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THE STUDY OF EFFECT PROBIOTIC IN ACNE AND ROSACEA : A SYSTEMATIC REVIEW

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ABSTRACT

Background: *Alternative remedies have long been utilized by patients to treat skin diseases in addition to or instead of traditional medical care. Research on the relationship between probiotics, the skin microbiota, and inflammatory dermatoses is only getting started.*

Aims : *This systematic review is to review the association of probiotic and its effect in acne and rosacea.*

Methods: *This study demonstrated compliance with all requirements by means of a comparison with the standards established by the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020. Thus, the specialists were able to guarantee that the research was as current as feasible. Publications released between 2014 and 2024 were considered for this search strategy. This was accomplished by utilizing a number of distinct online reference sites, including Pubmed, ScienceDirect, and SagePub. It was determined that reviews, previously published works, and partially completed works would not be included.*

Result: *In the PubMed database, the results of our search brought up 19 articles, whereas the results of our search on SCIENCE DIRECT brought up 166 articles, our search on SAGEPUB brought up 10 articles. The results of the search conducted for the last year of 2014 yielded a total 18 articles for PubMed, 122 articles for SCIENCE DIRECT and 7 articles for SAGEPUB. In the end, we compiled a total of 6 papers, 3 of which came from PubMed, 2 of which came from SCIENCE DIRECT and 1 of which came from SAGEPUB. We included six research that met the criteria.*

Conclusion: *In summary, manyof the studies that are currently available in the literature only involved a limited number of patients, did not state which species or dosage of probiotics were utilized, or did not run their trials long enough to fully assess the effects of probiotics on the microbiome of the skin and stomach.*

Keyword: *Probiotic, acne, rosacea*

INTRODUCTION

Elie Metchnikoff published the first research on probiotics in 1907, describing a link between longer life expectancy and lactic acid-producing bacteria consumed in yogurt. Probiotics have garnered attention in recent years for their potential to improve both digestive health and the treatment of inflammatory illnesses. "Living microorganisms which, when consumed in adequate amounts, confer a health effect on the host" is the definition of probiotic. Two of the most widely utilized probiotics are now Lactobacillus and Bifidobacterium, however research on more recent strains, including Bacillus coagulans, is showing promising benefits.[1–3]

Probiotics' immunomodulatory effects on keratinocytes and epithelial cells point to a physiological mechanism that justifies their use as an adjuvant acne therapy. In epithelial cells and keratinocytes, strain K12 of S. salivarius reduced the production of the pro-inflammatory cytokine IL-8, most likely by blocking the NK-kappaB pathway. When administered directly to the epithelium, S. salivarius may function as an immunological modulator, as evidenced by the suppression of many inflammatory pathways. Human skin cultures treated with L. paracasei NCC2461 demonstrated suppression of substance-P-induced skin inflammation as shown by decreased edema, mast cell degranulation, vasodilation, and production of tumor necrosis factor alpha (TNF-alpha). Although substance-P may increase sebum production and inflammation, its suppression makes it possible to treat acne therapeutically.[4–7]

Rosacea is a chronic skin condition that affects 5.5% of the general population, mostly women and men between the ages of 45 and 60. Rosacea mostly affects the forehead, chin, nose, and cheeks. There are remission and exacerbation phases to the condition. Persistent erythema, papules, pustules, flushing, hypertrophy of the sebaceous glands, and fibrosis are examples of cutaneous symptoms. Furthermore, even in cases when cutaneous symptomatology is absent or just mildly present, over 50% of rosacea patients exhibit ocular rosacea. Ocular rosacea symptoms and indicators include burning, itching, dryness, photophobia, hazy vision, foreign body feeling, lid margin, conjunctival telangiectasia, collapse of the meibomian glands, and in extreme cases, corneal inflammation and perforation, scarring, or loss of vision.[8–12]

The symptomatology of rosacea can have an emotional impact and can negatively influence social connections, leading to stigmatization, which is one of the major reasons why novel therapy techniques are being sought for. Numerous research have demonstrated a detrimental effect on rosacea patients' health-related quality of life. Fascinatingly, in a large number of individuals, the degree of rosacea does not correspond to the severity of psychosocial issues. Because of the symptoms' position on the face, moderate instances may already have a significant psychological impact. Rosacea frequently coexists with psychological comorbidities such as anxiety and depression. In a descriptive research with 827 European rosacea patients, one third reported feeling stigmatized in regard to related mental health issues. Compared to patients who did not feel stigmatized, those with rosacea had a greater prevalence of sadness (36.7 vs. 21.1%) and were more prone to avoid social settings (54.2% vs. 2.0%). In any event, stigmatization feeds a vicious cycle by making things worse. Furthermore, almost half of patients with rosacea-associated facial erythema believe that it interferes with their ability to do their job, which is directly connected to the psychological burden.[10,13–17]

