Journal of Community Health Provision
Vol. 6, Issue 2, 2026
Page 656-667
DOI: https://doi.org/10.55885/jchp.v6i2.1041

Microbiome Modulation in Acne Vulgaris: Comprehensive Narative Review of Oral-Topical Biotics and Future Challenges

Dzakiyya Nur Dhiya[1], Imelda Matruty[1], Rahma Ziska[1]
[1]Master's Program in Pharmaceutical Sciences, Faculty of Pharmacy, Universitas Bhakti Kencana, Bandung, Indonesia
Email: 251ff07019@bku.ac.id, 251ff07012@bku.ac.id, rahma.ziska@bku.ac.id

Abstract. *Acne vulgaris is a skin disease with a high prevalence, whose pathophysiology involves microbiome dysbiosis, inflammation, and dysregulation of skin barrier function. The long-term use of antibiotics as the primary therapy can raise concerns about resistance, necessitating alternative approaches based on microbiome modulation. Objective: This narrative review aims to synthesize the latest primary evidence on biotic interventions (prebiotics, probiotics, postbiotics, and synbiotics) for acne vulgaris, administered via both oral and topical routes, and to compare the mechanisms of action, benefits, and limitations of each route of administration. Methods: Primary literature search in several databases, such as PubMed, MDPI, SpringerLink, Wiley Online Library, ScienceDirect, and Google Scholar. Priority literature examples are RCTs (randomized controlled trials) or clinical trials published within the last 7 years that discuss the use of biotic interventions for acne vulgaris. Results: Data synthesis indicates that topical biotic interventions containing postbiotics provide faster and more consistent clinical improvement in reducing inflammatory lesions, acne severity scores, and sebum parameters. Conversely, oral biotic interventions show longer-lasting and more variable effects, primarily through modulation of the gut-skin axis and systemic inflammation. Conclusion: Biotic interventions have potential as an alternative or supportive therapeutic approach for acne vulgaris, with oral postbiotics showing the most consistent benefit profile. However, further research with standardized designs and direct comparative testing is needed to strengthen the clinical evidence and its mechanistic action.*

Keywords: *Acne Vulgaris, Postbiotic, Prebiotic, Probiotic, Synbiotic*

Received: June 8, 2026 Received in Revised: July 30, 2026 Accepted: August 5, 2026

INTRODUCTION

Physical appearance, particularly the face, remains one of the aspects that receives considerable attention from most individuals worldwide (Todorov et al., 2015; Little, 2014). One common problem is the occurrence of acne, or Acne vulgaris. Recent studies show that the global prevalence of Acne vulgaris among populations aged 10–24 years has increased significantly, particularly among those aged 15–19 years (Zhu et al., 2025). Prevalence data in Indonesia show a similar pattern, with this condition occurring in 83–85% of females aged 14–17 years and 95% of males aged 16–19 years (Latifah et al., 2024; Isfandari, S., & Lolong, 2014; Rahman & Fajar, 2024).

This disease may develop into scarring and potentially have negative impacts on an individual's quality of life (De La Garza et al., 2025; Tan et al., 2022). Proper management of *Acne vulgaris* before it progresses to scarring is therefore important to prevent these consequences.

Pathophysiologically, this condition arises from a complex interaction among follicular hyperkeratinization, sebum production, immune response, and microbiome alterations within the skin pilosebaceous unit (Vasam et al., 2023; Mosca et al., 2025; Malicka et al., 2026; Kreouzi et al., 2025).

One treatment for *Acne vulgaris* is conventional therapy using antibiotics (Vasam et al., 2023). However, recent studies indicate that long-term antibiotic use as therapy for *Acne vulgaris* may lead to increased antibiotic resistance (Paul et al., 2025). This has resulted in a paradigm shift in the treatment of *Acne vulgaris*. One alternative to antibiotic therapy for *Acne vulgaris* is the use of biotic interventions, including prebiotics, probiotics, postbiotics, and synbiotics, which focus on restoring microbiome balance and suppressing inflammatory pathways through both local and systemic mechanisms (Sánchez-Pellicer et al., 2022; Niedźwiedzka et al., 2024; Wojciechowska & Dos, 2025; Chia et al., 2026; Umekar et al., 2026).

Although this paradigm shift is positive, it still has limitations and challenges. These can be seen in the substantial heterogeneity of current literature study designs, including variations in strains and formulations, differences in dosage and duration, and differences in clinical outcomes, all of which affect the formulation of firm clinical recommendations (Mohamed et al., 2025; Tjiu & Lu, 2025).

Based on this background, this narrative review was prepared to synthesize the latest primary evidence on biotic interventions for *Acne vulgaris* through oral and topical routes, as well as to compare the mechanisms of action, benefits, and limitations of each route, with the expectation that it may guide further experimental or clinical studies.

METHODS

Literature Search Strategy

The writing of this narrative review article was conducted through a search for international studies published in reputable journals from various databases, including PubMed, MDPI, SpringerLink, Wiley Online Library, ScienceDirect, and Google Scholar. The database search used variations of keywords such as “("acne vulgaris" OR acne OR pimple) AND (probiotics OR prebiotics OR postbiotics OR synbiotics) AND (oral OR topical) AND (efficacy OR "healing duration") AND ("randomized controlled trial")”.

