Probiotics for gastrointestinal diseases

- ***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***

- ***Interactions** between intestinal microbes and the host are the subject of intensive **ongoing research** since they may **influence a variety of diseases***

- ***The greatest experience has been in the inflammatory bowel diseases, ulcerative colitis, Crohn disease, pouchitis, and irritable bowel syndrome, although clinical trials are emerging in several other conditions***

- *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)*

DEFINITION

- ***Probiotics are microorganisms that have beneficial properties for the host.***
- ***Most commercial products have been derived from food sources, especially cultured milk products***

- ***The International Scientific Association of Probiotics and Prebiotics panel defined probiotics in 2014 as "live microorganisms which when administered in adequate amounts confer a health benefit on the host" (Hill et al., 2014)***

- ***strains of lactic acid bacilli (eg, Lactobacillus and Bi dobacterium), a nonpathogenic strain of Escherichia coli (eg, E. coli Nissle 1917), Clostridium butyricum, Streptococcus salivarius, and Saccharomyces boulardii (a nonpathogenic strain of yeast)***

- ***Also under development are strains of bacteria that have been genetically engineered to secrete immunomodulators (such as interleukin-10, trefoil factors, or defensins, or express altered surface proteins such as lipoteichoic acid), which have the potential to favorably influence the immune system***

MECHANISMS OF BENEFIT

- ***Suppression of growth or epithelial binding/invasion** by pathogenic bacteria*
- *Improvement of **intestinal barrier function***
- ***Modulation of the immune system**. induce protective cytokines, including IL-10 and TGF-beta, and suppress proinflammatory cytokines, such as TNF*
- ***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*

- ***Additionally, B. longum strains alleviate stress fatigue, depression, and symptoms of UC (Yoo et al., 2022),***
- ***making them potential probiotics for the treatment of patients with UC who also have neuropsychiatric disorders.***

- ***Probiotics** differ in their ability to resist **gastric acid and bile acids**, **colonize** the intestinal tract, and influence **cytokines** secreted by intestinal epithelial cells*

- ***Although yogurt is commonly recommended as a source of probiotics, not all of the live cultures contained in yogurt survive well in an acidic environment nor do they colonize the microbiota efficiently***
- ***Lactose intolerance***

- ***Fermented dairy beverages*, such as *keffir*, that contain *much higher concentrations* of live cultures than yogurt or cultures that are *relatively resistant to gastric acid* are also available**

- ***Interesting observations indicate that it may not be necessary to administer living organisms to achieve a benefit(proteins and DNA)***
- ***The effects depended upon the specific DNA from the different bacterial species that were components of the preparation***

- ***Some studies demonstrate that products of endogenous resident microbiota can have benefficial effects,***
- ***creating opportunities for therapeutic manipulation beyond the traditional Lactobacillus and Bifidobacterium species.***

- ***the documentation of their efficacy and safety has suffered from the lack of large rigorous trials.***
- ***This, in part, is because probiotics are classified as food additives and, therefore, are not required to undergo US Food and Drug Administration approval for use***

Prebiotics

- ***Defined by the International Scientific Association for Probiotics and Prebiotics as 'a substrate that is selectively used by host microorganisms conferring a health benefit***

- ***Most prebiotics are indigestible dietary fibres derived from various food and nutritional sources.***
- ***They are distinct from probiotics and synbiotics (combinations of prebiotics and probiotics)***
- ***They are not significantly impacted by the oral transit through the GI tract.***

- ***This contrasts with the viability challenges faced by certain oral probiotics***
- ***which can be hindered by the acidic gastric environment before they colonise the intestine***

- ***Prebiotics vary based on their monomeric and linkage type, polymer or oligomer length, and these differences result in unique responses in the host and shifts in the gut microbiota***

- ***SCFAs*, *generated by the microbiota's fermentation of prebiotics, are critical in this context and extensively reviewed by Keshteli et al***

- ***These metabolites activate receptors like free fatty acid receptors, on various cells, including intestinal and immune cells, leading to either inflammatory or anti- inflammatory responses, crucial for maintaining gut homeostasis***

β-fructans

- ***β-fructans has been shown to increase anti- inflammatory mucosal IL- 10- positive dendritic cells in patients with active CD***
- ***prebiotic intervention notably elevated the expression of Toll- like receptor 4 (TLR- 4) on colonic dendritic cells,***

