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Review Article

The Role of *Lactiplantibacillus plantarum* in Modulating the Gut-Skin Axis: A Comprehensive Review on Its Potential in Managing Atopic Dermatitis

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Abstract: Atopic Dermatitis is a chronic inflammatory skin condition marked by impaired skin barrier function, immune system irregularities, and microbial imbalance. This research examines the efficacy of *Lactiplantibacillus plantarum,* a probiotic recognized for its established safety and advantageous characteristics, in the management of atopic dermatitis. The pathophysiology of atopic dermatitis encompasses genetic, environmental, and immunological components, with dysbiosis of skin and gut microbiota being essential. *L. plantarum* has shown beneficial effects in controlling gut and skin microbiota, improving skin barrier integrity, and modulating immunological responses via processes including short-chain fatty acid (SCFA) synthesis, cytokine regulation, and competitive exclusion of pathogens. Clinical investigations demonstrate that *L. plantarum* supplementation can diminish the severity of atopic dermatitis, as assessed by the SCORAD index, and enhance skin barrier integrity. The effectiveness of probiotic therapy may be affected by genetic, nutritional, and environmental variables. This review emphasizes the promise of *L. plantarum* as a therapeutic agent for atopic dermatitis, while also discussing the limitations and future possibilities for probiotic-based therapies in managing this intricate condition.

Keywords: Atopic dermatitis; *Lactiplantibacillus plantarum*; Gut-Skin Axis; Microbiota Dysbiosis; Immune Modulation

1. INTRODUCTION

Atopic dermatitis, sometimes referred to as atopic eczema, is a persistent inflammatory skin condition marked by xerosis, rash, and severe pruritus [1]. It frequently manifests as recurrent eczematous lesions and is linked to various atopic disorders, including asthma, allergic rhinitis, and food allergies [2]. One, four, five. The condition impacts a considerable segment of the population, exhibiting greater prevalence in youngsters (10-20%) than in adults (1-3%) [3][1]. The pathogenesis of atopic dermatitis entails a complex interaction of genetic, environmental, and immunological variables, resulting in immune system dysregulation and compromised skin barrier function [4][5]. The skin and gut microbiota are integral to the development and progression of atopic dermatitis.

Dysbiosis, the imbalance of microbial populations, is a crucial element in the development of Atopic dermatitis [5][4][6][7].

The skin microbiome, comprising bacteria, fungi, and viruses, aids in preserving skin homeostasis and inhibiting pathogen colonization. In atopic dermatitis, there is a significant decline in microbial diversity, accompanied by an increase in *Staphylococcus aureus* colonization, which is associated with disease severity [8][9][10]. The gut microbiota impacts the skin via the gut-skin axis, influencing immune responses and skin barrier functions. Changes in gut microbiota can affect the progression of atopic dermatitis by impacting systemic inflammation and immunological control [5][7][11]. Probiotics have demonstrated potential in altering gut microbiota to mitigate atopic dermatitis symptoms, while their therapeutic efficacy is still under examination [6][7][10].

Probiotics have emerged as a promising therapeutic strategy for modulating the gut-brain axis. Multiple studies have shown their capacity to restore microbial equilibrium, improve skin barrier function, and modulate immune responses. Most existing reviews primarily examine the role of general probiotics or the gut microbiome in atopic dermatitis [5][6][7]. Numerous significant reviews have enhanced our comprehension of the gut-skin axis and microbial therapy in atopic dermatitis. Wrześniewska et al. (2024) examined the significant role of microbiota in the pathogenesis and treatment strategies of atopic dermatitis [5]. Alam et al. (2022) investigated microbiota manipulation and its therapeutic implications [6], whereas Moniaga et al. (2022) highlighted the connection between altered microbiota and itch modulation in atopic dermatitis[7]. Nonetheless, none of these studies offered a strain-specific of *L. plantarum*, highlighting the necessity for the current review. *L. plantarum*, previously known as *L. plantarum*, is a multifaceted lactic acid bacterium renowned for its probiotic characteristics [12][13][14].

A number of strains of *L. plantarum* have demonstrated encouraging outcomes in in vitro experiments regarding their acid and bile resistance, adhesiveness, and antibacterial characteristics [13][15]. These characteristics render it a viable option for therapeutic uses, including the regulation of gut microbiota to enhance skin health and potentially mitigate disorders such as atopic dermatitis [12][13][16]. This study fills the identified gap by providing a thorough and targeted examination of *L. plantarum* in relation to atopic dermatitis. In contrast to earlier reviews that cover probiotics in broad strokes, this article explores the biological mechanisms through which *L. plantarum* maintains gut and skin homeostasis, including its immunoregulatory effects through the production of short-chain fatty acids (SCFA) and cytokine modulation. Furthermore, it compiles clinical data showing how well the strain works to treat atopic dermatitis. The review offers more focused and clinically relevant insights for researchers and practitioners looking for strain-specific, alternative, or adjunctive therapies for atopic dermatitis by focusing on this particular probiotic.

