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A Review on Significance of Probiotics in GI Diseases

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ABSTRACT

Probiotics means 'let good microbes work for you in different fields get their benefits and take a rest'. The human gut harbours a complex community of bacteria whose relationship with their host is normally mutually beneficial. Recent studies suggest a disturbance of this relationship in GI diseases and the potential to correct this by using probiotics. Many authors have described the history and the progress of probiotics and their different applications. In this review, we will focus mainly on three points, health improvement, infection control and disease management, which could be eliminated by the use of different types of direct uses of probiotics.

Keywords: Probiotics, Disease management, Health, Infections, Microbes.

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INTRODUCTION

Probiotics are defined as ‘mono-or mixed cultures of live micro-organisms which, when applied to animal or man beneficially affect the host by improving the properties of the indigenous microflora’¹. Both Lactobacilli spp. and Bifido bacterium spp. are frequently applied as probiotics. Probiotic bacteria for humans are preferably of human origin: they have to be safe for the host, genetically stable, and capable of surviving passage through the gastrointestinal tract². Among the effects claimed for probiotics are beneficial immunomodulation, reduction of serum cholesterol, improved lactose digestion and protection against colon cancer^{2,3}.

The mechanisms of action of probiotic bacteria are thought to result from modification of the composition of the indigenous intestinal microbiota and its metabolic activity, prevention of overgrowth and colonization of pathogens, and stimulation of the immune system⁴. Probiotics have been studied in several disease entities, especially when intestinal bacteria are thought to be involved in their pathogenesis. In this review, the available evidence of clinical trials on probiotics in GI and liver diseases will be summarized with a major focus on irritable bowel syndrome (IBS), inflammatory bowel disease.

Probiotic bacteria have to survive passage through the gastrointestinal (GI) tract containing gastric juice, bile and pancreatic juice. Furthermore, adhesion to the intestinal mucosa is considered to be a prerequisite for the interaction with the immune system and this is more likely to occur with host-specific strain.

Common microbes used as probiotics:⁵

The microbes used as probiotics represent different types such as bacteria, yeast or mold. However, there are more

Common species of each such as:

1- Bacteria:

- (i) Lactobacillus: acidophilus, sporogenes, plantarum, rhamnosum, delbrueck, reuteri, fermentum, lactus, cellobiosus, brevis, casei, farciminis, paracasei, gasseri, crispatus;
- (ii) Bifidobacterium: bifidum, infantis, adolescentis, longum, thermophilum, breve, lactis, animalis;
- (iii) Streptococcus: lactis, cremoris, alivarius, intermedius, thermophilis, diacetyllactis;
- (iv) Leuconostoc mesenteroides;
- (v) Pediococcus;
- (vi) Propionibacterium; Bacillus; Enterococcus; Enterococcus faecium;

2- Yeast and molds:

- (i) *Saccharomyces cerevisiae*,
- (ii) *Saccharomyces boulardii*,
- (iii) *Aspergillus niger*,
- (iv) *Aspergillus oryzae*,
- (v) *Candida parapsilosis*,
- (vi) *Saccharomyces boulardii*.

The type of the microbes used as probiotics increased due to the increase in the research concerning the subject as well as by the increase of the newly discovered and identified microbes, which could be used as probiotics. One should update his microbial flora from time to time and follow the research and the published data about probiotics to gain more knowledge and ideas.

Irritable bowel syndrome:

Irritable bowel syndrome is a functional GI disorder, characterized by symptoms such as abdominal pain, bloating, diarrhea or constipation. A few studies have examined the fecal flora of IBS patients and found a decrease in *E.coli*, *Lactobacilli* and *bifidobacteria* and an increase in other microbes in comparison with healthy volunteers^{5,6}.

Probiotics are applied in IBS as they may change the composition and metabolic activity of intestinal microbiota such as the production of short chain fatty acids and gas. Furthermore, they may affect gut motility and exert an anti-inflammatory effect.

Risk Factors:

- While the causes of IBS are still unknown, it is believed that the entire gut- brain axis is affected^{7,8}.
- The risk of effecting IBS increases six folds after acute gastro intestinal infection.
- Stress
- Small intestinal bacterial overgrowth.

Probiotics Used:

Lactobacillus salivarius was compared with *Bifidobacterium infantis* and placebo in 77 IBS patients defined by Rome II criteria⁹. Although *L. salivarius* resulted in a significantly better bowel movement measured by the Bristol stool scale in comparison with placebo, the *B. infantis* group had significant better scores for abdominal pain, bloating, bowel movement and overall GI function compared with both the *L. salivarius* and the placebo group.

