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Contents

Thrice Monthly Volume 11 Number 32 November 16, 2023

## EDITORIAL



## ORIGINAL ARTICLE

### Retrospective Cohort Study



### Retrospective Study



### Prospective Study



### Randomized Controlled Trial

*World Journal of Clinical Cases*

**Thrice Monthly Volume 11 Number 32 November 16, 2023**

## Contents

*World Journal of Clinical Cases*

**Thrice Monthly Volume 11 Number 32 November 16, 2023**

## Contents

*World Journal of Clinical Cases*

**Thrice Monthly Volume 11 Number 32 November 16, 2023**

## Contents

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EDITORIAL

# Efficacy of probiotics supplementation in amelioration of celiac disease symptoms and enhancement of immune system

Mostafa Hossam-Eldin Moawad, Ibraheem M Alkhawaldeh, Abdulqadir J Naswhan

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## Abstract

Patients with celiac disease (CD) have a mucosal layer that is unable to regulate the gut microbiota, leaving the host vulnerable to dangerous infections and antigens. When compared to healthy people, this dysbiosis is marked by a decrease in intra- and intergeneric biodiversity, which demonstrates an imbalance between helpful bacteria and possibly harmful or proinflammatory species. The early gut microbiota is influenced by the genotype of newborns with the HLA-DQ2 haplotypes, and this may modify how gluten is handled in the intestinal lumen, polarize innate or adaptive immune responses, and result in gluten-sensitive enteropathy. The outcome of gluten digestion can vary depending on the composition of the intestinal gut bacteria and the partial conversion of gluten into peptides larger than ten amino acids in the small intestines, which can be immunogenic. In the small intestine, 114 different bacterial strains belonging to 32 different species have 27 of them exhibiting peptidolytic activity. Thus, the individual risk of developing a gluten-related illness is further influenced by microbial composition and gluten degrading capacity. The conclusion that *lactobacilli* and *Bifidobacterium* spp. may be used as a probiotic supplement in CD patients is based on their shared possession of the most extensive peptidolytic and proteolytic activity thought to be engaged in the breakdown of gluten among all potential bacterial genera present in the gut microbiota. In children with CD autoimmunity, daily oral dose of *Lactobacillus. plantarum* HEAL9 and *Lactobacillus. paracasei* 8700:2 was found to modify the peripheral immune response. *Bifidobacterium. breve* strains have demonstrated a beneficial effect on reducing pro-inflammatory cytokine TNF- production in CD children on gluten-free diets.

**Key Words:** Celiac disease; Gut microbiota; Probiotics; Probiotics supplementation; Efficacy; Immune system

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**Core Tip:** In the context of celiac disease (CD), probiotics emerge as a multifaceted therapeutic approach with promising implications. Clinical trials demonstrate their potential to modulate immune responses, alleviate gastrointestinal symptoms, and reshape the gut microbiota in CD patients. Notably, specific probiotic strains have shown the ability to enzymatically break down immunotoxic gluten peptides, addressing a central challenge in CD pathogenesis. This dual-pronged role positions probiotics as a holistic means of CD management, offering immunomodulation and symptom relief to patients while potentially mitigating the toxicity of gluten peptides. Probiotics thus represent an encouraging avenue for enhancing the quality of life for individuals living with CD, underscoring their significance in the evolving landscape of CD treatment.

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## INTRODUCTION

The small intestine is primarily affected by celiac disease (CD), an autoimmune ailment that develops in those with a hereditary predisposition to gluten and is characterized by symptoms on both the intestinal and extraintestinal levels. The increasing body of research provides support for the hypothesis that changes in the composition and functionality of the gut microbiome are associated with various chronic inflammatory conditions such as inflammatory bowel disease, cancer, and Crohn's disease[1].