Inclusion and Exclusion Criteria

The literature in the form of experimental studies used as primary data in this narrative review article was selected based on inclusion and exclusion criteria. The inclusion criteria applied to the literature included research articles with a true experimental design, such as randomized controlled trials and clinical trials, published in reputable international English-language journals, and discussing the treatment of acne vulgaris using biotic interventions. The included literature also had to be published within the last seven years to ensure high scientific relevance. The exclusion criteria included non-English international articles, articles that were irrelevant or did not discuss the scope of data to be synthesized, and articles published more than seven years ago. For evidence synthesis, eligible reports were classified into three categories: direct controlled evidence (randomized, placebo-controlled, split-face, or active-comparator studies enrolling participants with acne vulgaris and reporting clinical acne outcomes), direct exploratory evidence (open-label, pilot, self-controlled, or uncontrolled studies with acne-specific clinical outcomes), and indirect/supportive evidence (studies with non-acne populations, biomarker-only outcomes, or very small acne subgroups). Indirect/supportive evidence was used only for mechanistic interpretation and was not treated as proof of clinical efficacy.

RESULT AND DISCUSSION

Study Selection and Evidence Classification

After duplicate and clearly irrelevant records had been removed during search management, 15 unique primary reports were formally identified and screened. All 15 reports

were assessed in full text. Twelve studies met the criteria for direct clinical evidence because they enrolled participants with acne vulgaris and reported acne-related clinical outcomes. Three reports were excluded from the direct clinical-efficacy synthesis but retained as indirect/supportive evidence: Tsai et al. (2021) enrolled healthy adults and evaluated general skin-health outcomes; Rahmayani et al. (2019) enrolled participants with acne but primarily reported serum IL-10 without a direct clinical acne outcome; and Rybak et al. (2023) included only seven participants with acne within a broader study population. The study-selection flow was therefore 15 records screened, 15 full texts assessed, 12 studies included in the direct synthesis, and three studies retained only as indirect/supportive evidence.

Among the 12 direct studies, nine used controlled designs, including randomized, placebo-controlled, split-face, or active-comparator approaches, whereas three were direct exploratory studies with pilot, open-label, or self-controlled designs. The direct evidence comprised prebiotics (n = 1), probiotics (n = 3), synbiotics (n = 2), and postbiotics (n = 6). The three indirect/supportive reports evaluated probiotic interventions. Direct clinical outcomes included acne severity scores, total and inflammatory or non-inflammatory lesion counts, sebum parameters, and skin-barrier measures. Biomarker-only and general skin-health outcomes were described separately and were not combined with direct acne efficacy outcomes.

Table 1. Characteristics and Evidence Classification of Primary Literature

Reference	Study Design	Study Subjects	Intervention Duration	Evidence category
(Majeed et al., 2020)	Open-label comparative RCT	n = 64 (F and M); aged 18–35 years; mild to moderate acne	3 weeks	Direct controlled
(Ho et al., 2022)	RCT	n = 20 (F and M); aged 18–40 years; mild to moderate acne	4 weeks	Direct controlled
(Sathikulpakdee et al., 2022)	Double-blind RCT	n = 104 (F and M); aged 18–45 years; mild to moderate acne	4 weeks	Direct controlled
(Han et al., 2022)	Split-face RCT	n = 20 (F and M); aged 19–39 years; mild to moderate acne	4 weeks	Direct controlled
(Cui et al., 2022)	Pilot clinical study	n = 30 (F and M); aged 18–45 years; mild to moderate acne	4 weeks	Direct exploratory
(Li et al., 2025)	Self-controlled study	n = 20 (mostly F); aged 18–35 years; mild to moderate acne	4 weeks	Direct exploratory
(Afzal et al., 2025)	Open-label prospective	n = 30 (F and M); aged 18–40 years; mild to moderate non-cystic acne	7 weeks	Direct exploratory
(Tsai et al., 2021)	Clinical trial + in vitro study	n = 36 healthy adults (F and M); aged 20–50 years; not diagnosed with acne	8 weeks	Indirect/supportive
(Rahmayani et al., 2019)	Pre–post clinical study	n = 33 (F and M); aged 18–25 years; acne severity not reported	30 days	Indirect/supportive
(Kim et al., 2021)	Double-blind, placebo-controlled RCT	n = 30 (F and M); aged 19–39 years; mild to moderate acne	12 weeks	Direct controlled

(Rybak et al., 2023)	Prospective placebo-controlled	n = 25 total (7 with acne; F and M); aged 18–45 years; acne severity not reported	8 weeks	Indirect/supportive
(Rinaldi et al., 2022)	Double-blind RCT	n = 114 (F and M); aged 18–45 years; mild to moderate acne	8 weeks	Direct controlled
(Eguren et al., 2024)	Double-blind, placebo-controlled RCT	n = 74 (F and M); aged 12–30 years; mild to moderate acne	12 weeks	Direct controlled
(Min et al., 2025)	Comparative RCT	n = 36 (mostly F); aged 18–35 years; mild to moderate non-cystic acne	8 weeks	Direct controlled
(Atefi et al., 2025)	Double-blind RCT	n = 80 (F and M); aged 18–35 years; moderate acne	3 months	Direct controlled

Topical studies generally used shorter intervention periods than oral studies. Most direct topical studies lasted 3-7 weeks, whereas controlled oral studies commonly assessed outcomes after 8-12 weeks or three months. This descriptive difference should not be interpreted as proof that topical biotics act faster, because route of administration was confounded by study design, comparator selection, formulation, outcome definitions, and timing of assessment. No head-to-head trial directly comparing oral and topical biotic interventions was identified.

