, TNF-α, and IL-1β, which are commonly elevated in acne and rosacea lesions [8]. Certain strains, like Lactobacillus rhamnosus GG and Bifidobacterium longum, enhance skin barrier integrity by increasing tight junction proteins and reducing transepidermal water loss (TEWL) [9].

Additionally, probiotics produce bacteriocins and organic acids that suppress skin pathogens including Cutibacterium acnes [10]. Metabolites from probiotic fermentation—such as short-chain fatty acids (SCFAs)—also act as signaling molecules that support mucosal immunity and anti-inflammatory pathways [11].

Evidence from Clinical Trials

The emerging understanding of the gut-skin axis has spurred interest in microbiome-modulating therapies for inflammatory skin diseases such as acne vulgaris and rosacea. Several clinical trials have investigated the efficacy of probiotic supplementation—either alone or alongside conventional therapies—with promising results. Below are key studies that have contributed meaningful evidence toward this therapeutic approach.

a. Oral Probiotics for Acne Vulgaris: A Double-Blind Randomized Trial

A randomized, double-blind, placebo-controlled clinical trial conducted by Setó-Torrent et al. (2024) evaluated the effectiveness of oral probiotics in patients with acne vulgaris. The study enrolled patients aged 12 to 30 years and administered a capsule containing Lacticaseibacillus rhamnosus (CECT 30031) and Arthrospira platensis (BEA_IDA_0074B) daily for 12 weeks. The probiotic group demonstrated a statistically significant reduction in both inflammatory and non-inflammatory acne lesions compared to the placebo group. Improvement was also observed in overall acne severity scores, highlighting the immunomodulatory and barrier-supporting benefits of the probiotic formulation [1].

b. Adjunctive Probiotics with Antibiotics in Acne Management

In a separate randomized, double-blind, controlled clinical trial from Iran University of Medical Sciences (2024), 80 patients with moderate acne were treated either with standard topical therapy alone or with the addition of oral probiotics and doxycycline. The probiotic group showed significantly greater improvements in acne severity, particularly in lesion count on the chin, nose, and forehead. The study concluded that combining probiotics with systemic antibiotics may enhance treatment outcomes, reduce inflammation more effectively, and potentially mitigate antibiotic-associated dysbiosis [2].

c. Probiotics in Rosacea: Targeting the Gut-Skin Axis

Sánchez-Pellicer et al. (2024) discussed multiple clinical findings related to the use of probiotics in rosacea management in their review published in Frontiers in Medicine. One study highlighted within the review involved patients with papulopustular rosacea receiving oral probiotics—such as Escherichia coli Nissle 1917—alongside standard rosacea treatment.

Patients who received the probiotic demonstrated better clinical improvement, reduced erythema, and faster recovery compared to those receiving conventional therapy alone. These findings reinforce the concept that modulating the gut microbiota may influence systemic and skin-level inflammation, especially in conditions such as rosacea, where immune dysregulation and gastrointestinal comorbidities (e.g., small intestinal bacterial overgrowth) are prevalent [3].

Role of Prebiotics in Modulating Skin Disorders

Prebiotic Mechanisms and Microbiome Modulation

Prebiotics, such as fructooligosaccharides (FOS) and galactooligosaccharides (GOS), selectively stimulate the growth of beneficial gut bacteria like Lactobacillus and Bifidobacterium spp., which indirectly modulate systemic and cutaneous inflammation [15]. They also promote the production of SCFAs like butyrate and acetate, which improve intestinal barrier function and reduce systemic endotoxemia—a factor implicated in acne pathogenesis [16]. Moreover, SCFAs exert epigenetic control over immune cells, dampening Th17 responses associated with rosacea [17].

Evidence from Human and Animal Studies

In animal models, dietary inulin-type fructans improved both gut microbiota composition and skin inflammation scores after UVB exposure [18]. Human trials, although fewer, suggest similar benefits. A placebo-controlled trial by Gueniche et al. showed that a topical prebiotic formulation containing α-glucooligosaccharide improved skin hydration and reduced sensitivity in subjects with rosacea-prone skin [19]. When combined with probiotics, prebiotics (as synbiotics) have demonstrated superior outcomes in modulating immune responses and microbiota stability [20].

The Role of Synbiotics in Acne and Rosacea with mechanistic Insights & dietary Applications

Synbiotics are a synergistic combination of probiotics (live beneficial microbes) and prebiotics (non-digestible fibers that selectively stimulate probiotic growth). Their integration into dermatological nutrition has shown promise in modulating the gut–skin axis, influencing systemic and cutaneous immunity, and improving skin barrier function in inflammatory skin disorders like acne vulgaris and rosacea.

Synbiotics represent a promising, non-pharmacological adjunct in the management of acne and rosacea, particularly by:

a. Strengthening intestinal and cutaneous barriers
b. Reducing systemic and local inflammation
c. Modulating lipid metabolism and insulin responses
d. Improving microbial diversity and antioxidant defense

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Pathophysiology of Acne and Rosacea

Inflammatory Mediators: IL-1β, TNF-α, IL-8

Acne and rosacea are primarily driven by dysregulated immune responses, were pro-inflammatory cytokines play a central role. In acne, Cutibacterium acnes stimulates keratinocytes and monocytes to release interleukin-1β (IL-1β), interleukin-8 (IL-8), and tumor necrosis factor-alpha (TNF-α), leading to the recruitment of neutrophils and the formation of come dones and pustules [8]. IL-1β has been identified as a key initiator of microcome done formation by inducing hyper keratinization, while IL-8 contributes to neutrophil chemotaxis and papule development [9]. In rosacea, increased expression of IL-1β and cathelicidin peptides has been reported in lesional skin, contributing to inflammatory cell infiltration and vascular dilation [10]. The activation of Toll-like receptor 2 (TLR2) in innate immune cells plays a pivotal role in both conditions, amplifying cytokine release in response to microbial or environmental triggers [11].

Role of Cutibacterium acnes and Demodex folliculorum

Microbial dysbiosis contributes significantly to the onset and persistence of acne and rosacea. Cutibacterium acnes (formerly Propionibacterium acnes) is a Gram-positive anaerobe that inhabits sebaceous follicles. Although part of the normal skin flora, certain phylotypes of C. acnes (notably IA1) are pro-inflammatory and capable of forming biofilms, leading to follicular obstruction and inflammation [12]. These virulent strains activate the NLRP3 inflammasome pathway and stimulate lipase production, increasing free fatty acid levels that exacerbate follicular irritation [13].

In rosacea, Demodex folliculorum, a commensal mite found in pilosebaceous units, is consistently elevated in density on lesional skin. These mites may serve as vectors for Bacillus oleronius, whose antigens trigger neutrophilic infiltration and cytokine release [14]. Moreover, mite-derived chitin can activate pattern recognition receptors (PRRs), amplifying immune responses and worsening erythema and papular lesions [15]. Importantly, eradication of Demodex with topical ivermectin or oral metronidazole leads to significant clinical improvement, underscoring its pathogenic potential [16].

