
IN THE NAME OF GOD

Prebiotics , probiotics and posbiotics in treatment of GI disease

Dr.L.Alizadeh

Assisstant professor of gastroenterology &hepatology

TBZ.MED

The intestinal tract is host to a vast ecology of microbes that are necessary for health, but also have the potential to contribute to the development of diseases in susceptible individuals by a variety of mechanisms.

Genetic or environmentally triggered perturbations in intestinal epithelial barrier function or innate immune bacterial killing, for example, can lead to an inflammatory response caused by increased uptake of bacterial and food antigens that stimulate the mucosal immune system

- **The gut microbiota and its homeostasis play a crucial role in human health.**
- **for some diseases related to the gut microbiota, current traditional medicines can only relieve symptoms, and it is difficult to solve the root causes or even cause side effects like disturbances in the gut microbiota.**





There are four general methods by which the intestinal microbiota can be altered:

- administration of antibiotics
- therapeutic diets and prebiotics (ie, dietary components that promote the growth and metabolic activity of beneficial bacteria)
- probiotics (ie, beneficial bacteria)
- fecal microbial transplant (FMT).

Combination of these methods is also possible (synbiotics).

The term probiotic, derived from the Greek words “pro” and “bios” meaning “for life.”

Today, the most widely accepted definition is that issued by the Food and Agriculture Organization of the United Nations (FAO) and the World Health Organization (WHO) in 2001, which defines probiotics as “live microorganisms which, when administered in adequate amounts, confer a health benefit on the host.

- **there are many types of probiotics that come from different families of bacteria and yeasts.**

- **Some of the most commonly recognized genera of bacteria used as probiotics include *Lactobacillus*, *Bifidobacterium*, *Enterococcus*, and *Streptococcus*, as well as the yeast *Saccharomyces cerevisiae*.**

MECHANISMS OF BENEFIT

- **Probiotics can alter the gut microbiota composition,**
- **compete with pathogens for nutrients and binding sites on the intestinal wall**
- **enhance the intestinal barrier function**
- **modulate the immune system(induce protective cytokines, including IL-10 and TGF-beta, and suppress proinflammatory cytokines, such as TNF)**
- **produce antimicrobial substances and other metabolites that can directly or indirectly influence host health**
- **can influence the nervous system of the host, communicating through the gut–brain axis.**
- **Modulation of pain perception.**

Some Lactobacillus strains appear to induce expression of micro-opioid and cannabinoid receptors in intestinal epithelial cells and mediate analgesic functions in the gut in a manner similar to the effects of morphine

Prebiotics

Prebiotics were first defined in 1995 as “non-digestible food ingredients that beneficially affect the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon.”

today prebiotics are recognized as dietary components that are selectively utilized by host beneficial microorganisms conferring a health benefit.

Most prebiotic compounds are carbohydrates with a variety of molecular structures that occur naturally in the human diet.

Common types of prebiotics include inulin, fructooligosaccharides (FOS), galactooligosaccharides (GOS), and lactulose

They can be found in various foods such as whole grains, onions, garlic, and bananas.

Prebiotics work primarily by providing a food source for beneficial bacteria in the gut.

They are nondigestible by human enzymes, so they reach the colon intact where they are fermented by the gut bacteria.

This fermentation process results in the production of SCFAs, including acetate, propionate, and butyrate.

Prebiotics selectively stimulate the growth and activity of beneficial gut bacteria such as *Bifidobacteria* and *Lactobacilli*, reduce the abundance of pathogenic bacteria, and thus help to maintain a balanced gut microbiota.

Simultaneously produced metabolites can provide energy to the cells lining the colon, regulate the immune system, enhance gut barrier function, and even influence brain function through the gut–brain axis.

postbiotics

postbiotics refers to preparation of inanimate microorganisms and/or their components that confers a health benefit on the host.

They include a wide range of components, such as inactivated microbial cells, cell wall components, functional proteins, peptides, SCFAs, polyamines, vitamins, bacteriocins, and other bioactive metabolites.

Postbiotics mechanisms of action:

- They can modulate the gut microbiota composition by inhibiting the growth of harmful bacteria and enhancing the function of beneficial bacteria,
- enhance the gut barrier function
- exhibit anti-inflammatory and antioxidant properties
- modulate the immune response.

Because they are nonviable and do not replicate in the gut, postbiotics present a safer alternative to probiotics for immunocompromised individuals or critically ill patients.

TABLE 1. A comparison of the differences between probiotics, prebiotics, and postbiotics.

	Probiotics	Prebiotics	Postbiotics
Definition	Live microorganisms that, when administered in adequate amounts confer a health benefit on the host.[19]	Nondigestible food ingredients that beneficially stimulate the growth and/or activity of gut bacteria.[20]	A preparation of inanimate microorganisms and/or their components that confers a health benefit on the target host.[21]
Source	Bacteria or yeast, often from fermented foods like yogurt. Examples: *Lactobacillus, Bifidobacterium*.	Typically dietary fibers or other carbohydrates. Examples include inulin, FOS, and GOS.	Typically metabolic byproducts from probiotic bacteria. Can be extracted and administered without live bacteria.
Function	Can colonize the gut, enhancing its microbial balance. They can produce postbiotics.[90]	Provide food for beneficial bacteria, promoting their growth and activity.[97]	May not directly affect microbiota composition but exert beneficial effects on host health.[100]
Stability	Sensitive to environmental conditions like temperature and stomach acid.[103]	Generally stable and not affected by temperature or stomach acid.	Stable; not sensitive to temperature, stomach acid, or digestive enzymes.

