

Probiotics and Gut Health

Varsha A. Singh, Ruhi Bungler

Department of Microbiology, MMIMSR Mullana, India

Abstract: The health promoting benefits and efficacy of probiotics has been demonstrated in many models of gastrointestinal disease. Probiotics have an antimicrobial effect through modifying micro flora, secreting antibacterial substances, competing with pathogens to prevent their adhesion, competing with nutrients necessary for pathogen survival, producing an antitoxin effect and reversing some of the consequences of infection on the gut epithelium. Fermented milks, cheese, enriched yoghurt, yoghurt-like products are the commonly used Probiotic food preparation.

INTRODUCTION

The immune system of mammals includes complex colonies of cells and molecules which interact to provide protection from challenges by pathogenic microbes (bacteria, viruses, parasites). The intestinal micro biota exerts both harmful and beneficial effects on human health and hence is the largest source of microbial stimulation. The term *PROBIOTICS* is a relatively new word meaning “for life” and is currently used to name bacteria associated with beneficial effects for humans and animals. ¹

WHAT IS A PROBIOTIC?

‘Let food be thy medicine and medicine be thy food’, the age-old quote by Hippocrates, is certainly the tenet of today. Probiotics was defined by Fuller in 1989 “as a viable microbial dietary supplement that beneficially affects the host through its effects in the intestinal tract “. Initially it was thought to be used as animal feed product. Many definitions of Probiotics have been published, starting from Fuller, who defined a probiotic as “a live microbial feed supplement which beneficially affects the host by improving its intestinal microbial balance”.¹

Recently FAO/WHO has defined it as: “Live microorganisms that when being administered in appropriate dose, they confer benefit of health to the receiver.”²

HISTORY

Fermented milk used for human consumption had been recorded as the first probiotic. After that, probiotics became popular with animal nutrition. The original observation of the positive role of these bacteria has been credited to the pioneering work of Metchnikoff from Pasteur Institute in the early 1900s.³

FEATURES OF A GOOD PROBIOTIC

A good Probiotic agent must be non-pathogenic, nontoxic, resistant to gastric acid /bile, should adhere to gut epithelial tissue and produce antibacterial substances (Figure 1).The survival of probiotics organisms in the gut depends on the colonization factors that they possess, organelles which enable them to resist the antibacterial mechanisms that operate in the gut. Besides antibacterial mechanisms, they need to avoid the effects of peristalsis, which tends to flush out bacteria with food. This can be achieved either by immobilizing themselves or by growing at a much faster rate than the rate of removal by peristalsis. When Probiotics are administered in combination with antibiotics, they increase the eradication rate and decrease the adverse effects associated with antibiotic therapy. ⁴

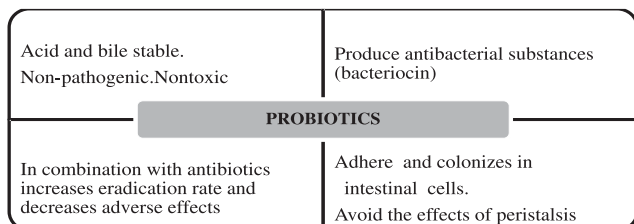


Figure 1: Probiotics Strain Characteristics

Correspondence: Dr. Ruhi Bungler, Assistant Professor, Flat No. D-32, M.M. University, Mulana -133207, India M: 8059931888 e-mail: ruhi.dr@gmail.com

COMPOSITION OF PROBIOTICS

Probiotics can be bacteria or yeast. But most Probiotics are bacteria. Microorganisms that are used as potential probiotic agents are listed in table 1.

Table 1: Composition of Probiotics

LACTOBACILLUS (Popular Probiotic)	BIFIDOBACTERIA (Popular Probiotic)	OTHER BACTERIA	YEASTS (Potential Probiotic)
L.acidophilus spp. L. acidophilus La-1 L. casei spp. L. rhamnosus GG L. reuteri L. plantarum spp L. fermentum KLD L. johnsonii	Bifidobacterium bifidum B. breve B. infantis B. longum	Enterococcus faecium Escherichia coli Nissle 1917 Streptococcus Salivarius subsp. thermophilus	Saccharomyces boulardii

