



MICROBIOTA MANIPULATION: A LITERATURE REVIEW OF ORAL AND TOPICAL PROBIOTIC EFFICACY IN ACNE VULGARIS

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ABSTRACT

Acne Vulgaris (AV) is a chronic inflammatory skin condition affecting global population, especially adolescents and young adults. Recent study highlighted the potential role of probiotics in managing AV by controlling the gut-skin microbiome axis. Objective: This review aimed to examine the role of human microbiota in controlling AV and explore how probiotics can contribute to the prevention and treatment of AV. Methods: A literature search was conducted from multiple databases (Google Scholar, PubMed, Hindawi, Science Direct, Proquest, and Cochrane) from 2014 to 2024. The inclusion criteria is study written in English that focus on probiotics effects on AV, with a total of 1,435 articles early identified and 1,217 articles carefully screened. Results: Multiple studies showed the potential of both oral and topical probiotics in managing AV. Key findings include: Probiotics can inhibit bacteria that can cause acne like *Cutibacterium acnes*, some probiotic strains (e.g., *Lactobacillus* and *Bifidobacterium*) showed promising improvements in reducing inflammatory lesions, probiotics help controlling immune responses and reduce inflammation. Conclusion: Probiotics show promising potential as an alternative or additional treatment for AV by balancing gut and skin microbiomes. However, further research is needed to be explored to understand the molecular mechanisms and optimizing probiotic treatment strategies.

Keywords: acne vulgaris; gut microbiome; probiotics; skin microbiome

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INTRODUCTION

AV is a long-term inflammatory skin condition affecting the pilosebaceous units, characterized by the development of comedones, papules, pustules, nodules, and scars, predominantly on the face, upper trunk, and occasionally on the extremities (Sánchez-Pellicer et al., 2022). AV is a prevalent skin condition, affecting approximately 8.96% of men and 9.81% of women worldwide at any age. AV typically begins in adolescence and early adulthood, impacting up to 85% of people between the ages of 12 and 25 (Lynn et al., 2016). Several factors contribute to the development of AV, including the enlargement of sebaceous glands, their tendency to produce excessive sebum, follicular keratosis, colonization by *Cutibacterium acnes*, and skin inflammation. Diets high in fat and glycemic index can elevate insulin-like growth factor-1 (IGF-1) levels, which in turn promotes lipogenesis, inflammation, and androgen production which can cause AV (Cruz et al., 2023; Rao et al., 2021).

Another factor contributing to AV development is the microbiome and its interactions with the innate immune system which cause skin dysbiosis and contributes to the development of

AV (Hall et al., 2018). *Cutibacterium acnes*, a commensal bacterium primarily found in sebaceous skin, plays a role in maintaining the skin's physiological pH and microbial balance, which helps prevent the invasion of potentially harmful pathogens. However, a decrease in the skin's α -diversity and an overgrowth of specific *Cutibacterium acnes* phylotypes, can lead to the development of AV (Cavallo et al., 2022; Dréno et al., 2020; Lee et al., 2019). Mild to moderate cases of AV are typically managed with topical treatments that have antibiotic and anti-inflammatory properties, such as topical retinoids, hormonal antiandrogens, benzoyl peroxide, and topical clindamycin, among others. For more severe cases, oral retinoids and antibiotics are recommended (Nast et al., 2016). Although effective, many of these treatments come with unwanted side effects, such as local irritation, skin dryness, headaches, nausea, and even systemic or teratogenic issues. Additionally, the use of antibiotics can lead to bacterial resistance. As a result, non-pharmacological therapies offer a valuable alternative to traditional AV treatments (Dessinioti & Katsambas, 2022). Probiotics can be considered an alternative approach for AV prevention because they directly prevent growth and colonization by pathogenic bacteria and control inflammation, constituting a non-invasive, less aggressive therapy with less side effects and can avoid gastrointestinal degradation when used topically (Dapkevicius et al., 2023).