2. MATERIALS AND METHODS

The method used is a literature review derived from various relevant studies. This review was conducted by collecting research data and scientific articles online. The research data obtained comes from the Scopus database. The keywords in this article review: atopic dermatitis, skin microbiota, gut-skin axis, probiotics, *Lactiplantibacillus plantarum*, immune modulation, SCFA, dysbiosis, and microbiome. Articles were selected based on their relevance to the research objectives and were limited to publications from the last 12 years.

3. RESULTS AND DISCUSSION

3.1. Lactiplantibacillus plantarum: Characteristics and Mechanisms of Action

3.1.1. Scientific classification and biological characteristics

Lactiplantibacillus plantarum is a species of gram-positive lactic acid bacteria. *L. plantarum* demonstrates ecological and metabolic adaptability, enabling it to inhabit various ecological niches, including fermented foods, meats, plants, and the mammalian gastrointestinal tract [17].

Scientific Classification of *L. plantarum*
Domain: Bacteria
Phylum: Firmicutes
Class: *Bacilli*
Order: *Lactobacillales*
Family: *Lactobacillaceae*
Genus: *Lactiplantibacillus*
Species: *Lb. plantarum*

L. plantarum has Qualified Presumption of Safety (QPS) certification from the European Food Safety Authority (EFSA) and Generally Recognized as Safe (GRAS) classification from the U.S. Food and Drug Administration (FDA). Moreover, it is recognized as a microorganism with a recorded history of culinary use. The safety of any probiotic strain must be verified using rigorous procedures prior to any practical implementation. The administration of probiotics in immunocompromised individuals necessitates further scrutiny and likely the establishment of particular protocols [18]. The complex adaptation strategy used by L. plantarum's acid tolerance mechanisms to deal with acid stress included altering fatty acid biosynthesis, controlling the transcription level of genes related to glycolysis and proton pumps, generating alkaline substances, and enhancing protein folding and translational accuracy [19]. Four strategies, induction of bile salt hydrolases, modification of membrane composition and fluidity, protection against oxidative damage, and maintenance of the proton motive force are thought to be crucial for L. plantarum's ability to withstand the stress of exposure to bile salts [12]. In L. plantarum, a mannose-specific adhesin has been found; this adhesin may play a role in intestinal colonization [20] L. plantarum has shown the ability to modify epithelial barrier function in both in vitro and in vivo settings. The benefits were shown to arise from many interconnected pathways, including the preservation of key tight-junction proteins, the attenuation of pro-inflammatory cytokine production, and the modulation of gut microbiota composition [12] [21].

3.1.2. Role in gut and skin microbiota homeostasis

The presence of L. plantarum on the skin has the potential to improve skin barrier function and influence local immune responses, thereby decreasing excessive inflammation and supporting overall skin health [22], [23], [24]. The intake of L. plantarum may result in alterations in gut bacterial populations, including an increase in beneficial bacteria such as Bifidobacterium and a reduction in harmful bacteria like Proteobacteria. The modifications contribute to a decrease in gut and systemic

inflammation, which may have a positive impact on skin health [22]. Strains of L. plantarum exhibit antimicrobial properties against skin pathogens including Staphylococcus aureus, Cutibacterium acnes, and Candida albicans. The antimicrobial action plays a significant role in sustaining a balanced skin microbiota, which is essential for preventing and managing atopic dermatitis [25] [26].

The presence of L. plantarum on the skin has the potential to improve skin barrier function and influence local immune responses, thereby decreasing excessive inflammation and supporting overall skin health. [26]According to studies, probiotics, such as L. plantarum, can considerably lessen the severity of atopic dermatitis. This is assessed through enhancements in clinical metrics like the Scoring Atopic Dermatitis (SCORAD) index [27] [28]. The positive impacts of L. plantarum on atopic dermatitis stem from its capacity to influence immune responses, lower pro-inflammatory cytokines, and boost anti-inflammatory cytokines. This contributes to the alleviation of skin inflammation and enhances symptom management [23] [27] [29].