GUT MICROFLORA- THE SOURCE OF PROBIOTICS

Colonization of the gut with micro flora begins in the infant, shortly after birth. During the birth and during the first few days of life, the gut is inoculated with bacteria. Thus, children born vaginally are exposed very early to maternal flora. In most breastfed infants, the Bifidobacteria counts increase rapidly to constitute 80%–90% of the total flora. Lactobacilli and bacteroides increase to a lesser extent and Enterobacteria counts decrease. On the other hand, Formula-fed infants tend to have a flora that is more complex, consisting mostly of coliforms and Bacteroides, with significantly lower prevalence of bifidobacteria.⁵ After weaning, the micro flora of children begins to resemble that of adults. The human gastrointestinal tract contains about 10¹⁴ bacteria, with small numbers in the stomach (<10³/ml) rising with descent of the tract to 10¹¹–10¹²/ml in the colon. Here the anaerobes outnumber the aerobes by 100– 1000 fold.⁶ Normal human GI flora has many roles including immune modulation, digestion, metabolic activity, and a competitive effect on other GI microbes

PROBIOTICS AND GASTROINTESTINAL INFECTIONS

Gastrointestinal infections lead morbidity and mortality worldwide, particularly in developing countries. Fig 2 shows the list of disorders on which probiotics act.

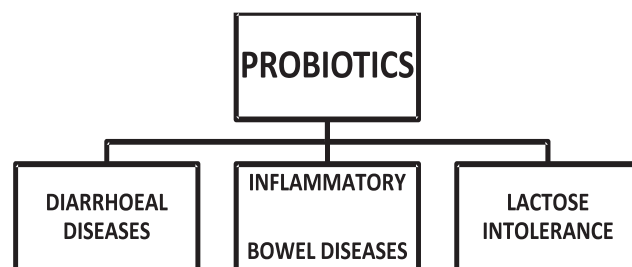


Fig: 2 List Of Disorders On Which Probiotics Acts

Diarrhoeal Disease

Each year gastrointestinal infections are responsible for significant morbidity and mortality worldwide. The World Health Organization (WHO) estimates it to be more than four billion episodes of diarrheal disease annually, while there were 2.2 million deaths attributable to diarrheal disease in 2004, making it the fifth leading cause of death at all ages worldwide.⁷ Probiotics have been used in the treatment and prevention of many forms of diarrheal disease.

Antibiotic-Induced Diarrhoeal Disease.

Clostridium difficile and *Klebsiella oxytoca* are two bacteria commonly thought to contribute to the occurrence of antibiotic-associated diarrhea (AAD) by releasing two exotoxins, toxin A and toxin B. Hyperosmolarity due to undigested carbohydrates and decreased formation of colonic short-chain fatty acids also thought to contribute to AAD.⁸ Probiotics may be efficacious in preventing AAD by stabilizing the microbial population of the colon by restoring resident flora and by stimulating the immune system

Traveller's Diarrhoea

Various infectious agents can cause traveller's diarrhea, enterotoxigenic *E. coli* is the most common. Enterotoxins produced by ETEC include heat-labile enterotoxin (LT) and heat-stable enterotoxin (ST).⁹ LT increases the level of cAMP in intestinal cells and this causes an increase in electrolyte and water excretion (diarrhoea). ST stimulates the production of cGMP, leading to increased fluid excretion and diarrhoea. *Lactobacillus* bacteria are most commonly used in the prevention of traveller's diarrhea

Acute Diarrhoea Caused By Rota Virus

Human rotavirus primarily infects intestinal epithelial cells of the distal small intestine. Malabsorption occurs because of the destruction of gut cells called enterocytes. They stimulate the overgrowth of urease producing bacteria. Urease is proinflammatory mediator that predisposes gut mucosa to ammonia-induced destruction. The Probiotics appeared to normalize fecal urease concentration, thereby stabilizing the gut microbial environment.¹⁰

Diarrhoea In Immunocompromised Subjects

Diarrhea is a very serious consequence of human immunodeficiency virus (HIV) infection and patients receiving Chemo and radiotherapy. This frequently causes severe disturbances of the immune system and the indigenous intestinal micro flora accompanied by diarrhea and/or increased cell counts of the *Candida albicans* in the gastrointestinal

tract and other organs. *S. boulardii*, probiotic bacteria decreases the side effects of the administration of radiotherapy.¹¹

Inflammatory Bowel Disease

Inflammatory bowel disease (IBD) is a term applied to a group of bowel disorders in which inflammation is a major feature, but where there is no proven evidence that infection is the causative agent. Rare forms of inflammatory bowel disease exist but the two main entities are ulcerative colitis and Crohn's disease. Both share some clinical, pathological and epidemiologic features and are diverse in others. The pathogenesis of IBD is not fully understood, the aetiology of both diseases is multi factorial (figure 3) However, more and more evidence shows gut micro flora plays an important part in initiating and maintaining the mucosal inflammatory response in IBD.