Probiotics are living microorganisms which when administered in adequate amounts confer a health benefit on the host (Hill et al., 2014). The skin microbiome consists of 'normal' commensal microbes that coexist in balance with the host, forming the resident microbiome, and environmental pathogen microbes that temporarily inhabit the skin, forming the transient microbiome (Grice & Segre, 2011). In AV, the resident microbiome includes *Cutibacterium acnes* (previously known as *Propionibacterium acnes*) and *Staphylococcus epidermidis*, while the transient microbiome features *Staphylococcus aureus* (Lee et al., 2019). An imbalance or 'dysbiosis' in the microbial population, compared to the normal distribution seen in healthy skin, has been implicated in the development of inflammatory AV (Ramasamy et al., 2019). Probiotics can be administered either topically or orally. Their effects involve attaching to the epidermal surface, inhibiting harmful pathogens, producing antimicrobial substances, and enhancing immune system modulation. When applied topically, probiotics can serve as a protective barrier, preventing the colonization of other pathogens.

Among the new strategies being explored, fostering a healthy microbial community by encouraging the growth of beneficial bacteria, rather than solely targeting harmful pathogens, appears promising. Additionally, because AV can be influenced by various factors, effective treatments should consider combined approaches that address both skin and gut microbiota (Sánchez-Pellicer et al., 2022). The aim of this review was to examine the role of human microbiota in the development of AV and to explore how probiotics can contribute to prevention and treatment of AV, either as an adjunct or alternative treatment, and impact the progression of AV.

METHOD

We conducted a search in the Google Scholar, PubMed, Science Direct, Proquest and Epistemonikos databases from 2014 to 2024 using the keywords "Gut Microbiome," "Skin Microbiome," "Topical Probiotics", "Oral Probiotics", and "Acne Vulgaris." Our focus was on controlled studies related to the skin microbiome and chronic inflammatory skin conditions. Four authors independently evaluated each title and abstract to determine their eligibility for inclusion. We specifically targeted literature aimed at exploring the relationship between probiotics and AV based on our inclusion and exclusion criteria. The inclusion criteria were researched in English, published in the last 10 years, participants using either topical or oral probiotics and discussed the effect of Probiotics on AV. The exclusion criteria encompassed studies not conducted in English, those published beyond the last 10 years, and

other forms of literature, including books and similar publications, and also studies which are not irrelevant with the topics. The total number of articles found is 623, and after screening, 25 articles are eligible to be used in this literature review.