3.1.3. Short-chain fatty acid (SCFA) production and immunomodulatory effects

SCFAs, including butyrate, acetate, and propionate, are metabolites generated by gut bacteria during the fermentation of food fibers. They regulate the host's metabolism, intestinal function, and immunological responses. SCFAs have been demonstrated to alter immunological responses and reduce inflammation, including atopic dermatitis. They affect the function and fate of immune cells, helping to prevent and treat inflammatory disorders [30] [31]. L. plantarum has demonstrated a significant increase in the total SCFA content within the cecal contents of mice, contributing positively to intestinal health [32]. L. plantarum enhances the synthesis of advantageous metabolites like short-chain fatty acids, contributing to the regulation of immune responses and the preservation of gut health. Short-chain fatty acids generated by gut microbiota, including those derived from L. plantarum, have the potential to impact the immune system by interacting with different immune cells and pathways, including T cells, B cells, macrophages and cytokine production [30] [33].

L. plantarum strains can alter immune responses by altering cytokine production. L. plantarum NCIMB8826 releases IL-10, IL-12, and TNF-α, which balance Th1 and Th2 responses [34]. L. plantarum has the potential to lower blood IgE levels, which are commonly raised in atopic dermatitis's patients. This reduction causes a decrease in Th2 cytokines (e.g. IL-4, IL-5) and an increase in Th1 cytokines (e.g. IFN-γ), leading to a more balanced immune response [34] [35]. L. plantarum treatment has been proven to enhance the numbers of regulatory T cells (Tregs), which play an important role in maintaining immunological tolerance and limiting excessive inflammatory responses [35], [36].

3.1.4. Mechanisms of adhesion and colonisation in the gut and skin

L. plantarum uses unique surface proteins to cling to the gut lining. For example, the EnoA1 alfa-enolase protein interacts to fibronectin, an extracellular matrix protein, increasing the adherence of intestinal cells [37]. The adhesive ability of L. plantarum is affected by pH. Bacteria adhere more to mucin and intestinal cells in acidic conditions, whereas in alkaline ones, adhesion decreases [38]. Glyceraldehyde-3-phosphate dehydrogenase (GAPDH) on the surface of L. plantarum binds to human colonic mucus, particularly to ABO blood group antigens, increasing adhesion (Wang dkk.,

2018). L. plantarum strains have mannose-specific adhesion, which is necessary for adhering to intestinal mucus and competing with pathogens for adhesion sites [39]. L. plantarum strains like as RS-09 demonstrate significant adhesion and long-term colonization ability, notably in the cecum and colon, which are crucial for gut health [40]. L. plantarum might alter the skin microbiome, potentially lowering the colonization of dangerous bacteria such as Staphylococcus aureus, which is frequently related with atopic dermatitis[41][42]. L. plantarum inhibits pathogen attachment to epithelial cells, which may help in treating skin infections and inflammation linked with atopic dermatitis[43].

3.1.5. Preservation of Key Tight-Junction Proteins in Ephitelial Barrier Function

L. plantarum has demonstrated the ability to augment transepithelial electrical resistance (TEER), signifying enhanced barrier integrity[44][45][46]. This is accomplished by inhibiting the degradation of TJ proteins and regulating inflammatory responses. L. plantarum aids in preserving the expression and distribution of tight junction proteins, including claudin-1, occludin, and ZO-1, which are essential for barrier integrity [44][47][45]. It inhibits the degradation and alteration of these proteins induced by pathogens such as E. coli [47]. The probiotic diminishes the expression of pro-inflammatory cytokines (e.g., IL-8, TNF-α) and alters signaling pathways such as NF-κB and MAPK, which are implicated in inflammatory reactions[44][45]. Through the preservation and enhancement of TJ protein expression, L. plantarum may help atopic dermatitis patients regain the function of their skin barrier, which would lessen symptoms and improve skin health[48][44][47].

3.2. Pathophysiology of Atopic Dermatitis

3.2.1. Skin barrier dysfunction and the role of filaggrin

The skin barrier, which is largely found in the stratum corneum (SC), is critical for guarding against external stressors and reducing water loss. Dysfunction in this barrier is the characteristic of atopic dermatitis [49]. Filaggrin aggregates keratin filaments, forming a keratin network that binds cornified envelopes and collapses keratinocytes into flattened corneocytes, contributing to the physical strength of the skin [50] [51]. Filaggrin is an important structural protein in the SC that maintains skin barrier integrity. It collects keratin filaments, forming a network that supports the skin and contributes to its hydration, breaking down into natural moisturizing factors (NMFs) [50] [49] [51]. Mutations in the filaggrin gene (FLG) are highly related with atopic dermatitis. These mutations cause a lack or malfunction of filaggrin, which results in reduced skin barrier function [51] [52] [53]. Individuals with FLG mutations frequently display more severe atopic dermatitis symptoms, greater skin dryness, and a higher chance of acquiring other atopic disorders such as asthma, allergic rhinitis [54][52]. Filaggrin deficiency causes decreased skin barrier function, allowing allergens and pathogens to permeate the skin more easily, triggering inflammatory reactions and exacerbating atopic dermatitis [55][56] [57].