Within the direct controlled evidence, topical postbiotic studies reported reductions in inflammatory lesions, acne severity scores, porphyrin levels, and sebum-related parameters (Majeed et al., 2020; Ho et al., 2022; Sathikulpakdee et al., 2022; Han et al., 2022). These controlled studies provide the strongest support for a local clinical effect, although confidence remains limited by small samples, short follow-up, and, in the study by Majeed et al. (2020), an open-label design. Direct exploratory studies also reported lesion reduction, sebum improvement, or better skin-barrier parameters (Cui et al., 2022; Li et al., 2025; Afzal et al., 2025), but the absence of an adequate control group means that treatment effects cannot be separated from natural acne fluctuation, concurrent skincare, regression to the mean, or placebo effects. The findings of Tsai et al. (2021) regarding porphyrin reduction and hydration were classified as supportive rather than direct evidence because the participants were healthy adults without acne vulgaris.

For oral interventions, controlled studies reported improvements in lesion counts or acne severity after probiotic or synbiotic supplementation, either alone or as an adjunct to conventional therapy (Kim et al., 2021; Rinaldi et al., 2022; Eguren et al., 2024; Min et al., 2025; Atefi et al., 2025). Nevertheless, the consistency of this evidence is reduced by differences in strains, multi-agent formulations, concomitant treatment, comparator groups, and outcome definitions. Rahmayani et al. (2019) was interpreted only as mechanistic support because an increase in serum IL-10 does not by itself demonstrate clinical acne improvement. Rybak et al. (2023) was also classified as supportive because the acne analysis was based on only seven participants, resulting in low precision and limited generalizability. Accordingly, controlled oral studies suggest potential benefit, but biomarker-only findings and small subgroup analyses should not be interpreted as equivalent to evidence from adequately powered acne-specific trials.

Table 2. Clinical Outcome Results from Primary Data

Reference	Biotic Type	Route	Strain / Component	Main Mechanism of Action	Clinical Outcomes	Limitations
(Majeed et al., 2020)	Postbiotic	Topical	*Bacillus coagulans* (LactoSporin®)	Antibacterial activity against *C. acnes*, 5α-reductase	↓ comedones, papules, sebum; comparable to BPO	Short duration; open-label

Reference	Biotic Type	Route	Strain / Component	Main Mechanism of Action	Clinical Outcomes	Limitations
				inhibition, ↓ sebum		
(Ho et al., 2022)	Postbiotic	Topical	TYCA06/AP-32/CP-9 co-fermentation + collagen	Antimicrobial, anti-inflammatory effects (↓ TSLP, IL-33), wound healing	↓ inflammation, porphyrin, acne lesions	Small sample; no active comparator
(Sathikulpakdee et al., 2022)	Postbiotic	Topical	*L. paracasei* MSMC 39-1 (cell-free supernatant)	Antibacterial activity, ↓ TNF-α	↓ inflammatory lesions comparable to BPO; milder side effects	Did not assess the microbiome
(Han et al., 2022)	Postbiotic	Topical	*Enterococcus faecalis* CBT SL-5 ferment	Microbiome modulation, bacteriocins	↓ acne scores, ↓ dysbiosis	Limited barrier parameters
(Cui et al., 2022)	Postbiotic	Topical	*Lactiplantibacillus plantarum* ferment lysate	↓ sebum, ↓ TEWL, antibacterial activity	Significant ↓ acne lesions	No control group; pilot study
(Li et al., 2025)	Postbiotic	Topical	*Lactobacillus ferment lysate*	*Barrier repair, microbiota modulation*	↓ GAGS >50%, ↑ satisfaction	No control group
(Afzal et al., 2025)	Prebiotic	Topical	*Prebiotic gel cream*	Selection of healthy *C. acnes* strains, ↑ genetic barrier function	↓ total and inflammatory lesions	*Open-label; no comparator*
(Tsai et al., 2021)	Probiotic	Topical	*Lactobacillus plantarum* GMNL6	Skin microbiome modulation, ↓ *C. acnes* and *S. aureus*, ↑ collagen	↓ porphyrin, ↑ hydration, improved skin condition	Not an acne-specific study; small sample
(Rahmayani et al., 2019)	Probiotic	Oral	Multi-strain, not specified	↑ systemic IL-10 anti-inflammatory response	Significant ↑ IL-10	Did not measure direct clinical outcomes
(Kim et al., 2021)	Probiotic	Oral	*L. plantarum CJLP55, 10^{10} CFU/day*	Gut–skin axis modulation, ↓ sebum TG, ↑ ceramide	↓ number and severity of acne lesions	Limited sample; indirect biomarkers

Reference	Biotic Type	Route	Strain / Component	Main Mechanism of Action	Clinical Outcomes	Limitations
(Rybak et al., 2023)	Probiotic	Oral	*Spore-based probiotic*	*Gut–skin axis, ↑ SCFA*	↓ acne lesions, ↓ sebum trend	Small acne subanalysis
(Rinaldi et al., 2022)	Sinbiotik	Oral	*B. breve, L. casei, L. salivarius + botanicals*	*Rebalancing of gut microbiota*	↓ inflammatory lesions and sebum	Specific effects difficult to separate
(Eguren et al., 2024)	Probiotik	Oral	*L. rhamnosus + Arthrospira platensis*	↑ SCFA, ↓ inflammation	↓ non-inflammatory lesions and GAGS	Did not assess the skin microbiome
(Min et al., 2025)	Sinbiotik	Oral	*Multi-strain + botanicals and prebiotics*	*Gut–skin axis, androgen regulation*	Significant ↓ total acne lesion count	Multi-agent formulation; mechanism difficult to isolate
(Atefi et al., 2025)	Probiotik	Oral adjuvant	*Multi-strain, Lactobacillus and Bifidobacterium*	Antibiotic synergy, ↓ inflammation	Greater ↓ GAGS compared with control	Did not evaluate the microbiome

Strength of Evidence According to Study Design

The highest level of evidence in this review came from double-blind placebo-controlled or randomized controlled studies that enrolled acne-specific populations and measured clinical lesion or severity outcomes (Dall'Oglio et al., 2021; Sugandhi & Bharata, 2025; Jaiswal et al., 2024). These studies support the potential efficacy of both topical and oral biotic interventions, but they do not establish superiority of one administration route because no direct oral-versus-topical comparison was available. Open-label comparative and split-face studies provide useful but more moderate evidence because outcome assessment may be influenced by lack of blinding, short follow-up, or within-person treatment effects.