Inflammatory skin conditions like rosacea, psoriasis, acne vulgaris, hidradenitis suppurativa, and atopic dermatitis are explained by the gut-skin axis as the result of a complex interaction between the immune system, lifestyle, and genetics that is constantly in sync with the neurological and endocrine systems. Significantly, as the skin and colon both exhibit ongoing interactions between bacteria and the immune system, the cutaneous and gut microbiota are important in these partnerships. Furthermore, the development and integration of next-generation sequencing (NGS) in recent years has made it possible to gather hitherto unheard-of data on the microbiome.[18–20]

METHODS

Protocol

The author of this study ensured that it complied with the standards by adhering to Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) 2020 guidelines. This is done to guarantee the accuracy of the results that are derived from the investigation. Thus, the specialists were able to guarantee that the research was as current as feasible. Publications released between 2014 and 2024 were considered for this search strategy. This was accomplished by utilizing a number of distinct online reference sites, including Pubmed, ScienceDirect, and SagePub. It was determined that reviews, previously published works, and partially completed works would not be included.

CRITERIA FOR ELIGIBILITY

In order to completse this literature evaluation, we looked at published research that discusses the association of probiotic and its effect in acne and rosacea. This is done to enhance the patient's therapy management and to offer an explanation. This paper's primary goal is to demonstrate the applicability of the issues that have been noted overall.

To be eligible to participate in the study, researchers had to meet the following requirements: 1) English must be used to write the paper. The manuscript must fulfill both of these conditions in order to be considered for publication. 2) A few of the examined studies were released after 2013 but prior to the time frame considered relevant by this systematic review. Editorials, submissions without a DOI, already published review articles, and entries that are nearly exact replicas of journal papers that have already been published are a few examples of research that are prohibited.

SEARCH STRATEGY

We used "probiotic", "rosacea" and "acne" out using the PubMed and SAGEPUB databases by inputting the words: (("probiotic s"[All Fields] OR "probiotical"[All Fields] OR "probiotics"[MeSH Terms] OR "probiotics"[All Fields] OR "probiotic"[All Fields]) AND ("skin"[MeSH Terms] OR "skin"[All Fields]) AND ("therapeutics"[MeSH Terms] OR "therapeutics"[All Fields] OR "treatments"[All Fields] OR "therapy"[MeSH Subheading] OR "therapy"[All Fields] OR "treatment"[All Fields] OR "treatment s"[All Fields])) AND ((clinicalstudy[Filter]) AND (2014:2024[pdat])) used in searching the literature.

DATA RETRIEVAL

After reading the abstract and the title of each study, the writers performed an examination to determine whether or not the study satisfied the inclusion criteria. The writers then decided which previous research they wanted to utilise as sources for their article and selected those studies. After looking at a number of different research, which all seemed to point to the same trend, this conclusion was drawn. All submissions need to be written in English and can't have been seen anywhere else.