3.2.2. Immune system dysregulation: Th2-dominant response, increased IL-4, IL-13, IL-31, and IgE

Atopic dermatitis is defined by a Th2-dominant immune response, which is pivotal in its development. This response is mostly regulated by cytokines including IL-4, IL-13, IL-31, and IgE, which play a role in the inflammatory mechanisms and manifestations linked to atopic dermatitis. Dysregulation of the immune response is pivotal in atopic dermatitis, characterized by a Th2-

dominant immune response as a significant component. Th2 cytokines, such as interleukin (IL)-4, IL-5, IL-13, and IL-31, are synthesized by diverse innate immune cells in the affected skin of atopic dermatitis, facilitating type 2 inflammation [58]. Cytokines generated from epithelial cells, including thymic stromal lymphopoietin (TSLP), IL-33, and IL-25, induce type 2 inflammation by regulating different cells, such as group 2 innate lymphoid cells. IL-31, a recently discovered type 2 cytokine, elicits pruritus by interacting with sensory neurons. IL-22, a hallmark cytokine produced by TH22 cells, is markedly expressed in atopic dermatitis skin and plays a role in the pathogenesis of atopic dermatitis [59].

IL-4 and IL-13 are essential in the Th2 immune response and have a substantial role in the development of atopic dermatitis. IL-4 and IL-13 reduced expression of epidermal barrier proteins and inhibition of keratinocyte development, resulting in skin barrier impairment, The creation of IgE and isotype switching by B-lymphocytes, a characteristic feature of allergic responses, degranulation of mast cells and basophils contributes to inflammation and pruritus. IL-4 and IL-13 are also involved in the recruitment of inflammatory cells into tissues and the pruritic response [60] [61]. IL-31 is predominantly synthesized by activated Th2 cells and is linked to the onset of pruritus in atopic dermatitis. Increased concentrations of IL-31 have been detected in individuals with atopic dermatitis, and IL-31-transgenic mice exhibit atopic dermatitis-like dermal inflammation. IL-31 contributes to pruritus and inflammation in atopic dermatitis, however it does not directly provoke localized cutaneous inflammation [62] [63]. IgE-mediated reactions are a crucial component of atopic dermatitis, as allergen sensitization results in the synthesis of IgE. This pathway encompasses both IgE-mediated and non-IgE-mediated Th2 responses to allergens [60] [64]. Increased IgE levels are linked to the allergic cascade and exacerbate the persistent inflammation observed in atopic dermatitis [65].GATA-3 is a transcription factor essential for the development of Th2 immunity. Increased GATA-3 mRNA levels have been detected in patients with atopic dermatitis, indicating its potential role in the disease's development. SOCS-3, a negative regulator of cytokine signaling, is also upregulated in atopic dermatitis, signifying its involvement in cytokine imbalance [66]. Mast cells and basophils secrete several mediators upon activation, facilitating the inflammatory processes and pruritus in atopic dermatitis. Eosinophils are involved in tissue remodeling and inflammation [67].

3.2.3. Relationship between gut microbiota dysbiosis and Atopic Dermatitis pathogenesis

Dysbiosis of gut microbiota can profoundly affect the immune system, which is essential in atopic dermatitis. Dysbiosis may result in immunological dysregulation, exacerbating the onset and severity of atopic dermatitis [68] [5] [69] [70]. The gut microbiota specifically modulates the immunological response via bacterial metabolites, including short-chain fatty acids (SCFAs), which participate in the signaling pathways of the gut-skin axis [5] [70]. The gut microbiota can impact the makeup of the skin microbiome, thereby affecting the integrity of the skin barrier. A compromised skin barrier is a characteristic of atopic dermatitis, and gut dysbiosis can aggravate this illness by enhancing inflammation and diminishing barrier integrity [5] [70] [71]. Research indicates that persons with DA frequently display modified gut microbiota profiles, marked by a reduction in advantageous bacteria such as Bifidobacterium and an elevation in potentially detrimental bacteria like Clostridium difficile [70] [72]. This imbalance may result in heightened intestinal permeability

("leaky gut"), permitting endotoxins to infiltrate the bloodstream and incite systemic inflammation [71].

