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## **Probiotic supplementation as a supportive treatment in inflammatory bowel diseases - literature overview**

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## **Abstract**

**Introduction and purpose:** The human body hosts a diverse ecosystem of commensal microbes, known as the human microbiome. This review aims to assess the current state of knowledge regarding the effectiveness, mechanisms of action, and potential benefits of probiotic supplementation in patients with inflammatory bowel diseases.

**Materials and methods:** A literature review was conducted using the “PubMed” and “Google Scholar” databases with the keywords “Probiotics”, “Gut Microbiome”, “Probiotics and the treatment of Crohns Disease”, “Probiotics and the treatment of Colitis Ulcerosa”.

**State of knowledge:** Dysbiosis is known to disrupt the function of the intestinal mucosa and has been associated with chronic tissue inflammation. The use of probiotics is a promising method to improve the state of gut microbiota. It is known that the gut microbiome is disrupted in inflammatory bowel diseases.

**Summary:** The use of probiotics in Ulcerative Colitis is supported by a significant amount of evidence supporting its effectiveness. In the case of Crohn's Disease there is a lack of evidence to definitively determine whether the use of probiotics yields therapeutic benefits. Therefore there is a need for further research in this area.

**Keywords:** Probiotics, Crohn's Disease, Colitis Ulcerosa, Gut microbiome.

## **Introduction**

The human body hosts a diverse ecosystem of commensal microbes, known as the human microbiome. The imbalance of the microbiome is defined as dysbiosis and may contribute to the development of certain diseases. However, maintaining the homeostasis of the intestinal microbiota may improve the patient's condition and be an additional supportive treatment for some diseases, including inflammatory bowel diseases.

In this review, we will analyze the available literature in terms of effectiveness, mechanisms of action and potential benefits of probiotic supplementation in patients with Crohn's disease and Colitis Ulcerosa.

## **State of knowledge**

### **Intestinal microbiota**

The intestinal microbiota includes a number of microorganisms such as bacteria, viruses and fungi. Intestinal microbiota plays a role in metabolizing nutrients, xenobiotics and drugs, but also in maintaining the integrity of the intestinal mucosa and immunomodulation [3]. There is

no universal pattern of healthy intestinal microflora, it depends on lifestyle and environment. The composition of the gut microbiota differs between populations in developed and developing countries. We also observe differences between the populations of developing countries depending on their lifestyle. Therefore, the concept of a healthy microbiota is relative and depends on the cultural and environmental factors [4]. Dysbiosis is associated with many digestive system diseases. It may result in inflammation and damage to the intestinal mucosa. The pathological development of *Escherichia Coli* and *Bacteroides Fragilis* bacteria is also associated with chronic inflammation of the intestinal mucosa [1]. It is believed that imbalance in microbiome may result in the colonization of resistant pathogens in the intestines, which increases the risk of an immune reaction in the intestinal mucosa and promotes the development of inflammatory diseases.[5]. Therefore, it should be considered whether improving the intestinal microbiota in these patients may have a positive impact on their health.

### **Microbiota and Inflammatory Bowel Diseases**

Inflammatory bowel diseases are chronic gastrointestinal disorders characterized by periods of exacerbation and periods of remission. There are two main types of inflammatory bowel diseases: Crohn's Disease (CD) and Ulcerative Colitis (UC) [6]. Inflammatory bowel diseases are increasingly being diagnosed in clinical practice, driven both by the improvement of diagnostics, which is becoming more effective and accessible, and the growing number of people suffering from these conditions. Early disease identification and immediate initiation of recommended intensive pharmacological therapy yield the best treatment outcomes [7]. In the case of Crohn's disease and ulcerative colitis, the age of onset is similar, with its peak occurring between the second and fourth decades of life. There is no significant difference in prevalence based on gender [8]. Inflammatory bowel disease is believed to primarily result from an abnormal immune response to microorganisms in the intestines in genetically susceptible individuals. Despite the etiology of inflammatory diseases remaining a mystery and largely unknown, it is recognized to be the outcome of interactions among environmental, genetic, and microbiological factors and the body's immune response [9]. Research conducted as part of the Integrative Human Microbiome Project has revealed a strong correlation between modifications in the taxonomic and functional composition of the gut microbiota and the occurrence of non-specific inflammatory bowel disease [10]. In one study, which examined stool samples collected from patients with inflammatory bowel diseases experiencing fatigue, it was observed that the gut

microbiome was less diverse, and the number of butyrate-producing bacteria, including *Faecalibacterium prausnitzii* ( $P = 0.0002$ ,  $q = 0.007$ ) and *Roseburia hominis* ( $P = 0.0079$ ,  $q = 0.105$ ), was significantly reduced [11]. In another study, which utilized mucosal biopsy samples collected from the colon and terminal ileum of patients with inflammatory bowel disease and healthy individuals, it was demonstrated that the tissue microbiota of Crohn's disease patients is less diverse compared to patients without signs of intestinal inflammation [12]. Furthermore, evidence confirming the significant role of the gut microbiome in the occurrence of inflammatory bowel diseases is that both ulcerative colitis and Crohn's disease patients often exhibit a characteristic dysregulation of gut flora [13].

### **Probiotics**

Probiotics are defined as "live microorganisms that, when administered in adequate amounts, confer health benefits to the host." They are intended to improve the internal microbiota balance of the human body [14]. Probiotics work through various mechanisms to limit the access and growth of other pathogens, such as competing for adhesion to intestinal epithelial cells, producing antimicrobial compounds, acidifying the gut contents, and also exerting immunomodulatory effects [15]. Probiotics can be found and used in the form of dietary supplements, food, as well as medicinal products. It's worth noting that some strains, even those belonging to the same species, may exhibit different probiotic effects. When choosing a probiotic, it is advisable to opt for one that contains identified strains with documented effects [16]. The use of probiotics is recommended and beneficial, particularly in aiding the treatment of autoimmune diseases and gastrointestinal disorders [15]. There are many strains that show potential in alleviating symptoms and treating inflammatory bowel diseases, including *Bacteroides fragilis*, *Bifidobacterium longum*, *Lactococcus lactis*, and *Lactobacillus plantarum*, among others. By stabilizing the integrity of the gut barrier and regulating the gut microbiome in murine models, they show potential in preventing the occurrence and development of inflammatory bowel diseases [17].