Pilot, open-label uncontrolled, self-controlled, biomarker-only, and small-subgroup studies were treated as hypothesis-generating evidence. Their results may clarify biological plausibility and inform future trial design, but they cannot independently establish treatment efficacy or equivalence with benzoyl peroxide, antibiotics, or placebo. Consequently, the synthesis gives greater interpretive weight to controlled acne-specific trials and uses exploratory or supportive studies only to contextualize mechanisms, feasibility, and research gaps.

Mechanisms Underlying Topical and Oral Routes of Biotic Product Intervention

The differences in clinical outcomes examined in the two interventions, namely the oral and topical routes, may be caused by mechanisms of action that depend on effector molecules (Lebeer et al., 2018). Effector molecules are molecules that can influence the regulation of other molecules, either by inhibiting or activating them, such as proteins, hormones, immune responses, and others (Arce-Sillas et al., 2016; Ramírez-Valdespino et al., 2019; Abdul et al., 2020). This has been explained in previous studies, in which examples of probiotic effector molecules from *Lactobacillus* and *Bifidobacterium* strains include anatomy-specific pili, S-layer proteins, exopolysaccharides, muropeptides, and metabolites produced by these strains (Lebeer et al., 2018). Studies by(Han et al., 2022) showed differences in phylogenetic diversity that may act as effector molecules in each sample taken from the skin of participating subjects. These were measured based on alpha diversity, which quantifies the variety of microbiomes at one site on the skin, and beta diversity, which describes differences in microbiome variety across several skin

sites within the same individual or between different individuals. These findings indicate the influence of clinical outcome severity between participants who were satisfied with topical therapy and those who were not satisfied (Han et al., 2022).

Another factor is the difference in target pathways of action. The oral route does not directly target microbiome variation on the skin, but works systemically and contributes to the improvement of overall inflammatory conditions in the individual's body, rather than focusing only on the skin (Deng et al., 2024). The topical route may have a faster onset and a shorter estimated duration of therapy because it offers the advantage of allowing biotic products to interact directly with the skin microbiome of individuals with acne vulgaris (Deng et al., 2024;. Zhao et al., 2023). This is consistent with the study by Li et al. (2025), which showed that a combination of postbiotic formulation and microneedling technology improved skin microbiome repair, reduced sebum and inflammation, and enhanced skin barrier function in a shorter duration (Li et al., 2025).

Mechanistically, the oral route works systemically by modulating the gut microbiome, which affects the systemic immune response, lipid metabolism, and interactions with metabolites produced by microbes in the body. These processes indirectly influence sebaceous gland activity and skin inflammation (Salem et al., 2018; Zhao et al., 2025). Although this systemic mechanism provides the main basis for the use of oral biotic products in acne vulgaris, oral route interventions may produce delayed outcomes and allow significant variation between individuals. This occurs because each individual may respond differently, especially when the intervention is delivered orally and enters the systemic circulation, where the level of tolerability and sensitivity varies among individuals. These mechanistic differences between topical and oral route interventions contribute to a slower onset and greater heterogeneity in the clinical outcomes of clinical trials using oral biotic products (Kim et al., 2021; Rinaldi et al., 2022).

Postbiotics as a Primary Modality in Topical Therapy

In the field of topical formulation research, postbiotics have become an increasingly attractive therapeutic modality. Compared with probiotics, which contain live beneficial bacterial strains, postbiotics usually consist of dead bacteria, metabolites, or fermentation products that retain the biological activity of the biotic product itself without concerns related to microbial viability, contamination, and storage stability of the formulation (Dinić et al., 2025; Hashemi et al., 2025).

Two controlled studies evaluated topical postbiotic formulations against conventional topical management. Majeed et al. (2020) used an open-label randomized comparative design, whereas Sathikulpakdee et al. (2022) used a randomized controlled design. Both reported clinical improvement broadly comparable to benzoyl peroxide with favorable tolerability; however, these findings should be interpreted as preliminary comparative evidence rather than definitive equivalence because of short treatment periods and limitations in blinding, sample size, and outcome standardization.

From a mechanistic perspective, products with postbiotics as the main active ingredient offer multifaceted activities, including antimicrobial effects against *C. acnes*, modulation of inflammatory signaling pathways, and improvement of skin barrier function (Dinić et al., 2025; Li et al., 2025). Other experimental studies have also shown that specific postbiotic components, such as bacteriocins and short-chain fatty acids, can exert immunomodulatory effects on keratinocytes without inducing cytotoxicity (Dinić et al., 2024; Huang et al., 2021; Pat et al., 2026).

However, the term postbiotic is still defined inconsistently across different studies. There is often considerable variability in fermentation processes, strain selection, and non-standardized metabolite composition, creating substantial limitations and research gaps. These challenges must be addressed before postbiotic-based treatment can be widely implemented in clinical practice.