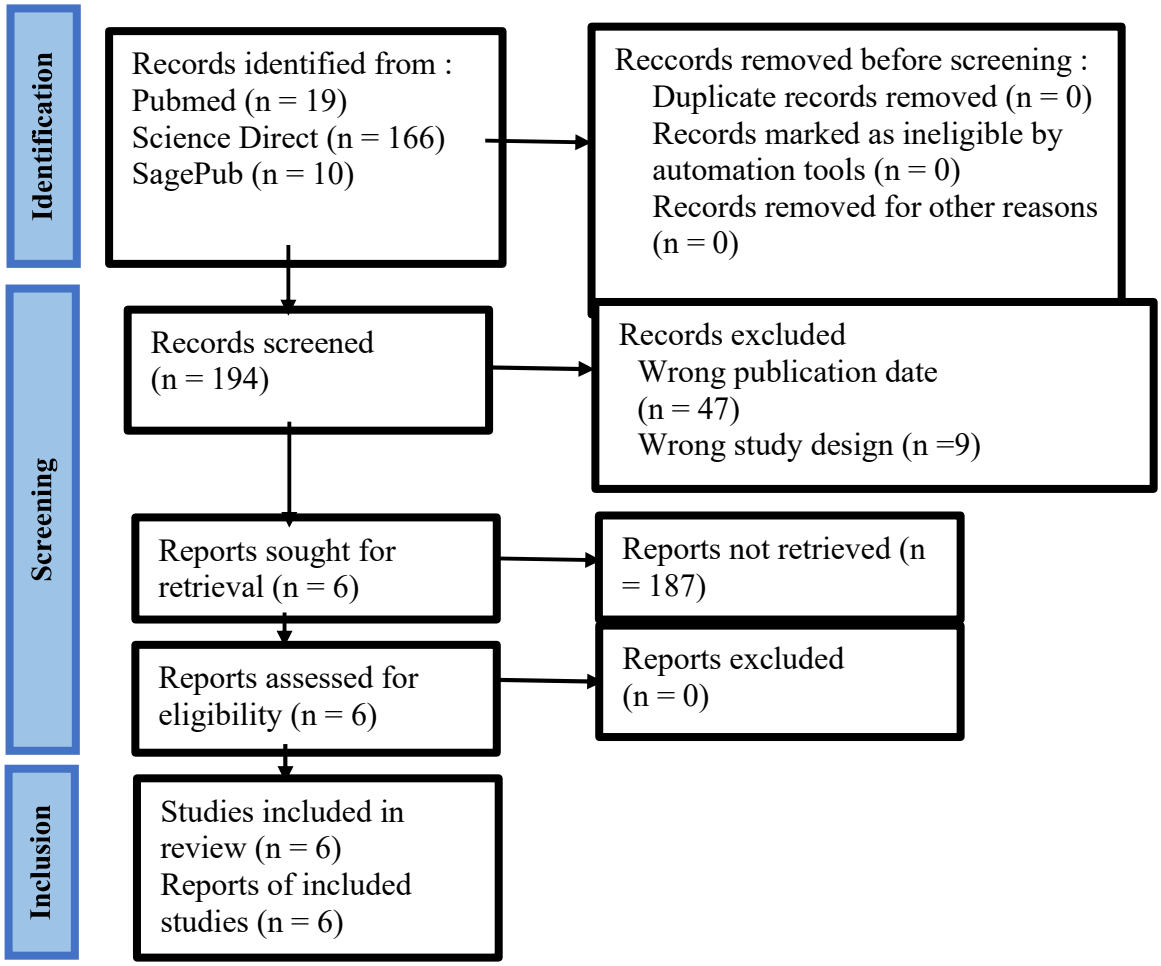

Figure 1. Prisma Flow Diagram

Only those papers that were able to satisfy all of the inclusion criteria were taken into consideration for the systematic review. This reduces the number of results to only those that are pertinent to the search. We do not take into consideration the conclusions of any study that does not satisfy our requirements. After this, the findings of the research will be analysed in great detail. The following pieces of information were uncovered as a result of the inquiry that was carried out for the purpose of this study: names, authors, publication dates, location, study activities, and parameters.

Quality Assessment and Data Synthesis

Each author did their own study on the research that was included in the publication's title and abstract before making a decision about which publications to explore further. The next step will be to evaluate all of the articles that are suitable for inclusion in the review because they match the criteria set forth for that purpose in the review. After that, we'll determine which articles to include in the review depending on the findings that we've uncovered. This criteria is utilised in the process of selecting papers for further assessment. in order to simplify the process as much as feasible when selecting

papers to evaluate. Which earlier investigations were carried out, and what elements of those studies made it appropriate to include them in the review, are being discussed here.

RESULT

In the PubMed database, the results of our search brought up 19 articles, whereas the results of our search on SCIENCE DIRECT brought up 166 articles, our search on SAGEPUB brought up 10 articles. The results of the search conducted for the last year of 2014 yielded a total 18 articles for PubMed, 122 articles for SCIENCE DIRECT and 7 articles for SAGEPUB. In the end, we compiled a total of 6 papers, 3 of which came from PubMed, 2 of which came from SCIENCE DIRECT and 1 of which came from SAGEPUB. We included six research that met the criteria.

Manzhalii, et al[21] (2016) showed that by promoting the development of a beneficial gut microbiota with reduced immunoreactive potential, E. coli Nissle shields the mucous barrier and ultimately improves the clinical course of intestine transmitted dermatoses.