Inflammatory bowel disease:

Crohn's disease (CD) and Ulcerative colitis (UC) are chronic inflammatory bowel disease (IBD) characterized by unpredictable periods of active and inactive diseases. Evidence suggests that (luminal) bacteria, loss of oral tolerance and an impairment of the mucosal barrier function play a role in the pathogenesis of IBD¹⁰.

An exaggerated T-cell response causing mucosal hyper-responsiveness is thought to be an important factor driving inflammation in IBD^{10,11}. T-cells from the lamina propria of CD patients respond with a Th1 polarized response;¹⁰ in UC patients, a preferential expression of Th2 cytokines IL-4 and IL-5 has been described¹². In addition, reduced numbers of regulating T- cells which produce IL-10 and/or transforming growth factor- β are found in both UC and CD. Finally, mutations in the NOD2/CARD 15 gene (involved in the intracellular recognition of bacterial components) are associated with CD,¹¹ and increased expression of toll- like receptors (Trans membrane receptors that recognize conserved structures of micro-organisms) is found in both UC and CD^{13,14}.

Risk Factors:

- Loss of integrity of intestinal epithelium
- High protein intake
- Genetics

Probiotics Used:

The first evidence for the use of probiotics in IBD comes from animal models of colitis. For example, *Lactobacillus reuteri* and *L.plantarum* were found to reduce the severity of methotrexate-induced and acetic acid-induced colitis. A reduction in the development of colitis was demonstrated in IL-10 knock-out mice treated with *Lactobacillus spp*¹⁵⁻¹⁷.

DIARRHOEA:

Diarrhea is the condition of having at least three loose or liquid bowel movements each day. It often lasts for few days and can result in dehydration due to fluid loss.

Many studies have been performed on the effect of probiotics in antibiotic- associated diarrhea (AAD) and acute diarrhea. AAD occurs in 4-30% of antibiotic treated patients and is caused by a disturbance of the intestinal microflora, direct tissue damage or modulation of the immune system.¹⁸⁻²⁰ *Clostridium difficile* is found in 10-25% of AAD patients and can cause pseudo-membranous colitis¹⁸.

Risk Factors: ¹⁹⁻²²

- A virus such as rotavirus, winter vomiting disease (Norwalk virus or norovirus), enterovirus or hepatitis virus
- Bacteria, such as E.coli, salmonella, shigella, c diff (clostridium), or cholera (Vibrio cholera).
- Children who have lowered levels of zinc have a greater number of instances of diarrhea, severe diarrhea and diarrhea associated with fever.
- Lack of clean water
- Open defecation.

Probiotics Used:

L. GG was found to decrease the duration of this diarrhea within 1-2 days in combination with an increase in IgA and a decrease in rotavirus shedding²³⁻²⁶. No such effects was found for *L. acidophilus*, *L. rhamnosis*, *L. delbrueckii* and *S. thermophile*.²⁷⁻²⁹.

HELICOBACTER PYLORI ERADICATION, CONSTIPATION AND LACTULOSE MALABSORPTON:

Probiotics have also been tested as eradication therapy for *H. pylori*. *In vitro*, specific lactobacilli and bifidobacteria have been found to exert bactericidal effects against *H. pylori*, probably by the production of bacteriocins or organic acids³⁰.

Probiotics Used:

Beneficial effects were found on self-reported severity of constipation in 70 chronically constipated adults treated with *L. casei Shirota*³¹ or placebo for 4 weeks. A small beneficial effect of a 24% increase in defecation frequency has been observed after *L. rhamnosis* intake in combination with *Propioni bacterium freudenreichii*³².

Yoghurt and probiotic bacteria are also often given to improve and lactose digestion and to reduce symptoms of intolerance in lactulose malabsorbers, as fermented milk products have been observed to be tolerated better than milk.⁴ Beneficial effects can be caused by microbial β -galactosidase, a delayed GI transit time, a reduced sensitivity to symptoms and positive effects on intestinal functions and the colonic microbiota³³.

Table 1: Different types of Probiotic microbial strains and their usage.³⁴

Disease name	strain
Eczema	<i>Escherichia coli</i>
	<i>Bifidobacterium bifidum</i>
	<i>Bifidobacterium lactis</i>
	<i>Lactococcus lactis</i>
Food allergies immunity	<i>Escherichia coli</i>