### **The use of probiotics in therapy :**

#### **Ulcerative colitis**

Ulcerative colitis (UC) is a chronic inflammatory bowel disease. The inflammatory process affects the mucosal and submucosal layers and is limited to the colon [18]. In the supportive treatment of ulcerative colitis, the use of probiotics is recommended as they contribute to

extending the period of disease remission. The selection of appropriate probiotics is an essential component of pharmacological therapy when the disease is in remission [19]. Although the currently available evidence for the benefits of using probiotics in patients with ulcerative colitis is limited, probiotics are commonly used as supportive therapy. They are often recommended by doctors and generally considered safe [20]. In one study involving 26 patients with ulcerative colitis, it was demonstrated that patients who supplemented their treatment with a rectally administered probiotic containing strains of *Lactobacillus paracasei* CNCM I-1572 modified the gut microbiota, leading to an increase in *Lactobacillus* spp. and a decrease in Enterobacteriaceae, thus having a beneficial impact on the treatment of ulcerative colitis [21]. Other research suggests that there is limited evidence that the use of probiotics in combination with 5-aminosalicylic acid as a combination therapy may be more effective in inducing disease remission compared to using 5-aminosalicylic acid alone [22]. Furthermore, it has been demonstrated that individuals using probiotics containing various bacterial species, including *Bifidobacterium* and *Lactobacillus*, more frequently experienced a reduction in stool frequency and abdominal pain, as well as observed an improvement in stool consistency. Additionally, in combination with mesalazine, probiotics significantly improved symptoms of rectal bleeding and bowel movement frequency compared to mesalazine alone [23]. A study conducted in a murine model of ulcerative colitis (*T-bet*<sup>-/-</sup>*Rag2*<sup>-/-</sup>) showed that *Bifidobacterium lactis* reduces inflammation and colitis in the early stages of the disease and decreases the amount of Enterobacteriaceae, which appear to contribute to the development of intestinal disease [24].

### **Crohn's Disease**

Crohn's disease is a chronic idiopathic gastrointestinal disorder characterized by the presence of transmural granulomatous inflammatory lesions that can affect any part of the digestive tract from the mouth to the anus. The treatment of this disease involves pharmacological therapy aimed at controlling inflammation and inducing clinical remission. However, the majority of patients will eventually require surgery. Unfortunately, surgery does not cure the patient of the disease, which often recurs. For these reasons, Crohn's disease is associated with many therapeutic challenges [25]. Due to these challenges, many researchers have been seeking more effective methods for treating this disease, and there was some hope placed in probiotic therapy. In two randomized controlled trials conducted on a total of 46 Crohn's disease patients, no statistically significant difference in the achievement of remission was observed between the control group and the probiotic group [26]. As indicated by an analysis

of 9 clinical studies in this field, the use of probiotics did not yield statistically significant effects in patients with Crohn's disease ( $p=0.07$ ) [27]. Despite the considerable interest among researchers, there is still a lack of evidence that definitively confirms or refutes the effectiveness of probiotics in the treatment of Crohn's disease, and this topic remains an open subject for further scientific research [28].

## **Summary**

Conclusions regarding the impact of probiotic use in non-specific inflammatory bowel diseases such as ulcerative colitis (UC) and Crohn's disease (CD), are still a subject of research and deliberation in the medical community. It's worth noting that the effectiveness of probiotics varies, and research results on the impact of probiotics on non-specific inflammatory bowel diseases are diverse and dependent on the specific species and strain of probiotic as well as individual patient characteristics. There is a greater amount of scientific research confirming the effectiveness in supportive treatment of ulcerative colitis compared to Crohn's disease, although there is no definitive prescription for their efficacy. Probiotics appear to achieve better results in maintaining remission than during exacerbation periods. Furthermore, they are described as potentially reducing mild to moderate symptoms such as abdominal pain or stool disturbances. Although probiotics are generally considered safe, further research is still needed to precisely determine their effectiveness in the treatment of non-specific inflammatory bowel diseases. It should be emphasized that the use of probiotics is not recommended as a substitute for traditional pharmacological therapy for non-specific inflammatory bowel diseases, such as anti-inflammatory drugs. Probiotics can be used as a part of supportive therapy, but the decision to use them should be made after consulting with a doctor, who is the primary person responsible for the care and treatment of patients with non-specific inflammatory bowel diseases.

## **Author's contribution:**

Conceptualization: A.G., M.G.-S.; methodology: A.G., M.G.-S.; software: A.G., M.G.-S, K.M., B.M., J.R., formal analysis: A.G., M.G.-S, K.M., B.M., J.R., P.B., M.R., P.R.; investigation: A.G., M.G.-S, K.M., B.M., J.R., P.B., M.R., P.R.; resources: A.G., M.G.-S, K.M., B.M., J.R. data curation: A.G., M.G.-S, K.M., B.M., J.R.; writing - rough preparation: A.G., M.G.-S, K.M., B.M., J.R., writing - review and editing: A.G., M.G.-S, K.M., B.M., J.R., P.B., M.R., P.R.; visualization: A.G., M.G.-S.; supervision: A.G., M.G.-S., project administration: A.G., M.G.-S.

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The authors declare that they have no conflict of interest.

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