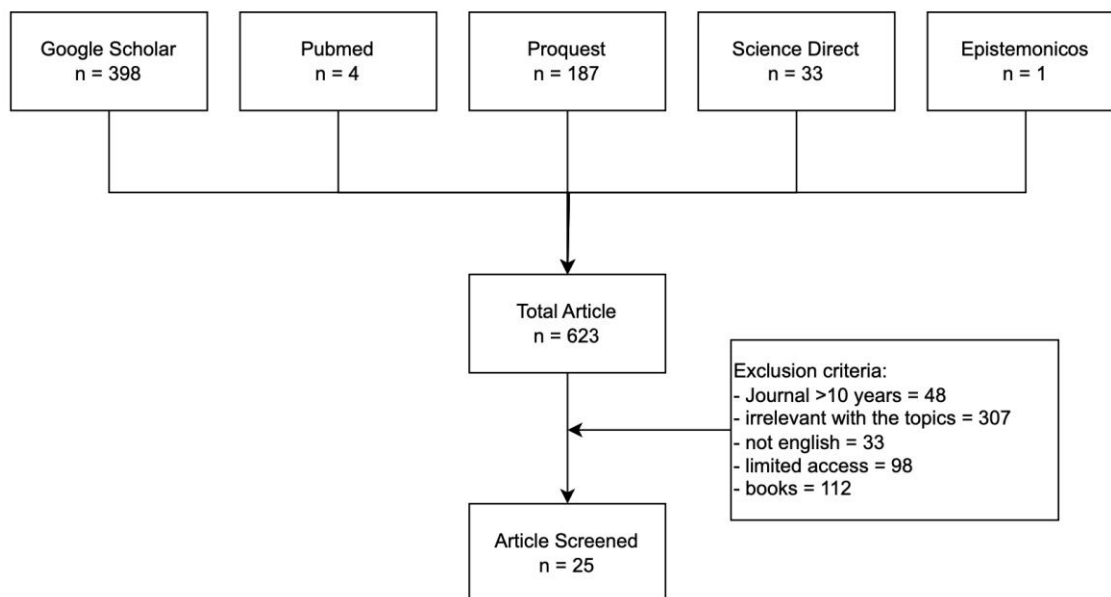


Figure 1. Research Screening Flow

RESULT

Table 1.
Results found from multiple researches

| Author | Year of Research | Research Outcome |
|-----------------------------|------------------|--|
| Fabbrocini G <i>et al.</i> | 2016 | Fabbrocini <i>et al.</i> studied the effects of <i>L. rhamnosus</i> (3×10^9 CFU per day) as a standalone treatment for adult AV over 12 weeks and noted significant improvement in back AV lesions. |
| Kitkuakosol & Khunngam | 2018 | 25 female patients, aged between 20-40 years old, with mild to moderate acne divided equally into two groups and randomly assigned either TS6 probiotics (100×10^9 CFUs/day) or placebo to be taken for 12 weeks. The percentage reduction of inflammatory lesions in the probiotic group was higher compared to the placebo group at week 12. |
| Paetzold <i>et al.</i> | 2019 | After sequential applications of a donor microbiome, the recipient microbiome becomes more similar to the donor. After intervention, an initial week-long phase is characterized by the dominance of donor strains. The level of engraftment depends on the composition of the recipient and donor microbiomes, and the applied bacterial load. We observed higher engraftment using a multi-strain donor solution with recipient skin rich in <i>Cutibacterium acnes</i> subtype H1 and <i>Leifsonia</i> . |
| Xu <i>et al.</i> | 2019 | The study underscores the complex interplay between acne, the skin microbiome, and antibiotic treatment. It highlights how <i>Cutibacterium acnes</i> dominates the microbiome in acne-prone areas but plays both beneficial and pathogenic roles, depending on its strain. Antibiotics such as macrolides, clindamycin, and tetracyclines have been central to acne treatment, but their long-term use has contributed to significant antibiotic resistance, particularly in <i>C. acnes</i> and other skin bacteria. |
| Dapkevicius L <i>et al.</i> | 2020 | Probiotics can be considered an alternative approach for acne prevention because they directly prevent growth and colonization by pathogenic bacteria and control inflammation, constituting a less aggressive therapy, when compared to antibiotics, with less side effects. |
| Dreno <i>et al.</i> | 2020 | Interactions between <i>C. acnes</i> and <i>Staphylococcus epidermidis</i> influence skin homeostasis and inflammation. |