Clinical Role and Limitations of Oral Probiotics and Synbiotics

Oral probiotic and synbiotic preparations were generally evaluated as complementary therapies or as components of multi-agent regimens rather than as uniform monotherapies. The most persuasive findings came from controlled acne-specific trials reporting reductions in lesion counts or severity (Kim et al., 2021; Rinaldi et al., 2022; Eguren et al., 2024; Atefi et al., 2025). Comparative findings from Min et al. (2025) were considered direct controlled evidence, but the multi-component formulation makes it difficult to isolate the effect of the synbiotic component. Biomarker-only and small-subgroup studies were not used to establish clinical efficacy.

However, because oral probiotics and synbiotics show significant heterogeneity in strain composition, dosage, and formulation, their clinical utility remains difficult to generalize for broader therapeutic application. Many studies still only use the term "multi-strain," which hinders the actual synthesis of evidence regarding which strains play the most important role and how they work in the treatment of acne vulgaris (Rinaldi et al., 2022). Several studies have also directly assessed changes in the skin microbiome or the correlation between systemic biomarkers and local skin outcomes, meaning that the clarity of the mechanisms of action of oral probiotics or synbiotics remains limited. Therefore, the limitations of oral probiotics and synbiotics include the absence of an established optimal formulation, variability in intervention dosage, and uncertainty regarding patient criteria suitable for this therapy.

Methodological Considerations and Research Implications

Methodological heterogeneity substantially limits the certainty and comparability of the available evidence. The 15 reports included nine direct controlled studies, three direct exploratory studies, and three indirect/supportive studies. Common limitations included small samples, short intervention periods, incomplete blinding, non-standardized acne severity measures, variation in strains and formulations, concomitant therapies, and inconsistent microbiome assessment. Because this narrative review applied a design-based evidence classification rather than a formal risk-of-bias instrument, the categories indicate relative evidentiary strength but should not be interpreted as a complete methodological quality score.

From a scientific perspective, future studies need to prioritize standardized reporting, including biotic composition, dosage, and formulation stability, accompanied by the use of clinical and microbiological outcomes. The integration of skin and gut microbiome analyses, combined with metabolomic approaches, has the potential to provide a deeper understanding of the mechanisms through which biotic interventions work. Efforts to address these limitations not only strengthen the evidence base but also open opportunities for relevant further research, particularly in the fields of formulation science, dermatology, and clinical pharmacology.

CONCLUSION

Overall, controlled acne-specific studies indicate that biotic interventions may contribute to the management of acne vulgaris through microbiome and inflammatory modulation. Topical postbiotic interventions showed relatively consistent short-term reductions in inflammatory lesions, severity scores, and sebum-related parameters, whereas controlled oral probiotic or synbiotic studies suggested more variable improvements over longer assessment periods. These conclusions are based primarily on direct controlled evidence; exploratory studies and the indirect/supportive reports by Tsai et al. (2021), Rahmayani et al. (2019), and Rybak et al. (2023) were not treated as independent proof of clinical efficacy. Based on the consistency of findings, postbiotics derived from *Lactobacillus plantarum*, *Lactobacillus paracasei*, and *Bacillus coagulans* show strong potential, particularly when applied as topical preparations compared with the use of live probiotics, which tend to produce effects over a longer duration. In line with the objective of this narrative review, the synthesis of current evidence confirms clear differences between oral and topical biotic interventions in terms of mechanisms of action, clinical benefits, and methodological limitations. Future research should focus on the standardization of biotic types and dosages, direct comparative clinical trials between routes of administration, and the use of standardized clinical outcomes to support the development of more effective and applicable microbiome-based therapies for acne vulgaris.

ISSN 2776-1150 (Print), ISSN 2776-1169 (online)

ACKNOWLEDGEMENTS

The authors would like to express their gratitude to all parties involved in the preparation of this article, particularly those who provided guidance and support.

REFERENCES

Abdul Malik, N. A., Kumar, I. S., & Nadarajah, K. (2020). Elicitor and receptor molecules: orchestrators of plant defense and immunity. *International journal of molecular sciences*, *21*(3), 963. https://doi.org/10.3390/ijms21030963

Afzal, L., Dulai, A. S., Khan, Z. e. huma, Nguyen, N., Afzal, N., Gunt, H. B., & Sivamani, R. K. (2025). Open-Label, Prospective Study of a Prebiotic Gel Cream on Its Efficacy of Mild to Moderate Acne Management and Effects on the Functional Skin Microbiome. *Journal of Cosmetic Dermatology*, *24*(10). https://doi.org/10.1111/jocd.70138

Arce-Sillas, A., Álvarez-Luquín, D. D., Tamaya-Domínguez, B., Gomez-Fuentes, S., Trejo-García, A., Melo-Salas, M., ... & Adalid-Peralta, L. (2016). Regulatory T cells: molecular actions on effector cells in immune regulation. *Journal of immunology research*, *2016*(1), 1720827. https://doi.org/10.1155/2016/1720827

Atefi, N., Mohammadi, M., Bodaghabadi, M., Mehrali, M., Behrangi, E., Ghassemi, M., Jafarzadeh, A., & Goodarzi, A. (2025). Evaluating the Effectiveness of Probiotic Supplementation in Combination With Doxycycline for the Treatment of Moderate Acne: A Randomized Double-Blind Controlled Clinical Trial. *Journal of Cosmetic Dermatology*, *24*(1). https://doi.org/10.1111/jocd.16614

Chia, J., Carma, A., Alwyn, A., Cho, R., Hill, D. S., & Borrello, M. T. (2026). The Skin Microbiome Revolution: The Science and Challenges of Prebiotics, Probiotics, and Postbiotics in Skincare. *Cosmetics*, *13*(1), 43. https://doi.org/10.3390/cosmetics13010043

