# Probiotics: Benefits Against the Risks

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**Abstract**

probiotics (usually lactobacilli and bifidobacteria) It has been shown to be helpful in preventing certain medical conditions in addition to the potential to enhance certain aspects of health. In The current review, evidence from clinical trials of the benefits of probiotics to promote health for many diseases, it has been mentioned, as well as a comparison between the benefits and disadvantages of using it as a food additive or food supplement.
Probiotics may be beneficial Malnutrition, especially in the case of lactose and calcium intolerance Absorption and constipation. Done probiotics Clearly shown to boost immunity in the elderly, however the clinical significance of this remains to be clarified.
The results are encouraging, and further studies are large-scale it seems justified to create a place for probiotics.

## Probiotics history

Probiotics have a long history [1] and are closely linked to the consumption of fermented foods. It is reasonable to assume that around 10,000 years ago, when farming began to replace hunting and gathering, the man began to produce fermented foods and beverages.
Consumption of milk and dairy products is linked to a long and healthy life in ancient Indian Ayurvedic texts. Nonetheless, the first pictorial evidence of milking (whose technique remained unchanged until the early 1900s, when they invented the first milking machines) was discovered during excavations of Ur, Mesopotamia's ancient capital, dating back to 3100 BC.
Both the seal on display at the Museum of Natural History in Chicago, in which a goat offers her own milk to the pastor under the watchful eye of a goddess of fertility, and a polychrome Sumerian fresco from 2500 BC in the Baghdad Museum, depict large cows like Aurochs with their young; near them, large jars collect milk, while the cream is poured into a churn from a churn from a churn from a Sumerian priests carry the milking in the so-called "frieze of the dairy" [2].
Fermented milk can be traced back to the ancient Egyptians, Phoenicians, and Eastern cultures. Ancient Oriental peoples, white, Phrygian, and Macedonian nomadic shepherds kept milk from cows, sheep, goat, horse, and camel in bottles made from the skin or stomach of the same animal, where milk came into contact with bacteria, most likely the ancestors of the acidophilus and bulgaricus that have become so well-known today. Legend has it that while traveling in the hot sun of the Turkish desert, one of these shepherds forgot milk in a goatskin bag for a period of time, and when he returned, it had transformed into a thick, creamy, and delicious custard. “Yogurt” was the name given to this novel product. Whatever its origin, yogurt and other fermented milks have been known for their beneficial health properties and therapeutic use since the dawn of time, long before bacteria were discovered.

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Yogurt was the elixir of life for the Turks. They believed that yogurt could provide physical and mental well-being as well as extend life [2].

## Probiotics definition

Probiotic has a variety of meanings for different people, so its definition has evolved over time. In 1965, Lilly and Stillwell used the word of probiotics for the first time. According to them, Probiotics are substances secreted by one microorganism that stimulate the growth of other microorganisms. Probiotics were defined by Sperti in 1971 as tissue extracts that have a promote on the growth of other microbes. Probiotics, according to Parker (1974), are organisms and substances that play an important role in intestinal microbial balance. Crawford defined probiotics in 1979 as "a culture of specific living microorganisms, primarily Lactobacillus spp., implanted in the animal to ensure the effective establishment of intestinal populations of both beneficial and pathogenic organisms".

The definition of probiotics has been changed to include a live microbial feed supplement that enhances the host animal by improving the microbial balance of its intestine [3]. This is proposed that probiotics are live microorganism cultures (monocultures or mixed cultures) that are beneficial to the host when applied to an animal or a person because they improve the host's indigenous microflora. Probiotics are bacteria, yeast, and fungi that are direct fed microbials of naturally occurring microorganisms, according to the United States National Food Ingredient Association (USNFIA) [4].

Probiotics are live microbial cultures or cultured dairy products that have beneficial effects on the host's health and nutrition, according to Salminen in 1996. Schaafsma broadened the definition in 1996. Oral probiotics, he claimed, are living microorganisms that have beneficial health effects as well as nutritional value when consumed in certain amounts [5].