3.2.4. The role of regulatory T cells (Tregs) in controlling inflammation in Atopic Dermatitis

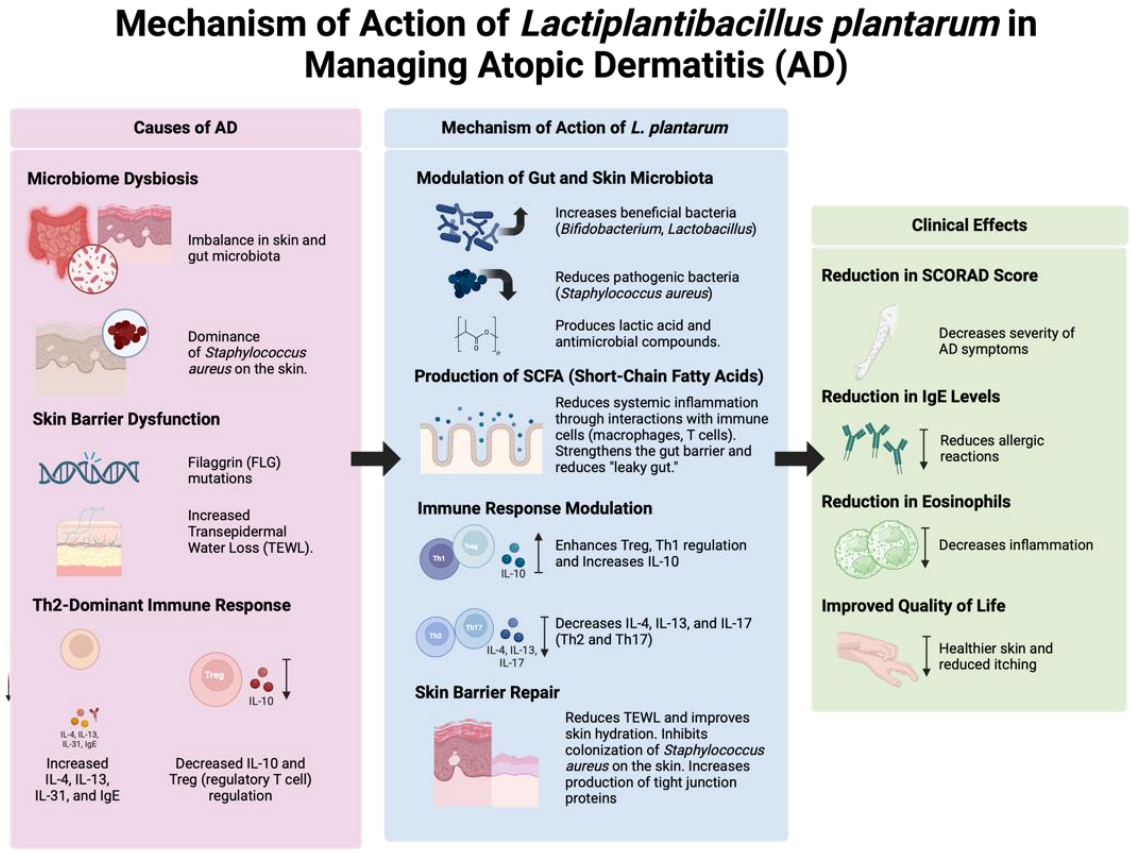

Figure 1. Mechanism of Action of *L. plantarum* in the Management of Atopic Dermatitis. The figure illustrates the primary methods via which *L. plantarum* regulates the gut-skin axis to mitigate symptoms of atopic dermatitis.

Regulatory T cells (Tregs) are essential in controlling immunological responses and preserving immune homeostasis, particularly in relation to atopic dermatitis, a chronic inflammatory skin disorder. Tregs are crucial for inhibiting the activation and multiplication of effector T cells (Teffs), which mediate the inflammatory response in atopic dermatitis. In patients with severe atopic dermatitis, Tregs exhibit a diminished capacity to inhibit Teff growth, hence contributing to the immunological responses characteristic of the condition [73]. Tregs secrete immunosuppressive cytokines, including IL-10 and TGF-β, that regulate inflammation. In atopic dermatitis patients, the levels of these cytokines are frequently diminished, suggesting impaired regulatory function [74] [73]. Evidence indicates that Tregs can differentiate into Th2 cells, which play a role in the allergic response associated with atopic dermatitis. This bidirectional conversion may intensify the inflammatory response in atopic dermatitis [75] [61]. Reduction of Foxp3+ Tregs in mouse models results in intensified skin inflammation, heightened recruitment of inflammatory cells, and increased levels of Th2 cytokines [76] [77]. Tregs modulate cutaneous allergic inflammation by governing IFN-γ-induced neutrophilic infiltration and NETosis (neutrophil extracellular traps). The reduction of Tregs leads to heightened neutrophil activity and skin inflammation, which can be alleviated by

neutralizing IFN-γ [77]. Various subpopulations of Tregs, including Th2-Tregs and Th17-Tregs, are elevated in patients with atopic dermatitis, especially in those possessing filaggrin (FLG) null mutations. These subpopulations contribute to the immunological aberration noted in atopic dermatitis [78].