| Author | Year of Research | Research Outcome |
|-----------------------------|------------------|--|
| Yu <i>et al.</i> | 2020 | Probiotic intervention showed positive results for improving skin conditions including acne vulgaris. |
| Mi-ju Kim <i>et al.</i> | 2021 | <i>Lactobacillus Plantarum</i> CJLP55 supplement reduced acne lesion count and severity, lowered sebum triglycerides (TG), and enhanced skin hydration and ceramide 2 levels. |
| Navarro-lópez <i>et al.</i> | 2021 | Probiotic is a promising adjunctive therapy for acne vulgaris by improving skin barrier and reducing <i>P. acnes</i> . |
| Marcela <i>et al.</i> | 2021 | Both oral and topical administration of UCO-SMC3 resulted in significantly lower <i>Cutibacterium acnes</i> counts in skin samples compared to the infected control mice. The topical application of <i>Weissella viridescens</i> UCO-SMC3 was more effective than the oral treatment in decreasing <i>Cutibacterium acnes</i> loads in the skin. |
| Kim <i>et al.</i> | 2021 | Inflammatory lesion count (ILC), total lesion count (TLC), and acne grade significantly decreased in the CJLP55 group compared to baseline. ILC decreased by 42.09%, TLC decreased by 49.67%, and acne grade decreased by 28.99% in the CJLP55 group compared to the placebo group over 12 weeks. Skin hydration increased by 14.52% and sebum content decreased by 16.27% in the CJLP55 group compared to the placebo group. Triglyceride (TG) levels, the major sebum lipid, decreased by 28.44% in the CJLP55 group compared to the placebo group. |
| Fabio <i>et al.</i> | 2022 | There was an impact, on the quantity of surface level inflammatory marks observed throughout the research timeframe in participants consuming the research product (group II), plant extracts (group III), and probiotics (group IV). These groups showed decreases of 56,67%, 40% and 38,89% respectively compared to the placebo groups decrease of 10%. |
| Marasca <i>et al.</i> | 2022 | 30 AV patients with mild to moderate AV were given supplement contained with 3 strains of lactic ferments (<i>Lactobacillus plantarum</i> ICIM01, <i>Lactobacillus reuteri</i> ICIM02, <i>Lactobacillus rhamnosus</i> ICIM0) for not less than 1 billion CFU per strain orally once a day, combined with a topical gel product (Bionike Aknet Azelike Plus®) enhanced by the combination of azelaic acid 6%, hydroxypinacolone retinoate 0.1% and α -hydroxy acids, applied once a day at acne's lesions. After 60 days there were a reduction of 37.4% of GAGS score. |
| Rocha <i>et al.</i> | 2022 | Study with 212 patients aged from 12 to 35 years was divided into two phases of 90 days each. In the first phase, patients received treatment with adapalene 0.1% and benzoyl peroxide 2.5% associated with a probiotic (IT), or adapalene 0.1% and benzoyl peroxide 2.5% associated with placebo (CT). In the second phase (90 days), patients received only oral treatment with a probiotic or placebo. |
| Lebeer <i>et al.</i> | 2022 | A significant reduction in inflammatory lesions after 8–12 weeks of using topical lactobacillus cream. |
| Habeebuddin <i>et al.</i> | 2022 | By promoting a balanced microbial environment, topical probiotics can help restore the skin's natural defenses, leading to a reduction in acne lesions. |
| Pellicer P S <i>et al.</i> | 2022 | Orally administered probiotics would give beneficial functions through the modulation of the intestinal microbiota, generating an anti-inflammatory response, restoring intestinal integrity, or through metabolic pathways involving IGF-1. Topical probiotics seem to produce their effects through the inhibition of growth of <i>C. acnes</i> in the pilosebaceous unit. |
| Chilicka <i>et al.</i> | 2022 | The use of probiotics may reduce skin eruptions. The use of internal supplementation and probiotic containing cosmetics give hope for the improvement of the skin condition of people with acne. |
| De Almeida <i>et al.</i> | 2023 | Oral and topical probiotic can improve skin health by promoting immune system modulation and reduce inflammation. |
| Podrini <i>et al.</i> | 2023 | A notable reduction in the production of inflammatory cytokines, sebum, and the prevalence of <i>C. acnes</i> after the combination of <i>Lactiplantibacillus plantarum</i> , mannitol, hyaluronic acid, and vitamin |

| Author | Year of Research | Research Outcome |
|----------------------------|------------------|---|
| | | B1. |
| Manfredini M <i>et al.</i> | 2023 | The study found that the topical application of SkinDuo™ serum containing <i>Lactiplantibacillus plantarum</i> resulted in a statistically significant reduction in both the number and severity of acne lesions compared to the placebo group. |
| Shi Z <i>et al.</i> | 2024 | A significant increase in skin hydration was achieved by probiotic group compared to the placebo. |
| Eguren <i>et al.</i> | 2024 | Patients with improvement in the Acne Global Severity Scale were 10/34 (29.41%) in the placebo group compared with 20/40 (50%) in the probiotic group. |
| Atefi <i>et al.</i> | 2024 | Probiotic capsule combined with doxycycline 100 mg showed a significant reduction in acne lesion severity and better overall treatment response. |
| Gowda <i>et al.</i> | 2024 | By inhibiting the growth of <i>P. acnes</i> probiotic may improve skin health and reduce inflammation in acne vulgaris. |