The gut microbiota plays a crucial role in promoting tolerance in normal physiological conditions. However, any disruption in the microbiota, known as dysbiosis, can disturb the balance between immune responses that promote tolerance and those that induce inflammation. This imbalance can contribute to the development of diseases such as Crohn's disease, which is characterized by an overactive Th1 immune response. The small intestine of people who have CD makes partial metabolism (due to dysbiosis) to gluten leading to its breakage into large chains of more than 10 amino acids which is immunogenic. The principal probiotic bacteria are *Lactobacillus* and *Bifidobacterium* species, which are found in the intestinal environment. *Bifidobacteria* produce exopolysaccharides that serve as fermentable substrates for additional human intestinal bacteria, whereas *lactobacilli* can secrete mucins, reinforce the epithelial barrier, improve tight-junction activities, and inhibit the epithelial cells death . It was discovered that microbiota composed of *Bifidobacterium* and *lactobacilli* can produce more active peptidases to break down those long chain amino acids, thus protecting the intestine from severe immunological reaction when ingesting gluten[2].

Increased interferon (IFN)-γ synthesis in CD causes TNF-α secretion, which is crucial for causing intestinal mucosal injury and inflammation. Increased production of TNF-α is also associated with lower *Firmicutes/Bacteroidetes* ratio which is considered a major dysbiosis in CD patients. Klemenak *et al*[3] and Quagliariello *et al*[4] demonstrated a decline in TNF-α and the increase of the *Firmicutes/Bacteroidetes* ratio, respectively, after treatment with *B.breve* which is in line with Primec *et al*[5] who showed that after 3 mo of *B.breve* treatment, TNF-α was reduced with parallel increase in *Firmicutes*.

Khorzoghi *et al*[6] studied how probiotic administration affected the composition of the intestinal microbiota and how clinical symptoms in CD patients improved as a result. In this investigation, the ingestion of a probiotic combination containing *Bifidobacterium* spp., *Lactobacillus* spp., and *S. thermophilus* resulted in a reduction in the intensity of clinical symptoms (fatigue, muscle discomfort, bloating, and a gassy feeling) compared to placebo. The relative levels of *Lactobacillus*, *Bacteroidetes*spp., *Bifidobacterium* spp., *Clostridium* cluster I, *Enterobacteriaceae*, and *Firmicutes* were higher in the probiotics group than they were in the control group, with the exception of *Staphylococcus* spp. In light of this, a 12-week probiotic multi-strain treatment plan could alter the make-up of the intestinal microbiota and lessen gastrointestinal symptoms in CD patients. According to Klemenak *et al*[3] and Quagliariello *et al*[4], *B. breve* strains combined with GFD act on a decrease in TNF- α production, which may have an impact on preventing a pro-inflammatory milieu in children with CD. The effects of this probiotic pill, however, only last while being consumed. Three months following the end of the intervention, Klemenak *et al*[3] discovered that TNF-α levels have nearly completely returned to baseline levels. Therefore, further trials are required to investigate a long-lasting effect of probiotic pills and control the microbiota environment of the CD patients.

Håkansson *et al*[7] conducted a randomized, double-blind, placebo-controlled clinical trial for children with CD. The main result was the steady alteration in the peripheral immune response; demonstrated by T cells regulation and decreased their concentration and responses in the probiotic group compared to placebo group indicating that *L. paracasei* 8700:2 and *L. plantarum* HEAL9 were capable of modulating the peripheral immune response in CD autoimmunity. The median levels of IgA-tTG also decreased as a result of the probiotic therapy ($P$ = 0.013).

In a major prospective, randomized study, Francavilla *et al*[8] combined five strains of lactic acid bacteria and *bifidobacteria*: *L. casei* LMG 101/37 P-17504, *L. plantarum* CECT 4528, *B. animalis* subsp. lactis Bi1 LMG P-17502, *B. breve* Bbr8 LMG P-17501, and B. breve Bl10 LMG P-17500. They recruited 109 CD patients who strictly adhered to a GFD and had signs and symptoms of irritable bowel syndrome (IBS). They were randomly assigned for six weeks to receive