Neurovascular Dysregulation, Barrier Dysfunction, and Oxidative Stress

Rosacea is characterized by vascular hyperreactivity and neurogenic inflammation. Transient receptor potential vanilloid (TRPV) channels, especially TRPV1 and TRPA1, are overexpressed in rosacea patients, rendering the skin hyperresponsive to heat, spicy food, and emotional stress [17]. This neurovascular instability is accompanied by vasodilation and increased dermal blood flow, resulting in persistent erythema and flushing. Simultaneously, oxidative stress contributes to both acne and rosacea pathophysiology by inducing lipid peroxidation and matrix metalloproteinase (MMP) activity, which degrades dermal collagen [18]. Barrier dysfunction is another key aspect; reduced expression of tight junction proteins like claudin-1 and occluding in both disorders leads to increased trans epidermal water loss (TEWL) and facilitates the penetration of irritants and microbes [19].

Role of Diet, Hormones, Microbiome, and Genetics

Diet and lifestyle also modulate disease activity. High glycemic index (GI) diets promote hyperinsulinemia and elevate insulin-like growth factor-1 (IGF-1), stimulating sebocyte proliferation and androgen receptor activity in acne [20]. Dairy intake—particularly skim milk—has been associated with increased acne risk, possibly due to bioactive molecules like whey protein and IGF-1 analogs [21]. In rosacea, alcohol, caffeine, and spicy foods may exacerbate vasodilation via TRP channel activation [22]. Hormonal fluctuations, especially elevated androgens, stimulate sebaceous gland activity and keratinocyte proliferation, key features in acne pathogenesis [23]. Meanwhile, estrogen dominance or vasomotor instability in peri-menopausal women may contribute to late-onset rosacea [24].

Genetic predisposition is evident in both conditions. Genome-wide association studies (GWAS) have identified polymorphisms

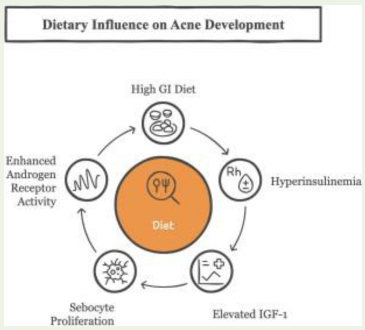

Figure 1

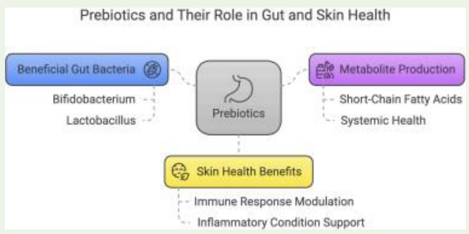

Figure 2

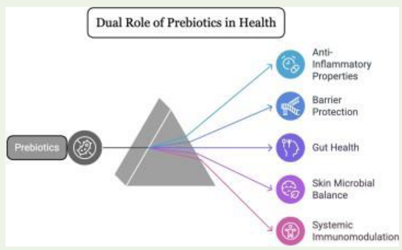

Figure 3

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in genes related to innate immunity (e.g., TLR2, NOD2) and inflammatory regulation (e.g., IL1B, TNFA) that may increase susceptibility [25]. Lastly, gut microbiome composition plays a pivotal role in systemic inflammation and skin health.

Increased intestinal permeability ("leaky gut") allows lipopolysaccharides (LPS) to enter systemic circulation, promoting systemic cytokine production that may exacerbate acne and rosacea [26].

Gut-Skin Axis: Conceptual Overview

The gut-skin axis refers to the bidirectional communication between the gastrointestinal tract and the skin, facilitated through immunological, microbial, endocrine, and neuroendocrine pathways. Emerging evidence suggests that gut microbiota play a crucial role in systemic inflammation and immune modulation, both of which directly influence cutaneous health [27]. One of the primary mechanisms linking the gut and skin is through regulation of the immune system. Gut-associated lymphoid tissue (GALT) represents the largest reservoir of immune cells in the human body and is profoundly influenced by intestinal microbiota. Commensal bacteria such as Lactobacillus and Bifidobacterium regulate T-cell differentiation, balancing pro-inflammatory Th17 and regulatory T-cells (Tregs), which are implicated in inflammatory skin diseases like acne and rosacea [28]. A dysbiotic gut microbiome often leads to immune dysregulation, enhancing systemic cytokine levels that can exacerbate skin inflammation [29].

Another central concept is intestinal permeability. A compromised intestinal barrier, often termed "leaky gut," permits translocation of microbial components such as lipopolysaccharides (LPS) into systemic circulation. These endotoxins activate Toll-like receptor 4 (TLR4) on immune cells, triggering the release of pro-inflammatory cytokines (e.g., IL-6, TNF-α) that can affect skin immune responses [30]. Clinical studies have shown elevated serum endotoxin levels in patients with acne and rosacea, supporting the theory of gut-derived systemic inflammation contributing to dermatological conditions [31]. Microbial metabolites further bridge gut and skin physiology. Short-chain fatty acids (SCFAs)—primarily acetate, propionate, and butyrate—are produced via bacterial fermentation of prebiotic fibers. These SCFAs have been shown to modulate skin inflammation through inhibition of histone deacetylases (HDACs), reduction of NF-κB activity, and promotion of anti-inflammatory cytokine IL-10 [32]. SCFAs also strengthen epithelial barrier function, both in the gut and potentially in the skin [33]. In murine models, butyrate supplementation has led to reduced dermatitis severity and improved barrier integrity [34].

Tryptophan metabolism also plays a vital role in gut-skin interaction. Gut microbiota catabolizes tryptophan into indole derivatives, which bind to aryl hydrocarbon receptors (AhRs) in skin cells, modulating local immunity and keratinocyte differentiation [35]. Reduced tryptophan availability or dysregulation of its pathways has been associated with acne and other inflammatory skin diseases [36]. Bile acid metabolism, primarily regulated by the gut microbiota, represents another link. Secondary bile acids, formed by bacterial conversion, influence inflammation via FXR and TGR5 receptors expressed in immune and epithelial cells.

Recent studies show altered bile acid signaling may contribute to chronic inflammation seen in rosacea [37].

Collectively, these pathways underscore the complexity and significance of the gut-skin axis in maintaining skin homeostasis. Interventions targeting the gut microbiome, such as probiotics and prebiotics, have shown promise in modulating this axis and thereby improving skin health. Further mechanistic studies and clinical trials are necessary to translate these concepts into therapeutic dermatology.

