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PROBIOTICS IN THE MANAGEMENT OF PEDIATRIC ATOPIC DERMATITIS: A SYSTEMATIC REVIEW

PROBIÓTICOS NO MANEJO DA DERMATITE ATÓPICA PEDIÁTRICA: UMA REVISÃO SISTEMÁTICA

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Abstract. The aim of this study is to analyze what the literature presents regarding the use of probiotics as complementary therapies in the treatment of atopic dermatitis (AD) in children and adolescents. A systematic review was carried out of articles indexed in the PubMed, Lilacs, Scielo and Embase databases, which included interventions with probiotics. The selection followed the PRISMA strategy, focusing on randomized clinical trials published between 2014 and 2024. Fifty-seven articles were identified, of which 14 met the inclusion criteria. The studies analyzed the SCORAD index (Severity Scoring of Atopic Dermatitis) and indicated a significant reduction in AD symptoms in 53.8% of the clinical trials that used probiotics, with emphasis on the strains Lacticaseibacillus rhamnosus GG, Bifidobacterium bifidum, Lactobacillus sakei proBio65, among others. The results have also shown an improvement in patients' quality of life in some studies and a reduction in the use of medication in others, although the evidence varies depending on the type of probiotic and the context of the treatment. The use of probiotics has potential as a therapeutic adjuvant for AD, but the methodological variability between studies limits definitive conclusions.

Keywords: Atopic dermatitis; Pediatrics; Child; Therapeutics; Probiotics.

Resumo. O objetivo deste estudo é analisar o que a literatura apresenta sobre o uso de probióticos como terapias complementares no tratamento da dermatite atópica em crianças e adolescentes. Foi realizada uma revisão sistemática de artigos indexados nas bases de dados PubMed, Lilacs, Scielo e Embase, que incluíram intervenções com probióticos. A seleção seguiu a estratégia PRISMA, focando em ensaios clínicos randomizados publicados entre 2014 e 2024. Foram identificados 57 artigos, dos quais 14 cumpriram os critérios de inclusão. Os estudos analisaram o índice Severity Scoring of Atopic Dermatitis (SCORAD) e indicaram uma redução significativa nos sintomas de DA em 53,8% dos ensaios clínicos que usaram probióticos, com destaque para as cepas Lacticaseibacillus rhamnosus GG, Bifidobacterium bifidum, Lactobacillus sakei proBio65, entre outras. Os resultados também mostraram uma melhora na qualidade de vida dos pacientes em alguns estudos e uma redução no uso de medicamentos em outros, embora as evidências variem dependendo do tipo de probiótico e do contexto do tratamento. O uso de probióticos apresenta potencial como adjuvante terapêutico para a dermatite atópica, mas a variabilidade metodológica entre os estudos limita conclusões definitivas.

Palavras-chave: Dermatite atópica; Pediátrico; Criança; Terapêutica; Probióticos.

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Introduction

Atopic dermatitis (AD), also known as atopic eczema, is a chronic inflammatory disease that affects the skin and involves genetic, immunological, and environmental factors in its etiology[1-3]. Symptoms, including xeroderma (skin dryness) and pruritus, can interfere with sleep and negatively impact patients' quality of life[1-4]. Lesions vary depending on age and disease stage, potentially presenting as erythema, papules, and crusts[1-2].

AD typically arises in childhood, especially during the first year of life (60%), and in most cases, manifests in a mild form[12]. In industrialized countries, it affects between 10% and 30% of children, with symptom improvement in 70% of cases by adolescence. However, 2% to 10% of individuals continue to experience symptoms into adulthood, and the prevalence of the condition has been increasing in recent decades[5-6].

AD is often associated with other allergic conditions, such as asthma and allergic rhinitis, characterizing the so-called "atopic march"[1-2]. Standard treatment includes skin hydration and the use of anti-inflammatory medications. Emollient moisturizers and topical corticosteroids are commonly used to control inflammation; however, they may cause adverse effects such as skin atrophy. Moreover, prolonged use of corticosteroids can lead to increased percutaneous absorption, potentially resulting in systemic effects such as hypothalamic-pituitary-adrenal axis suppression, although this is rarely reported. Systemic corticosteroids can lead to clinical improvement, but discontinuing their use is often associated with symptom recurrence[2-4].

