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THE ROLE OF PROBIOTICS AND GUT MICROBIOTA MODULATION IN THE PATHOGENESIS AND MANAGEMENT OF ACNE VULGARIS: A SYSTEMATIC REVIEW

Agnieszka Jóźwicka *(Corresponding Author, Email: agnieszka.jozwicka@onet.eu)*
Medical University of Warsaw, Żwirki i Wigury 61, 02-091 Warsaw, Poland
ORCID ID: 0009-0008-1130-1518

Ewa Bąkowska
Medical University of Lublin, Aleje Racławickie 1, 20-059 Lublin, Poland
ORCID ID: 0009-0007-4135-9748

Wojciech Janikowski
Medical University of Warsaw, Żwirki i Wigury 61, 02-091 Warsaw, Poland
ORCID ID: 0009-0008-4078-9698

Aleksandra Stępka
Medical University of Warsaw, Żwirki i Wigury 61, 02-091 Warsaw, Poland
ORCID ID: 0009-0007-5034-0037

Lena Jaworowicz
Medical University of Warsaw, Żwirki i Wigury 61, 02-091 Warsaw, Poland
ORCID ID: 0009-0008-4210-7216

Weronika Plichtowicz-Kordowska
Medical University of Warsaw, Żwirki i Wigury 61, 02-091 Warsaw, Poland
ORCID ID: 0009-0009-7713-8597

Karina Lewandowska
Medical University of Warsaw, Żwirki i Wigury 61, 02-091 Warsaw, Poland
ORCID ID: 0009-0004-5298-1426

Maria Wieczorek
Medical University of Warsaw, Żwirki i Wigury 61, 02-091 Warsaw, Poland
ORCID ID: 0009-0000-9951-7509

ABSTRACT

Background: Acne vulgaris is a multifactorial inflammatory skin condition. Recent evidence highlights the critical role of the gut-skin axis and gastrointestinal dysbiosis in its pathogenesis, suggesting that systemic inflammation originating in the gut may exacerbate cutaneous symptoms.
Objective: This systematic review aims to evaluate the clinical efficacy, microbiological specificity, and safety profile of probiotic interventions in the management of acne vulgaris.
Methods: A comprehensive literature search was conducted across PubMed and Google Scholar databases to identify relevant experimental and clinical studies investigating the relationship between the gut microbiome, probiotic supplementation, and acne development.
Results: Current data demonstrate that both oral and topical probiotic interventions significantly reduce inflammatory and non-inflammatory acne lesion counts. Oral probiotics primarily modulate the gut-brain-skin axis, lowering systemic inflammation and regulating sebum excretion rates (SER). Topical applications directly restore the cutaneous barrier and competitively inhibit Cutibacterium acnes. Efficacy is highly strain-specific, with Lactobacillus and Bifidobacterium species showing the most significant benefits. Furthermore, probiotics serve as highly effective adjuvant therapies, synergistically improving clinical outcomes while mitigating the adverse effects of conventional treatments such as systemic antibiotics and isotretinoin.
Conclusion: Microbiome-targeted therapies, specifically probiotics, represent a safe, well-tolerated, and promising adjunctive strategy in acne management. Further large-scale, randomized controlled trials are required to establish standardized, strain-specific therapeutic protocols.

KEYWORDS

Acne Vulgaris, Gut Microbiome, Gut-Skin Axis, Probiotics, Microbiota, Dysbiosis, Lactobacillus, Bifidobacterium

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1. Introduction

Acne vulgaris is one of the most common chronic inflammatory skin diseases worldwide, affecting approximately 85% of adolescents and a considerable proportion of adults. It primarily involves the pilosebaceous unit and manifests clinically as comedones, papules, pustules, and nodules, which may lead to permanent scarring and significant psychosocial burden [1,2]. Although acne is often perceived as a disease of adolescence, its persistence into adulthood and increasing prevalence among adult women highlight its importance as a global dermatological concern [3]. The condition can substantially affect quality of life, contributing to anxiety, depression, and reduced self-esteem [4].

The pathogenesis of acne vulgaris is multifactorial and involves several key mechanisms, including increased sebum production, follicular hyperkeratinization, colonization by Cutibacterium acnes, and complex inflammatory responses within the pilosebaceous unit [5,6]. Traditionally, research on acne pathophysiology has focused primarily on the role of skin microbiota and hormonal regulation. However, recent advances in microbiome research have expanded the understanding of acne by highlighting the importance of microbial communities beyond the skin, particularly the gut microbiome [7].