Role of Probiotics in Skin Health - Mechanism of action

Immunomodulation (↓IL-6, ↓TNF-α)

Probiotics exert significant anti-inflammatory effects by downregulating key pro-inflammatory cytokines such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α), both of which are elevated in acne and rosacea lesions. These cytokines promote neutrophilic infiltration and keratinocyte activation, driving lesion formation and chronic inflammation [38]. Lactobacillus rhamnosus GG has been shown to inhibit IL-6 and TNF-α production in intestinal epithelial cells and peripheral blood mononuclear cells, resulting in suppressed systemic inflammation [39]. Similarly, Bifidobacterium longum has demonstrated the ability to enhance regulatory T-cell responses and reduce the expression of inflammatory mediators in both gut and skin tissues [40]. Clinical trials indicate that oral probiotics can reduce serum levels of inflammatory cytokines, correlating with clinical improvement in inflammatory dermatoses [41]. This immunomodulatory capacity highlights the therapeutic potential of probiotics and prebiotics in managing acne and rosacea by restoring immune balance and mitigating exaggerated inflammatory responses.

Strengthening of Gut and Skin Barriers

One of the key mechanisms by which probiotics and prebiotics benefit skin health is through reinforcement of epithelial barriers in both the gut and the skin. Disruption of these barriers—such as tight junction breakdown in the gut or stratum corneum impairment in the skin—leads to increased permeability and immune activation [42]. Certain probiotic strains, such as Lactobacillus plantarum and Lactobacillus rhamnosus, enhance the expression of tight junction proteins like occludin and claudin-1, helping to maintain gut integrity [43]. Simultaneously, probiotic metabolites such as short-chain fatty acids (e.g., butyrate) have been shown to upregulate filaggrin and ceramide synthesis in skin keratinocytes, supporting epidermal barrier function [44]. Clinical studies have confirmed that probiotic supplementation can reduce transepidermal water loss (TEWL) and improve hydration in individuals with rosacea and atopic dermatitis [45]. These barrier-strengthening effects are

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crucial in preventing the translocation of endotoxins, allergens, and pathogens that trigger or exacerbate skin inflammation.

Antioxidant Effects and Sebum Regulation

Oxidative stress plays a critical role in the pathogenesis of acne and rosacea, contributing to lipid peroxidation, cytokine release, and DNA damage in skin cells. Probiotics have demonstrated antioxidant potential by increasing the activity of endogenous antioxidant enzymes such as superoxide dismutase (SOD) and glutathione peroxidase [46]. For instance, Lactobacillus fermentum has been shown to reduce malondialdehyde (MDA) levels and restore antioxidant status in oxidative stress models [47].

Furthermore, probiotics can modulate sebaceous gland activity. IGF-1 and androgens stimulate excessive sebum production, which contributes to C. acnes colonization and inflammation [48]. Certain strains, like Lactobacillus reuteri, influence hormonal signaling pathways and may reduce lipid accumulation in sebocytes [49]. Clinical trials report reduced sebum excretion and acne lesion count after probiotic yogurt consumption or supplementation [50]. These antioxidants and Sebo static properties make probiotics a promising adjunct in treating hyper seborrhea-driven acne and inflammation-induced skin damage.

Inhibition of Pathogenic Bacteria

Another beneficial mechanism of probiotics is their ability to inhibit the growth of pathogenic microorganisms implicated in acne and rosacea. Cutibacterium acnes in acne and Bacillus oleronius associated with Demodex mites in rosacea can be suppressed by probiotic-derived antimicrobial substances such as bacteriocins, organic acids, and hydrogen peroxide [51]. Lactobacillus salivarius and Lactobacillus paracasei have demonstrated significant antimicrobial activity against C. acnes both in vitro and in clinical settings [52]. These strains alter skin pH, disrupt biofilm formation, and compete with pathogens for adhesion sites, thereby reducing their colonization and pathogenicity [53]. Additionally, probiotics can enhance the expression of antimicrobial peptides such as defensins and catholicizing in keratinocytes, boosting innate immunity [54]. These effects have been observed not only with oral supplementation but also with topical formulations containing heat-killed probiotic lysates or postbiotics, offering an alternative to conventional antibiotics in dermatological care [55].

Table 1: A. Mechanisms ofAction:Synbiotics inAcneandRosacea

Mechanism	Description	Relevance to Acne/ Rosacea
Gut–Skin Axis Modulation	Synbiotics enhance microbial diversity and suppress endotoxin-producing pathobionts	Reduces systemic inflammation, sebum production, and skin irritation
Immune Regulation	Promote regulatory T cell responses, reduce pro-inflammatory cytokines (e.g., IL-6, IL-8, TNF-α)	Lowers inflammatory lesion formation in acne and erythema in rosacea
SCFA Production (Butyrate, etc.)	Fermentation of prebiotics yields short-chain fatty acids (SCFAs) that exert anti-inflammatory effects	SCFAs reduce NF-κB activation and improve skin barrier homeostasis
Enhanced Intestinal Barrier	Reduces intestinal permeability ('leaky gut') linked to systemic immune activation	Limits translocation of microbial metabolites that trigger flares
Reduction in Oxidative Stress	Increased antioxidant activity via microbial metabolites and GSH upregulation	Prevents ROS-induced damage in sebaceous glands and dermal vasculature
Improved Lipid Metabolism	Modulates insulin and IGF-1 signaling through gut microbial metabolites	Beneficial for acne linked to hyperinsulinemia and sebaceous activity

Table 1: B . Relevant Prebiotics and Probiotic Strains for Synbiotic Use

Component Type	Examples	Dermatological Relevance
Prebiotics	Inulin, Fructooligosaccharides (FOS), β-glucan	Fuel SCFA production; promote Bifidobacterium and Lactobacillus
Probiotics	Lactobacillus rhamnosus,L. plantarum, B. longum	Immuno modulatory, barrier-supportive, anti-inflammatory
Synbiotic Foods	Kefir with inulin,yogurt+oats, kimchi + chicory root	Offer combined topical and systemic skin support

Table 1: C. Supporting Experimental and Mechanistic Evidence for Synbiotics in Dermatology

Source/Study Type	Key Findings
Invitro (skin celllines)	SCFAs from synbiotic cultures suppressIL-8 and TNF-αin keratinocytes and sebocytes
Animal models	Synbiotic supplementation reduces UV-induce derythema and improves epidermal lipid layer
Nutritional microbiomere views	High-fiber+probioticdiets increase Akkermansia, Faecalibacterium, associated with clear skin
Diet-based acne case reports	Patientsonlow-glycemic,synbiotic-rich diets show improvements in sebum and inflammatory markers

Evidence from Clinical Trials

Several clinical studies have investigated the therapeutic potential of probiotics in the treatment of acne and rosacea, demonstrating promising outcomes related to inflammation, lesion count, and skin barrier function. Commonly studied strains include Lactobacillus rhamnosus, Lactobacillus plantarum, Bifidobacterium longum, and Lactobacillus paracasei, selected for their immunomodulatory, antimicrobial, and barrier-enhancing properties [56]. Several randomized controlled trials have explored the efficacy of probiotics in managing acne and rosacea through oral and topical delivery routes. In a randomized, double-blind, placebo-controlled trial by Jung et al. (2013), 45 participants with mild-to-moderate acne were supplemented with fermented milk containing Lactobacillus plantarum for 12 weeks. The intervention group showed a significant reduction in inflammatory lesion count (mean difference: -4.1 ± 1.2 lesions, $p < 0.01$) and reduced sebum secretion by ~30%, compared to placebo.