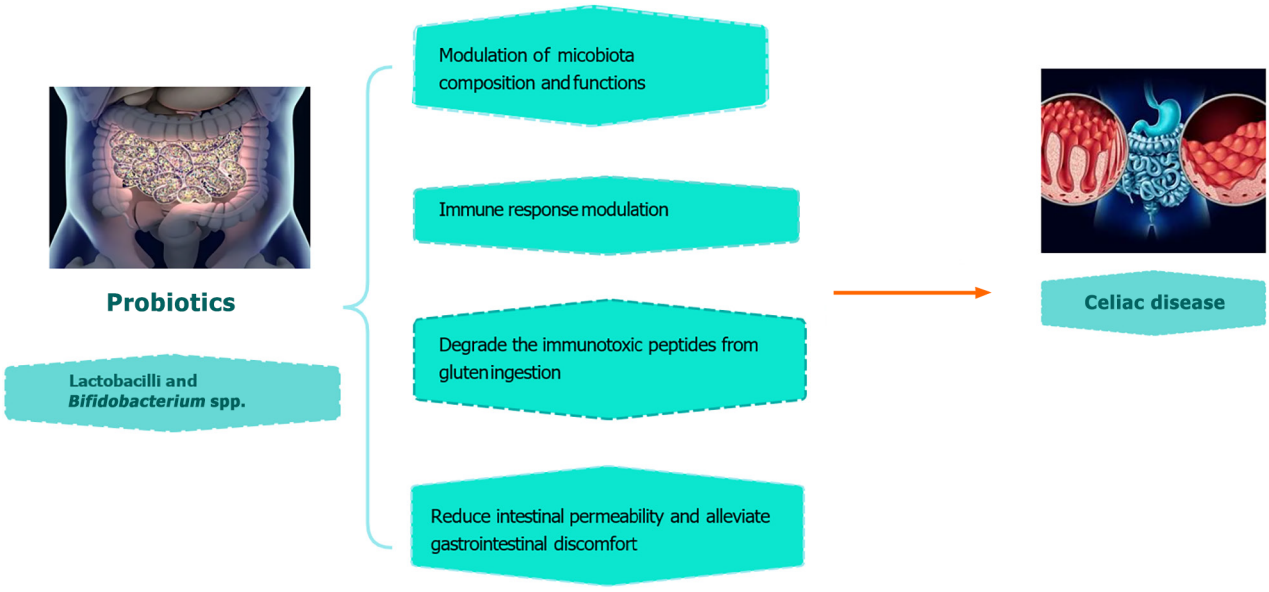


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**Figure 1 The possible advantages of using probiotics in celiac disease patients.**

probiotics or a placebo, and then were monitored for another six weeks. The findings showed that this probiotic mixture was effective in reducing the severity of gastrointestinal symptoms, with a decreased feeling of pain on various clinical assessments and a significantly greater percentage of treatment success (defined as at least a 50% decrease in the symptom scores). With a rise in lactic acid bacteria, *Bifidobacterium*, and *Staphylococcus* that was remained observable six weeks after the withdrawal of probiotics, they were able to demonstrate a favorable modification of the gut microbiota (Figure 1).

In a different trial[9], 20 CD patients received hydrolyzed wheat gluten bread with *L. alimentaris*, *L. brevis*, *L. sanfranciscenis*, and *L. hilgardi* for six days. In comparison to healthy controls, the findings revealed no substantial rise in IFN-γ. Thus, clinical trials have recently produced growing and positive outcomes. Serological, histological, and immunohistochemical characteristics were unaffected when CD patients were fed a diet of baked goods with less than 10 ppm of gluten prepared from fermented wheat flour. Similar outcomes were attained when CD patients in remission were exposed to *lactobacilli* that had already digested gluten for 60 d[10]. Patients' symptoms, intestinal permeability, or serological markers did not worsen, indicating that lactobacilli-derived endopeptidases may be capable of completely breaking down gluten and reducing gluten toxicity in CD patients[10].

## CONCLUSION

Due to this findings, present research aims to identify probiotic strains that can totally degrade the immunotoxic peptides from gluten ingestion. Therefore, probiotics are the uprising mainstay of treatment of CD patients whether by their administration to them or by their effect of gluten peptides that cause autoimmune reactions.

## FOOTNOTES

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