3.3. Effects of L. plantarum on Atopic Dermatitis

3.3.1. In Vitro Studies: Regulation of inflammatory cytokine expression (IL-10, IL-12, IFN-γ, IL-4, IL-6, IL-17, IL-23)

L. plantarum has demonstrated the ability to enhance IL-6 expression in human PBMCs and Caco-2 cells [79] [80]. Nonetheless, it may also suppress IL-6 production under specific situations, such as in the presence of ETEC K88 [81]. IL-12 is increased by L. plantarum, facilitating a Th1 response [82], [83]. L. plantarum can stimulate IFN-γ production, hence facilitating a Th1 immune response [84] [83]. L. plantarum enhances TNF-α expression in multiple cell types, including PBMCs and Caco-2 cells [80], [84] . L. plantarum is recognized for augmenting IL-10 production, which is essential for its anti-inflammatory properties. This phenomenon has been reported in peripheral blood mononuclear cells, dendritic cells, and macrophages [84] [85] [86] [87]. L. plantarum can diminish IL-4 production, thereby attenuating Th2 responses [83] [82]. L. plantarum has a complex effect on IL-17. It can both increase and decrease IL-17A and IL-17F production depending on the specific strain and experimental conditions [88] [89]. Analogous to IL-17, L. plantarum can influence these cytokines, with certain strains diminishing their levels in stimulated PBMCs [88].

3.3.2. In Vivo Studies: Effects of L. plantarum on immune response, microbiota homeostasis, and skin barrier function.

L. plantarum has demonstrated the ability to improve immune function in immunosuppressed mice by reinstating the expression of particular immunological markers in the spleen and augmenting the quantity of goblet cells in the intestine [90]. It can regulate immunological responses by promoting T helper (Th) 1 or T regulatory cells, which are essential for balancing Th1/Th2 immune responses, vital for controlling allergic reactions [91]. The oral treatment of L. plantarum lysates in mice diminished epidermal thickness and enhanced skin barrier function, indicating its potential for treating inflammatory disorders [83]. L. plantarum can alter gut microbiota composition, evidenced in immunosuppressed mice, where it reduced Firmicutes and elevated Verrucomicrobia and Actinobacteria [90]. L. plantarum has demonstrated the ability to boost skin barrier function by enhancing moisture retention, decreasing transepidermal water loss (TEWL), and mitigating hot flushes in clinical trials [92]. It can safeguard against epithelial barrier damage induced by pathogens such as enteroinvasive Escherichia coli by preserving the integrity of tight junction proteins [47].

3.4. Clinical Studies in Atopic Dermatitis Patients

3.4.1. Impact of *L. plantarum* supplementation on clinical symptoms (SCORAD Index, TEWL, IgE, eosinophils)

Numerous investigations have demonstrated that L. plantarum markedly decreases the SCORAD index, signifying a reduction in atopic dermatitis severity. L. plantarum CCFM8610 markedly reduced the SCORAD index in patients with atopic dermatitis [93]. Furthermore, the

supplementation of L. plantarum IS-10506 led to a notable decrease in SCORAD scores among both pediatric and adult patients with atopic dermatitis [35] [94]. The SCORAD scores of another trial using L. plantarum CJLP133 likewise showed a considerable decline [95] [96]. TEWL, an indicator of skin barrier function, was markedly decreased following the administration of a probiotic blend containing L. plantarum, signifying enhanced skin barrier integrity [97]. The effect of L. plantarum on IgE levels seems to be inconsistent. Certain investigations indicated no significant alteration in serum IgE levels following supplementation with L. plantarum [35], [94], [96]. Nevertheless, some research saw a decrease in IgE levels, indicating a possible immunomodulatory impact [98]. Eosinophil counts, commonly raised in allergic situations, were markedly decreased in individuals administered L. plantarum CJLP133 [96]. The decrease in eosinophil counts corresponds with the noted clinical enhancements in atopic dermatitis symptoms .

3.4.2. Effects on gut microbiota composition and immune balance

L. plantarum CCFM8610 markedly affected the gut microbiota in atopic dermatitis patients by elevating the proportion of Bacteroidetes and diminishing the Firmicutes/Bacteroidetes (F/B) ratio. This strain downregulated functional genes related to Staphylococcus aureus infection and elevated steroid hormone production [93] . L. plantarum ZDY2013 was demonstrated to modulate changes in intestinal microbiota induced by allergens, namely diminishing Rikenella, Ruminiclostridium, and Lachnospiraceae UCG-006 [99]. The administration of L. plantarum CCFM8610 led to a notable reduction in the SCORAD index, signifying an enhancement in atopic dermatitis symptoms. It also elevated serum IL-10 levels, an anti-inflammatory cytokine, indicating an immunomodulatory action [93]. Supplementation with L. plantarum IS-10506 in adults with mild to severe atopic dermatitis dramatically reduced IL-4 and IL-17 levels while elevating IFN-γ and Foxp3+ levels, suggesting a transition towards a more equilibrated immune response [35]. L. plantarum ZDY2013 and Lactobacillus rhamnosus GG were observed to mitigate allergy responses by reducing serum IgE levels and facilitating the development of T helper (Th) 1 and T regulatory cells, hence decreasing the Th2-dominant response [99].