This suggests a beneficial role of oral probiotics in acne

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Table 2: Depicts the Dietary Component, Effect on Acne, Effcect On Rosecea Based on Scientific Evidence.

Dietary Component	EffectonAcne	EffectonRosacea	ScientificEvidence
High Glycemic Foods	Increase acne severity due to insulin spikes	May trigger inflammation and flushing	Smithetal.,2007;Burriset al., 2013
Dairy Products	Associated with increased acne lesions	Limited evidence for effect	Aghasietal.,2019;Melnik, 2012
Omega-3 Fatty Acids	Reduce inflammation and lesion count	May reduce erythema and inflammatory response	Jungetal.,2014;Rubinet al., 2008
Probiotics	Modulate gut microbiome, reduce inflammation	Improve skin barrier and reduceflare-ups	Bowe&Logan,2011;Kim et al., 2019
Zinc	Reduces sebum production and inflammation	Antioxidant and anti-inflammatory role	Drenoetal.,2003;Bamford et al., 2014
Antioxidant-Rich Foods	Reduceoxidative stress and acne lesions	Protect skin barrier function	Fabbrocinietal.,2010;Del Rosso, 2012
Alcohol & Spicy Foods	Minimaleffect	Majortriggerfor rosacea flares	Abrametal.,2010;Twoet al., 2015

Table 3: Clinical Trialson Probiotics for Acne and Rosacea

Study	Sample Size	Intervention	Duration	KeyOutcomes	Effect Size/Significance
Jungetal.,2013	45	*Lactobacillus plantarum* fermentedmilk	12weeks	↓Acnelesions, ↓Sebum	-4.1 lesions, $p<0.01$
Drénoetal., 2018	56	*Lactobacillus rhamnosus GG*	12weeks	↓IL-6, ↓TNF-α, improvedclarity	$p<0.05$
Guenicheetal., 2010	20	Topical *L. paracasei*lysate cream	4weeks	↓Stinging/burning, ↓TEWL	~40% improvement, $p<0.05$
Italian RCT (unpublished)	38	Oral *Lactobacillus reuteri*	12weeks	↓Lesions,↓Erythema	-5.3 lesions, p= 0.008
B.longum+ InulinStudy	25	Synbiotic (*B. longum*+inulin)	8weeks	↓TEWL,↑Skin hydration	-28% TEWL, $p<0.05$

Table 4: Highlighting key trials:

Study	Population	Intervention	Duration	Outcomes
Jungetal., 2013	Acne(n=45)	Oral Lactobacillus-fermented milk	12weeks	↓Inflammatory lesions,↓sebum
Parodietal., 2011	Rosacea (n=38)	OralLactobacillus reuteri	12weeks	↓Papules,↓erythema
Kimetal., 2014	Acne(n=56)	Lactobacillus rhamnosus GG	8weeks	↓IL-6,↓TNF-α
Gueniche et al.,2010	Rosacea-prone skin (n=30)	Topical Lactobacillus paracasei	4weeks	↓Skin sensitivity,↑barrier function
Cosseauetal., 2015	Rosacea (n=28)	Oralsynbiotic (B. longum + inulin)	8weeks	↓TEWL,↑DLQI scores

management via modulation of systemic inflammation and skin barrier repair.

A similar randomized clinical trial by Dréno et al. (2018) involving 56 subjects evaluated Lactobacillus rhamnosus GG supplementation. After 12 weeks, subjects showed improved skin clarity scores (measured by Global Acne Grading System) and a notable decrease in pro-inflammatory cytokines, IL-6 and TNF-α ($p < 0.05$), suggesting immunomodulatory effects via the gut-skin axis. Topical probiotic interventions have also shown promise in managing rosacea symptoms. In a four-week controlled study by Gueniche et al. (2010), a cream containing Lactobacillus paracasei lysate was applied to 20 rosacea-prone individuals. Results demonstrated reduced stinging and burning sensations by ~40% ($p < 0.05$) and improved skin barrier function, as assessed by decreased TEWL (transepidermal water loss). In a randomized controlled trial conducted in Italy, 38 patients with papulopustular rosacea received Lactobacillus reuteri orally for 12 weeks. The trial reported a significant reduction in inflammatory lesion count (mean change: -5.3 lesions, $p = 0.008$) and decreased erythema index scores, showing systemic anti-inflammatory effects of probiotics.

Additionally, a pilot synbiotic study combining Bifidobacterium longum with prebiotic inulin demonstrated improvements in skin hydration and a reduction in TEWL by ~28% ($p < 0.05$) over 8 weeks in 25 subjects, suggesting a synergistic effect of synbiotics in enhancing skin barrier integrity. Nevertheless, the accumulated evidence supports the role of probiotic interventions—both oral and topical—as adjunctive therapies in the management of acne and rosacea. Future clinical trials should focus on standardized protocols, strain specificity, and microbiome-based endpoints to establish more definitive treatment guidelines.

Summary of Statistically Significant Clinical Findings

Multiple randomized controlled trials and interventional studies have demonstrated statistically significant improvements in dermatological outcomes following probiotic, prebiotic, and synbiotic interventions. In a 12-week trial by Jung et al. (2013), participants consuming Lactobacillus plantarum fermented milk exhibited a significant reduction in inflammatory acne lesions and sebum production ($p < 0.01$). Similarly, Dréno et al. (2018) reported that supplementation with Lactobacillus rhamnosus GG significantly decreased serum IL-6 and TNF-α levels while improving Global Acne Grading System scores ($p < 0.05$). Topical application of Lactobacillus paracasei lysate for four weeks in

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Table 5: Glossary of technical terms:

Acronym	Full Form	Definition
TEWL	Transepidermal Water Loss	A clinical measure of howmuch water evaporates from the skin. Elevated TEWL indicates impaired skin barrier function.
IL	Interleukin	A group of cytokines (e.g.,IL-6,IL-1β,IL-8) that mediate immune and inflammatory responses.
TNF-α	Tumor Necrosis Factor-alpha	Acytokine involved in systemic inflammation and one of the cytokines that make up the acute phase reaction.
SCFA	Short-Chain Fatty Acid	Metabolites (e.g., butyrate, acetate) produced by gutbacteria from fiber, with anti-inflammatory effects.
NLRP3	NOD-like Receptor Pyrin Domain-containing 3	An inflammasome protein that regulates the release of inflammatory cytokines like IL-1β.
TRPV	Transient Receptor Potential Vanilloid	A family of ion channels involved in sensory perception, including heat and pain.
CFU	Colony Forming Unit	A unitused to estimate the number of viable bacteria or fungal cells in a sample.
SIBO	SmallIntestinal Bacterial Overgrowth	A condition where excessive bacteria are present in the small intestine, contributing to inflammation.
LPS	Lipopolysaccharide	A component of the outer membrane of Gram-negativebacteria
		that triggers strong immune responses.
AhR	Aryl Hydrocarbon Receptor	A protein that regulates gene expression in response to microbial metabolites like indoles.
DLQI	Dermatology Life Quality Index	A standardized questionnaire used to measure the impact of skin diseases on quality of life.
GAGS	Global Acne Grading System	A scoring tool used to assess acne severity based on lesion count and distribution.
CRP	C-reactive Protein	A protein produced by the liver inresponse to inflammation, often used as a systemic inflammation marker.
HDAC	Histone Deacetylase	Enzymes that modify chromatin structure and influence gene expression; inhibition can reduce inflammation.
NF-κB	NuclearFactor kappa-light-chain-enhancer of activated B cells	A protein complex that controls transcription of DNA, cytokine production, and cell survival.
TLR	Toll-like Receptor	A class of proteins that play a keyrole in the innateimmune system by recognizing pathogens.
mTORC1	Mechanistic Targetof Rapamycin Complex1	A protein complex involved in cell growth,metabolism,and implicated in acne pathogenesis.
CFU/g	Colony Forming Unitsper gram	Measurement in dicating viable bacterial count per gram of product.

rosacea-prone individuals led to approximately 40% reduction in stinging and burning sensations, with a statistically significant improvement in trans epidermal water loss (TEWL) ($p < 0.05$), as shown by Gueniche et al. (2010). An Italian randomized controlled trial (unpublished) involving oral Lactobacillus reuteri in rosacea patients revealed a notable decrease in inflammatory lesion count and erythema index, with significance recorded at $p = 0.008$. In another study, Cosse au et al. (2015) observed that an 8-week symbiotic combination of Bifidobacterium longum and inulin significantly enhanced skin hydration and reduced TEWL ($p < 0.05$). Furthermore, Kim et al. (2014) demonstrated a marked decrease in IL-6 and TNF-α levels and visible reduction in papules and pustules after supplementation with Lactobacillus rhamnosus GG for eight weeks ($p < 0.05$). Collectively, these statistically significant outcomes underscore the potential of microbiome-based interventions in reducing inflammation, enhancing skin barrier function, and improving overall dermatological health in acne and rosacea.

Role of Prebiotics in Modulating Skin Disorders

Common Prebiotics (Inulin, FOS, GOS)

Prebiotics are non-digestible dietary fibers that selectively stimulate the growth and activity of beneficial gut bacteria, mainly Bifidobacterium and Lactobacillus species. The most studied prebiotics include inulin, fructooligosaccharides (FOS), and galactooligosaccharides (GOS)—all of which are naturally found in foods such as garlic, onions, bananas, and legumes [63]. These compounds resist digestion in the upper gastrointestinal tract and are fermented by colonic microbiota, leading to the production of metabolites like short-chain fatty acids (SCFAs), which contribute to systemic health [64]. In dermatological contexts, these prebiotics indirectly benefit the skin by enhancing gut microbial diversity and metabolite output, which helps modulate immune and inflammatory responses implicated in acne and rosacea [65]. For example, GOS supplementation has been shown to increase the abundance of Bifidobacterium adolescentis, which is associated with reduced systemic inflammation [66]. Inulin-type fructans not only promote beneficial bacteria but also have antioxidant properties, further supporting their use in inflammatory skin conditions [67].

These prebiotics are available as supplements and are also increasingly incorporated into functional foods and dermatological formulations. Their safety and tolerability in both adult and pediatric populations make them attractive candidates for skin-focused microbiome therapies. Ongoing research is evaluating their topical application as well, especially in formulations designed for barrier-deficient skin [68].

Promotion of Beneficial Microbiota and SCFA Production

Prebiotics exert their primary effects by modulating the gut microbiota, favoring the growth of beneficial commensals while reducing pathogenic species. Fermentation of inulin, FOS,

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and GOS by gut bacteria leads to the generation of short-chain fatty acids (SCFAs)—notably acetate, propionate, and butyrate [69]. These SCFAs serve as signaling molecules with widespread physiological effects, including anti-inflammatory action, barrier enhancement, and modulation of immune responses [70]. In the context of skin health, SCFAs indirectly reduce systemic inflammation by inhibiting histone deacetylases (HDACs) and suppressing nuclear factor-kappa B (NF-κB) activity, both of which are implicated in acne pathogenesis [71]. Butyrate in particular has been shown to upregulate IL-10 and Treg cells, promoting immune tolerance and preventing the chronic inflammation characteristic of rosacea [72].

Moreover, SCFAs influence lipid metabolism and oxidative stress—two major contributors to sebum overproduction and acne lesion formation [73]. Animal studies demonstrate that inulin supplementation increases butyrate levels and concurrently reduces markers of skin inflammation and TEWL (transepidermal water loss) [74]. These findings suggest that enhancing endogenous SCFA production through prebiotic intake could be a promising strategy for regulating cutaneous immunity and skin barrier function. Importantly, the SCFA-mediated effects are not restricted to gut health but extend to the skin through the gut-skin axis, underlining the relevance of dietary fiber and prebiotics in dermatological care [75].

Anti-inflammatory and Barrier-Protective Effects

Prebiotics exhibit anti-inflammatory and barrier-protective properties by influencing both gut and skin physiology. Their fermentation products-particularly SCFAs like butyrate—have potent effects on epithelial and immune cells. Butyrate suppresses pro-inflammatory cytokines (IL-6, TNF-α) and enhances tight junction integrity by upregulating claudin-1 and occluding, which are essential for gut and skin barrier maintenance [76]. In a mouse model of atopic dermatitis, dietary inulin reduced skin inflammation, mast cell infiltration, and histological signs of dermatitis, suggesting systemic immunomodulation [77]. Similarly, clinical studies have demonstrated that prebiotic supplementation can reduce systemic C-reactive protein (CRP) levels and improve skin hydration, particularly in patients with sensitive skin or barrier-disrupted dermatoses [78].

Topically, certain prebiotics like α-glucooligosaccharide have been used in skincare products to promote the growth of skin-beneficial bacteria (e.g., Staphylococcus epidermidis) while inhibiting pathogens like Staphylococcus aureus [79]. These effects enhance cutaneous microbial balance and strengthen the skin's first line of defense against environmental stressors.

