

# Probiotic Microorganisms in Diet and Their Effect on Crohn's Disease

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**Abstract:** *Ulcerative colitis (UC) and Crohn's disease (CD) are common types of inflammatory bowel diseases (IBD). Investigations have revealed that some neurological factors, intestinal flora, etc., are effective in getting infected by the Crohn's disease, which affects various parts of the gastrointestinal tract. Standard treatment methods for Crohn's disease are based on the alteration of the immune system with corticosteroids, immunosuppressants, and surgery, along with using synthetic drugs. The side effects of each of these methods, along with the awareness of the role of enteric bacteria in the development of Crohn's disease have attracted researchers' attention toward the probiotics as an effective factor in the treatment of this disease. Probiotics can be used as a part of the food or as probiotic supplements and enter the body. Due to some uncertainties in the production and measurement of probiotic supplements, it is recommended that food products containing probiotics to be used as the main source of these microorganisms. However, in case of emergency and treatment of inflammatory bowel diseases, probiotic supplements are recommended along with probiotic foods.*

**Keywords**—Diet; Inflammatory Bowel Disease; Microorganism; Probiotic; Crohn's Disease

## 1. INTRODUCTION

Probiotics are commensal organisms that, when they are consumed in sufficient quantities, show positive effects on the health of the consumer. Probiotics are usually catalase-negative and gram-positive lactic acid bacteria without any spores and also are able to tolerate acidic conditions. These bacteria are fermenters, and lactic acid is their major end product in sugar fermentation [1]. As noted, although most probiotics are bacteria and the type of lactic acid, they can also be mold or yeast. Species such as *Carnobacterium*, *Enterococcus*, *Lactobacillus*, *Lactococcus*, *Lactosphaera*, *Leuconostoc*, *Melissococcus*, *Oenococcus*, *Pediococcus*, *Streptococcus*, *Tetragenococcus*, *Vagococcus*, and *Weissella* are considered as lactic acid bacteria (LAB) [2-4]. In this category, some species, such as *Lactococcus* and *Streptococcus*, are homofermentative, while others are heterofermentative such as *Leuconostoc* and *Weissella*. Homofermentative species convert the glucose molecule into two lactates, while heterofermentative species convert the glucose molecules into lactate, ethanol, and carbon dioxide. It should be noted that all probiotic bacteria are lactic acid bacteria, but not all lactic acid bacteria are probiotic [5]. On the other hand, there are prebiotics that are not alive, unlike probiotics; however, they are non-digestible foods (usually oligosaccharides or polysaccharides) that effectively affect

the health of the host by selective stimulation of growth and activity of some bacterial species. More precisely, it can be said that prebiotics refers to the component that was selectively fermented and allows for specific changes in the composition and/or activity of the gastrointestinal microbiota that ultimately leads to beneficial effects the health of the host. Prebiotics should not be hydrolyzed by human intestinal enzymes but should be selectively fermented by beneficial bacteria to cause beneficial effects on the health of the host. The combination of probiotics and prebiotics is called synbiotic [6,7]. In order for a microorganism to be considered as a probiotic, it is required to have a human origin and safe conditions (GRAS). Other essential features include acid and bile stability, the ability to adhere to intestinal cells, and the capability of being stable in the human intestine for a while. These microorganisms should also be able to resist pathogenic bacteria and regulate the immune response [8]. surface active compounds including surface layer protein, lipoteichoic acid, lipopolysaccharide, and heat-killed antigen, molecular metabolites such as bacteriocin, vitamins, short-chain fatty acids, and long-chain fatty acids, antihistamine production,  $\gamma$ -aminobutyric acid, citrullination, biohydrogenation property such as the production of conjugated linoleic acid, with properties such as being antioxidant and cholesterol assimilation. The production of beta-galactosidase, immunomodulation, pathogen suppression, competition with pathogens and harmful microorganisms for grabbing food and space are some factors that have made it possible to recommend and emphasize the

use of probiotic microorganisms in the diet [9-17]. Fig. 1 indicates some features of probiotic microorganisms that lead to a health-promoting feature in the host [18].

the health of the host. Dairy and fruit are the main sources of probiotic bacteria [20].