3.5. Clinical Implications and Challenges in Probiotic Use for Atopic Dermatitis

3.5.1. Factors influencing the success of probiotic therapy (genetics, diet, environment)

The effectiveness of probiotic therapy, such as *L. plantarum*, may be affected by hereditary variables. The C-159T polymorphism of the CD14 receptor gene has been linked to the onset of atopic dermatitis. Probiotics may influence chronic inflammation by activating the CD14 receptor, indicating that genetic variations can affect the efficacy of probiotic therapies [100]. Genetic predispositions influencing immunological responses, including elevated total IgE levels and heightened production of transforming growth factor (TGF)-β, have been associated with improved clinical outcomes in atopic dermatitis patients undergoing *L. plantarum* therapy [95]. The amalgamation of *L. plantarum* with additional dietary supplements, such as β-1,3/1,6-glucan, has demonstrated superior immunomodulatory benefits, mitigating atopic dermatitis symptoms more efficiently than *L. plantarum* in isolation. This combination markedly reduced Th2 and Th17 cell transcription factors while elevating Th1 and Treg cell markers [36]. The gut microbiota's makeup,

shaped by nutrition, is essential for the efficacy of probiotic therapy. Treatment with *L. plantarum* has been demonstrated to modify gut microbiota composition, enhancing beneficial bacteria such as *Bacteroidetes* and decreasing the *Firmicutes*/*Bacteroidetes* ratio, which correlates with ameliorated atopic dermatitis symptoms [93]. The microbial milieu, encompassing beneficial bacteria, profoundly affects atopic dermatitis. Extracellular vesicles (EVs) derived from *L. plantarum* have demonstrated efficacy in diminishing skin inflammation and enhancing skin barrier integrity in atopic dermatitis models, indicating that environmental microbial elements can affect the efficacy of probiotic interventions [101]. Patients of younger age and extended treatment durations have demonstrated significant alleviation of atopic dermatitis symptoms when administered *L. plantarum* [27].

3.5.2. Potential combination with other therapies

The combination of *L. plantarum* with prebiotics has shown notable clinical enhancements in individuals with atopic dermatitis. A study involving children with atopic dermatitis shown that a synbiotic combination of *Lactobacillus rhamnosus* GG and prebiotics resulted in a greater overall therapeutic effect, shorter exacerbation durations, and enhanced SCORAD index relative to antiallergic medication alone. The combined use of probiotics and prebiotics can augment the gut microbiota, elevating beneficial bacteria such as *Bifidobacteria* and *Lactobacilli*, which are correlated with ameliorated atopic dermatitis symptoms [102] [103].

Table 1. *Summary of Studies on L. plantarum for Atopic Dermatitis*

Study Type	Strain	Model/System	Key Findings	Reference
In Vitro	*L. plantarum* NCIMB8826	PBMCs, dendritic cells	Induced IL-10, IL-12, TNF-α; modulated Th1/Th2 balance	[34]
In Vitro	*L. plantarum* 299v	Human PBMCs	Modulated cytokine profile; enhanced IL-10	[85]
In Vitro	*L. plantarum* OLL2712	Intestinal dendritic cells	Promoted IL-10 production; anti-inflammatory effects	[86]
In Vitro	EVs from *L. plantarum*	Human keratinocyte cell culture (HaCaT)	Protected against inflammation caused by S. aureus EVs; reduced IL-6 and TNF-α	[101]
In Vitro	*L. plantarum* CJLP55	Mouse splenocyte & macrophage cultures	Downregulated inflammatory cytokines; upregulated regulatory T cell markers	[98]
In Vitro	*L. plantarum* (unspecified strain)	Human intestinal epithelial cells & immune cells	Suppressed pro-inflammatory cytokines (IL-6, TNF-α); enhanced Treg-related markers	[104]
In Vivo	*L. plantarum* + β-glucan	Atopic dermatitis - induced mice	Enhanced Treg/Th1 markers; reduced Th2/Th17	[36]

continued Table 1..