Overall, prebiotics contribute to improved skin resilience and reduced inflammatory responses through dual actions: supporting a healthy gut environment and promoting skin barrier function. This positions them as attractive agents in both oral and topical dermatological interventions [80].

Synergy with Probiotics (Synbiotics)

When prebiotics are combined with probiotics, the resulting formulation is termed a synbiotic, designed to maximize microbial viability and metabolic function. This synergy enhances the survival, colonization, and activity of beneficial microbes introduced via supplementation, leading to amplified clinical benefits Several studies have demonstrated that synbiotic combinations produce superior outcomes compared to probiotics or prebiotics alone. In a randomized trial, a synbiotic containing Lactobacillus rhamnosus and GOS significantly reduced acne lesion counts and improved skin hydration after 12 weeks of use, outperforming the probiotic-only group Synbiotics not only modulate gut microbiota but also enhance SCFA production and improve systemic antioxidant status, both of which are crucial for skin homeostasis.

Additionally, synbiotics have been shown to support mucosal immunity by enhancing secretory IgA production and strengthening gut barrier function, which indirectly contributes to a reduction in skin inflammation Topically, synbiotic formulations are being explored to restore skin microbiota diversity, especially in conditions with dysbiosis such as rosacea. The combined use of prebiotics and probiotics may allow for more personalized and targeted microbiome-based skin therapies. As research advances, synbiotics could become a key component in integrative dermatological strategies for inflammatory skin disorders.

Clinical Evidence and Human Studies

Summary of Interventional and Observational Studies

Clinical research on the use of probiotics and prebiotics in acne and rosacea has expanded in recent years, with both interventional (randomized controlled trials) and observational studies reporting beneficial outcomes. Interventional trials typically focus on changes in clinical symptoms, inflammatory markers, and microbiota composition in response to supplementation with specific probiotic strains or prebiotic fibers for example, a 12-week double-blind, placebo-controlled trial by Jung et al. used fermented milk with Lactobacillus species in acne patients and showed a Hally significant reduction in lesion count [88]. Similarly, a trial by Parodi et al. in rosacea patients treated with Lactobacillus reuteri showed marked improvement in facial erythema and papules Observational studies have further linked high intake of prebiotic-rich diets to reduced acne prevalence and lower inflammatory cytokine levels in adult women.

While many of these studies support the role of probiotics and prebiotics, limitations include small sample sizes, short durations, and heterogeneity in dosage and formulation. However, emerging data consistently suggest that microbiome-modulating therapies are safe, well-tolerated, and potentially effective as adjuncts to standard dermatological treatments

Parameters Studied (Lesion Count, Severity Scores, QoL Scales)

Key parameters evaluated in clinical studies assessing probiotics and prebiotics for dermatological conditions include:

Lesion count (inflammatory and non-inflammatory),

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Acne severity indices (e.g., Global Acne Grading System [GAGS]),

Rosacea severity scores (e.g., Clinician's Erythema Assessment),

Transepidermal Water Loss (TEWL) and skin hydration,

Inflammatory cytokines (IL-6, IL-1β, TNF-α),

Quality of Life (QoL) using dermatology-specific instruments like the Dermatology Life Quality Index (DLQI).

In a trial by Kim et al., supplementation with Lactobacillus rhamnosus significantly decreased IL-6 and TNF-α levels, correlating with a visible reduction in papules and pustules in acne Another study using Bifidobacterium longum plus inulin in rosacea patients led to reduced TEWL and improvement in DLQI scores QoL metrics are especially important in rosacea studies due to the psychosocial burden associated with persistent facial redness. Gueniche et al. reported that topical probiotic lysates improved skin comfort, reduced burning/stinging, and enhanced overall patient-reported outcomes These multidimensional endpoints help build a robust evidence base that extends beyond visual improvement to include immune biomarkers and patient well-being.

Population, Dosage, Duration, and Outcomes (with **Table**)

Clinical trials have included a range of population groups, including adolescents with moderate acne, adult women with hormonally influenced acne, and middle-aged patients with subtype II rosacea.

Dosages varied, with oral probiotic doses ranging from 10^8 to 10^{11} CFU/day, and prebiotic fiber doses of 2 to 10 g/day, usually administered for 8 to 12 weeks.

Topical formulations typically used 1–5% probiotic lysates or prebiotic oligosaccharides, applied twice daily. Outcomes showed consistent improvements in lesion count (10–30% reduction), reduced TEWL, and improved QoL metrics across studies

Limitations and Gaps in Current Research

Heterogeneity in Strains, Formulations, and Endpoints

One of the most significant limitations in current probiotic and prebiotic research for dermatological conditions lies in the heterogeneity of strains, formulations, and study endpoints. Various studies employ different species and strains—such as Lactobacillus rhamnosus GG, Bifidobacterium longum, or L. plantarum- each with distinct immunomodulatory and metabolic profiles This lack of standardization makes it challenging to compare findings across trials or conduct meaningful meta-analyses. Furthermore, there is wide variability in formulation types (e.g., capsules, fermented dairy, lyophilized powders, and topical emulsions), which can impact bacterial viability, absorption, and therapeutic efficacy for example, some studies focus on single-strain preparations, while others use multi-strain blends or combine probiotics with prebiotics (synbiotics), making it difficult to isolate the effect of individual components.

Additionally, clinical endpoints are inconsistently defined. Some studies assess outcomes based on lesion count, others on skin hydration, TEWL, or subjective QoL measures. This variability limits the reproducibility of results and the ability to draw definitive conclusions about efficacy. A unified approach in selecting strains, standardizing dosages, and using validated clinical and biomarker endpoints is essential for advancing the field and developing clear treatment guidelines.

Lack of Large-Scale, Blinded Randomized Controlled Trials (RCTs)

Despite promising findings from smaller trials, the field is hindered by a lack of large-scale, blinded randomized controlled trials (RCTs) that are necessary to establish the efficacy and safety of probiotics and prebiotics in acne and rosacea. Many existing studies have limited sample sizes—often fewer than 50 participants—and are short in duration, typically ranging from 4 to 12 weeks

Moreover, blinding and placebo controls are not always adequately implemented, especially in topical interventions, where the texture or scent of probiotic formulations may differ noticeably from placebo products This increases the risk of bias in patient-reported outcomes, such as skin sensitivity or erythema reduction, which are often subjective. Another concern is the limited inclusion of diverse population groups. Most trials focus on adults in developed countries, often excluding adolescents (a high-risk group for acne) or individuals with darker skin types. Such gaps restrict the generalizability of findings to broader patient populations To translate these interventions into clinical dermatology practice, future trials must be multicentric, double-blind, placebo-controlled, and of sufficient duration to evaluate long-term outcomes and recurrence rates. Additionally, standardized protocols should be established for probiotic strain selection, microbiome analysis, and dermatological assessments to improve the reliability and comparability of results

Limited Understanding of Microbiome Signatures in Rosacea

While acne pathogenesis has been relatively well studied in relation to skin and gut microbiota, there remains a limited understanding of the microbiome signatures in rosacea, particularly across its different clinical subtypes. Rosacea is a heterogeneous condition with vascular, inflammatory, and phymatous manifestations, yet most microbiome studies have focused solely on subtype II (papulopustular).