Han, et al[22] (2022) showed that for individuals with mild-to-moderate acne, E. faecalis CBT SL-5 extract may be a practical and well-tolerated way to improve skin microbiome dysbiosis and acne severity.

Sathikulpakdee, et al[23] (2022) showed that a lotion made from probiotics is safe and efficient in treating mild to moderate cases of acne vulgaris; the results are similar to those obtained with 2.5% benzoyl peroxide. It could be a different approach to treating acne that has less serious side effects.

Table 1. The litelature include in this study

Author	Origin	Method	Sample	Result
Manzhalii et al, 2016[21]	Ukraine	Randomized prospective study	82 patients	Eighty-nine percent of the patients with acne, papular-pustular rosacea and seborrhoic dermatitis responded to E. coli Nissle therapy with significant amelioration or complete recovery in contrast to 56% in the control arm ($P < 0.01$). Accordingly, in the E. coli Nissle treated patients life quality improved significantly ($P < 0.01$), and adverse events were not recorded. The clinical improvement was associated with a significant increase of IgA levels to normal values in serum as well as suppression of the proinflammatory cytokine IL-8 ($P < 0.01$ for both parameters). In the E. coli Nissle treated group a shift towards a protective microbiota with predominance of bifidobacteria and lactobacteria (> 10(7) CFU/g stool) was observed in 79% and 63% of the patients, respectively ($P < 0.01$), compared to no change in the control group without E. coli Nissle. Moreover, the detection rate of a pathogenic flora dropped from 73% to 14 % of the patients in the experimental arm ($P < 0.01$) with no significant change in the control arm (accounting 80% before and 70% after the observation period, $P > 0.05$). Accordingly, stool

				consistency, color and smell normalized in the E. coli Nissle treated patients.
Han et al, 2022[22]	South Korea	Randomized controlled study	20 patients	This was a split-face, randomized, placebo-controlled trial with twenty patients. For four weeks, the patients' faces were treated with lotion containing E. faecalis on one side and a vehicle lotion on the other. Improvements in the researchers' evaluation of the severity of acne, patient satisfaction, modifications to skin characteristics, and diversity of the skin microbiome were among the effectiveness outcome measures. After 2 weeks ($p = 0.009$) and 6 weeks ($p < 0.0005$), the investigators' assessment score was considerably higher on the test side compared to the control side. Skin moisture and TEWL, however, did not differ much between the two groups. In the skin samples from the test side, the phylogenetic diversity of the skin microbiota declined with time.
Sathikulpakdee et al, 2022[23]	Thailand	Randomized controlled study	104 patients	This was a split-face, randomized, placebo-controlled trial with twenty patients. For four weeks, the patients' faces were treated with lotion containing E. faecalis on one side and a vehicle lotion on the other. Improvements in the researchers' evaluation of the severity of acne, patient satisfaction, modifications to skin characteristics, and diversity of the skin microbiome were among the effectiveness outcome measures. After 2 weeks ($p = 0.009$) and 6 weeks ($p < 0.0005$), the investigators' assessment score was considerably higher on the test side compared to the control side. Skin moisture and TEWL, however, did not differ much between the two groups. In the skin samples from the test side, the phylogenetic diversity of the skin microbiota declined with time.
Eguren et al, 2024[24]	Spain	Randomized clinical study	40 patients	The probiotic Lacticaseibacillus rhamnosus (CECT 30031) and the

				cyanobacterium Arthrospira platensis (BEA_IDA_0074B) were combined to create a capsule that served as the research product. On the Acne Global Severity Scale, patients who showed improvement were 10/34 (29.41%) in the placebo group and 20/40 (50%) in the probiotic group (p = 0.03). The number of non-inflammatory acne lesions was significantly lower (p = 0.03) in the probiotic group (-18.60 [-24.38 to -12.82]) than in the placebo group (-10.54 [-17.43 to -3.66]). In terms of total lesions, the probiotic group had a decrease that was nearly statistically significant (p = 0.06) (-27.94 [-36.35 to -19.53]) as compared to the placebo group (-18.31 [-28.21 to -8.41])
Ho et al, 2022[25]	Taiwan	Randomized clinical study		In vitro, the TAC/Collagen postbiotics demonstrated effective growth suppression against P. acnes and decreased TSLP and IL-33 inflammation. The TAC/Collagen combination improved HaCaT cell culture wound healing. The clinical trial's outcome demonstrated that the TAC/Collagen gel enhanced the skin's in vivo moisture score and inflammation index. Furthermore, in volunteers with acne vulgaris, this TAC/Collagen gel also enhanced the healing of acne-related wounds. Additionally, this TAC/Collagen gel lessened the quantity of brown patches and porphyrins on the skin of the face.
Berardesca et al, 2023[26]	Canada	Randomzied clinical study		At both time intervals, erythema considerably improved with M89PF ($p<0.01$ at D15 and $p<0.001$ at D30). When compared to baseline and standard skin care, skin sensitivity as measured by the skin stinging test improved dramatically ($p<0.01$) with M89PF at D30. In comparison to the baseline and the untreated side, skin erythema, tightness, dryness, hydration, and TEWL significantly improved ($p\leq0.05$) with M89PF at D15 and D30. At D15 and D30, subjects expressed great satisfaction

