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Potential role of Lactobacilli spp. postbiotics in atopic dermatitis

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ABSTRACT:

Chronic itchiness and irritation are the hallmarks of atopic dermatitis. Although the precise etiology is yet unknown, environmental, and genetic factors are involved. Patches of red, irritated skin commonly develop on flexural parts, such as the knees and elbows. Scratching makes the problem worse and increases the risk of infection and broken skin. Although it mostly affects children, it can also impact adults. Moisturizing, avoiding triggers, and occasionally applying topical steroids are all part of management. Beyond just causing bodily discomfort, the effects also have an influence on mental health. Research on novel therapies and the function of the immune system never stops. Beneficial microorganisms called probiotics show potential in the treatment of atopic dermatitis. They might alter the gut flora, which would affect the immune system. Research indicates that some strains may lessen inflammation and enhance the function of the epidermal barrier. Lactobacilli spp. are probiotics that have anti-allergic activity because of their cell-wall components. But due to their relative instability in normal room temperature and conditions, these probiotics are treated with heat attenuation process to form Lactobacilli spp. postbiotics. These postbiotics by modulating the Th1/Th2 imbalance, can reduce the level of IgE and cause improvement in various symptoms of atopic dermatitis. Based on the clinical study evidence, we can conclude that Lactobacilli spp. postbiotics are an important therapeutic option that can be used in real-world clinical settings for the management of atopic dermatitis and related skin allergic conditions.

Keywords: Atopic dermatitis, Allergy, *Lactobacilli spp.*, IgE, Th1/Th2, Postbiotic.

Introduction

Atopic dermatitis (AD), is a chronic inflammatory skin ailment that affects millions of people globally. It is a complex and diverse condition. With an emphasis on clinical presentation, diagnosis, pathophysiology, epidemiology, etiology, and therapy techniques, this introduction explores its complex character. A comprehensive approach is necessary to comprehend atopic dermatitis because of its significant effects on people's social, mental, and physical health. Although it can arise anywhere on the body, AD typically presents as red, itchy patches of skin that are often distributed in a specific pattern, especially affecting the flexural surfaces of the elbows, knees, and neck. The ailment's defining feature, the constant itching, prompts people to scratch, which exacerbates the inflammation and may result in consequences including skin infections. Due to the chronic nature of AD, patients may go through periods of remission punctuated by flare-ups, which can be brought on by a number of things, such as environmental allergens, irritants, stress, and shifting climatic conditions.(1-3)

Over the past few decades, the incidence of AD has been progressively increasing, especially in developed countries. The disease affects people of all ages, but it primarily affects youngsters. In fact, up to 20% of children worldwide may experience symptoms at some point, making AD one of the most prevalent skin conditions in childhood. Many people outgrow the disease by adolescence, but a sizable percentage struggle with it well into adulthood, emphasizing the necessity for long-term management techniques. AD affects people of all ages, but mostly affects youngsters. Its incidence has been gradually increasing over the past few decades, especially in developed nations. In fact, AD is frequently regarded as one of the most prevalent skin conditions in children, affecting up to 20% of children worldwide at some point. Effective management measures are necessary throughout the lifespan, even though many people outgrow the illness by adolescence and a large portion continue to struggle with it into adulthood.(4-6)

Atopic dermatitis is largely hereditary, and families affected by the condition exhibit a significant familial clustering. Its growth, however, depends critically on the interaction of genetic susceptibility and environmental variables. The pathogenesis of AD is linked to variables such changes in the function of the epidermal barrier, immune system dysregulation, and microbial dysbiosis. The idea that AD progresses to other atopic disorders including allergic rhinitis and asthma is known as the "atopic march," which emphasizes the disease's systemic character and wide-ranging effects. Atopic dermatitis is diagnosed mostly by clinical assessment, which includes the patient's medical history, physical examination results, and symptoms. Clinicians can more reliably diagnose and classify AD with the help of established diagnostic criteria, such as the Hanifin and Rajka

criteria as well as the more current criteria put out by the American Academy of Dermatology. Laboratory tests can be used to rule out other disorders or gauge the severity of a disease, although they are usually not required for diagnosis.(3,7-9)

The treatment of atopic dermatitis is complex and frequently calls for a customized strategy based on the unique requirements and circumstances of the patient. The application of thorough skincare procedures targeted at preserving and repairing the skin barrier function is essential to its maintenance. While topical corticosteroids and calcineurin inhibitors can reduce inflammation during flare-ups, emollients and moisturizers are essential for moisturizing the skin and decreasing dryness. Furthermore, recognizing and avoiding triggers—such as certain foods, allergies, and environmental elements—can help control symptoms and lessen the likelihood of disease exacerbations. For more severe or resistant forms of atopic dermatitis, systemic therapy may be necessary in addition to topical ones. These could include immunosuppressive drugs, biological agents that target particular immunological pathways linked to the pathophysiology of AD, or oral corticosteroids. However, using systemic medicines requires close monitoring for unfavorable occurrences and careful evaluation of possible side effects. The use of probiotics, bleach baths, and phototherapy as complementary and alternative therapies for atopic dermatitis has gained popularity in recent years. Although there is conflicting evidence regarding their effectiveness, they offer other choices that might help certain people or supplement traditional treatments.(1,10,11)

