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Probiotics and Their Role in Celiac Disease: A Review of Animal, Cellular, and Human Studies

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A B S T R A C T

Objective: Celiac disease is a chronic autoimmune disorder of the small intestine, characterized by gluten sensitivity and villous atrophy, which leads to nutrient malabsorption and gastrointestinal complications. Emerging evidence suggests that alterations in the gut microbiota may significantly influence the severity of celiac symptoms. Consequently, probiotics have received increasing attention as a potential adjunctive therapeutic strategy.

Methods: This review systematically examined studies published between 2010 and 2025, identified through searches in major databases, including PubMed, Scopus, and Web of Science. The search focused on studies investigating the effects of probiotics on gut microbiota modulation, regulation of inflammatory immune responses, and improvement of gastrointestinal symptoms in individuals with celiac disease.

Results: Evidence from clinical and preclinical studies indicates that probiotic supplementation particularly strains from the genera *Bifidobacterium* and *Lactobacillus* may confer beneficial effects by modulating gut microbial composition, attenuating inflammatory immune responses, and alleviating gastrointestinal symptoms in celiac patients. However, some studies report inconsistent effects on systemic immune markers and celiac-specific antibodies. Overall, probiotics appear to be safe when administered alongside a gluten-free diet and may positively influence inflammation, microbial balance, and patient quality of life. Nonetheless, current evidence remains insufficient to draw definitive conclusions regarding long-term efficacy, emphasizing the need for larger, well-designed clinical trials.

Conclusion: Current evidence suggests that probiotics may serve as a useful adjunct to a gluten-free diet in managing celiac disease by promoting gut microbial balance and modulating inflammatory immune responses. However, heterogeneity in study outcomes and limitations in human trials highlight the necessity for more extensive, standardized clinical research to determine optimal strains and dosing regimens.

Keywords: Probiotics, Celiac Disease, Gut Microbiota, Intestinal Inflammation, Malabsorption

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Introduction

Celiac disease is a chronic autoimmune disorder of the small intestine, characterized by an abnormal immune response to gluten, a protein found in wheat, barley, and rye [1]. In affected individuals, gluten intake triggers persistent inflammation of the small intestinal mucosa, villous atrophy, and impaired nutrient absorption [2]. The global prevalence of celiac disease is rising, and delayed diagnosis can result in malnutrition, growth retardation, anemia, and long-term health complications [3]. Beyond its physical manifestations, the disease also imposes psychological and social burdens that can substantially affect patients' quality of life [3]. The etiology of celiac disease is multifactorial, involving genetic predispositions particularly HLA-DQ2 and HLA-DQ8 environmental triggers, and immune system dysregulation [4]. The immune response to gluten damages the intestinal mucosa and can disrupt systemic immune function [5]. Additionally, imbalances in gut microbiota have been implicated in exacerbating disease severity and gastrointestinal symptoms [4,5]. Pathophysiologically, celiac disease is characterized by T lymphocyte activation, localized inflammation, increased production of pro-inflammatory cytokines, and villous destruction [6]. These processes collectively impair nutrient absorption and contribute to systemic weakness [6,7]. Recent studies have emphasized the critical role of the gut–microbiota axis in modulating immune responses and influencing the severity of celiac symptoms [7,8]. Complications of untreated celiac disease include malnutrition, weight loss, anemia, osteoporosis, growth disturbances in children, and an elevated risk of malignancies, such as intestinal lymphoma [9]. Diagnosis relies on a combination of clinical evaluation, serological tests (e.g., anti-tissue transglutaminase [anti-tTG] and endomysial antibodies [EMA]), and small intestinal biopsy [10]. Early detection is essential for preventing complications and guiding appropriate management [9,10]. Management of celiac disease primarily involves non-pharmacological and pharmacological strategies [11]. Non-pharmacological interventions focus on strict adherence to a gluten-free diet and lifestyle modifications, whereas pharmacological approaches are mainly directed at controlling inflammation and gastrointestinal symptoms [12]. No specific drugs have been approved for celiac disease; dietary management remains the cornerstone of therapy. In select cases, anti-inflammatory agents and immunomodulators have been explored under clinical research settings [11,12]. Complementary approaches in celiac disease management have attracted increasing interest, aiming to reduce intestinal inflammation, enhance immune function, and restore microbial balance as potential adjunctive therapies [13]. Probiotics live microorganisms that confer health benefits when administered in adequate amounts have emerged as a promising option [14]. By modulating gut microbiota, probiotics can support intestinal health and systemic well-being [13,14]. Evidence from colorectal cancer research further highlights their potential, demonstrating that probiotics can attenuate inflammation, enhance anti-tumor immune responses, and suppress harmful bacteria [15,16]. Additionally, adjunctive probiotic therapy has been associated with reduced chemotherapy-related side effects and improved patient quality of life [16].