Additionally, various environmental and dietary factors may influence the risk and severity of AD. Studies suggest that exclusive breastfeeding for three to four months may reduce the risk of AD development in children, although this relationship remains controversial[5,7-8]. The gut microbiota, which plays a key role in immune system modulation, has also been linked to AD; for example, breastfed infants tend to have a microbiota predominantly composed of Bifidobacteria, which is associated with a lower incidence of eczema[7].

Probiotics are live microorganisms that, when administered in adequate amounts, confer health benefits to the host, primarily by modulating the gut microbiota and influencing systemic immune responses. Several strains of Lactobacillus rhamnosus have demonstrated probiotic properties with immunomodulatory effects, improving Severity Scoring of Atopic Dermatitis (SCORAD) in AD cases[9]. Despite positive results, some studies have not observed statistically significant differences compared to placebo, suggesting a possible natural recovery of the condition[10].

Limitations such as the lack of consensus on inflammatory biomarkers, variability in assessment methods, and dietary and geographical influences highlight the need for more standardized studies to better understand the impact of probiotics[11,12].Considering the influence of probiotics on atopic dermatitis, this article aims to review recent literature on the use of nutritional interventions, particularly probiotics, as complementary therapies to conventional AD treatment. We will assess the efficacy of these interventions in reducing signs and symptoms, disease severity, and improving the quality of life in children and adolescents with the condition.

Method

This study presents a systematic literature review based on articles retrieved from the PubMed, Lilacs, Scielo, and Embase databases, focusing on the analysis of probiotic interventions as complementary therapies for the treatment of atopic dermatitis (AD) in children and adolescents. The review methodology followed the principles of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) strategy, ensuring rigor and transparency in the search and selection process of the included studies. The guiding research question established was: "Can probiotics be used as complementary therapies to traditional treatments for atopic dermatitis in children and adolescents?"

The literature search was conducted using a combination of specific terms, employing the Health Sciences Descriptors (DeCS) and the Medical Subject Heading (MeSH) terms: "Dermatitis, Atopic" AND "Pediatrics OR Child" AND "Therapeutics" AND "Probiotics." The search strategy was adjusted according to the specificity of each database to capture the maximum amount of relevant literature. The search covered randomized clinical trials published between 2014 and 2024, and the article selection took place between February 2014 and February 2024. Strict exclusion criteria were applied, eliminating letters to the editor, reviews, personal opinions, book chapters, commentaries, editorials, and any publication lacking primary data or not addressing the use of probiotics for the treatment or prevention of atopic dermatitis. This approach aimed to select studies that provided robust and relevant evidence for the review's objective.

The search strategy was structured according to the Peer Review of Electronic Search Strategies (PRESS) checklist, ensuring adherence to best practices for systematic reviews. The search was conducted by two authors with experience in systematic reviews and fluency in both Portuguese and English. The analysis was limited to studies published in the last 10 years. The review of the search strategy was performed between December 2023 and February 2024.