Th1/Th2 imbalance in Atopic dermatitis

AD is an allergic condition which is caused due to imbalance in the immune system activity leading to overactive immune system. In normal conditions, the entry of allergen in the body causes a chain of actions, initiated by the intake of the pathogen by nearby Antigen Presenting Cells (APCs). These APCs initially destroy the allergen and present a molecular pattern of the allergen to Th-0 cell in the nearby lymph node. This molecular pattern gets recognized by the Th0 cells, which then converts the Th0 cells to Th1 cells. Th1 cells are responsible for the formation and release of IgG and IgM antibodies effective against the particular antigen. Further exposure of the same antigen causes the IgG and IgM antibodies to tag the antigen for immune-mediated destruction by the neutrophils and natural killer cells.(12-14)

In atopic dermatitis, the presentation of allergen by the APC to Th0 cells causes altered modulation of the Th0 activity, which leads to formation of Th2 cells instead of Th1 cells. These Th2 cells causes release of IgE antibodies, which are considered as biomarker of allergic condition. The level of IgE is found to be increased in various allergic conditions including atopic dermatitis. The released IgE travels in the systemic circulation and reaches the resident mast cells on skin and airways. The binding of IgE to the mast cells results in the sensitization of the mast cells. Mast cells, as denoted as machine guns of immune system, are always filled with granules containing inflammatory cytokines mainly histamine, leukotrienes, and prostaglandins. The further exposure of the same allergen in the body, now travels to the mast cells where it binds with the surface bound IgE antibodies. Binding of antigen to IgE causes the mast cells to release all the inflammatory cytokines in the skin and airways, which leads to allergic condition like atopic dermatitis and allergic rhinitis.(12-14)

Postbiotic *Lactobacilli spp.* in Atopic dermatitis

Live bacteria known as probiotics have gained a lot of attention due to their potential medicinal uses in treating a number of illnesses, including AD. Their potential to affect the make-up and activities of the gut microbiome—a complex ecosystem of bacteria living in the gastrointestinal tract—is the basis of their method of action in AD. Growing data indicates that dysbiosis, which is defined by changes in the diversity and composition of the gut microbiota, may exacerbate inflammatory responses and disturb immunological homeostasis, which may contribute to the pathogenesis of AD.(15,16)

Lactobacilli spp. are potential probiotics that has been studied for their role in allergic conditions like atopic dermatitis and allergic rhinitis. The cell wall of these probiotics contains essential components (including lipoteichoic acid and peptidoglycans) that can interact with the Toll-like receptor-2 (TLR2) and CD14 present on the Payer's patch of intestines. This interaction of cell wall components results in the alteration of immune system activity, which shifts the formation of Th0 from Th2 to Th1. This shift results in increased formation of Th1 cells instead of Th2 cells, which eventually reduces the formation of IgE, and reduces sensitization of mast cells. But because of various environmental factors, these probiotics gets degraded in tropical climate. The degradation of these probiotics results in initiation of reactive chain that eventually causes the degradation of all the essential cell wall components as well. As the cell wall components are the main ingredients responsible for the anti-allergic activity of *Lactobacilli spp.*, the prevention of the cell wall components is crucial. Heat attenuation is a process in which the probiotics are subjected to high temperature for short period of time followed by immediate cooling which thereby attenuates the probiotics but prevents the cell wall components. This particular method was adopted for the production of *Lactobacilli spp.* postbiotics, which thereby prevents the destruction of essential cell wall components and also renders superior stability compared to the live probiotics. The detailed mechanism of action of postbiotic *Lactobacilli spp.* in atopic dermatitis is presented in Figure 1.(12-14,17-21)