Cui, H., Guo, C., Wang, Q., Feng, C., & Duan, Z. (2022). A pilot study on the efficacy of topical lotion containing anti-acne postbiotic in subjects with mild -to -moderate acne. *Frontiers in Medicine*, *9*. https://doi.org/10.3389/fmed.2022.1064460

Dall'Oglio, F., Nasca, M. R., Fiorentini, F., & Micali, G. (2021). Diet and acne: review of the evidence from 2009 to 2020. *International journal of dermatology*, *60*(6), 672-685. https://doi.org/10.1111/ijd.15390

De La Garza, H., Trepanowski, N., Flores, R., Visutjindaporn, P., Patzelt, N., & Vashi, N. A. (2025). The Impact of Acne Scarring on Quality of Life, Willingness-to-pay, and Time Trade-off: A Cross-sectional Analysis. *The Journal of Clinical and Aesthetic Dermatology*, *18*(3), 71–73.

Deng, K., Fan, X., Yuan, Z., & Li, D. (2024). Probiotic effects on skin health: comprehensive visual analysis and perspectives. In *Frontiers in Microbiology* (Vol. 15). Frontiers Media SA. https://doi.org/10.3389/fmicb.2024.1453755

Dinić, M., Burgess, J. L., Lukić, J., Catanuto, P., Radojević, D., Marjanović, J., Verpile, R., Thaller, S. R., Gonzalez, T., Golić, N., Strahinić, I., Tomic-Canic, M., & Pastar, I. (2024). Postbiotic lactobacilli induce cutaneous antimicrobial response and restore the barrier to inhibit the intracellular invasion of *Staphylococcus aureus* in vitro and ex vivo. *The FASEB Journal*, *38*(14). https://doi.org/10.1096/fj.202400054RR

Dinić, M., Gonzalez, T., Caridad Hernandez, M., Radojević, D., Fernandez, L., Golić, N., & Pastar, I. (2025). Postbiotics as microbial-derived therapeutics for wound healing disorders: from molecular mechanisms to future application. *Cell Communication and Signaling*, *23*(1), 504. https://doi.org/10.1186/s12964-025-02494-4

Eguren, C., Navarro-Blasco, A., Corral-Forteza, M., Reolid-Pérez, A., Setó-Torrent, N., García-Navarro, A., Prieto-Merino, D., Núñez-Delegido, E., Sánchez-Pellicer, P., & Navarro-López,

V. (2024). A Randomized Clinical Trial to Evaluate the Efficacy of an Oral Probiotic in Acne Vulgaris. *Acta Dermato-Venereologica*, *104*. https://doi.org/10.2340/actadv.v104.33206

Han, H. S., Shin, S. H., Choi, B. Y., Koo, N., Lim, S., Son, D., Chung, M. J., Park, K. Y., & Sul, W. J. (2022). A split face study on the effect of an anti-acne product containing fermentation products of Enterococcus faecalis CBT SL-5 on skin microbiome modification and acne improvement. *Journal of Microbiology*, *60*(5), 488–495. https://doi.org/10.1007/s12275-022-1520-6

Hashemi, S., Rafati, A., Roohinejad, S., Yaghoobi, F., & Salehi, A. (2025). Postbiotics as Emerging Therapeutics for Skin Wound Healing and Dermatological Care: Clinical Trends and Mechanistic Insights. *International Wound Journal*, *22*(12). https://doi.org/10.1111/iwj.70799

Ho, H. H., Chen, C. W., Yi, T. H., Huang, Y. F., Kuo, Y. W., Lin, J. H., Chen, J. F., Tsai, S. Y., Chan, L. P., & Liang, C. H. (2022). Novel application of a Co-Fermented postbiotics of TYCA06/AP-32/CP-9/collagen in the improvement of acne vulgaris—A randomized clinical study of efficacy evaluation. *Journal of Cosmetic Dermatology*, *21*(11), 6249–6260. https://doi.org/10.1111/jocd.15228

Huang, F., Teng, K., Liu, Y., Cao, Y., Wang, T., Ma, C., Zhang, J., & Zhong, J. (2021). Bacteriocins: Potential for Human Health. *Oxidative Medicine and Cellular Longevity*, *2021*(1). https://doi.org/10.1155/2021/5518825

Isfandari, S., & Lolong, D. B. (2014). Analisa faktor risiko dan status kesehatan remaja Indonesia pada dekade mendatang. *Buletin Penelitian Kesehatan*, *42*(2), 122-130.

Jaiswal, S., Jawade, S., Madke, B., Gupta, S., & Gupta, S. N. (2024). Recent trends in the management of acne vulgaris: a review focusing on clinical studies in the last decade. *Cureus*, *16*(3).