DISCUSSION

Acne Vulgaris

Acne vulgaris is a chronic skin disease which affecting the sebaceous gland, it is induced by multifactorial causes including hormonal dysregulation, state of immune of the human itself, diet, excessive sebum production, and colonization of *Propionibacterium acnes* (Polak et al., 2021). It primarily affects the face, upper chest, and back, and is most prevalent among adolescents and young adult (Polak et al., 2021). Specific region of the body inhabited by different species of bacteria which can be lead to potential of AV with different severity (Navarro-López et al., 2021). Sebaceous regions, including the face, scalp, and back, are predominantly colonized by lipophilic species such as *Propionibacterium acnes*. This genus is particularly abundant in oily skin areas and plays a crucial role in the pathophysiology of AV (Navarro-López et al., 2021). Moist region like the armpits, groin, and soles of the feet are rich in *Staphylococcus* and *Corynebacterium* species. These bacteria thrive in humid environments and contribute to the diverse microbial ecosystem of the skin (Navarro-López et al., 2021). Dry regions, such as the forearm, host a more diverse microbial community with a mixture of all four major phyla: Actinobacteria, Proteobacteria, Bacteroidetes, and Firmicutes. This diversity reflects the skin's ability to harbor a wide range of microorganisms depending on its condition and location (Navarro-López et al., 2021). The highest prevalence of AV is observed in adolescents, with 80-85% of individuals aged 15-18 years affected (Hay et al., 2014). In Indonesia, studies have shown that the prevalence of AV has increased from 60% in 2006 to 80% in 2007 (Jumiati et al., 2022). Clinicians often use a range of classifications, such as inflammatory versus non-inflammatory acne, to guide treatment (Boeddinghaus & Whyte, 2020). The management of AV typically involves a combination of topical and systemic therapies, depending on the severity of the condition (Assefa, 2023; Heng & Chew, 2020; Henshaw & Olasode, 2019). Probiotic supplementation has also been explored as a potential adjunct therapy for AV management (Heng & Chew, 2020).

It's important to assess how severe AV is to determine the treatment and track its progression over time. The Global Acne Grading System (GAGS) has become an accepted method, for evaluating acne severity in a manner for healthcare providers. The GAGS categorizes the face into six sections. Forehead, cheek, left cheek, nose, chin and chest. The GAGS gives a score to each area depending on the seriousness of comedones and inflammatory lesions found (Bae et al., 2024). AV intensity, in every section is ranked from 0, to 4; where 0 signifies no lesions and 4 signifies the ones. The scores, for each region are multiplied by their factors. Added together to calculate the overall GAGS score that ranges from 0 to 44. The AV severity is then classified into four grades based upon the final GAGS: Mild (1-18), Moderate (19-30), Severe (31-38), Very severe (>38) (Bae et al., 2024).

Gut and Skin Microbiome

The skin is commonly known as the organ of the body and plays a vital role in connecting the human body with its surroundings by acting as a protective shield and hosting various types of microorganisms (Bay et al., 2020). Similarly the gut microbiome consists of microorganisms living in the human digestive system and is now widely acknowledged for its importance, in preserving overall well being and balance (Bull & Plummer, 2014). Recent studies indicate that there is a connection between gut and skin microbiomes. Imbalances in these communities may play a role in causing different skin issues, like AV. AV is a skin condition characterized by various types of lesions that can vary from mild to severe. The collection of microorganisms, in the skin microbiome is crucial for keeping the skin healthy. Studies indicate that AV formation is linked to both the skin and gut microbiomes. Even though *Propionibacterium acnes* is commonly linked with AV development, *Staphylococcus epidermidis* plays a role in balancing and preserving skin health as a defense. The connection between the gut-brain-skin axis affects inflammation and hormonal equilibrium which impacts the development of AV (Polak et al., 2021).