This review aims to synthesize current evidence on the application of probiotics in celiac disease management, focusing on their effects on gut microbial balance, mucosal inflammation, gastrointestinal symptoms, and overall patient health. By consolidating these findings, the study seeks to clarify the potential role of probiotics as a safe and effective adjunctive therapy for celiac disease.

Methods

This study constitutes a systematic and narrative review of the existing literature on the effects of probiotics in the prevention, management, and treatment of celiac disease.

Data Sources

Relevant studies were identified through comprehensive searches of major international databases, including PubMed, Scopus, Web of Science, Embase, and the Cochrane Library, as well as Persian-language sources such as SID and Magiran.

Search Period:

The search focused on articles published between 2010 and 2025 to capture the most recent and reliable evidence regarding the impact of probiotics on gut

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microbiota, immune responses, and clinical management in celiac disease.

Keywords and Search Strategy: A combination of main keywords and Medical Subject Headings (MeSH) terms was employed to identify relevant studies. Key search terms included:

Probiotics

Celiac disease OR Gluten-sensitive enteropathy

Gut microbiota OR "Microbiota-gut axis"

Lactobacillus, *Bifidobacterium*

Immune modulation OR Inflammation

The search strategy was structured using Boolean operators as follows: *(Probiotics OR Lactobacillus OR Bifidobacterium) AND ("Celiac disease" OR "Gluten-sensitive enteropathy") AND ("Gut microbiota" OR "Microbiota-gut axis")*

Inclusion Criteria:

Original research articles, review papers, clinical trials, and experimental studies investigating the effects of probiotics in individuals with celiac disease.

Studies published in English or Persian.

Full-text availability.

Reports addressing clinical, immunological, anti-inflammatory effects, or changes in gut microbiota.

Exclusion Criteria:

Articles unrelated to celiac disease or probiotics.

Abstracts, conference proceedings, letters, and studies without full text.

Studies of insufficient quality or with incomplete data.

Animal studies whose results were not directly generalizable to humans (unless included in the discussion to provide preclinical evidence).

Study Selection Process: All articles identified through the search were initially screened based on keywords. Titles and abstracts were reviewed to exclude irrelevant studies. Full texts of remaining articles were then assessed according to the inclusion and exclusion criteria to determine the final selection.

Key data were extracted from each study, including study type, population, probiotic strain, dosage, duration of intervention, and reported outcomes related to clinical effects, immune modulation, and gut microbiota alterations.

Results

Randomized clinical trials indicate that strains of *Bifidobacterium*, particularly *B. longum* and *B. breve*, may help mitigate intestinal inflammation in celiac disease patients by reducing pro-inflammatory cytokines such as TNF-α and modulating mucosal immune responses.

Interventional studies in children with celiac disease adhering to a gluten-free diet have shown that probiotic supplementation can partially restore gut microbial composition, increase populations of beneficial bacteria, and, in some cases, improve growth parameters and nutritional status.

In patients with active celiac disease, particularly during gluten exposure, certain probiotic strains, such as *Bifidobacterium infantis*, have been reported to alleviate gastrointestinal symptoms and suppress innate immune markers in the gut, including α-defensin and Paneth cell activity.

Multispecies formulations containing *Lactobacillus* and *Bifidobacterium* have been associated with reductions in abdominal pain, improved quality of life, and enhanced stability of gut microbiota. However, their effects on celiac-specific antibodies have not been consistent across studies.

Some trials, including those utilizing the VSL#3 formulation, indicate that not all probiotic preparations produce significant changes in immune markers or microbiota composition, suggesting that treatment outcomes may depend on the specific strain, dosage, and duration of administration.