Kim, M. J., Kim, K. P., Choi, E., Yim, J. H., Choi, C., Yun, H. S., Ahn, H. Y., Oh, J. Y., & Cho, Y. (2021). Effects of lactobacillus plantarum cjlp55 on clinical improvement, skin condition and urine bacterial extracellular vesicles in patients with acne vulgaris: A randomized, double-blind, placebo-controlled study. *Nutrients*, *13*(4). https://doi.org/10.3390/nu13041368

Kreouzi, M., Theodorakis, N., Nikolaou, M., Feretzakis, G., Anastasiou, A., Kalodanis, K., & Sakagianni, A. (2025). Skin microbiota: mediator of interactions between metabolic disorders and cutaneous health and disease. *Microorganisms*, *13*(1), 161. https://doi.org/10.3390/microorganisms13010161

Latifah, U., Maulida, I., & Henda K, A. (2024). The Influence of Stress on the Severity of Acne Vulgaris in Adolescents. *Indonesian Journal of Global Health Research*, *7*(1), 117–124. https://doi.org/10.37287/ijghr.v7i1.4010

Lebeer, S., Bron, P. A., Marco, M. L., Van Pijkeren, J. P., O'Connell Motherway, M., Hill, C., Pot, B., Roos, S., & Klaenhammer, T. (2018). Identification of probiotic effector molecules: present state and future perspectives. In *Current Opinion in Biotechnology* (Vol. 49, pp. 217–223). Elsevier Ltd. https://doi.org/10.1016/j.copbio.2017.10.007

Li, Z., Li, P., Xu, Y., Yan, C., Ma, X., Wang, H., Cheng, H., Zeng, J., Li, T., Li, X., Zhou, J., Zhang, J., Zhou, J., Yang, R., Wu, Y., Li, L., Lai, W., Zhao, J., Liu, Z., & Meng, Q. (2025). Efficacy of a Postbiotic Formulation Combined With Microneedling for Mild-to-Moderate Acne: A Self-Control Study. *Journal of Cosmetic Dermatology*, *24*(2). https://doi.org/10.1111/jocd.16703

Little, A. C. (2014). Facial attractiveness. *Wiley Interdisciplinary Reviews: Cognitive Science*, *5*(6), 621-634. https://doi.org/10.1002/wcs.1316

Majeed, M., Majeed, S., Nagabhushanam, K., Mundkur, L., Rajalakshmi, H. R., Shah, K., & Beede, K. (2020). Novel topical application of a postbiotic, lactosporin®, in mild to moderate acne: A randomized, comparative clinical study to evaluate its efficacy, tolerability and safety. *Cosmetics*, *7*(3). https://doi.org/10.3390/COSMETICS7030070

Malicka, N., Tłustochowicz, K., Łuczak, K., Krajewska, A., Korba, M., Polkowska, W., ... & Dębczak, J. (2026). Pathophysiology of Acne Vulgaris: An Integrative Narrative Review. *Quality in Sport*, *53*, 69766-69766. https://doi.org/10.12775/QS.2026.53.69766

Min, M., Afzal, N., Maloh, J., Dulai, A. S., Ahmad, N., Pinzauti, D., & Sivamani, R. K. (2025). Prospective Comparative Study of an Oral Synbiotic and a Myoinositol-Based Herbal Supplement in Modifying Hormone Levels and the Gut Microbiome in Non-cystic Acne. *Dermatology and Therapy*, *15*(6), 1331–1350. https://doi.org/10.1007/s13555-025-01411-4

Mohamed, M., Ullah, A., Hassan, R., Hamza, M., Mohamed, I., & Salam, M. (2025). The Impact of Probiotics on Acne Vulgaris: A Meta-Analysis of Randomized Controlled Trials. *Cureus*. https://doi.org/10.7759/cureus.97010

Mosca, S., Ottaviani, M., Briganti, S., Di Nardo, A., & Flori, E. (2025). The sebaceous gland: a key player in the balance between homeostasis and inflammatory skin diseases. *Cells*, *14*(10), 747. https://doi.org/10.3390/cells14100747

Niedźwiedzka, A., Micallef, M. P., Biazzo, M., & Podrini, C. (2024). The role of the skin microbiome in acne: challenges and future therapeutic opportunities. *International journal of molecular sciences*, *25*(21), 11422. https://doi.org/10.3390/ijms252111422

Pat, Y., Yazici, D., Babayev, H., Ardicli, S., Bu, X., Simmons, S., Almada, A., Avena, C., Jensen, T., Dhir, R., Westermann, P., Garcia-Sanchez, A., Li, M., Ardicli, O., Zeyneloglu, C., Pane, M., Amoruso, A., Messner, C., Ogulur, I., … Akdis, C. A. (2026). Postbiotics and Nicotinamide Utilize Distinct Mechanisms to Improve Skin Barrier Integrity, Inflammation, and Keratinocyte Differentiation. *Allergy*. https://doi.org/10.1111/all.70225

Paul, N. A., Bhat M, R., Antony, B., & Jayaraman, J. (2025). Antibiotic resistance and biofilm formation in Cutibacterium acnes: A descriptive cross-sectional study. *Indian Journal of Dermatology, Venereology and Leprology*, *91*, 315. https://doi.org/10.25259/IJDVL_539_2024

Rahman, R. A., & Fajar, N. A. (2024). Analisis faktor risiko kejadian anemia pada remaja putri: Literatur review. *Jurnal kesehatan komunitas (Journal of community health)*, *10*(1), 133-140. https://doi.org/10.25311/keskom.Vol10.Iss1.1403

Rahmayani, T., Putra, I. B., & Jusuf, N. K. (2019). The effect of oral probiotic on the interleukin-10 serum levels of acne vulgaris. *Open Access Macedonian Journal of Medical Sciences*, *7*(19), 3249–3252. https://doi.org/10.3889/oamjms.2019.718

Ramírez-Valdespino, C. A., Casas-Flores, S., & Olmedo-Monfil, V. (2019). Trichoderma as a model to study effector-like molecules. *Frontiers in microbiology*, *10*, 1030. https://doi.org/10.3389/fmicb.2019.01030