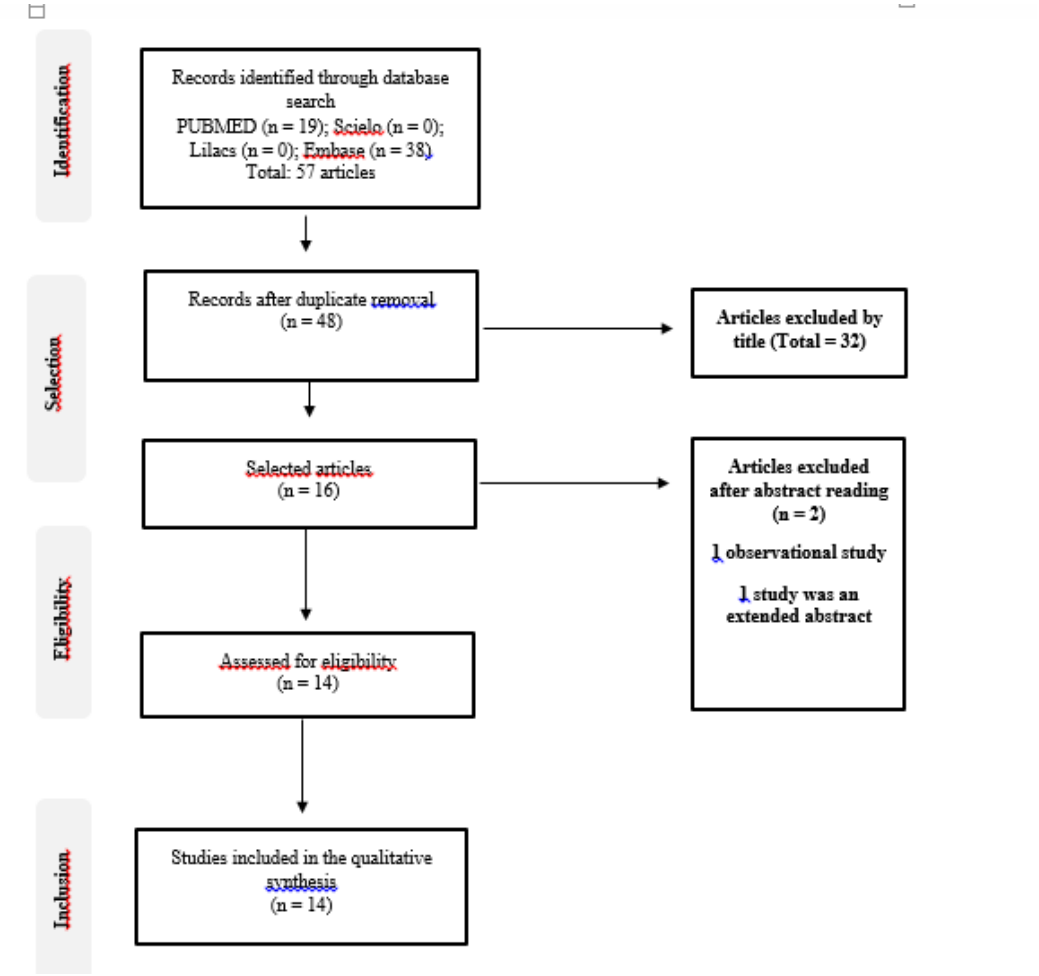
To manage the records, data were exported to Mendeley® software, where duplicates were removed, and an initial screening of the studies was performed. The selected records were then transferred to a Microsoft Excel spreadsheet, facilitating the organization and screening of the studies. The selection process was conducted in two stages: first, by analyzing the titles and abstracts, followed by a full-text review of potentially eligible articles. In case of disagreement between the reviewers, the inclusion or exclusion of articles was resolved by consensus.

Data extraction was performed by two independent reviewers, and the information was entered into a standardized spreadsheet with the following fields: author, study year, publication year, location, study design, participant age, sample size (control and intervention groups), method, intervention duration, and outcomes achieved.

To assess the methodological quality of the studies, the Oxford checklist (2001) was used, consisting of 14 evaluation criteria. These included items such as randomization, allocation concealment, blinding of participants and assessors, dropout rates, adherence to the intervention protocol, and intention-to-treat analysis. This assessment ensured that only studies with appropriate methodological rigor were considered in the final analysis.

The selected articles were categorized into two main sections: interventions that proved effective and interventions that were not effective in improving atopic dermatitis symptoms. The results were presented in tables highlighting the essential characteristics of the studies and their main conclusions.

FIGURE 1. Flowchart of article selection according to the PRISMA methodology.