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Evidence from systematic reviews and preclinical studies further suggests that probiotics may exert beneficial biological effects in celiac pathophysiology by reducing intestinal permeability, inhibiting inflammatory pathways, and degrading gluten-derived peptides.

Overall, current findings support the adjunctive use of probiotics alongside a gluten-free diet. Nevertheless, heterogeneity in study design and reported outcomes underscores the need for more robust, well-designed human trials to determine sustained clinical efficacy and to identify optimal probiotic strains. Detailed results are summarized in Table 1.

Table 1: Clinical and Preclinical Evidence on the Effects of Probiotics in Celiac Disease

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Study Design	Population / Model	Probiotic (Dose / Duration)	Main Outcomes	Ref.
3-month RCT	Children with CD on GFD	*Bifidobacterium longum* CECT 7347	↑ Height growth; ↓ serum TNF-α; ↓ HLA-DR$^+$ T cells	[17]
3-month RCT	Children with CD	*B. breve* BR03 + B632 (2×10^9 CFU/day)	↓ TNF-α; modulation of immune response	[18]
3-month RCT	Children with CD	*B. breve* 16604 + B632	↑ Actinobacteria; partial restoration of gut microbiota	[19]
12-week double-blind RCT	45 CD patients	VSL#3™ (5 g, twice daily)	No significant changes in microbiota or immune markers	[20]
6-week RCT	Children with CD	Multispecies *Lactobacillus* + *Bifidobacterium*	↓ Abdominal pain; ↑ *Bifidobacterium* (stable up to 6 weeks post-intervention)	[21]
3-week gluten challenge RCT	Patients with active CD	*Bifidobacterium infantis*	↓ GI symptoms; ↓ α-defensin and Paneth cell activity	[22]
Double-blind RCT, newly diagnosed children	78 children with CD	*L. plantarum* HEAL9 + *L. paracasei* 8700:2 (6 months)	↑ Lactobacillaceae; limited effect on tTGA	[23]
Double-blind RCT	78 children with CD	HEAL9 + 8700:2 (10^{10} CFU/day, 6 months)	↓ IgA-tTG; modulation of immune cells	[24]
Double-blind RCT	31 CD patients	Multispecies (10^9 CFU/day, 12 weeks)	↓ Fatigue; improved symptoms; ↑ beneficial bacteria	[25]
RCT, newly diagnosed children	96 children with CD	Multispecies + GFD (12 weeks)	↑ Faster BMI-Z gain; other parameters similar to placebo	[26]
Randomized cross-sectional study	170 children with CD	Probiotics + GFD (28 days)	↓ Bowel movement frequency; improved GI symptoms	[27]
Comparative prospective study	50 CD patients	Probiotic yogurt (200 mL/day, 3 months)	↓ EMA; ↓ Abdominal pain; ↑ Vitamin D and ferritin	[28]

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Longitudinal cohort	6,520 children	Probiotic intake in first year of life	No significant association with CD incidence	[29]
Systematic review & meta-analysis of RCTs	—	Various *Lactobacillus*/*Bifidobacterium* strains	↓ GI symptoms; improved immune markers; safe	[30]
Systematic review (2011–2022)	—	Probiotics	↓ TNF-α and IL-1β; improved clinical parameters	[31]
Analytical review (in vitro / animal / RCT)	—	*Bifidobacterium* spp.	↓ Intestinal permeability; ↓ inflammatory pathways	[32]
Narrative / interdisciplinary review	—	Probiotics, enzymes	Potential adjunct for CD management; limited clinical evidence	[33]
Narrative review	—	*Lactobacillus* and *Bifidobacterium*	Improved microbiota; reduced inflammation; limited clinical effect	[34]
Evidence review	—	Focus on *Bifidobacterium*	Targeted microbiota modulation; potential prevention/therapy	[35]
In vitro experimental study	—	*B. longum*, *L. acidophilus*, *L. plantarum* mix	Gluten hydrolysis; reduced gliadin levels	[36]
Narrative review (postbiotics)	—	Postbiotics	Modulation of CD pathways; limited clinical evidence	[37]

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Discussion

Celiac disease is not solely dependent on adherence to a gluten-free diet (GFD); persistent disruptions in gut microbiota and activation of immune-inflammatory pathways are often observed, which are not fully corrected by gluten exclusion alone. Increasing evidence suggests that probiotics can play a complementary role in mitigating celiac disease symptoms and immune dysfunction by modulating gut microbial composition, reducing intestinal permeability, and suppressing inflammatory responses. Consequently, targeted probiotic use as an adjunctive therapeutic strategy has garnered growing attention for improving quality of life and preventing long-term complications.