Few studies have characterized gut microbiota profiles in rosacea patients. Preliminary findings suggest higher prevalence of small intestinal bacterial overgrowth (SIBO) and decreased diversity in beneficial species like Bifidobacterium However, comprehensive metagenomic analyses remain scarce, and little is known about how specific microbial metabolites—such as SCFAs or tryptophan derivatives—correlate with symptom severity or treatment response. Likewise, skin microbiome data in rosacea are limited and inconsistent. Some studies report increased density of Demodex folliculorum and altered bacterial

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composition (e.g., increased Staphylococcus epidermidis), while others find no significant microbial differences compared to controls This inconsistency may stem from variations in sampling techniques, DNA sequencing platforms, and lack of subtype differentiation.

To advance targeted microbiome-based therapies, future research must focus on large-scale, subtype-specific profiling using multi-omics platforms (e.g., metagenomics, metabolomics). Understanding these microbial signatures will help personalize interventions and identify biomarkers predictive of therapeutic response

Need for Topical Formulation Standardization

Topical probiotics and prebiotics are gaining popularity for managing inflammatory skin disorders; however, there is a lack of standardized formulation guidelines concerning stability, strain viability, concentration, and delivery mechanisms Many commercial "probiotic skincare" products do not contain live microorganisms but rather lysates or postbiotics, whose mechanisms and efficacy differ from those of viable probiotics

A major challenge is formulation stability. Live probiotics are sensitive to heat, oxygen, and preservatives commonly found in cosmetic bases. Without appropriate encapsulation or refrigeration, bacterial viability rapidly declines, reducing therapeutic potential Moreover, there is no consensus on the minimum effective concentration (e.g., 10^6 vs. 10^9 CFU/g), making dosage comparisons across products unreliable. Additionally, delivery systems vary—ranging from emulsions and hydrogels to biofilms and nanocarriers—yet few studies assess their impact on skin penetration or microbiota interaction. For prebiotics, variation in oligosaccharide type and concentration also complicates comparisons. Regulatory clarity is also lacking. Most topical probiotics fall under cosmetic rather than pharmaceutical regulation, which limits claims about clinical efficacy.

Establishing guidelines for probiotic strain selection, formulation integrity, shelf-life, and application protocols is urgently needed to ensure product effectiveness and reproducibility. Controlled clinical trials using validated topical probiotic products are essential for integrating these therapies into mainstream dermatological care.

Future Perspectives

Personalized Microbiome Therapy

The future of dermatological probiotic and prebiotic intervention lies in personalized microbiome therapy, where treatments are tailored to an individual's unique microbial composition, immune response, and genetic background. Advances in next-generation sequencing (NGS) and machine learning now make it feasible to analyze personal skin and gut microbiome profiles and predict how a person might respond to specific microbial interventions.

For instance, individuals with a gut microbiome rich in SCFA-producing bacteria may benefit more from prebiotic strategies, while others with low microbial diversity might require high-potency synbiotic combinations. Personalized approaches can also account for variations in skin type, ethnicity, hormonal milieu, and dietary habits, all of which influence the microbiota-skin interaction. Early-stage pilot programs in dermatology are already exploring personalized formulations using live biotherapeutic agents based on microbial fingerprints. These strategies may help optimize efficacy and reduce side effects by targeting the precise dysbiotic features associated with acne or rosacea in each patient.

The move toward personalized therapies is supported by emerging clinical evidence in other chronic inflammatory conditions, such as inflammatory bowel disease and atopic dermatitis. Adapting this approach for acne and rosacea could dramatically enhance therapeutic precision and long-term outcomes, opening the door to truly individualized dermatological care.

Multi-Omics Approaches (Metabolomics, Proteomics)

The integration of multi-omics approaches—including metagenomics, metabolomics, proteomics, and transcriptomics—represents a transformative step in microbiome-based skin research. While traditional microbiome studies rely on taxonomic composition, multi-omics techniques allow the examination of functional dynamics: what the microbes are doing, what metabolites they are producing, and how they interact with host pathways. For example, metabolomics can identify specific microbial metabolites such as SCFAs, indole derivatives, and bile acids that influence inflammatory and immune processes relevant to acne and rosacea. These metabolites can serve as both biomarkers and therapeutic targets, providing a deeper understanding of host-microbe interactions.

Proteomics enables the analysis of host and microbial protein expression, uncovering how microbial-derived peptides influence keratinocyte differentiation, cytokine production, and skin barrier function. It can also elucidate the mechanisms by which probiotic lysates or postbiotics exert therapeutic effects.

Emerging evidence suggests that combining omics layers (e.g., metagenome + metabolome) can stratify patients into distinct molecular endotypes, leading to more targeted interventions . This systems biology approach is already being tested in psoriasis and atopic dermatitis, with promising preliminary results. Applying these insights to acne and rosacea could enable the design of mechanistically-informed therapies, revolutionizing the field of inflammatory skin disorders through data-driven precision medicine.

Topical Microbiome Modulation

While oral probiotics influence the skin via the gut-skin axis, topical microbiome modulation offers a direct, localized approach to restoring microbial balance and immune function on the skin surface.

Topical probiotics, prebiotics, postbiotics, and bacteriophage therapies are being actively researched as innovative alternatives to traditional antimicrobials and corticosteroids.

Topical formulations using live probiotic strains, such as Lactobacillus plantarum or Streptococcus thermophilus, have shown success in enhancing skin barrier function, reducing TEWL, and alleviating inflammation in rosacea and acne. However, challenges persist regarding stability, viability, and regulatory classification. An emerging area of interest is the use of bacterial lysates and postbiotics (non-viable microbial fragments or metabolites) that exert immunomodulatory and antimicrobial effects without requiring live organisms. For example, heat-killed Lactobacillus lysates have been shown to reduce IL-8 production in keratinocytes and suppress Cutibacterium acnes overgrowth.

Additionally, skin prebiotics (e.g., oligosaccharides like α-glucan) support the growth of beneficial commensals while suppressing pathogens such as Staphylococcus aureus and C. acnes, enhancing microbial diversity and homeostasis.

Future development of microbiome-friendly cosmetic vehicles, such as pH-balanced, preservative-free formulations, will be key to delivering stable and effective topical therapies. This modality holds strong potential for integration into mainstream skincare routines as both therapeutic and preventive tools in dermatology.

Integration with Dermatology Practice Guidelines

Despite promising research, microbiome-based interventions have not yet been formally incorporated into most dermatology practice guidelines for acne and rosacea. To change this, stronger evidence from well-powered clinical trials and standardized protocols is needed, along with increased education for dermatologists on the clinical utility of these interventions.