Rinaldi, F., Marotta, L., Mascolo, A., Amoruso, A., Pane, M., Giuliani, G., & Pinto, D. (2022). Facial Acne: A Randomized, Double-Blind, Placebo-Controlled Study on the Clinical Efficacy of a Symbiotic Dietary Supplement. *Dermatology and Therapy*, *12*(2), 577–589. https://doi.org/10.1007/s13555-021-00664-z

Rybak, I., Haas, K. N., Dhaliwal, S. K., Burney, W. A., Pourang, A., Sandhu, S. S., Maloh, J., Newman, J. W., Crawford, R., & Sivamani, R. K. (2023). Prospective Placebo-Controlled Assessment of Spore-Based Probiotic Supplementation on Sebum Production, Skin Barrier Function, and Acne. *Journal of Clinical Medicine*, *12*(3). https://doi.org/10.3390/jcm12030895

Salem, I., Ramser, A., Isham, N., & Ghannoum, M. A. (2018). The Gut Microbiome as a Major Regulator of the Gut-Skin Axis. *Frontiers in Microbiology*, *9*. https://doi.org/10.3389/fmicb.2018.01459

Sánchez-Pellicer, P., Navarro-Moratalla, L., Núñez-Delegido, E., Ruzafa-Costas, B., Agüera-Santos, J., & Navarro-López, V. (2022). Acne, Microbiome, and Probiotics: The Gut–Skin Axis. *Microorganisms*, *10*(7), 1303. https://doi.org/10.3390/microorganisms10071303

Sathikulpakdee, S., Kanokrungsee, S., Vitheejongjaroen, P., Kamanamool, N., Udompataikul, M., & Taweechotipatr, M. (2022). Efficacy of probiotic-derived lotion from Lactobacillus paracasei MSMC 39-1 in mild to moderate acne vulgaris, randomized controlled trial. *Journal of Cosmetic Dermatology*, *21*(10), 5092–5097. https://doi.org/10.1111/jocd.14971

Sugandhi, D. A. A. G., & Bharata, P. E. V. N. (2025). Efficacy and Safety of Topical Tretinoin Monotherapy versus Vehicle in the Treatment of Acne Vulgaris: A Meta-Analysis of Randomised Controlled Trials. *Scientific Journal of Dermatology and Venereology*, *3*(2), 86-95. https://doi.org/10.59345/sjdv.v3i2.297

Tan, J., Beissert, S., Cook-Bolden, F., Chavda, R., Harper, J., Hebert, A., Lain, E., Layton, A., Rocha, M., Weiss, J., & Dréno, B. (2022). Impact of Facial Atrophic Acne Scars on Quality of Life: A Multi-country Population-Based Survey. *American Journal of Clinical Dermatology*, *23*(1), 115–123. https://doi.org/10.1007/s40257-021-00628-1

Tjiu, J.-W., & Lu, C.-F. (2025). Oral Probiotics in Acne vulgaris: A Systematic Review and Meta-Analysis of Double-Blind Randomized Clinical Trials. *Medicina*, *61*(12), 2152. https://doi.org/10.3390/medicina61122152

Todorov, A., Olivola, C. Y., Dotsch, R., & Mende-Siedlecki, P. (2015). Social attributions from faces: Determinants, consequences, accuracy, and functional significance. *Annual review of psychology*, *66*(1), 519-545. https://doi.org/10.1146/annurev-psych-113011-143831

Tsai, W. H., Chou, C. H., Chiang, Y. J., Lin, C. G., & Lee, C. H. (2021). Regulatory effects of lactobacillus plantarum-GMNL6 on human skin health by improving skin microbiome. *International Journal of Medical Sciences*, *18*(5), 1114–1120. https://doi.org/10.7150/ijms.51545

Umekar, M., Chaudhary, A., Koche, S., Dhule, D., Shidhaye, S., Khobragade, R., ... & Trivedi, R. (2026). Redefining acne treatment: emerging role of probiotics in dermatology. *Archives of Microbiology*, *208*(1), 27. https://doi.org/10.1007/s00203-025-04582-y

Vasam, M., Korutla, S., & Bohara, R. A. (2023). Acne vulgaris: A review of the pathophysiology, treatment, and recent nanotechnology based advances. In *Biochemistry and Biophysics Reports* (Vol. 36). Elsevier B.V. https://doi.org/10.1016/j.bbrep.2023.101578

Wojciechowska, K., & Dos Santos Szewczyk, K. (2025). The skin microbiome and bioactive compossunds: mechanisms of modulation, dysbiosis, and dermatological implications. *Molecules*, *30*(22), 4363. https://doi.org/10.3390/molecules30224363

Zhao, L., Chen, J., Bai, B., Song, G., Zhang, J., Yu, H., Huang, S., Wang, Z., & Lu, G. (2023). Topical drug delivery strategies for enhancing drug effectiveness by skin barriers, drug delivery systems and individualized dosing. In *Frontiers in Pharmacology* (Vol. 14). Frontiers Media SA. https://doi.org/10.3389/fphar.2023.1333986

Zhao, Y., Yu, C., Zhang, J., Yao, Q., Zhu, X., & Zhou, X. (2025). The gut-skin axis: Emerging insights in understanding and treating skin diseases through gut microbiome modulation (Review). *International Journal of Molecular Medicine*, *56*(6), 1–15. https://doi.org/10.3892/ijmm.2025.5651

Zhu, Z., Zhong, X., Luo, Z., Liu, M., Zhang, H., Zheng, H., & Li, J. (2025). Global, regional and national burdens of acne vulgaris in adolescents and young adults aged 10–24 years from 1990 to 2021: a trend analysis. *British Journal of Dermatology*, *192*(2), 228–237. https://doi.org/10.1093/bjd/ljae352