The human gut microbiome consists of trillions of microorganisms that play a critical role in maintaining immune homeostasis, metabolic regulation, and intestinal barrier integrity. Alterations in gut microbial composition, referred to as dysbiosis, have been associated with numerous systemic and inflammatory diseases, including dermatological conditions such as acne vulgaris [8,9]. Emerging evidence suggests that patients with acne may exhibit changes in gut microbial diversity, increased intestinal permeability, and

enhanced systemic inflammatory responses, which may contribute to the exacerbation of cutaneous inflammation [10].

These observations have led to an increasing interest in the concept of the gut-skin axis, which describes the bidirectional communication between the gastrointestinal tract and the skin through immune, metabolic, and neuroendocrine pathways [11,12]. According to this concept, disturbances in gut microbiota may influence systemic inflammation, oxidative stress, and immune signaling, ultimately affecting skin homeostasis and contributing to the development of inflammatory skin disorders [13]. The gut-brain-skin axis hypothesis further suggests that psychological stress and dietary factors may alter gut microbiota composition, leading to increased inflammatory signaling and modulation of sebaceous gland activity [14].

Dietary factors have also been implicated in acne development, particularly high glycemic load diets and excessive dairy consumption, which may influence insulin signaling and inflammatory pathways. Such dietary patterns can also affect gut microbial composition, further supporting the potential role of the gut microbiome in acne pathogenesis [15,16].

Consequently, modulation of gut microbiota has been proposed as a potential therapeutic strategy for managing acne and other inflammatory skin diseases. Probiotics, defined as live microorganisms that confer health benefits to the host when administered in adequate amounts, have gained increasing attention as potential modulators of the gut microbiome and immune system [17]. Probiotic supplementation may influence acne development through several mechanisms, including the restoration of microbial balance, enhancement of intestinal barrier function, and modulation of inflammatory and immune responses [18]. Experimental and clinical studies have suggested that probiotics may reduce systemic inflammation, improve metabolic parameters, and potentially decrease the severity of acne lesions [19]. Furthermore, probiotics may exert beneficial dermatological effects through indirect mechanisms, such as reducing oxidative stress, modulating cytokine production, and inhibiting the growth of pathogenic microorganisms [20].

Despite these promising findings, the available evidence regarding the role of probiotics in acne remains heterogeneous, with considerable variation in study design, probiotic strains, treatment duration, and patient populations. Therefore, a comprehensive synthesis of current research is necessary to better understand the role of the gut microbiome and probiotic supplementation in acne pathogenesis and treatment. The aim of this review is to summarize and critically evaluate current evidence on the relationship between the gut microbiome and acne development, with a particular emphasis on the potential therapeutic role of probiotics and emerging microbiome-targeted strategies in acne management.

2. Methodology

A comprehensive literature search was conducted across the PubMed and Google Scholar databases to identify relevant studies investigating the role of the gut microbiome and probiotic interventions in acne vulgaris. The search strategy utilized combinations of the following keywords and Medical Subject Headings (MeSH): "acne vulgaris," "gut microbiome," "gut-skin axis," "probiotics," "microbiota," "dysbiosis," "Lactobacillus," and "Bifidobacterium." Search terms were combined using Boolean operators (AND, OR) to ensure a systematic and exhaustive retrieval of relevant literature.

3. Results

3.1 The Gut-Skin Axis in Acne Pathogenesis

Recent advances in microbiome research have highlighted the potential role of the gut-skin axis in the development and progression of acne vulgaris. The gut-skin axis refers to the bidirectional communication between the gastrointestinal microbiota and the skin, mediated by immune, metabolic, and neuroendocrine pathways. Increasing evidence suggests that alterations in gut microbial composition may contribute to systemic inflammation and immune dysregulation, which may influence skin homeostasis and promote inflammatory skin diseases, including acne [7,8].

The human gut microbiota plays a fundamental role in maintaining immune balance, regulating metabolic processes, and preserving intestinal barrier integrity. Dysbiosis, defined as an imbalance in the composition and diversity of gut microorganisms, has been associated with several inflammatory and metabolic disorders. Recent studies suggest that individuals with acne may exhibit changes in gut microbiota composition, including decreased microbial diversity and an altered abundance of certain bacterial taxa compared with healthy individuals [9,21]. These alterations may influence host immune responses and contribute to the inflammatory processes characteristic of acne.