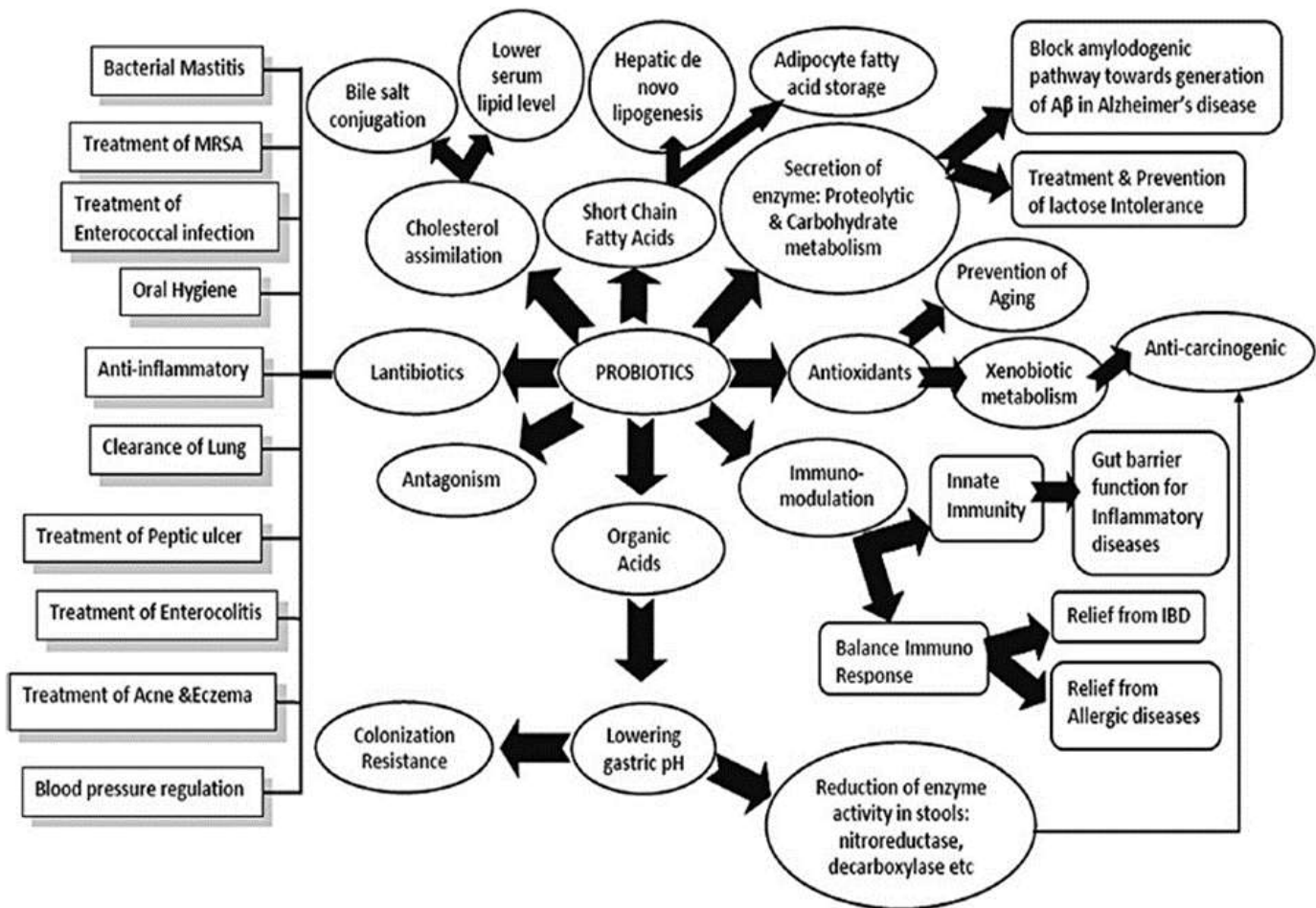


Fig. 1. indicates some features of probiotic microorganisms that lead to a health-promoting feature in the host [19]

## 2. METHODS AND MATERIALS

### 2.1 Methods

The present article is the result of investigating articles and books related to the topic and keywords of research in various databases such as Google Scholar, Science Direct, PubMed, Medline, and other related databases. Inflammatory bowel diseases are divided into two common types of ulcerative colitis and Crohn's disease. It should be noted that the purpose of this study is to evaluate the tests and studies on Crohn's disease in these databases.

### 3. PROBIOTIC FOOD OR PROBIOTIC SUPPLEMENTS

The foods containing probiotic microorganisms are referred to as functional foods. These kinds of foods contain micronutrients and also nutrients that have positive effects on

In general, probiotic products are divided into three categories; probiotic dairy products (fermented milk and yogurt, cheese, and ice cream), non-dairy probiotic products (juices and desserts), and supplements (in the forms of capsules and pills) [20,21]. Yogurt, which is one of the high-consumed dairy products, is obtained from the fermentation of milk by various bacteria and mainly lactic acid bacteria and bifidobacteria [22].

Due to the variety of foods that include probiotic microorganisms, the use of probiotic-containing supplements was not recommended except under specific conditions and as a substitute for probiotics present in foods. Most supplements on the market are labeled in milligrams (mgs), but probiotic supplements are labeled in colony-forming units (CFUs). In general, it is expected that a bottle containing

probiotic supplements to possess  $\geq 10$  billion CFU. However, investigations have indicated that only one sample of fermented vegetables contains 10 trillion CFU of probiotic microorganisms [23]. In addition, probiotic foods naturally possess more pragmatic "super food" benefits than probiotic supplements. On the other hand, due to the lack of established regulatory laws, probiotic supplements are not regulated, and the exact number of CFUs in these products is questionable [24,25].