Gaurner and Schaafsman refined the definition in 1998, explaining that probiotics are living microorganisms that, when consumed in sufficient quantities, provide health benefits beyond those provided by basic nutrition. According to a joint report published by the Food and Agriculture Organization (FAO) and the World Health Organization (WHO) in 2002, these are cultures of live microorganisms that can be mono or mixed cultures. When these cultures are given to animals or humans in large enough quantities, they have a positive impact on the host's health [6].

According to researches, probiotics are defined as microbial cell preparations or components of microbial cells that, when given in adequate doses, have a beneficial effect on the host's health and well-being [7].

## Probiotic Properties

Customers are becoming more interested in foods, not only because of their taste and immediate nutritional needs, but also because of their ability to provide specific health benefits in addition to their basic nutritional value. Nutraceutical activities of LAB include vitamin B production and improved digestibility. They also have a variety of therapeutic properties, such as alleviating lactose intolerance, restoring ecological balance, and boosting immunity through the detoxification of harmful products, the removal of carcinogenic products, and the suppression of food-borne pathogens [8]. Foods aim to improve the balance and activity of the intestinal micro flora. Now these foods making up the largest segment of the functional food market.

Consumption of foods containing live bacteria, also known as "probiotics," is one of

the most effective ways to increase the number of beneficial bacteria in the intestinal tract [7].

During storage, the majority of foods deteriorate. Microbiological changes in foods can cause a wide range of spoilage reactions, including food poisoning, in addition to physical, chemical, and enzymatic factors that alter sensory characteristics [9]. So, it is very important to inhibit the growth of spoilage microorganisms in foods. The use of antimicrobial compounds produced by LAB as a safe and natural way of food preservation has grown in popularity as a result of a strong demand for natural and minimally processed foods. In addition to nisin which is widely used in foods, another antimicrobial compound that has been proposed for use in food preservation is reuterin produced by *L. reuteri* [10] fig (1).

**Health aspects**

Lactic acid bacteria have become increasingly popular as probiotics in recent years. A LAB strain's ability to produce antimicrobial compounds against pathogenic and cariogenic bacteria, as well as adhere to and colonize human intestinal mucosa, are important features for it to be a probiotic. The production of antimicrobial compounds may help probiotics colonize the gut mucosa by giving them a competitive advantage over normal gastrointestinal microflora [11]. The Exopolysaccharides EPS has been discovered in adherent biofilms; the EPS could serve as both initial and permanent adhesion compounds [12].