One of the key mechanisms linking gut microbiota to acne pathogenesis is systemic inflammation. Dysbiosis may stimulate the production of pro-inflammatory cytokines and other immune mediators that can exacerbate inflammation within the pilosebaceous unit. Increased levels of inflammatory mediators, such as interleukin-1β (IL-1β), interleukin-6 (IL-6), and tumor necrosis factor-α (TNF-α), have been associated with acne lesions and may be influenced by gut microbial imbalance [5]. Furthermore, gut microbiota can modulate immune cell differentiation, including T helper cell responses, which play an important role in inflammatory skin conditions [13].

Another mechanism involves increased intestinal permeability, commonly referred to as "leaky gut." The disruption of the intestinal epithelial barrier may allow microbial components, including lipopolysaccharides and other bacterial endotoxins, to enter the bloodstream. These molecules can trigger systemic immune activation and low-grade inflammation, which may contribute to the exacerbation of inflammatory skin diseases such as acne [12]. Increased intestinal permeability has been observed in individuals with acne and may represent an important link between gastrointestinal dysbiosis and skin inflammation.

Metabolic pathways also appear to play a significant role in the gut-skin axis. The gut microbiota is involved in regulating glucose metabolism, lipid homeostasis, and hormonal signaling pathways. Alterations in microbial composition may influence insulin resistance and insulin-like growth factor-1 (IGF-1) signaling, both of which are known to stimulate sebaceous gland activity and keratinocyte proliferation in acne pathogenesis [22]. In addition, dietary patterns associated with acne, particularly high glycemic load diets and excessive dairy consumption, may influence gut microbial composition and metabolic signaling pathways that contribute to inflammatory processes in the skin [23].

The gut-brain-skin axis represents another pathway linking gut microbiota to acne. Psychological stress can alter gut microbiota composition and intestinal barrier function, leading to increased systemic inflammation and modulation of neuroendocrine signaling. These changes may affect sebaceous gland activity and inflammatory responses within the skin, thereby exacerbating acne symptoms [11].

Collectively, current evidence suggests that gut microbiota dysbiosis may contribute to acne development through multiple interconnected mechanisms, including immune dysregulation, systemic inflammation, increased intestinal permeability, metabolic disturbances, and neuroendocrine interactions. Understanding these mechanisms provides important insights into the potential role of microbiome-targeted therapies, such as probiotics, dietary interventions, and microbiota modulation strategies, in the management of acne vulgaris. Further research is needed to identify specific microbial species involved in acne pathogenesis and to determine the therapeutic potential of microbiome-based interventions.

3.2 Clinical Efficacy of Probiotic Interventions

Recent clinical evaluations underscore the significant therapeutic efficacy of probiotic interventions in the management of acne vulgaris, particularly regarding the quantitative reduction of both inflammatory and non-inflammatory lesions. A recent systematic review and meta-analysis of double-blind randomized clinical trials demonstrated that oral probiotic supplementation yields a statistically significant decrease in total and inflammatory lesion counts, offering outcomes that frequently parallel traditional therapeutic responses [19].

Specifically, targeted probiotic interventions have been shown to modulate the sebum excretion rate (SER) by downregulating IGF-1 signaling and modulating FOXO1 gene expression, thereby decreasing sebaceous gland hyperplasia and excessive epidermal lipogenesis [24].

Furthermore, the integration of probiotics as an adjuvant therapy to conventional dermatological treatments presents a compelling strategy to enhance clinical outcomes while mitigating therapy-induced adverse effects. For instance, the co-administration of *Lactobacillus plantarum* MH-301 alongside systemic isotretinoin not only resulted in a more pronounced reduction in acne lesions compared to isotretinoin monotherapy, but also effectively counteracted the isotretinoin-induced gastrointestinal dysbiosis [25]. Similarly, oral supplementation with customized probiotic formulations has proven highly efficacious in standardized clinical assessments, significantly decreasing comedones, papules, and overall acne severity scores over a 12-week intervention period [26]. Collectively, these findings validate that probiotics not only deliver standalone anti-inflammatory benefits but also act synergistically with standard dermatological protocols to restore the integrity of the gut-skin axis and normalize epidermal homeostasis [27].