In Vivo	*L. plantarum* lysates	NC/Nga mice	Improved skin barrier; reduced epidermal thickness	[83]
In Vivo	*L. plantarum* CJLP133	Atopic dermatitis - induced mice	Reduced SCORAD, IgE, IL-4; increased Tregs	[96]
In Vivo	*L. plantarum* CJLP133	NC/Nga mice with house dust mite-induced dermatitis	decreased serum IgE, modulation of Th1/Th2 cytokines, reduced skin inflammation	[105]
In Vivo	*L. plantarum* CJLP55	Atopic dermatitis - induced mice	Decreased skin inflammation and Th2 cytokines	[98]
In Vivo	*L. plantarum* IS-10506	BALB/c mice	increased T-reg cells and balancing Th1/Th2 cytokine responses	[106]
In Vivo	*L. plantarum* K8	Atopic dermatitis - induced mice	Increased skin hydration, improved barrier function	[107]
In Vivo	*L.plantarum* LM1004	Atopic dermatitis - induced rat and mice	Reduced vasodilation, pruritus, edema, serum histamine; altered gut microbiota	[108]
In Vivo	*L. plantarum* HD02 and MD159	Atopic dermatitis - induced mice	Reduced MCPT-1, IgE, TEWL; increased Foxp3+ T cells	[109]
Clinical	*L. plantarum* CCFM8610	Atopic dermatitis patients	Lowered SCORAD, improved gut microbiota and IL-10	[93]
Clinical	*L. plantarum* IS-10506	Adults and children with atopic dermatitis	Reduced IL-4, IL-17; increased IFN-γ and Foxp3+	[35][94]
Clinical	*L. plantarum* CJLP133	Children with atopic dermatitis	Lower SCORAD and eosinophil counts	[95][96]
Clinical	*L. plantarum* (multi-strain synbiotic)	Children with atopic dermatitis	Reduced TEWL; improved clinical symptoms	[97]

3.6. Product Development and Delivery Systems for Lactiplantibacillus plantarum

In order to treat atopic dermatitis, researchers have looked into a number of ways to get L. plantarum into the body. Utilizing this probiotic's immunomodulatory and gut microbiota-modulating qualities, the main emphasis has been on oral administration. Supplements containing a single strain of L. plantarum have also been tested. For instance, it has been demonstrated that the kimchi-derived L. plantarum CJLP133 suppresses atopic dermatitis symptoms and alters immune responses in both children and mouse models [96][105]. In atopic dermatitis-induced mice [98], a different strain of L. plantarum CJLP55, which was also isolated from kimchi, showed comparable

therapeutic effects. Probiotic mixtures, including L. plantarum, have been used in a number of studies to treat atopic dermatitis. For example, in an atopic dermatitis mouse model, a combination of Bifidobacterium longum and L. plantarum significantly decreased dermatitis scores and immune markers [104]. Children 's atopic dermatitis symptoms were considerably reduced in another study using a synbiotic supplement that contained L. plantarum in addition to other probiotics and prebiotics [110]. The anti- atopic dermatitis effects of herbal extracts fermented with L. plantarum have been studied. In mouse models, these extracts in topical application reduced atopic dermatitis symptoms by demonstrating significant immunosuppressive effects and increased bioavailability [111]. The application of extracellular vesicles made from L. plantarum has also been investigated. In atopic dermatitis models, these EVs were shown to improve skin barrier functions and decrease skin inflammation, indicating a new way to deliver the probiotic's advantageous effects [101].

4. CONCLUSION

Atopic dermatitis is a multifaceted disorder affected by genetic, immunological, and microbiological factors. *L. plantarum* demonstrates potential as a probiotic treatment for atopic dermatitis by altering microbiota, improving skin barrier integrity, and controlling immune responses. Clinical trials demonstrate its potential to diminish atopic dermatitis severity and enhance skin health. Nonetheless, efficacy may fluctuate due to genetic, nutritional, and environmental influences. Additional research is required to enhance its application; however, *L. plantarum* provides a secure and natural method for alleviating atopic dermatitis symptoms. The role of *L. plantarum* is likely to become more important in treating atopic dermatitis. Future research might concentrate on strain-specific mechanisms, effective dosage strategies, and personalized probiotic therapies customized to individual genetic and microbiome profiles. The incorporation of next-generation sequencing, metabolomics, and microbiota-targeted formulations may augment the efficacy of *L. plantarum*. Additionally, innovative delivery strategies such as topical formulations, encapsulated postbiotics, or modified vesicles may offer additional methods for targeting the skin barrier and modifying immune responses. Extended clinical trials involving heterogeneous groups will be essential to confirm safety and efficacy. *L. plantarum* has potential as both a therapeutic adjuvant for atopic dermatitis and as a model organism in the wider scope of microbiome-based dermatological treatments.

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