Role of probiotic for Acne Vulgaris

Probiotics are bacteria that can be useful for controlling AV by stopping the growth of bacteria that cause acne such as *Propionibacterium acnes*. When probiotics are used topically they can change the balance of bacteria and the immune system response on the skin types such, as *Enterococci faecalis* SL-5, *Nitrosomonas eutropha* and *Lactobacillus acidophilus* have demonstrated encouraging outcomes for enhancing skin health. An interesting instance is the *Chamaecyparis obtusa* fermented with *Lactobacillus* (known as LFCO) which outperformed tea tree oil in a study lasting 8 weeks by reducing acne lesions by 65.3% compared to 38.2%. Furthermore topical probiotics are beneficial, for skin health as they boost ceramide production improve skin hydration and offer protection against microbes. (Polak et al., 202; Dréno et al., 2020; Lee et al., 2019) While topical application of probiotics is more direct for skin conditions like AV, oral probiotics might also be beneficial. Oral probiotics can influence the skin microbiome indirectly by altering the gut microbiota, which interacts with the skin microbiome (Lee et al., 2019). Oral probiotics are believed to provide benefits by influencing the intestinal microbiota, triggering an anti-inflammatory response, restoring gut integrity, or through metabolic processes involving IGF-1. Oral probiotics like *Lactobacillus johnsonii* NCC 533 have been shown to enhance skin immune responses and reduce UV-induced skin damage, which could indirectly benefit acne-prone skin (Chang et al., 2014). Another study showed that *Bifidobacteria* and *Lactobacilli* who is commonly found in the gut, have been suggested as probiotics for the treatment of inflammatory skin diseases like AV. Their effects on AV may be mediated by reducing systemic oxidative stress, regulating cytokines, and reducing inflammatory markers (Dréno et al., 2020). These probiotics can also regulate the production of insulin-like growth factor-1 (IGF-1), which is implicated in AV development (Lee et al., 2019). Additionally, a study on *Streptococcus salivarius*, a key member of the oral microbiota in healthy individuals, showed its ability to inhibit *Propionibacterium acnes*.

In a research conducted by Fabbrocini et al. on 20 adults (14 females, 6 males, mean age 33.7 ± 3.3 years) with AV in a 12-week clinical trial. The probiotic group (n=10) received LSP1 supplement at 3×10^9 CFU daily, while the placebo group (n=10) received a control liquid. Results showed the probiotic group has a 32% reduction in lesions and 65% increase in IGF1 and FOXO1 gene expression ($P < 0.001$). The probiotic group had an odds ratio of 28.4 (95% CI = 2.2-411.1, $P < 0.05$) for improvement of the skin compared to placebo. The study proved that LSP1 probiotic supplementation improves skin gene expression related to insulin signaling and make AV in adults get better (Fabbrocini et al., 2016). In a 12 week trial

conducted by Kitkuakosol & Khunngam, 25 women between the ages of 20 and 40 with mild to acne were studied. One group was given TS6 probiotics (100×10^9 CFUs/day) which included six bacterial species and a prebiotic, while the other received a placebo. Both groups used topical benzoyl peroxide and clindamycin. The results revealed both groups had reduced inflamed lesions by week 2 and get fewer comedones by week 8. By week 12, both groups showed decreased sebum and redness, with the probiotic group always showing better improvements in all measurements around the study period (Kitkuakosol & Khunngam, 2018).