Pouchitis

Symptoms of pouchitis include increased stool frequency, urgency, hematochezia, abdominal pain, fever, and extraintestinal manifestations of inflammatory bowel diseases

Pouchitis affects approximately 20 percent of ulcerative colitis patients in the first year after creation of the IPAA and 50 percent of patients after five years, but less than 1 percent of patients with colectomies to treat familial polyposis.

- Detailed studies of the microbiota in patients with pouchitis have demonstrated unique patterns, including the persistence of Fusobacteria and enteric species, increased Clostridium perfringens, and the absence of Streptococcus and Faecalibacterium species in the inflamed pouch
- These observations and a high rate of response to various antibiotics support an important role for bacteria in the pathogenesis of pouchitis and provide a rationale for clinical trials aimed at altering the microbiota with probiotics.

Small controlled trials have suggested that at least one probiotic preparation (VSL#3; original Italian formulation) containing 5 X 10(11) per gram of four Lactobacillus species, three Bifidobacterium species, and one strain of Streptococcus salivarius subspecies thermophilus may be effective in prevention of recurrent pouchitis after antibiotic induction of remission.

- **Several systematic reviews have suggested that VSL#3 may be more effective than placebo for preventing relapse of chronic pouchitis and preventing onset of pouchitis .**

- **Results from a single randomized controlled trial indicate that VSL#3, commenced immediately after restorative proctocolectomy, is capable of preventing the onset of pouchitis**

Ulcerative colitis

Convincing data to support the use of probiotic preparations in ulcerative colitis are lacking

Although various probiotic species have shown promise in the treatment of ulcerative colitis, because of the small number of patients in these studies and the risks associated with probiotics, systematic reviews have reached variable conclusions regarding the use of probiotics for the induction and maintenance of remission of ulcerative colitis

The combination of a prebiotic and a probiotic (B. longum) was associated with improvement in histologic scores and measures of immune activation in a one-month randomized controlled trial

Postbiotics such as bacterial supernatants , inhibit NF-KB signaling , offering an alternative to live organisms in immunocompromised patients,

Crohn disease

Clinical trials of probiotics in Crohn disease have shown mixed results.

The reasons for the heterogeneity are unclear and use of probiotics in prevention of postoperative recurrence of Crohn disease has been unsuccessful.

the available data do not support clinical effectiveness of probiotic therapy for either induction or maintenance of remission in patients with Crohn disease.

Whether certain patient subgroups might benefit remains to be determined. A report of clinical improvement with combination of a probiotic, B. longum, and a prebiotic suggested the possibility of using a synbiotic approach to treating Crohn disease, although previous reports with other agents were less positive.

- **Diverticular colitis**
- Infrequently, patients with diverticular disease develop a segmental colitis, most commonly in the sigmoid colon, which can occasionally be symptomatic.
- Combination therapy with VSL#3 and oral beclomethasone dipropionate was beneficial in a case series.

Radiation enteritis

A meta-analysis of six randomized controlled trials of probiotics in radiation-induced diarrhea detected slight overall benefit in diarrhea, but no difference in Bristol Stool Scales or antidiarrheal medication use .

Basic research indicates that intestinal bacteria contribute to radiation-induced injury and repair, so this therapeutic application is open to investigation .

- The PREP trial demonstrated that *Bacillus licheniformis* prophylaxis starting 2 weeks before radiotherapy lowered acute RC incidence by 15% compared to placebo.
- Prebiotics are less studied in RC. Low-FODMAP fibers may mitigate dysbiosis caused by radiation, but their role in prevention or treatment remains unclear,
- SCFAs may also counteract radiation-induced oxidative stress.

infectious diarrhea

The use of probiotics in children with presumed acute infectious diarrheal illness has no benefit.

Probiotic use in adults with acute infectious gastroenteritis is unproven.

Older systematic reviews have demonstrated a modest reduction in the duration of infectious diarrhea with the use of probiotics, although there was heterogeneity among studies.

the AGA Technical Review on probiotics in gastrointestinal diseases concluded that probiotics were not beneficial for treating children with acute gastroenteritis (moderate evidence) .

It is whether probiotics reduce important complications of diarrheal illness such as dehydration and malnutrition.

Collagenous colitis

Collagenous colitis, a subtype of microscopic colitis, is a diarrheal illness characterized by the presence of a thickened subepithelial collagenous plate and lymphocytic infiltrate in the colonic mucosa,

A possible benefit of E. coli strain Nissle 1917 was suggested in an open-label study of 14 patients .

The authors hypothesized that the benefit may have been due to an antagonistic effect of the probiotic against strains of Yersinia species.