Based on the data summarized in Table 1, most human evidence on probiotics in celiac disease comes from randomized controlled trials (RCTs) conducted in pediatric populations, predominantly alongside a GFD. These studies indicate that various *Bifidobacterium* strains, particularly *B. longum* and *B. breve*, can reduce pro-inflammatory cytokines such as TNF-α and modulate mucosal immune responses, contributing to decreased intestinal inflammation and improvements in specific clinical parameters [17–19].

Three-month trials in children with celiac disease have shown that supplementation with *Bifidobacterium longum* CECT 7347 reduces inflammatory markers and activated T cells while promoting height growth a clinically significant finding, given that growth impairment is a common consequence of untreated pediatric celiac disease [17]. Similarly, *B. breve* strains (BR03, B632, and 16604) have been reported to attenuate inflammation and partially restore gut microbial balance through increases in Actinobacteria populations [18, 19].

Multispecies formulations containing *Lactobacillus* and *Bifidobacterium* have also been investigated, with several trials demonstrating reductions in abdominal pain, improved gastrointestinal symptoms, and sustained increases in beneficial bacteria. However, their effects on celiac-specific antibodies, such as tTG, have not been consistent across studies [21, 24–26]. This heterogeneity likely reflects differences in probiotic strains, dosages, intervention duration, and patient clinical status.

Conversely, some trials including a 12-week double-blind study using VSL#3™ reported no significant changes in microbiota composition or immune parameters, highlighting that not all probiotic formulations exert clinically meaningful effects [20]. These findings underscore the importance of precise strain selection and carefully designed interventions.

Short-term studies in patients with active celiac disease, particularly under gluten challenge conditions, suggest that *Bifidobacterium infantis* can reduce gastrointestinal symptoms and suppress innate gut immune responses, demonstrating the potential of probiotics to modulate inflammation even during gluten exposure [22].

Longitudinal cohort studies indicate that probiotic intake during the first year of life does not significantly alter the incidence of celiac disease, suggesting limited preventive effects and emphasizing the need to distinguish between therapeutic and prophylactic applications [29].

Systematic reviews, meta-analyses, and preclinical studies consistently support the notion that probiotics may influence celiac pathophysiology through mechanisms such as reducing intestinal permeability, suppressing inflammatory pathways, and degrading gluten-derived peptides [30–32, 36]. Nevertheless, heterogeneity in results and the limited number of large, long-term RCTs suggest that probiotics should currently be considered an adjunct to a GFD rather than a substitute for standard therapy. Future well-designed clinical trials are needed to determine optimal strains, dosages, and long-term efficacy [33–37].

Conclusion

Probiotics, particularly strains of *Bifidobacterium* and *Lactobacillus*, may serve as effective adjunctive therapy alongside a gluten-free diet by modulating gut microbiota and reducing immune-inflammatory responses in patients with celiac disease. Observed benefits include improved growth parameters, reduced intestinal inflammation, and partial restoration of gut microbial balance in pediatric populations, although results across studies are not entirely consistent. Strain selection, formulation, dosage, and duration of intervention are critical factors influencing efficacy. Preclinical studies and systematic reviews suggest additional mechanisms of benefit, including suppression of inflammatory pathways, reduction of intestinal permeability, and degradation of gluten peptides (30–32, 36). Given current limitations in human studies and heterogeneity of outcomes, larger, standardized, and long-term clinical trials are warranted to establish optimal strains, dosing regimens, and sustained clinical efficacy.

Statements and Declarations

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Competing interests

The authors have no competing interests to declare that are relevant to the content of this article.

Ethics approval

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This study was performed in line with the principles of the Declaration of Helsinki.

Consent to participate

Informed consent was obtained from all individual participants included in the study.

Author contributions

AH and MRH: Conceptualization, the original draft writing, investigation, writing including reviewing and editing and investigation and formal analysis; MRH: Conceptualization, supervision, and project administration; AH Conceptualization, the original draft writing, investigation, writing including reviewing and editing

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