Marcela et al. studied about *Weissella viridescens* UCO-SMC3's effects in the treatment of acne. Laboratory tests have shown this probiotic strain survives digestive conditions and fights *Cutibacterium acnes*. Study in mice, both oral and topical applications of UCO-SMC3 reduced skin inflammation and growth of *Cutibacterium acnes*. While oral probiotic showed better immune response, topical application was more effective at reducing bacteria on the skin. The research point up on how beneficial bacteria can help maintain skin health by fighting harmful bacteria and controlling inflammation, advising probiotics could be valuable in treating skin conditions (Marcela et al., 2021). M. J. Kim et al. did a research about the effects of *Lactobacillus plantarum* CJLP55 on AV for 12 weeks. The group which taking CJLP55 showed improvements compared to the placebo group, inflammatory lesions decreased by 42.09%, total lesions by 49.67%, and acne severity by 28.99%. They also experienced better skin health markers, including 14.52% increased moisture, 16.27% reduced in production of skin oil, 28.44% lower triglycerides, and higher levels of Ceramide 2, which can helps protect the skin barrier (M. J. Kim et al., 2021).

Rinaldi et al. studied about dietary supplement combining probiotics (*Bifidobacterium breve* BR03, *Lactobacillus casei* LC03, *Lactobacillus salivarius* LS03) with Lupeol and Echinacea extracts for treatment of AV. After 8 weeks, the combination of the supplement group showed the best results with a 56.67% reduction in inflammatory lesions compared to 40% in the extract only group, 38.89% in the probiotic only group, and 18.89% in the placebo group. The combination of the supplement also improved the balance of skin microbiome by decreasing harmful bacteria like *Cutibacterium acnes* and *Staphylococcus aureus* and on the other hand increasing beneficial bacteria like *Staphylococcus epidermidis* (Rinaldi et al., 2022). A study by Marasca et al. noted about combination treatment using a supplement that contains biotin and three probiotic strains (*Lactobacillus plantarum*, *Lactobacillus reuteri*, and *Lactobacillus rhamnosus*) together with topical azelaic acid gel. Results showed improvements in patients with 37.4% reduction of acne severity (GAGS score), 40.7% decrease in production of sebum (SEBUTAPE™), 18% reduction in water loss (TEWL), and 44% increase in saliva blue test results. The study also highlighted that acne patients usually have higher production of sebum and water loss, lower skin hydration, and lower in ceramide levels compared to people without acne (Marasca et al., 2022).

Rocha et al. studied the combination of probiotics (*Lactobacillus acidophilus* and *Bifidobacterium lactis*) with topical treatment (adapalene 0.1% and benzoyl peroxide 2.5%) for mild to moderate acne. The probiotic group revealed better improvements in IGA scores from day 30 and so on compared to the placebo group. After 90 day, the probiotic group showed lower IGA scores, and their total lesion count decreased from 76.2 to 25 within 180 days, proved that adding probiotics to standard topical treatment can enhance acne improvement (Rocha et al., 2022). Researchers led by Shi et al. conducted a study on a combination of probiotics (comprising *Lactobacillus plantarum* PBS067, *Lactobacillus rhamnosus* LRHO20 and *Lactobacillus reuterii* PBS072) to assess its effectiveness in treating acne in adult women. The group that received the probiotics showed enhancements in aspects compared to those who received a placebo. Notably the probiotic recipients experienced

increased skin hydration by day 56, reduced sebum levels starting from day 28, lower skin pH by day 70 and fewer non-inflammatory lesions from day 56. Both sets exhibited reduced spots. The group taking probiotics displayed more pronounced enhancements in the overall severity of acne and skin texture (Shi et al., 2024).