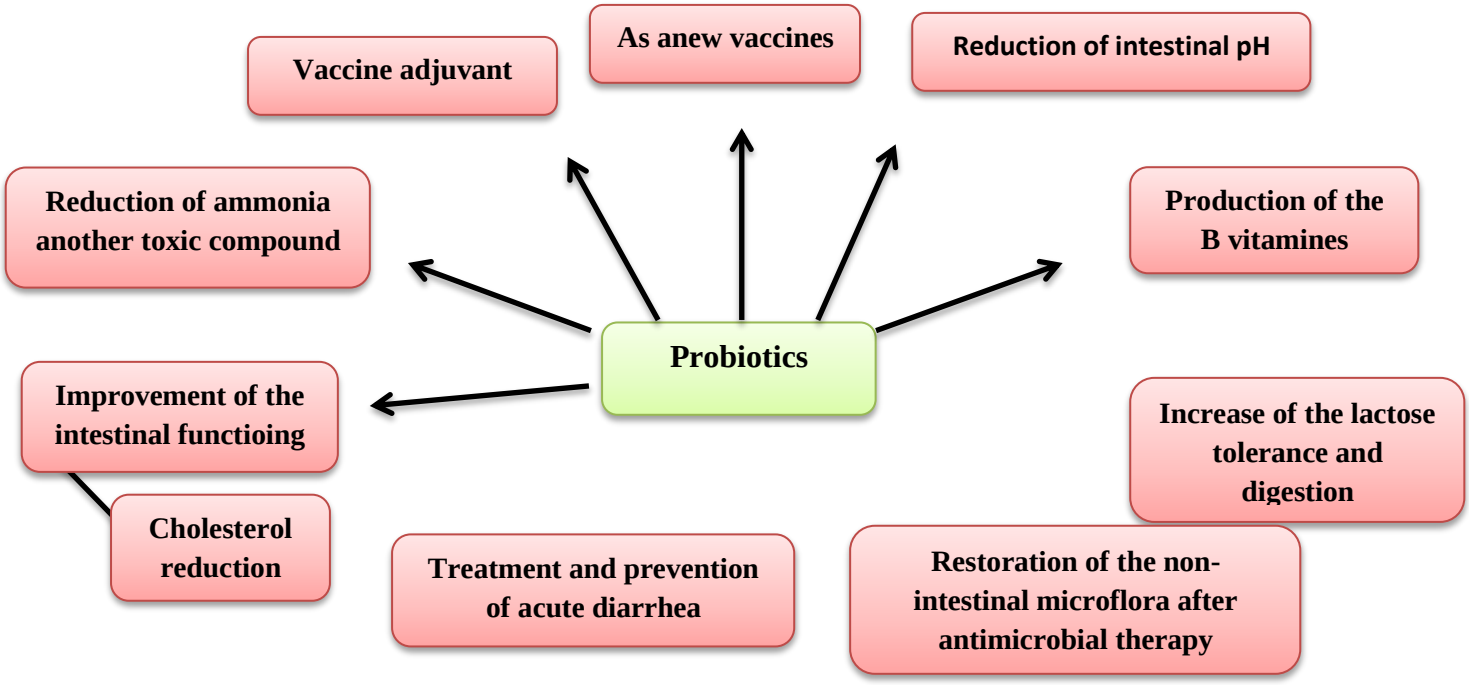


Figure (1) Function of probiotics [14].

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## Common Probiotics and its Mode of Action

The majority of probiotics come from the Lactobacillus and Bifidobacterium genera, which belong to the LAB group. This group's most well-known probiotics include: *Bifidobacterium bifidum, Bifidobacterium longum, Bifidobacterium breve, Bifidobacterium infantis, Lactobacillus acidophilus, Lactobacillus casei, Lactobacillus plantarum, Lactobacillus rhamnosus* and *Lactobacillus fermentum* [13]. LAB has been studied extensively and proven to be beneficial native inhabitants of the gastrointestinal tract (GIT). The GIT of the human body contains a diverse microbial population that mediates numerous interactions with the chemical environment, owing to the fact that the GIT has a much larger contact area with the environment than our skin surface. After or during antibiotic treatment, pharmaceutical preparations containing live microorganisms in capsules, such as probiotics, were used to restore the GIT population [14]. Probiotics are chosen based on their tolerance to gastrointestinal conditions (acid, phenol, and bile), ability to adhere to the gastrointestinal mucosa, competitive exclusion of pathogens, antimicrobial substance production, lack of toxicity, and resistance to technological processes [15].

The interface between a mammalian host and micro flora in the lumen is the mucous gel layer and the underlying cell coat (glycocalix), which consists of glycoconjugates on the apical surface of the epithelium. When compared to pathogenic strains, there have been very few studies on the mechanism of non-pathogenic bacteria (lactobacilli) adhesion to mucosa. It has been suggested that lectin-like components in lactobacilli surface-layered proteins play an important role in adhesion to receptors on the surface of intestinal epithelial cells, such as glycoproteins. Many factors affecting lactic acid bacteria adhesion have been identified, including non-specific hydrophobicity, non-specific charge, lectin-like proteins, fibronectin, and collagen. The ability of probiotics to adhere to the host epithelium is the most important factor in probiotic selection, but this is not a universal property of lactic acid bacteria and is not required for desired probiotic [16].