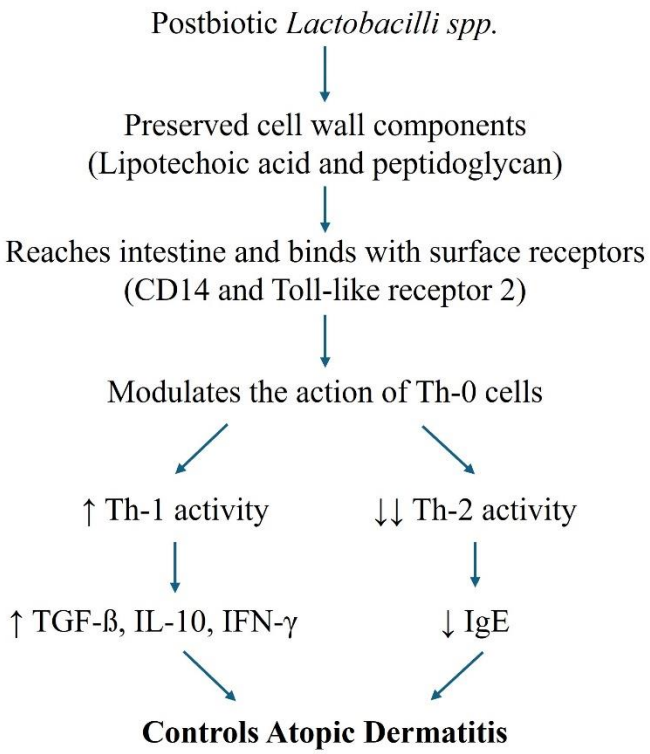

Fig. 1 – Mechanism of action of postbiotic *Lactobacilli spp.* in atopic dermatitis

Clinical evidence of *Lactobacilli spp.* in atopic dermatitis and allergic conditions

Various clinical studies have confirmed that postbiotic *Lactobacilli spp.* has comparable efficacy compared to the live *Lactobacilli spp.* in allergic conditions. In a clinical study, the therapeutic effect and safety of postbiotic *Lactobacilli spp.* was investigated in children with moderate AD. Postbiotic *Lactobacilli spp.* was administered to children aged 1-12 years with moderate AD for 12 weeks. The primary outcome, SCORing of AD (SCORAD) scores, showed a significant reduction in the postbiotic *Lactobacilli spp.* group compared to the control group. Levels of eosinophil cationic protein (ECP) and interleukin (IL)-31 tended to decrease in the postbiotic *Lactobacilli spp.* group, especially in children with AD for ⩾50 months. Safety analysis revealed no significant differences between the treated and control groups. The study concluded that oral administration of postbiotic *Lactobacilli spp.* demonstrated therapeutic effects on moderate AD, potentially correlated with reductions in ECP and IL-31 levels, particularly notable in longer-duration AD cases.(22)

A systematic review and meta-analysis were conducted which focused on the use of postbiotics, defined as dead microorganisms or their components, for treating AD. It covered studies from January 2012 to July 2022 and analyzed outcomes such as SCORAD scores, disease extension, intensity, and adverse events. The meta-analysis of three studies revealed that oral postbiotic *Lactobacillus spp.* significantly reduced SCORAD scores compared to placebo. The study concluded that oral postbiotic *Lactobacillus spp.* has the potential to alleviate AD severity, particularly reflected in reduced SCORAD scores.(23) Another systematic review evaluated the efficacy of oral *Lactobacilli spp.* postbiotics for managing AD symptoms in both pediatric and adult patients. Nine randomized controlled trials were included, involving 512 subjects. Trials in adults generally indicated symptomatic improvement. Dosage appeared to influence outcomes, and only one trial directly compared postbiotics with viable probiotics, reporting positive results in both groups. One trial reported shifts in gut microbial communities associated with postbiotic use. Overall, *Lactobacilli spp.* postbiotics may be effective as adjuvant therapy for AD.(24)

Conclusion

Probiotics hold sway in the realm of atopic dermatitis, aiding in the balance of gut flora, they bring vital respite. Their impact extends beyond mere gut health's scope, to calm the storm of inflammation where AD's symptoms lope. *Lactobacilli spp.* are probiotics that have anti-allergic potential

due to their cell wall components. But due to their relative instability in adverse environmental conditions, they are subjected to heat attenuation process to form postbiotics so that the cell wall components are retained with improved stability. Various studies have confirmed that postbiotic *Lactobacilli spp.* are comparable to live probiotics and able to improve symptoms in atopic dermatitis condition. Hence the use of postbiotic *Lactobacilli spp.* holds immense potential for real-world applications for the treatment of atopic dermatitis.