#### 4. CROHN'S DISEASE AND THE EFFECTS OF PROBIOTICS

Crohn's disease, which is the type of inflammatory bowel disease, can affect various parts of the gastrointestinal tract. In most cases, this disease affects the last part of the small intestine, the ileum, and the beginning part of the large intestine, the cecum. Specialists normally use induce remission and maintain remission approaches to treat these diseases. When using the induce remission approach of surgery, predicting strategies to prevent post-operative recurrence is very important. Standard treatments for Crohn's disease focus on the alteration of the immune system with corticosteroids, immunosuppressants, and biological therapies (biologic therapies). The awareness of the role of enteric bacteria in the development of Crohn's disease has attracted researchers' attention toward probiotics as an influential factor in the treatment of this disease. Researchers have investigated the use of surgery and drugs to treat active Crohn's disease with microbiome modification, but for microbiome modification, the focus is currently on dietary, antibiotics, probiotics, and fecal microbial transplantation [26]. Stopping of production and maintenance of microbiota has been recognized as a key factor in the development of diseases in individuals. It can be particularly said that this factor leads to local inflammation. Previous research has revealed that probiotic microorganisms, whether alive or dead, can regulate the microbial composition of the intestine to revive the lost microbiota and reduce the inflammation and its consequences. The probiotic microflora-mediated therapy is referred to as a new treatment approach for inflammatory diseases. Probiotics are of the most important components of functional foods. These microorganisms regulate the intestinal microflora and stabilize the homeostasis in the gastrointestinal tract. Probiotics are also involved in the normalization of intestinal colonization [27]. In most cases, the studies on the relationship between probiotics and their effects on the health of the host are associated with three functional fields of the gut microbiota, including metabolic effects, protective effects, and trophic effects [7]. Evidence suggests that probiotic bacteria in different species and strains may be applied as an anti-inflammatory agent in some chronic inflammatory diseases depending on the way of using them [29]. Most research conducted on the treatment of Crohn's disease by probiotics relates to *Lactobacillus* and *Bifidobacterium* microorganisms. Since patients with chronic

inflammation, including Crohn's disease, usually consume a wide range of drugs, they are exposed to some side effects such as diarrhea and loss of appetite. In order to overcome these problems, several investigations have been carried out to enrich foods with probiotic microorganisms. As an example of these investigations, the effect of probiotic yogurt enriched with two probiotic strains *Lactobacillus rhamnosus* GR-1 and *Lactobacillus reuteri* RC-14 on controlling mucosal infections and its anti-inflammatory properties on Crohn's disease have been evaluated. The reason for using yogurt was that it does not cause side effects contrary to medications, and it also reduces diarrhea problems as a nutritional supplement [30,31]. A study by Malin et al. on pediatric CD showed an increase in intestinal Immunoglobulin A (IgA) levels and, thus, the reinforcement of gut immunological barrier after consuming *Lactobacillus* GG [32]. McCarthy et al. conducted an open-label uncontrolled trial and showed that *Lactobacillus salivarius* UCC118 significantly reduced the Clinical Disease Activity Index in 25 patients with mild to moderate Crohn's disease [33]. Research by Lescheid et al. revealed that prescription of edible *Lactobacillus rhamnosus* GG in patients with Crohn's disease increases and enhances the IgA (Immunoglobulin A) immune response in the intestine and reduces the pains caused by the disease [3]. In an open-label trial conducted by Fujimori et al., the effect of synbiotic therapy on Crohn's disease was investigated. In this way, the effect of *Bifidobacterium breve*, *Lactobacillus casei*, *Bifidobacterium longum*, and *psyllium* on ten patients with active Crohn's disease was investigated. The test results revealed a significant enhancement of the Crohn's Disease Activity Index (CDAI) throughout the trial period [35]. In an uncontrolled open-label trial consisting of 4 patients, *Lactobacillus rhamnosus* GG was used for six months. The results indicated that the disease was associated with recovery in children with mildly to moderately active Crohn's disease [36]. In a randomized controlled study by Steed et al., on various synbiotic factors, it was found that *Bifidobacterium longum*, inulin, and oligofructose as a synbiotic compound led to the enhancement of CDAI in 35 patients with active Crohn's disease during a 6-month trial period [37]. In some studies, there was no significant difference between the consumption of probiotics and the use of chemical drugs in terms of disease treatment. In the study by Campieri et al., the probiotic cocktail VSL # 3 was compared with mesalazine to treat Crohn's disease. At the end of treatment, there was no meaningful statistical difference between probiotics and mesalazine [38]. In a study by Zocco et al., the effect of *Lactobacillus rhamnosus* GG on retention of Crohn's disease was investigated. After one year, the results indicated that there was no significant difference between probiotics and mesalazine [39].

#### 5. CONCLUSION

Side effects of synthetic and chemical drugs are major challenges in the treatment of patients, and the medications

for Crohn's disease are no exception. Some medications containing salicylate compounds (such as Sulfasalazine and Mesalazine) and immunosuppressive compounds (such as Mercaptopurine and Methotrexate) possess many side effects for consumers. Although many studies have revealed that Crohn's disease can be recovered by the consumption of probiotics, some studies reject their beneficial effects compared to chemical drugs. It seems that more research is needed on the effect of probiotics on the recovery of Crohn's disease, contrary to Ulcerative colitis, that the effect of probiotics on its recovery has been proven convincingly.

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