Many studies have found that lactobacilli that produce yogurt are more sensitive to gastric juice, whereas enteric species are more resistant. Gastric juice raises the pH of the stomach to around 3.0. As a result, potential probiotics must be able to tolerate the specific pH in order to survive in the stomach. With the addition of soymilk, the survival of potential probiotic dairy propionibacteria strains in pH 2.0 was significantly improved [17]. Also another research noticed that Lactobacilli and Lactococci strains were, kept there viability and growth for 3 hours at pH 2.0.

Lactobacilli survival in low pH conditions of the human stomach was compared using simulated gastric juice for 90 minutes (SGJ, pH 2.0). *Lactobacillus rhamnosus GG* had the best survival rate and maintained their initial viable cell numbers (9 log CFU/ml), while *L. paracasei* NFBC 338 had the worst survival rate, with dropping the concentrations to undetectable levels by 30 minutes of exposure [18].

Cellular stress is said to start in the stomach and upper intestinal tract, where bile is secreted into the gut. Bile salts are secreted into the duodenum in conjugated forms from the gall bladder. The majority of *Lactobacillus* and *Bifidobacterium* strains derived from humans can tolerate physiological bile and gastric juice concentrations [19].

## Probiotic preparation and viability

Probiotics come in a variety of forms, including liquid, tablet, capsule, powder, and acidophilus drinks. Yogurt or kefir, fermented

and unfermented milk, miso, tempeh, and some juices and soy beverages all contain probiotic bacteria. (Probiotics added downstream of the process or food items containing probiotics are subjected to mild processes that do not kill the probiotic bacteria). The bacteria in probiotic foods and supplements may have been present at the time of manufacture or added later.

On the other hand, low viability of probiotic strains in the gastrointestinal tract and final products can result in financial losses as well as a loss of health benefits. A recommended intake of probiotics is $10^8$-$10^9$ viable live cells daily in order to get the beneficial health effects [20]. Spray drying, freeze drying, and fluidized bed drying are common methods for converting probiotic cultures into concentrated powder form. The main steps in the production and preparation of probiotics are described in, but these techniques are insufficient to protect bacteria from the product environment or during their passage through the GIT because they completely release bacteria.

Encapsulating probiotic strains in hydrocolloid beads improves their stability during storage, protects them from bacteriophages, and increases survival during freeze-drying and freezing. They also demonstrated that encapsulating Lactobacillus delbrueckii ssp. bulgaricus in artificial sesame oil emulsions increased bile tolerance and viability by four log units.

Even after 6 months of storage at 4°C and 21°C, probiotic organisms encapsulated in 3 percent v/w sodium alginate in freeze-dried yogurt showed improved viability. Encapsulation in sodium alginate by either extrusion or emulsion technique was found to be effective in maintaining probiotic bacteria counts above the therapeutic minimum (>$10^7$ CFU/g), while non-encapsulated probiotic bacteria counts decreased by approximately 3 logs. Alginate beads are used for encapsulation because they are non-toxic and widely accepted as a food additive. The development of new technologies, such as probiotic strain encapsulation, may be able to overcome the disadvantages [21]. Fresh products, such as set-yoghurt, will not have a problem with probiotic viability because they will be stored at 4 °C until consumed within 2-15 days.

## Health benefits

Probiotics can help to balance intestinal bacteria and reduce the risk of bladder and colon cancer. Immune stimulation, vaccine adjuvant, adherence to human intestinal cells, enhancing help in the production of vitamin K and vitamin B, the protective barrier of the digestive tract, prevention of diarrhea caused by radiotherapy, antibiotics, rotavirus, and *Clostridium difficile*, treatment of constipation, and prevention of inflammatory bowel disease are just a few of the health benefits that probiotics provide [22]. According to some studies, certain lactobacilli strains have anti-oxidative activity and can reduce the risk of free radical accumulation.