The data analysis in Table 1 reveals that the groups treated with probiotics showed a significant reduction in SCORAD scores at the end of the treatment compared to the control group. This improvement was documented in studies such as: Carucci et al. ($p < 0.05$)[9]; Lin et al. ($p < 0.05$)[14]; Jeong et al. (difference of -13.89 ± 10.05, $p = 0.0283$)[15]; López et al. (-83% vs. -24%, $p < 0.001$)[12]; Rodríguez et al. (difference of -5.43, $p = 0.04$)[16]; Rather et al. (CV: $p = 0.0193$; CM: $p = 0.0242$)[17]; Prakoeswal et al. ($p = 0.000$)[18]. In total, 53.8% of the randomized clinical trials indicated a significant improvement in SCORAD scores for the groups that received probiotic interventions.

TABLE 1. Summary of randomized controlled trials using probiotics as an intervention in children and adolescents.

Author, Year, Country	Intervention/ Control (n)	Age	Microorganism, Duration	Dose	Summary of Results
Carucci et al., 2022, Italy[9]	46/45	6 – 36 months	Lacticaseibacillus rhamnosus GG, 12 weeks	CFU, once daily	In the intervention group, SCORAD improved ($p < 0.05$), a higher percentage of children reached MCID in SCORAD ($p < 0.05$), and the mean IDQOL was lower. The number of days without rescue medication was higher in the intervention group in two periods ($p < 0.05$). Both groups used emollients and had common infections. No adverse effects were reported.
Yan et al., 2019, Taiwan19	47/55	4 – 30 months	Lactobacillus paracasei GM-080, 16 weeks	1×10^{10} CFU equivalent/day	No significant differences were found between groups regarding SCORAD, IDQOL, TEWL, or CCL17/TARC. The intervention group showed higher IgE elevation ($p < 0.001$), and adverse effects were observed in both groups. SCORAD significantly reduced in both groups from week 2. No differences were observed between groups in the use of topical corticosteroids, symptom-free time, or IDQOL. Adverse events were not related to treatment.
Lin et al., 2015, China14	20/20	<12 – 36 months	Bifidobacterium bifidum, 4 weeks	1 capsule, three times a day	At T4, B. bifidum levels in feces and SCORAD were significantly better in the intervention group compared to the control ($p < 0.05$).
Jeong et al., 2020, Korea1	45/45 (FA), 33/33 (PP)	1 – 12 years	Lactobacillus rhamnosus IDCC 3201, 12 weeks	CFU per day	In the intervention group, SCORAD improved ($p = 0.0283$). In the subgroup with AD for 50+ months, IL-31 and eosinophil levels decreased ($p = 0.0431$ and $p = 0.0486$). Adverse events were reported but were not associated with treatment.
Navarro-López et al., 2018, Spain12	23/24	4 – 17 years	Bifidobacterium lactis CECT 8145, B. longum CECT 7347, L. casei CECT 9104, 12 weeks	CFU, once daily	Greater SCORAD reduction (-59%) and less use of topical steroids ($p < 0.001$) in the intervention group compared to control. No significant differences in IL-13, eosinophils, IL-4, IL-5, IL-10, IgE, and lactate dehydrogenase.
Yang et al., 2014, Korea20	37/34	2 – 9 years	Lactobacillus casei, L. rhamnosus, L. plantarum, B. lactis, 6 weeks	CFU, twice daily	Clinical improvement with no differences between groups at T6. The probiotic fecal cell count was higher in the intervention group ($p \leq 0.001$), but cytokine levels did not differ significantly between groups.
Wang & Wang, 2015, Taiwan21	159/53	1 – 18 years	L. paracasei, L. fermentum, 3 months	CFU (LP and LF), once daily	Lower SCORAD scores ($p < 0.001$) in the intervention group, sustained until month 4. At M3, FDLQI and CDLQI scores were lower ($p < 0.05$), with a significant reduction in IL-4 and allergen sensitization. No significant differences in steroid use and adverse effects.