	<i>Bacillus circulans</i> PB7
	<i>Lactobacillus plantarum</i>
	DSMZ 12028
Antibiotic effect removal	<i>Enterococcus mundtii</i> ST4SA
	<i>Lactobacillus plantarum</i>
	<i>Lactobacillus brevis</i> KB290
	<i>Lactobacillus</i> strains
	<i>Bifidobacterium</i> strains
Gastroenteritis	<i>Lactobacillus casei</i>
Therapeutics Intestinal hyper permeability	<i>Lactobacillus plantarum</i> species 299(LP299)
Vaginal candidiasis(thrush)	<i>Lactobacillus reuteri</i> RC-14
	<i>Lactobacillus rhamnosus</i> GR-1
Urinary tract infection	<i>Lactobacillus rhamnosus</i> GR-1
	<i>Lactobacillus reuteri</i> RC-14
Lactose Intolerance	<i>Lactobacillus acidophilus</i>
Non-steroidal anti- inflammatory drug	<i>Escherichia coli</i> strain Nissle 1917
Intestinal dysbiosis	<i>Lactobacillus johnsonii</i> La1
	<i>Lactobacillus</i> strain
	<i>Lactobacillus</i> GG
Irritable bowel syndrome	<i>Bifidobacterium</i> infantis 35624
	<i>Escherichia coli</i> DSM17252
	<i>Bifidobacterium</i> infantis 35624
Traveler's diarrhea	<i>Lactobacillus</i> GG
	<i>Lactobacillus plantarum</i>
Radiation –induced diarrhea	<i>Lactobacillus casei</i> dn-114 001
Crohn's disease	<i>Escherichia coli</i> strain Nissle 1917
Prevention of colon cancer	<i>Enterococcus faecium</i> M-74
	<i>Lactic acid</i> bacteria
Ulcerative colitis	<i>Lactobacillus acidophilus</i>
	<i>Escherichia coli</i> strain Nissle 1917
	<i>Bifidobacterium</i>
Peptic ulcer disease	<i>Lactobacillus acidophilus</i>
Prevention of atopy	<i>Lactobacillus rhamnosis</i> GG
Hypercholesterolemia and cardiovascular diseases	<i>Enterococcus faecium</i> M-74
	<i>Lactobacillus plantarum</i>
	<i>Propionibacterium</i> freudenreichii
	<i>Lactobacillus plantarum</i> PH07

Relation of Probiotics to our health:³⁴

1. Probiotics are useful and friendly microbes.
2. They are able to compete with the bad microbes and colonize our digestive system.
3. They are able to ferment our food to simpler by products and could promote our health by many different mechanisms.
4. Their amount could be deteriorated due to many factors, such as incorrect diet, alcohol, age and so on. This is why they should be taken through our regular diet.

5. In particular cases such as after antibiotic treatments, where they are expected to be affected severely, they should be taken orally in considerable amounts or with food.

6. Probiotics promote health while they:

- Remove the side effect of the pathogens or the harmful microbes.
- Supply the body with useful byproducts.
- Reduce the jobs of our digestive system.
- Reduce the effect of the first attack of harmful compounds, instead of our cells, by their biofilm, which protects our digestive system.
- Reduce the amount of food needed by our bodies due to the correct digestion and metabolism of any amount of food.
- Probiotics in some cases could complement the deficiency in our genetic materials by helping us to borrow the products of their genes (such as in case of the lactose fermentation deficiency).

Role of Probiotics in disease treatment and management:³⁴

1. Suppression of the putrefactive-type fermentation which was one of the Ilya Ilyich Metchnikoff postulations about the usefulness of Probiotics

2. Used to reduce the antibiotic destructive effect and to regenerate any type of loss in beneficial microflora. Some *Bacillus species* are recommended for use with antibiotics while they are resistant to them

3. Treating of the diarrheal disorder. *Saccharomyces cerevisiae var boulaardii* was used widely for treating various diarrheal disorders

4. Improving intestinal tract health

5. Enhancing the immune system, synthesis and enhancing the bioavailability of nutrients

6. Reducing symptoms of lactose intolerance and decreasing the prevalence of allergy in susceptible individuals

7. Reducing the risk of certain cancers

8. Control of serum cholesterol levels

9. Improved digestion of lactose against food containing lactose.

10. Probiotics may also influence the protective functions of the intestinal mucosa including the synthesis and secretion of antibacterial peptides

11. Hypertension (Blood pressure control)

12. Condition of the genitourinary tract

CONCLUSION:

The intestinal microbiota is a very complex ecosystem, which has several important functions for the host. Probiotic bacteria are increasingly used in several GI diseases, especially when intestinal bacteria might be involved in their pathogenesis. Evidence for the therapeutic or preventive application of particular probiotic strains is available for AAD, Rota-virus-associated diarrhea. Results are encouraging for IBS, UC and for reducing side effects by H.pylori eradication therapies but are less clear for CD, lactose intolerance and constipation. As different probiotic strains can have different effects, further insight into disease entities and into functioning of probiotic strains is required to be able to select well-characterized strains with specific health benefits.

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