This could be because probiotics regulate cytokine function, which modulates inflammatory and hypersensitivity responses. They improve milk allergies and reduce the risk of atopic eczema in children, as well as preventing recurrences of inflammatory bowel disease in adults. Probiotics improve immune function by increasing the number of IgA-producing plasma cells, increasing or improving phagocytosis, and increasing the proportion of T lymphocytes and Natural Killer cells, among other things [23]. Due to the production of ACE inhibitor-like peptides during fermentation, drinking milk fermented with various strains of lactic acid bacteria can result in modest blood pressure reductions. Probiotics may lower serum cholesterol levels in animals by breaking down bile in the gut and inhibiting its re-absorption (which enters the blood as cholesterol). Total and LDL cholesterol levels may be reduced slightly as a result of this [24]**.** The ability of probiotics to bind with hetro-cylic amines, carcinogenic

substances formed in cooked meat is thought to play a role in preventing colon cancer through anti-mutagenic effects. They also reduce the activity of a digestive enzyme called -glucuronidase, which can regenerate carcinogens [25].

The majority of studies on probiotics have focused on diseases of the gastrointestinal tract, but there have been studies on probiotics in allergic conditions such as atopic dermatitis, rhinitis, bacterial vaginosis, and food allergies. Eczema, also known as atopic dermatitis, is the most common chronic skin disorder. Probiotics like L. *rhamnosus* GG have been shown to prevent or reduce symptoms in studies. Even eczema can be avoided if pregnant women take probiotics and newborns take them for the first six months of their lives [26]. Lactococcus, Pediococcus, and Leuconostoc are probiotics that can help prevent or limit the growth of cycotoxinogenic mold [27].

Furthermore, LAB could bind aflatoxin B1 both in vivo and in vitro, according to their bacterial strain [28]**.** *L. paracasei* ST11 was found to reduce body and abdominal fat in studies. These probiotic bacteria appeared to have a weight-loss effect [29]. Intestinal bacteria are thought to influence the host's metabolic, neuroendocrine, and immune functions, which could help them, regulate body weight [28]. Furthermore, probiotics may have anticariogenic properties, preventing and treating dental caries, and may be effective in the oral cavity and the treatment of periodontal disease in general [30].

**Clinical therapeutic effects of probiotics and nutraceuticals**

**Helicobacter pylori infection**

Helicobacter pylori is a main infectious agent worldwide because of its carcinogenic potential and association with peptic ulcer disease. The use of a combination of antibiotics has become the gold standard for eradication. [31]. The ability of multiple strains of Lactobacilli [32, 33] The ability of probiotics to inhibit gastric mucosal adhesion of H. pylori and some flavonoids to inhibit H. pylori growth in vitro suggests that these compounds may have a therapeutic role. Attempts to improve H. pylori eradication rates using probiotics or nutraceuticals have had mixed results, despite promising preclinical evidence [34,35]. Their use in clinical settings should be limited. In this context, it's critical to highlight promising sulforaphane research [36]. An isothiocyanate found in abundance as a glucosinolate precursor in some broccoli varieties and broccoli sprouts. This compound, which is abundant in broccoli sprouts, prevents benzopyrene-induced gastric tumors by inhibiting extracellular, intracellular, and antibiotic-resistant strains of H. pylori. [36] In the context of H. pylori colonization, the use of broccoli sprouts as a "neutraceutical" for cancer prevention appears to be very appealing. Overall, probiotics may have a greater clinical role in the treatment of H. pylori by reducing antibiotic-related side effects and thus increasing patients' willingness to adhere to treatment regimens. [37, 38].