Cukrowska et al., 2021, Poland22	48/68 (M3), 48/53 (M9)	<2 year	L. rhamnosus ŁOCK 0900, L. rhamnosus ŁOCK 0908, L. casei ŁOCK 0918, 3 months	CFU, once daily	SCORAD decline showed improvement, but not significant. At M3, a higher proportion of children in the intervention group showed clinical improvement (p = 0.029). At M9, no beneficial probiotic effect was observed.
Sharma et al., 2022, India23	49/54	6 months – 12 years	Bacillus clausii, 8 weeks	2 billion spores/5 ml, twice daily	No significant difference in mean SCORAD between groups. No improvement in disease severity, but a positive correlation was observed between CDLQI and SCORAD.
Feíto-Rodríguez et al., 2023, England16	35/35	4 – 17 years	B. lactis, B. longum, L. casei, 12 weeks	CFU, once daily	A positive difference in mean SCORAD (-5.43) and improvement in IGA scores in the intervention group (p < 0.002). Adverse effects were proportional between groups.

SCORAD - Severity Scoring of Atopic Dermatitis; MCID - Minimal Clinically Important Difference; IDQOL - Infants' Dermatitis Quality of Life Index; TEWL - Transepidermal Water Loss; CCL17/TARC - Chemokine (C-C motif) ligand 17 / Thymus and Activation-Regulated Chemokine; IgE - Immunoglobulin E; ITT - Intention-To-Treat; PP - Per-Protocol; FA - Full Analysis; AD - Atopic Dermatitis; IL-31 - Interleukin-31; IL-13 - Interleukin-13; IL-4 - Interleukin-4; IL-5 - Interleukin-5; IL-10 - Interleukin-10; FDLQI - Family Dermatology Life Quality Index; CDLQI - Children's Dermatology Life Quality Index; M3 - Month 3 (time point in study); M9 - Month 9 (time point in study); IGA - Investigator Global Assessment.

The study by Cukrowska et al.[22] identified a decrease in SCORAD in the group treated with probiotics, although no statistically significant differences were found compared to the control group at the end of the treatment. However, in the treated group, a higher proportion of children showed clinical improvement (>30% reduction in SCORAD, p = 0.029), particularly in those sensitized to allergens (p = 0.003). This trend reflects a potentially beneficial impact for sensitized patients, reinforced by the loss of significant difference in baseline SCORAD between sensitized and non-sensitized patients (p < 0.00001). In the study by Ahn et al.[24], although the overall group did not show significant improvements, the sensitized subgroup showed advancements in subjective scores (p = 0.019), suggesting symptom relief specifically for this profile.

Five out of the 14 articles assessed patients' quality of life using the IDQOL and CDLQI instruments, with evidence of improvement in two studies that used probiotics. Carucci et al. reported a reduction in IDQOL (p < 0.05)[9], and Wang & Wang observed an improvement in CDLQI (p < 0.05) and FDQL (p < 0.02)[21]. These findings contrasted with neutral results in the studies by Sharma et al.[23], Wu et al.[10], and Yan et al.[19], indicating that the effectiveness of probiotics on quality of life may vary depending on treatment context.

The frequency of medication use was also evaluated, with reductions observed in three clinical trials. Carucci et al. reported a significant decrease in rescue medication use during two time intervals (p < 0.05)[9]. López et al. found a reduction in steroid use for symptom control (OR = 0.63; p < 0.001)[12], while Rodríguez et al. reported a decrease in medication use duration[16]. However, other studies did not observe significant changes.

Various inflammatory response indicators were investigated. Yan et al. [19] observed an increase in IgE levels (p = 0.038) in the intervention group, contrasting with other studies that documented a reduction in IgE[12,21]. Jeong et al. reported significant improvements in eosinophil cationic protein (ECP) in the intervention group (p = 0.0224)[15], while reductions in IL-4 were found in the studies of Wu et al. (p = 0.04)[10] and Prakoeswa et al. (p = 0.000)[18]. In patients with AD for more than 50 months, Jeong et al. identified a decrease in mean eosinophil count in the treated group (p = 0.0486)[15], while Rather et al. observed eosinophil reduction in patients treated with CV (p = 0.0331)[17].

Among inflammatory and immunological markers such as IL-5, IL-13, and TNF-α, no significant changes were observed in most studies. However, Carucci et al.[9] investigated fecal butyrate levels and recorded a significant increase in this metabolite in patients who achieved clinical improvement ($p < 0.05$). These findings suggest that response to probiotic treatment may depend on specific mechanisms that are not yet fully understood, emphasizing the need for further research on the relationship between probiotics and inflammatory markers in atopic dermatitis.