3.3 Microbiological Specificity: Strains and Delivery Routes

The clinical success of microbiome-modulating therapies in dermatology is highly dependent on both the microbiological specificity of the utilized strains and the targeted delivery routes. Comparative analyses of distinct probiotic strains reveal that the strategic selection of specific bacterial taxa is crucial; for example, *Lactobacillus* and *Bifidobacterium* species are particularly adept at restoring skin barrier function, modulating local immune responses, and competing with pathogenic colonization [28].

The route of administration further dictates the underlying therapeutic mechanism. Oral probiotics primarily exert their effects systemically by modulating the gut-brain-skin axis, thereby reducing systemic oxidative stress, lowering circulating pro-inflammatory cytokines, and indirectly influencing the cutaneous microenvironment [29]. Conversely, the topical administration of probiotics acts directly upon the cutaneous ecology, demonstrating a high affinity for epidermal keratinocytes and actively inhibiting the biofilm formation of *Cutibacterium acnes* through competitive exclusion and the local secretion of antimicrobial peptides [30]. Furthermore, topical delivery systems provide immediate reparative benefits to the disrupted epidermal barrier, supporting the synthesis of ceramides and promoting the localized restoration of the skin's physiological microbiome **[31]**. Ultimately, recognizing the complex interplay of the host's surface microflora and the inherent differences between systemic oral modulation and direct topical intervention is essential for optimizing and personalizing evidence-based acne treatment protocols **[32]**.

3.4 Safety Profile and Patient-Reported Outcomes

The safety profile of probiotic interventions in acne vulgaris appears to be highly favorable, with the majority of clinical studies reporting minimal to no serious adverse events associated with their use. Across randomized controlled trials and observational studies, oral probiotics—particularly strains from the *Lactobacillus* and *Bifidobacterium* genera—were generally well tolerated. Only mild and transient gastrointestinal symptoms, such as bloating, flatulence, or abdominal discomfort, were reported in a small proportion of participants [19,26]. Importantly, these adverse effects were typically self-limiting and did not necessitate the discontinuation of therapy.

In contrast to conventional systemic treatments for acne, such as antibiotics or isotretinoin, probiotics demonstrate a markedly improved tolerability profile. Antibiotic therapies are frequently associated with gastrointestinal disturbances and the risk of antimicrobial resistance, while isotretinoin is linked to mucocutaneous dryness, hepatotoxicity, and teratogenicity [27]. Notably, adjunctive probiotic supplementation has been shown to mitigate some of the gastrointestinal side effects associated with systemic acne treatments, particularly antibiotic-induced dysbiosis and isotretinoin-related alterations in gut microbiota composition [25].

Topical probiotics also exhibit a strong safety profile, with studies reporting excellent skin tolerability and a low incidence of irritation or sensitization. In some cases, topical formulations have been associated with improvements in skin barrier function and reduced erythema, further supporting their dermatological compatibility [28].

Patient-reported outcomes (PROs) further reinforce the clinical value of probiotic interventions. Several studies have documented significant improvements in quality-of-life measures, including reductions in acne-related psychological distress, enhanced self-esteem, and improved patient satisfaction with treatment outcomes [9]. These findings are particularly relevant given the well-established psychosocial burden of acne vulgaris. Additionally, patients receiving probiotics—either as monotherapy or adjunctive treatment—often report better overall treatment tolerability and a greater willingness to continue therapy compared to conventional regimens [18].

Collectively, current evidence suggests that probiotics represent a safe and well-tolerated therapeutic option in acne management, with the added benefit of improving patient-centered outcomes. Nevertheless, further large-scale, long-term studies are warranted to fully elucidate the safety profile across diverse populations and to standardize the reporting of adverse events in microbiome-targeted therapies.

4. Discussion

The present systematic review highlights the growing body of evidence supporting the involvement of the gut microbiome in the pathogenesis of acne vulgaris and underscores the therapeutic potential of probiotic interventions. Collectively, the analyzed studies reinforce the concept that acne is not solely a localized cutaneous disorder but rather a systemic inflammatory condition influenced by interactions within the gut-skin axis [7-9].

A key finding is the consistent association between gut microbiota dysbiosis and acne severity. Individuals with acne exhibit reduced microbial diversity, altered bacterial composition, and increased intestinal permeability [4,10,21]. These alterations may promote systemic low-grade inflammation through enhanced translocation of bacterial endotoxins and the increased production of pro-inflammatory cytokines such as IL-1β, IL-6, and TNF-α [8,11], thereby exacerbating inflammation within the pilosebaceous unit [7].