A study conducted by Eguren et al. learnt about probiotic mixture of *Lactobacillus casei* CECT 30031 and *Arthrospira platensis* BEA_IDA_0074B for treating mild to moderate acne for 12 weeks. The probiotic group showed better results than placebo group, here is the comparison: 50% vs 29.4% improved in GAGS score, a lot of reduction in non-inflammatory lesions (18.6 vs 10.5), and higher total lesion count reduction (27.9 vs 18.3). Additionally, 42.5% of patients treated with probiotic achieved at least 30% improvement in GAGS score compared to 20.6% in the placebo group, proved that probiotics is effective in managing acne (Eguren et al., 2024). A few of researcher did a review about oral and topical probiotic that play an important role in dermatology. It can improve skin health by promoting immune system modulation, inhibit *P. acnes*, and reduce inflammation in acne vulgaris (De Almeida et al., 2023; Gowda et al., 2024; Navarro-lópez et al., 2021; Yu et al., 2020). A study conducted by Lebeer et al. showed significant improvement in acne lesions in the group of patients treated with a cream supplemented with lactobacillus containing 10⁸ CFU of live *Lactobacilli* per application (± 1 g/application) twice daily for 8 weeks. Patients who applied live lactobacillus topically showed a significantly higher percentage of reduction in inflammatory lesions compared to the placebo group. A study by (Podrini et al., 2023) using the SkinDuo™ product containing mannitol, hyaluronic acid, and vitamin B1 along with the probiotic *Lactiplantibacillus plantarum*, showed that the positive colonies per strain tested for *C. acnes* and *S. epidermidis* significantly decreased after serum treatment. With the presence of lipopolysaccharide (LPS, which induces the expression of antimicrobial peptides and proinflammatory cytokines), the serum treatment significantly reduced lipid production (57% reduction). It also targets the production and secretion of proinflammatory cytokines, offering a potential therapeutic option for acne vulgaris (Lebeer et al., 2022).

A randomized controlled trial by Atefi et al. involving 80 moderate acne patients split into two groups of 40 compared treatments. The control group took one daily doxycycline capsule (100 mg), while the intervention group received doxycycline plus a daily probiotic capsule with over 10⁹ CFU. Acne severity was assessed using the global acne grading system (GAGS). Both groups improved, but the doxycycline plus probiotics group showed significantly better results on the forehead, chin, and nose ($p < 0.05$) (Atefi et al., 2024). Mi-Ju Kim et al. studied the effects of the *Lactobacillus Plantarum* CJLP55 supplement on patients with acne vulgaris. 14 participants per group took either the CJLP55 supplement or a placebo for 12 weeks. Results showed that compared to the placebo, the CJLP55 supplement reduced acne lesion count and severity, lowered sebum triglycerides (TG), and enhanced skin hydration and ceramide 2 levels, a key ceramide that helps maintain the epidermal lipid barrier (Mi-Ju Kim et al., 2021).

Habeebuddin et al. discusses topical probiotics help in restoring balance to the skin microbiome by introducing beneficial bacteria directly to the skin. This can enhance the skin's natural barrier function, modulate immune responses, and reduce inflammation by producing antimicrobial peptides that target pathogenic organisms. These probiotics may improve skin conditions by suppressing inflammatory pathways and strengthening the skin's defense against harmful microbes (Habeebuddin et al., 2022). In the research of Paetzold et al. it was found that the composition of human skin can be modulated by adding good quality bacteria from healthy individuals. Combining several bacterial strains can significantly enhances engraftment. The dose of applied bacteria plays an important role in the modulation capacity. During the first three days, the abundance of applied bacteria increases each day and then

decreases gradually after the termination of application. The applied dose determines the prolongation of the abundance of the applied strain on the tested skin (Paetzold et al., 2019).

CONCLUSION

After reviewing the research analysis provided it can be inferred that the connection between the gut and skin greatly influences the onset and advancement of AV. The analysis emphasizes the intricate relationships among the gut-skin microbiome and how disruptions in these mechanisms may lead to the development of AV. Both oral and topical probiotics have displayed potential as a treatment method for addressing AV. Incorporating probiotics can aid in rebalancing the gut and skin microbiomes by lessening inflammation and preventing the proliferation of AV triggering bacteria such as *Cutibacterium acnes*. Different research projects have proven the efficacy of probiotic strains, like *Lactobacillus* and *Bifidobacterium* species in enhancing AV conditions and promoting better skin health overall. Weaknesses and limitations of this research are most studies used small sample sizes (less than 50 participants), relatively short study durations, and insufficient detailed explanation of molecular mechanisms. To deepen our knowledge of the connection between the gut-skin microbiome and how probiotics can help manage AV we should delve further into various research aspects such as the specific impacts of different strains, the best dosage and duration for treatment long term outcomes, and the potential benefits of combining therapies.

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