Discussion

Among the 14 studies included in this review, 9 used probiotics composed of a single bacterial strain, while the others used strain mixtures. In total, 24 bacterial strains were analyzed, covering three genera: 17 strains belonged to the Lactobacillus genus, 6 strains belonged to the Bifidobacterium genus, 1 strain belonged to the Bacillus genus.

The Lactobacillus casei group stood out as the most widely used and studied, including species such as Lactobacillus casei, Lactobacillus paracasei, and Lactobacillus rhamnosus. These species are classified as lactic acid bacteria, Gram-positive, and metabolically dependent on carbohydrates as an energy source. These bacteria demonstrate immunomodulatory potential and impact cytokine regulation, as established in several studies[25-26].

The studies applied 11 different types of probiotics, each with specific dosages and protocols, reflecting significant variability in administration time and treatment monitoring. This heterogeneity complicates determining the optimal time for a metabolic response in symptom control, as some studies did not evaluate long-term effects. Additionally, variations in bacterial strain concentrations suggest that dose or duration may not be optimal for symptom control. The concomitant use of topical corticosteroids may also interfere with the perceived benefits of probiotics.

To assess atopic dermatitis severity and quality of life, studies employed validated tools such as the Severity Scoring of Atopic Dermatitis (SCORAD), the Children's Dermatology Life Quality Index (CDLQI), and the Family Dermatology Life Quality Index (FDLQI). These measurement instruments are widely accepted and used in the literature as comparative tools for evaluating the impact of inflammatory skin diseases on the quality of life of children and their families[27-30].

Among Lactobacillus rhamnosus strains, several are considered probiotics, with immunomodulatory properties that include competitive exclusion of pathogenic microorganisms. The study by Carucci et al. [9], for example, showed improvement in SCORAD in both the treated and control groups, with faster and stronger responses in the group that received Lacticaseibacillus rhamnosus GG (LGG). Additionally, there was an improvement in quality of life and reduction in corticosteroid use. The benefits persisted for up to four weeks after intervention. However, some studies found symptom improvement with probiotics but without statistical differences from placebo[10], suggesting that recovery may occur naturally, regardless of probiotic intervention.

Another important aspect is the limited response of inflammatory markers and subjective symptoms, even with SCORAD improvement. Despite the identification of cytokines and chemokines as potential inflammation biomarkers, there is no consensus on specific markers for AD assessment[11]. SCORAD and the Eczema Area and Severity Index (EASI) remain the gold standard in clinical trials, but method variability limits standardization.

The analysis suggests that Lacticaseibacillus rhamnosus GG, Bifidobacterium bifidum, L. sakei proBio65, Lactobacillus plantarum IS-10506, and various Bifidobacterium and Lactobacillus mixtures demonstrated efficacy in reducing SCORAD31-33. However, factors such as dietary patterns, participant age, and bacterial diversity indicate the need for more rigorous and standardized studies. Geographic and dietary influences, variability in inflammatory responses, and lack of specific biomarkers are limitations requiring methodological standardization to advance the understanding of the impact of probiotics on atopic dermatitis.

Conclusion

This review suggests that the use of probiotics has potential as an adjunct therapy in the treatment of atopic dermatitis, demonstrating significant improvements in SCORAD severity index, patients' quality of life, and reduction in the use of topical medications. These findings indicate a promising clinical applicability of probiotics in atopic dermatitis management.

However, the variability observed among studies regarding bacterial strain diversity, administered dosages, experimental designs, and monitoring protocols—including concomitant medication use, dietary control, and intervention duration—highlights the complexity in assessing probiotic efficacy. This methodological heterogeneity makes it challenging to draw consistent conclusions and underscores the need for more rigorously standardized studies.

Future trials should focus on a more uniform experimental approach to better understand the impact of probiotics on atopic dermatitis and to strengthen their inclusion as a therapeutic option in clinical practice.

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