**Colorectal cancer**

Colorectal cancer (CRC) is the second most common cancer in North America. Although numerous plant bioactive factors have been shown to have anti-carcinogenic effects in laboratory studies [39, 40]. The results of case-control and cohort studies examining the relationship between dietary components and the incidence of CRCs have been mixed [41,42]. Several confounding variables could be to blame for these inconsistencies. First, the timing of any dietary intervention with respect to the stage of colon cancer is an important contributing factor to the effectiveness of any dietary intervention in humans, as the most effective interventions in animal models are generally those that begin before the experimental induction of tumors [39]. Second, because the protective effects of a specific bioactive factor may be dependent on the presence or absence of other dietary

constituents, interactions between different dietary compounds within the lumen of the gastrointestinal tract are possible. The use of various nutritional supplements to prevent cancer is the subject of large epidemiologic studies and clinical trials. The preliminary results of this study, which show a decrease in CRC with increased fiber intake, have been published [42]. There is very little experimental evidence that probiotics can prevent cancer in humans. Following experimental ingestion of *Bacillus oligonitrophilus*, a recent case series of patients with a variety of cancer types showed apparent stabilization of cancer growth and patient survival that outperformed historical trends, but these data were uncontrolled observations [43]. The majority of the additional evidence for probiotics' potential use in the prevention and treatment of human cancer is indirect. [44, 45]. The effect of a synbiotic product containing the probiotic strains *Lactobacillus rhamnosus* GG and *Bifidobacterium lactis* Bb12 and the prebiotic oligofructose-enriched inulin (designed to enhance bacterial growth) on colon cancer risk biomarkers is being investigated in a human clinical trial [46]. To date, results have shown that this synbiotic combination modulates gut flora, as evidenced by an increase in bifidobacteria and lactobacilli levels and a decrease in coliforms [46]. It remains to be seen whether this intervention will result in a decrease in cancer incidence.

**Irritable bowel syndrome**

The most common functional gastrointestinal condition is irritable bowel syndrome (IBS), and treatment focuses mainly on symptom relief [47]. Abdominal discomfort or pain, bloating, flatulence, and faecal urgency are some of the most common symptoms. Phytochemicals like peppermint oil, artichoke leaf extract, and turmeric have shown some clinical benefit in small uncontrolled trials [48,49].

Probiotics have been studied in two recent randomized controlled trials for IBS [50]. The researchers looked at the effects of a probiotic formulation (VSL31; VSL Pharmaceuticals Inc., Florida) containing eight different probiotic species on gastrointestinal transit and symptoms in patients with diarrhea-predominant IBS. They discovered no significant difference in overall symptom relief between the placebo and VSL3-treated groups, though VSL3 treatment reduced abdominal bloating [51]. Compared placebo treatment with *L. salivarius* or B. infantis formulations. Patients taking B. infantis had lower symptom scores in most categories than those taking L. salivarius, which was similar to placebo.

**Pancreatitis**

In patients with severe acute pancreatitis, pancreatic necrosis and associated pancreatic infection are predictors of poor outcome, and the microbial species that inhabit the intestine can influence infection rates. The effects of naso-jejunal treatment with Lactobacillus plantarum in patients with acute pancreatitis were studied in two small randomized double-blind trials published by the same research group [52,53]. Both trials compared live *L. plantarum* to killed bacteria as a control, and both found that the groups given the live probiotic had significantly lower rates of infection. Replication of these findings, preferably in larger studies, would provide excellent evidence for the use of probiotics in this situation.

**Diarrhea**

**Infectious diarrhea**

Probiotics were found to be a useful adjunct to rehydration therapy in the treatment of acute infectious diarrhea by the Cochrane Collaboration, which conducted a comprehensive systematic review of the evidence for their use in infectious diarrhea [54]. Unfortunately, studies differed in terms of inclusion criteria, probiotic agent used, and outcome measurements, and subgroup analyses failed to clearly identify appropriate probiotic settings. Although the findings show strong evidence in favor of probiotics' efficacy

for infectious diarrhea, their cautions about heterogeneity are obvious to anyone trying to understand the literature. While probiotics are clearly effective in this setting, questions remain about which patients should receive them, which agents should be used, and when. Given that infectious diarrhea is usually a self-limiting condition, these questions remain difficult to answer.