Outcomes		
Histopathology	**Inflammation indicators**	**Microbial and metabolic profiles**
↓ Colonic histological scores	↓ Dialysate prostaglandin E2, thromboxane B2, leukotriene B4, ↓ Colonic MPO	↑ Faecal genus *Lactobacillus* ↓ Colonic luminal pH
↓ Caecal and colonic tissue damage	↓ Caecal IL-1β and TGF-β	↑ *Lactobacillus* and *Bifidobacterium* genera
↓ Colonic histological scores	↓ Caecal IL-1β	↑ Caecal/colonic *Lactobacillus* and *Bifidobacterium* genera ↑ Faecal/caecal genus *Bifidobacterium* ↓ Faecal/caecal family Enterobacteriaceae and genus *Lactobacillus* ↓ Faecal/caecal genus *Bacteroides* ↓ Faecal/caecal genus *Clostridium* cluster IV spp ↓ Faecal/caecal *C. difficile* ↑ Faecal/caecal total SCFA concentration
		↑ Distal colon butyrate concentration
↓ Colon weight, extent of necrosis ↓ Colonic damage	↓ Colonic RNA expression of IL-1β, NOSs, COX-2	↑ Caecal/colonic total SCFA concentration

Galacto- oligosaccharides (GOS)

- ***the reduction in proinflammatory cytokines may, in part, be due to GOS inhibiting nuclear factor-κB (NF-κB) signalling pathways***

- ***Interestingly, GOS and α-GOS enhanced the mRNA expression of tight junction proteins in the colon, namely zonula occludin (ZO)- 1, occludens and claudin- 1, which were reduced, indicating its regulation of gut barrier function***

β-glucans

- ***yeast- derived β-glucans administered for 14 days were found to significantly reduce the colonic histopathological score in rats***

- ***Stimulate the growth and activity of selected strains of bacteria that have a beneficial effect on health***
- ***Decrease the pH of the intestinal contents***
- ***To be resistant to hydrolysis and the action of gastrointestinal enzymes***
- ***To not be absorbed in the upper gastrointestinal tract***
- ***To provide a medium for one or more beneficial microorganisms in the colon***
- ***To be stable in the food processing process***

VSL#3 6 g/day or placebo in pouchitis

- *significantly fewer patients in the probiotic group had experienced a relapse (15 versus 100 percent)*
- *Within three months of stopping treatment, all patients in the VSL#3 group had relapsed*
- *Likewise, fecal Lactobacillus and bifidobacteria concentrations returned to pretreatment levels within one month after therapy was discontinued, indicating that permanent colonization with the probiotic species did not occur*

- ***Patients randomized to VSL#3 also had significantly better quality of life.***
- ***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***

Ulcerative colitis

- ***Benefits of probiotics in ulcerative colitis remain unproven,***
- ***but E. coli Nissle 1917 shows promise in maintaining remission and could be considered as an alternative to biologic approaches in patients with mild recurrent disease who are intolerant or resistant to 5-ASA preparations.***

- ***VSL#3 preparation may have some efficacy in treating active disease as an adjunctive approach***

- ***Relevant clinical trials are currently lacking***
- ***so the extension of animal experimental findings to clinical application requires a longer period of consideration for validation***

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Crohn disease

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

Diverticular colitis

- ***Combination therapy with VSL#3 and oral beclomethasone dipropionate (a locally acting corticosteroid not available in the United States) was beneficial in a case series.***
- ***Not recommended***

- ***● ● A 2010 meta-analysis that included 63 randomized controlled trials in adults and children found that probiotics reduced the overall risk of diarrhea lasting four or more days by 59 percent and the mean duration of diarrhea by 25 hours***

- ***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***

constipation

- ***Evidence to support the use of single or combination probiotics in children or adults with functional constipation are lacking***
- ***improvement in defecation frequency, stool consistency, and intestinal transit time with Bifidobacterium lactis***
- ***marked heterogeneity in study***

IRRITABLE BOWEL SYNDROME

- ***Evidence remains unconvincing for benefits of probiotics for treating irritable bowel syndrome (IBS), probably due to marked heterogeneity in this disorder and variability between the agents studied***

- ***It is possible that a clinically important benefit might be achieved in certain subgroups of patients, particularly those with diarrhea-predominant symptoms***

- ***A placebo-controlled blinded trial of a low fermentable oligo- di- and monosaccharides and polyols (FODMAP) diet with or without multi-strain probiotics in 104 IBS patients showed reduced symptom scores with the low FODMAP diet, but no added benefit of the probiotics***

LACTOSE INTOLERANCE

- ***Ingestion of lactase-containing probiotics has the potential to aid lactose digestion 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***

HEPATIC ENCEPHALOPATHY

- ***Lactulose as prebiotics***
- ***VSL#3 as probiotics***
- ***Lactobacillus and Bifidibacteria as the most effectious species***

- ***H.pylori treatment***
  - ***Maybe anti h.pyloti effect***
  - ***Diminish antibiotics side effects***
  - ***Increase acceptance and compliance***
  - ***Not recommended***

Postbiotics

- ***The term postbiotics, sometimes also not-quite-correctly called metabiotics, has been recently limited to metabolites/CFS (cell-free supernatants) and soluble factors (products or metabolic byproducts) secreted by live bacteria***
- ***SCFA,exopolysacharides,vitamins,bacteriocins***

- ***Generally recognized as safe(GARS) by the FDA***
- ***Qulified presumption of safe(QPS) by the EPSA***