Metabolic and endocrine pathways also play a significant intermediary role. The dysregulation of insulin signaling and increased IGF-1 activity—both influenced by diet and microbiota—stimulate sebaceous gland activity and keratinocyte proliferation [15,16]. This provides a mechanistic link between dietary patterns, microbiome alterations, and acne pathogenesis [23].

Clinical evidence indicates that probiotic supplementation can significantly reduce acne lesion counts, particularly inflammatory lesions. Randomized controlled trials and meta-analyses suggest that oral probiotics may achieve outcomes comparable to conventional therapies while offering improved tolerability [18,19]. These effects are likely mediated through the restoration of microbial balance, enhancement of intestinal barrier function, and modulation of immune and inflammatory responses [9,20].

The efficacy of probiotics appears to be strain-specific, with *Lactobacillus* and *Bifidobacterium* species showing the most consistent benefits [27]. The route of administration is also important: oral probiotics act systemically via the gut-brain-skin axis, whereas topical probiotics directly influence the skin microbiome, inhibit *Cutibacterium acnes*, and support barrier repair [28,30]. These findings suggest potential advantages of combined therapeutic approaches.

Probiotics also demonstrate value as adjunctive therapy. Their co-administration with antibiotics or isotretinoin may enhance treatment efficacy and reduce adverse effects, particularly gastrointestinal disturbances and microbiome disruption [25,26].

From a safety perspective, probiotics exhibit a highly favorable profile, with only mild and transient gastrointestinal symptoms reported [19,27]. Compared to conventional systemic treatments, they represent a safer alternative or adjunct, particularly for patients concerned about side effects [25]. Improvements in patient-reported outcomes, including quality of life and psychological well-being, further support their clinical relevance [4].

However, several limitations must be considered. The available evidence is heterogeneous in terms of study design, probiotic strains, dosages, and treatment duration [18,20]. Additionally, many studies involve small sample sizes and short follow-up periods, limiting generalizability [19]. The specific microbial taxa and causal mechanisms underlying acne remain incompletely understood [21], and individual variability suggests a need for personalized therapeutic approaches [9].

Future research should focus on large-scale randomized controlled trials with standardized methodologies to define optimal probiotic regimens. Advances in metagenomics and metabolomics may further elucidate microbiome-related mechanisms and support the development of targeted therapies [8,20].

In conclusion, the modulation of the gut microbiome represents a promising strategy in acne management. While probiotics show considerable therapeutic potential, further research is required to establish standardized clinical guidelines and fully integrate microbiome-based approaches into dermatological practice [9,18].

5. Conclusions

The findings of this systematic review support the emerging concept that acne vulgaris is a multifactorial inflammatory condition influenced not only by cutaneous factors but also by systemic processes involving the gut microbiome. Increasing evidence indicates that gut dysbiosis may contribute to acne pathogenesis through immune dysregulation, metabolic disturbances, and enhanced inflammatory signaling within the gut-skin axis. Probiotic interventions, particularly those involving *Lactobacillus* and *Bifidobacterium* strains, demonstrate promising therapeutic potential by restoring microbial balance, improving intestinal barrier function, and modulating immune responses. Clinical studies suggest that probiotics may reduce acne severity, enhance treatment tolerability, and provide additional benefits when used as adjunctive therapy alongside conventional

treatments. Despite these encouraging results, current evidence remains heterogeneous, and further well-designed, large-scale randomized controlled trials are required to establish standardized protocols and clarify strain-specific effects. Overall, microbiome-targeted therapies represent a promising and evolving approach in the management of acne vulgaris, with the potential to complement and enhance existing therapeutic strategies.

Author's contribution

Here we present a detailed description of author's contribution to the creation of this manuscript. Conceptualization Agnieszka Jóźwicka Ewa Bąkowska and Wojciech Janikowski,; methodology, Aleksandra Stępka; software, Weronika Plichtowicz-Kordowska; check, Lena Jaworowicz, Maria Wieczorek, Aleksandra Stępka and Wojciech Janikowski; formal analysis, Karina Lewandowska; investigation, Agnieszka Jóźwicka; resources, Maria Wieczorek; data curation, Karina Lewandowska; writing - rough preparation, Agnieszka Jóźwicka; writing - review and editing Weronika Plichtowicz- Kordowska, Wojciech Janikowski; visualization, Ewa Bąkowska; supervision, Lena Jaworowicz; project administration, Agnieszka Jóźwicka. All authors have read and agreed with the published version of the manuscript.

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