**Antibiotic-associated and C. difficile diarrhea**

The efficacy of probiotics in preventing diarrhea caused by C. difficile and antibiotics has been confirmed, with an odds ratio of 0.37 in favor of probiotic treatment over placebo in preventing antibiotic-associated diarrhea [55,65]. C. difficile-associated colitis is the subject of the world's largest randomized controlled trial [57]. Saccharomyces boulardii was shown to be effective in preventing disease recurrence, but only in people who had multiple C. difficile infections in a row. A later experiment with L. plantarum yielded similar results [58].

**Inflammatory bowel disease**

**Use of probiotics**

Inflammatory bowel disease is thought to be caused by a disruption in the gastrointestinal microflora or the host's response to this microflora (IBD). As a result of this information, probiotics have been used to try to change the bacterial flora, as discussed in detail elsewhere [59].

**Ulcerative colitis**

The largest study in the treatment of active ulcerative colitis (UC) included 116 patients who were randomly assigned to receive either E. coli Nissle 1917 or standard-care mesalamine therapy. [60]. Because there was no difference in clinical outcomes between the groups, the authors concluded that the therapies were equivalent. Despite the fact that this trial was not powered to detect equivalence, a subsequent study of 327 patients with inactive UC compared E. coli Nissle 1917 to mesalamine and found statistical equivalence [61]. However, another study evaluating maintenance of remission in 120 patients with E. coli Nissle 1917 found no difference between probiotics and placebo [62]. Patients with UC were given BIFICO capsules (Enterococci, Bifidobacteria, Lactobacilli) to maintain sulfasalazine-induced remission in a smaller study [62]. When compared to patients who received placebo, patients who received BIFICO had lower levels of pro-inflammatory cytokines and NF-kB and higher levels of interleukin-10, and relapse was significantly lower (20%) in the BIFICO treated group compared to placebo (93%) at one year. A synbiotic containing a prebiotic (Synergy) and a probiotic (Bifidobacterium longum) were used in another small doubleblinded randomized controlled trial to treat patients with active UC. Patients receiving synbiotic treatment showed improvement in all clinical parameters after one month of treatment [63]. In uncontrolled pilot studies, VSL3 was found to be effective in inducing remission in patients with mild to moderate UC [64]. With the use of Bifidobacteria-fermented milk, promising preliminary results have also been reported [65]. And S. boulardii [66]. Currently, randomized placebo-controlled trials using VSL3 to treat UC are being conducted to confirm the product's efficacy. In UC, a novel probiotic administration protocol involving fecal flora donation from healthy adults has shown promising preliminary results [67]. All patients were free of endoscopic and histologic evidence of UC 1–13 years after receiving human fecal infusion [67].

**Pouchitis**

Probiotics have proven to be extremely effective in the treatment of ill inflammation following colectomy and the formation of an ileal pouch (pouchitis). Randomized controlled trials have conclusively shown that the preparation VSL3 is effective in maintaining antibiotic-induced remission of

pouchitis and in preventing pouchitis after surgery [68,69,70,71]. Culture, a fermented milk product with Lactobacilli and Bifidobacteria, has also shown some promise in trials [72]. The use of Lactobacillus GG for the treatment of acute active pouchitis, on the other hand, did not show efficacy [73].

**Crohn's disease**

Only a few randomized controlled trials have looked into the use of probiotics in the treatment of Crohn's disease; unfortunately, there isn't enough evidence to recommend their use. These studies only looked at one strain, *L. rhamnosus* GG, and found no clinical benefit in the treatment of active disease. [74] or maintenance of drug-induced [74] or postoperative remission [75]. Similarly, a trial of E. coli Nissle 1917 as a maintenance therapy failed to show efficacy [76]. However, because these trials were small and only used one strain of bacteria, future larger trials using different multistrain probiotic compounds may yield more positive results.

## Conclusion

Literature review refers to the study of health benefits, beneficial and comparing benefits and disadvantages. These appropriate microorganisms are affected It is most suitable whether it is yoghurt or specific supplements. More work is needed to determine Long lasting results and the most suitable probiotic strains.

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