REFERENCES

1. Frazier W, Bhardwaj N. Atopic dermatitis: diagnosis and treatment. American family physician. 2020;101(10):590-8.
2. Torres T, Ferreira E, Gonçalo M, Mendes-Bastos P, Selores M, Filipe P. Update on atopic dermatitis. Acta medica portuguesa. 2019;32(9):606-13.
3. David Boothe W, Tarbox JA, Tarbox MB. Atopic dermatitis: pathophysiology. Management of atopic dermatitis: methods and challenges. 2017:21-37.
4. Bylund S, von Kobyletzki LB, Svalstedt M, Svensson Å. Prevalence and incidence of atopic dermatitis: a systematic review. Acta dermato-venereologica. 2020;100(12).
5. Fuxench ZC, Block JK, Boguniewicz M, Boyle J, Fonacier L, Gelfand JM, Grayson MH, Margolis DJ, Mitchell L, Silverberg JI, Schwartz L. Atopic dermatitis in America study: a cross-sectional study examining the prevalence and disease burden of atopic dermatitis in the US adult population. Journal of Investigative Dermatology. 2019;139(3):583-90.
6. Hadi HA, Tarmizi AI, Khalid KA, Gajdács M, Aslam A, Jamshed S. The epidemiology and global burden of atopic dermatitis: a narrative review. Life. 2021;11(9):936.
7. Kim J, Kim BE, Leung DY. Pathophysiology of atopic dermatitis: Clinical implications. InAllergy and asthma proceedings 2019 (Vol. 40, No. 2, p. 84). OceanSide Publications.
8. Malik K, Heitmiller KD, Czarnowicki T. An update on the pathophysiology of atopic dermatitis. Dermatologic Clinics. 2017;35(3):317-26.
9. Lyons JJ, Milner JD, Stone KD. Atopic dermatitis in children: clinical features, pathophysiology, and treatment. Immunology and Allergy Clinics. 2015;35(1):161-83.
10. Fishbein AB, Silverberg JI, Wilson EJ, Ong PY. Update on atopic dermatitis: diagnosis, severity assessment, and treatment selection. The Journal of Allergy and Clinical Immunology: In Practice. 2020;8(1):91-101.
11. Dattola A, Bennardo L, Silvestri M, Nisticò SP. What's new in the treatment of atopic dermatitis?. Dermatologic Therapy. 2019;32(2):e12787.
12. Fujimura Y, Kihara T. Immunohistochemical localisation of intercellular adhesion molecule-1 in follicle associated epithelium of Peyer's patches. Gut. 1994;35(1):46-50.
13. Hirota K, Turner JE, Villa M, Duarte JH, Demengeot J, Steinmetz OM, Stockinger B. Plasticity of TH17 cells in Peyer's patches is responsible for the induction of T cell–dependent IgA responses. Nature immunology. 2013;14(4):372-9.
14. Jung C, Hugot JP, Barreau F. Peyer's patches: the immune sensors of the intestine. International journal of inflammation. 2010 Sep 19;2010.
15. Rusu E, Enache G, Cursaru R, Alexescu A, Radu R, Onila O, Cavallioti T, Rusu F, Posea M, Jinga M, Radulian G. Prebiotics and probiotics in atopic dermatitis. Experimental and therapeutic medicine. 2019;18(2):926-31.
16. Lise M, Mayer I, Silveira M. Use of probiotics in atopic dermatitis. Revista da Associação Médica Brasileira. 2018;64:997-1001.
17. Huang CF, Chie WC, Wang IJ. Efficacy of Lactobacillus administration in school-age children with asthma: a randomized, placebo-controlled trial. Nutrients. 2018;10(11):1678.
18. Veerabhadraiah P, Muddiah D, Vaibhavi MK, Lavanya, Srinivas V, Pavitra. A Study on the Role of Probiotics In Nasal Allergy, UPJOHNS; 2022;10(1):35-41.
19. Peng GC, Hsu CH. The efficacy and safety of heat‐killed Lactobacillus paracasei for treatment of perennial allergic rhinitis induced by house‐dust mite. Pediatric allergy and immunology. 2005;16(5):433-8.
20. UP S, GB A, Chadha B. Comparative Case Study of Efficacy of Oral Bilastine Monotherapy to Concomittant Administration of Oral Bilastine with Probiotic in Patients with Allergic Rhinitis. Indian Journal of Otolaryngology and Head & Neck Surgery. 2023;75(3):2137-41.
21. Wang IJ, Wang JY. Children with atopic dermatitis show clinical improvement after Lactobacillus exposure. Clinical & Experimental Allergy. 2015;45(4):779-87.
22. Jeong K, Kim M, Jeon SA, Kim YH, Lee S. A randomized trial of Lactobacillus rhamnosus IDCC 3201 tyndallizate (RHT3201) for treating atopic dermatitis. Pediatric allergy and immunology. 2020;31(7):783-92.
23. Tanojo N, Irmadita Citrashanty I, Utomo B, Listiawan Y, Ervianti E, Tinduh D. Oral postbiotics derived from Lactobacillus sp. in treatment of atopic dermatitis: a meta-analysis. Acta Dermatovenerologica Alpina, Panonica et Adriatica. 2023;32(2):41-7.
24. Lima M, Paulino LC. Oral postbiotics as a therapeutic strategy for atopic dermatitis: A systematic review of randomized controlled trials. Journal of the American Nutrition Association. 2024;43(2):139-46.