In a second placebo-controlled trial, a combination of L. acidophilus and B. animalis strains had no

Microscopic Colitis

Focus on dietary modifications, budesonide for inflammation, and cautious probiotic use (e.g., VSL#3).

Postbiotics like butyrate warrant further study.

Celiac disease

Probiotics can degrade or alter gluten and gliadin, and Lactobacillus and Bifidobacterium concentrations are decreased in patients with celiac disease .

However, there is no evidence to support the use of probiotics in patients with celiac disease .

In a randomized controlled trial, 22 adults with celiac disease on a gluten-containing diet were randomized to treatment with B. infantis NLS super strain or placebo.

Although patients treated with B. infantis reported a significant improvement in constipation, indigestion, and gastroesophageal reflux as compared with placebo, there was no significant difference in diarrhea, abdominal pain, or celiac serologies.

- Probiotics like *Bifidobacterium* and *Lactobacillus* strains may help restore gut microbiota balance in CeD patients, who often exhibit dysbiosis (e.g., reduced *Lactobacillus* and *Bifidobacterium*, increased *Enterobacteriaceae*) even after a glutenfree diet (GFD).
- Certain strains (*L. paracasei*, *B. longum*) degrade immunogenic gluten peptides, reduce intestinal permeability, and modulate immune responses (e.g., lowering anti-tTG antibodies).
- High-FODMAP prebiotics (e.g., inulin) may trigger bloating in sensitive individuals.

CONSTIPATION

Evidence to support the use of single or combination probiotics in children or adults with functional constipation are lacking .

Multiple small, randomized, placebocontrolled trials of probiotics in patients with chronic constipation without irritable bowel syndrome, and in normal subjects with a tendency toward infrequent stools, suggest improvement in defecation frequency, stool consistency, and intestinal transit time with Bifidobacterium lactis, Lactobacillus casei Shirota, L. reuteri DSM 19738 and E. coli Nissle 1917 .

Limited heterogeneous studies do not support use of probiotics in children with functional

IRRITABLE BOWEL SYNDROME

- Probiotics, prebiotics, and postbiotics show promise in managing Irritable Bowel Syndrome (IBS) by addressing gut dysbiosis and potentially improving symptoms.

- Probiotics, prebiotics, and postbiotics offer potential benefits for managing IBS by modulating the gut microbiota and potentially reducing symptoms. However, individual responses can vary, and the best approach may require a personalized approach.
- Bifidobacterium infantis* 35624 improves symptoms like abdominal pain and bloating by modulating gut-brain axis communication .
- Prebiotics like galactooligosaccharides (GOS) increase fecal SCFA levels, alleviating constipation-predominant IBS .
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- Probiotics and carefully selected prebiotics are cornerstone therapies for IBS, supported by moderate evidence. Postbiotics and synbiotics show potential but require further research.

LACTOSE INTOLERANCE

Ingestion of lactase-containing probiotics has the potential to aid lactose digestion in patients with lactose intolerance. Several studies have evaluated the benefit of various probiotics in patients with lactose intolerance .

A systematic review of 15 controlled trials found inconsistent results among strains, but a positive effect of probiotics and suggested further studies on specific strains in which a benefit was suggested .

Probiotics, postbiotics, and liver disease

Recent studies have emphasized the important role of probiotics in treating and preventing liver diseases by modulating gut microbiota, strengthening the intestinal barrier, and interacting with the gut-liver axis .

How they work in liver disease

- **Gut-Liver Axis:**
- The gut microbiota plays a crucial role in liver health, and dysbiosis (imbalance of gut bacteria) can contribute to liver disease. Probiotics, prebiotics, and postbiotics can help restore gut health, reducing the impact of gut dysbiosis on the liver.
- **Inflammation:**
- Inflammation is a key feature of liver diseases. Probiotics, prebiotics, and postbiotics can modulate the gut's inflammatory response, reducing inflammation in the liver and potentially improving overall health.
- **Metabolic Effects:**
- These interventions can also influence metabolic processes in the liver, potentially improving lipid profiles, insulin resistance, and other metabolic factors.
- **Liver Function:**
- By restoring a healthy gut environment and reducing inflammation, probiotics, prebiotics, and postbiotics can improve liver function, as indicated by reduced levels of liver enzymes.

Nonalcoholic Fatty Liver Disease (NAFLD)

- Probiotics (*Lactobacillus* spp.) and synbiotics reduce liver fat content, ALT, and AST levels by improving gut barrier function and lowering LPS-induced inflammation .

- Meta-analyses confirm significant reductions in triglycerides and TNF-α with probiotic supplementation .

Alcoholic Liver Disease (ALD)

- Probiotics (*Bifidobacterium breve*) mitigate oxidative stress and hepatic fibrosis by reducing bacterial translocation and acetaldehyde production .

- - Postbiotics like butyrate enhance liver regeneration and reduce portal hypertension .

Liver cirrhosis and liver cancer

- **Probiotics and postbiotics have recently emerged as promising interventions for preventing and treating cirrhosis and liver cancer, and mitigating disease complications**
- **Postbiotics lower the ammunia level and HE risk**

- **Probiotics lower blood ammonia levels by modulating urease-producing gut bacteria, improving cognitive symptoms .**


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