				with M89PF. Excellent tolerance was shown in every topic.

Eguren, et al[24] (2024) showed that In the probiotic group, patients with improvement attending the Global Acne Grading System were 17/40 (42.50%) compared to 7/34 (20.58%) in the placebo group (p = 0.02). In both groups, the quantity of unfavorable occurrences was comparable. Patients with acne vulgaris should give consideration to the probiotic utilized in this trial, since it proved to be efficacious and well-tolerated.

Ho, et al[25] (2022) showed that in addition to improving skin health, these TAC/Collagen postbiotics can help people with acne vulgaris reduce their redness, inflammation, and acne symptoms.

Berardesca, et al[26] (2023) showed that even with protective masks on, M89PF dramatically lowers erythema, skin tightness, dryness, and TEWL while also enhancing skin hydration and sensitivity. M89PF has a good tolerance profile and a high degree of user satisfaction.

DISCUSSION

TEWL and skin hydration were not significantly different between the two groups. The phylogenetic diversity of the skin microbiota decreased over time in the skin samples of test side. In conclusion, E. faecalis CBT SL-5 extract can be a feasible and well-tolerated option for improving acne severity and skin microbiome dysbiosis in mild-to-moderate acne patients.[22] Manzhalii, et al in their study also showing the result, in patients receiving Nissle treatment for E. coli, feces consistency, color, and smell returned to normal. By promoting the development of a beneficial gut microbiota with reduced immunoreactive potential, E. coli Nissle shields the mucous barrier and ultimately improves the clinical course of intestine transmitted dermatoses.[21]

Probiotics have advantages in lessening acne. Lactobacillus paracasei was found to have anti-inflammatory properties in earlier research. Nevertheless, there is currently a dearth of clinical data supporting topical probiotic lotion as an acne therapy. In their study, Shatikulpakdee et al. found that a lotion generated from probiotics is safe and effective in treating mild to moderate cases of acne vulgaris, showing similar results to 2.5% benzoyl peroxide. It could be a different approach to treating acne that has less serious side effects.[23]

It has been highlighted that the gut microbiota has a role in some inflammatory skin conditions, such as acne vulgaris. Probiotics may be able to improve the clinical course of this illness by modulating the microbiota. Eguren et al. carried out a 12-week randomized, double-blind, placebo-controlled clinical experiment with individuals with acne vulgaris ages 12 to 30. In both groups, the quantity of unfavorable occurrences was comparable. Patients with acne vulgaris should give consideration to the probiotic utilized in this trial, since it proved to be efficacious and well-tolerated.[24]

A persistent inflammatory skin condition is acne vulgaris. Skin lesions can have a lasting effect on look and have a detrimental effect on self-confidence if they are not properly treated in a timely manner. Benzoyl peroxide, azeleic acid, and antibiotics are frequently used to treat acne symptoms. Nonetheless, prolonged usage of such drugs should be done so with caution due to their adverse consequences. Consequently, the creation of a material that is more appropriate for everyday usage while yet being safe and effective is required. Ho, et al. chose collagen because of its superior wound-healing properties when co-fermenting it with three probiotic strains, TYCA06/AP-32/CP-9 (TAC). The substance that had fermented was mixed with cosmetic gel and applied to the acne lesions of the individuals. In addition to improving skin health, these TAC/Collagen postbiotics can help people with acne vulgaris reduce their redness, inflammation, and acne symptoms.[25]

CONCLUSION

In summary, many of the studies that are currently available in the literature only involved a limited number of patients, did not state which species or dosage of probiotics were utilized, or did not run their trials long enough to fully assess the effects of probiotics on the microbiome of the skin and stomach.

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