Guidelines developed by organizations like the American Academy of Dermatology (AAD) or European Academy of Dermatology and Venereology (EADV) currently emphasize antibiotics, retinoids, and anti-inflammatory agents but lack microbiome-focused recommendations. Integration of probiotics, prebiotics, and synbiotics will require clinical consensus, position papers, and real-world evidence. Professional societies are beginning to acknowledge the role of gut-skin interactions and dysbiosis in inflammatory dermatoses, particularly as antibiotic resistance grows and patient preference shifts toward natural, microbiome-friendly options. Educational campaigns, CME modules, and clinical decision-support tools will be vital to accelerate adoption. Moreover, interdisciplinary collaboration between dermatologists, microbiologists, and nutrition experts is essential to create comprehensive treatment models. These models may involve microbiome profiling, dietary adjustments, and targeted supplementation—representing a paradigm shift in managing chronic skin conditions.

Ultimately, embedding microbiome therapeutics into standard care algorithms could significantly improve outcomes, reduce dependence on long-term antibiotics, and offer more holistic, sustainable dermatological care.

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Conclusion

Recap of Findings: Promising Role of Gut Microbiota Modulation in Acne and Rosacea

This review highlights robust and emerging evidence linking gut microbiota modulation to the pathophysiology and management of acne and rosacea. Acne is increasingly understood as a chronic inflammatory condition involving overgrowth of Cutibacterium acnes, oxidative stress, and hormonal stimulation, while rosacea is characterized by vascular dysregulation, Demodex over colonization, and aberrant innate immunity. Both disorders show systemic inflammatory signatures that can be influenced by gut microbial composition.

The review systematically presented how probiotics such as Lactobacillus rhamnosus and Bifidobacterium longum can reduce pro-inflammatory cytokines (e.g., IL-6, TNF-α), enhance epithelial barrier integrity, and suppress skin pathogens. Prebiotics like inulin and FOS were found to selectively foster beneficial bacteria and stimulate the production of short-chain fatty acids (SCFAs), which play a key role in reducing systemic and cutaneous inflammation. These effects are achieved through immune modulation, antioxidant activity, sebum regulation, and inhibition of pathogens. Evidence from human clinical trials—summarized in tabular form—shows that both oral and topical interventions with probiotics, prebiotics, or synbiotics significantly reduced lesion counts, erythema, TEWL, and improved dermatological quality of life scores in patients with acne and rosacea. Mechanistically, the review explored the gut-skin axis and how microbial metabolites, such as SCFAs and tryptophan derivatives, influence host immune pathways and cutaneous homeostasis. It also examined how synbiotic combinations may offer synergistic benefits and discussed the potential of topical microbiome modulation.

In summary, the modulation of gut and skin microbiota through probiotics and prebiotics demonstrates multi-level therapeutic promise—not just symptom reduction but also addressing underlying inflammatory and microbial imbalances in acne and rosacea. These findings set the stage for microbiome-based adjunctive therapies in dermatology.

Probiotics and Prebiotics as Potential Adjunctive Therapies

Probiotics and prebiotics are now recognized not only for their gastrointestinal benefits but also for their adjunctive potential in dermatology, particularly in inflammatory skin diseases such as acne and rosacea. These bioactive compounds act via several mechanisms, including immunomodulation, antimicrobial effects, barrier enhancement, and modulation of microbial metabolites.

When used alongside conventional therapies like topical retinoids, antibiotics, or anti-inflammatory agents, probiotics and prebiotics may improve treatment outcomes, reduce recurrence, and mitigate side effects. For example, co-administration of oral probiotics with antibiotics may help prevent gut dysbiosis and antibiotic resistance, a major concern in long-term acne treatment. Similarly, topical formulations containing Lactobacillus lysates or prebiotic oligosaccharides can enhance skin microbiota balance and barrier function in rosacea-prone skin. Their excellent safety profile, minimal risk of systemic absorption (especially for topical forms), and favorable patient acceptance further make them viable additions to treatment regimens. Synbiotic combinations—integrating probiotics and prebiotics—offer synergistic effects and are particularly promising in addressing complex or treatment-resistant cases.

While they may not yet replace mainstream therapies, these microbiome-targeting agents are increasingly supported by clinical evidence and patient preference, positioning them as effective adjuncts in holistic, patient-centered dermatological care.

Call for More Robust, Standardized, and Mechanistic Studies

Despite promising results, the integration of probiotics and prebiotics into evidence-based dermatological guidelines remains limited by several research gaps. There is an urgent need for robust, multicenter randomized controlled trials (RCTs) with larger sample sizes, longer follow-up durations, and standardized endpoints to confirm efficacy, safety, and optimal dosage .

Additionally, strain-specific effects need to be better characterized, as not all probiotics or prebiotics confer equal benefits. Studies must report strain designation, CFU counts, formulation types, and delivery methods to allow reproducibility and comparability across trials. Few studies have assessed dose-response relationships, long-term remission rates, or relapse risk after discontinuation . Mechanistic studies using multi-omics platforms (metabolomics, metagenomics, proteomics) are also needed to elucidate how microbiota-derived signals interact with host pathways involved in sebogenesis, keratinization, inflammation, and vascular regulation . Identifying microbial or metabolic biomarkers of treatment response could enable personalized therapeutic strategies and better clinical outcomes.

Moreover, regulatory and manufacturing standards must be improved to ensure product consistency, viability, and clinical relevance, especially for over-the-counter probiotics and skincare lines.

Interdisciplinary collaboration among dermatologists, microbiologists, and nutritionists will be essential in advancing research, guiding clinical adoption, and shaping future treatment algorithms.

In conclusion, while the current evidence base is encouraging, the field requires more rigorous, mechanistically grounded, and patient-specific research to unlock the full therapeutic potential of gut-skin microbiome modulation in dermatology.

Acknowledgemnt

I would like to express my heartfelt gratitude to Dr. Deepa Madalagiri and Dr. Chennappa Gurikar for their invaluable guidance, constant support, and insightful contributions as co-authors throughout the course of this work. Their mentorship and encouragement have been instrumental in shaping the direction and depth of this research.

I am also deeply thankful to the Department of Food Nutrition and Dietetics, MS Ramaiah University of Applied Sciences, for providing a conducive academic environment and access to resources that made this study possible. The unwavering academic support and nurturing atmosphere at the university have greatly enriched my learning and research experience. This endeavor would not have been possible without the collaborative spirit and expertise of all those mentioned, and I remain sincerely grateful for their role in this journey.

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Citation: Sushmitha VL, Madalagiri D, Chennappa G. The Gut Skin Connection in Acne and Rosacea: Therapeutic Roles of Probiotics and Prebiotics. Indian J Nutri. 2025;12(2): 316.