Lactose Intolerance

Lactose intolerance is a physiological state in human beings where they lack the ability to produce an enzyme named lactase or B-galactosidases. This lactase is essential to assimilate the disaccharide in milk and needs to be split into glucose and galactose. Individuals lacking lactase are not being able to digest milk and it often poses a problem in newborn infants. People with lactose intolerance problem express abdominal discomfort, diarrhea, cramps, flatulence, nausea, vomiting, etc. A person suffering from lactose intolerance is advised to take non-milk diet.

Lactose intolerance is of 3 types. In primary or adult-type lactose Malabsorption, lactase activity is high at birth, decreases in childhood and adolescence and remains low in adulthood. Secondary forms of lactose malabsorption may be due to inflammation or functional loss of the small intestinal mucosa and by protein-energy malnutrition. Although some forms are transient, disappearing after recovery from the original disease, others are irreversible.¹² Congenital lactose malabsorption, a rare autosomal-recessive heritable genetic defect, is evident immediately after birth. Afflicted newborns respond to their first milk feed with diarrhoea.¹³

H. Pylori Gastritis.

More than half of the world's human population is infected by *H. pylori* infection.¹⁴ Any alterations in the resident micro flora in the stomach contribute to the development and persistence of ulcers. Probiotics may help prevent or treat *Helicobacter pylori* infections responsible for type B gastritis, peptic ulcers and perhaps stomach cancer.¹⁵ Clinical studies demonstrate that Probiotics do not eradicate *H. pylori* alone, but they may increase the ability of antibiotics to accomplish this goal.

MECHANISMS OF ACTION OF PROBIOTICS

There are various proposed mechanisms by which probiotic may protect the host from intestinal disorders (fig 4). Probiotics have an antimicrobial effect through modifying micro flora, secreting antibacterial substances, competing with pathogens to prevent their adhesion, competing with nutrients necessary for pathogen survival, producing an antitoxin effect and reversing some of the consequences of infection on the gut epithelium – such as secretory changes and neutrophil migration.¹⁶ Inhibitory substances such as organic acids, hydrogen peroxide and bacteriocins inhibits bacterial metabolism or toxin produced by bacteria. They also block the receptor sites by competitive inhibition for bacterial adhesion sites on intestinal epithelial surfaces.¹⁷ In addition to that Probiotics also competes with pathogenic microorganisms for the nutrition. In *C. difficile* intestinal disease, *S. boulardii* protects through degradation of the toxin receptor on the intestinal mucosa. Other proposed mechanisms include strengthening tight junctions between enterocytes, increasing IG-A

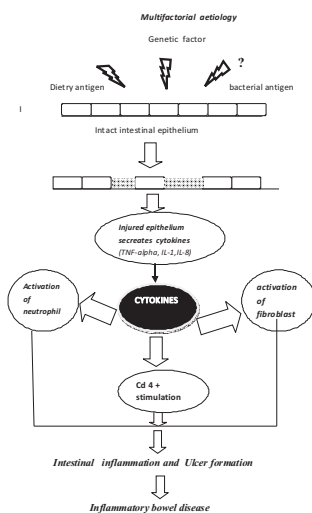


Fig 3: Pathogenesis Of Inflammatory Bowel Diseases

production and stimulation of specific and nonspecific immunity.¹⁸ In sum, Probiotics are generally thought to affect the gastrointestinal tract and the associated CD (local) immune system. Several studies have been performed to investigate the effects of different probiotic bacteria. From these studies it has become clear that different strains of lactobacilli induce very different effects. In addition, effects seen in a certain human population with one strain of bacteria can often not be reproduced. This makes a final overall conclusion very difficult.

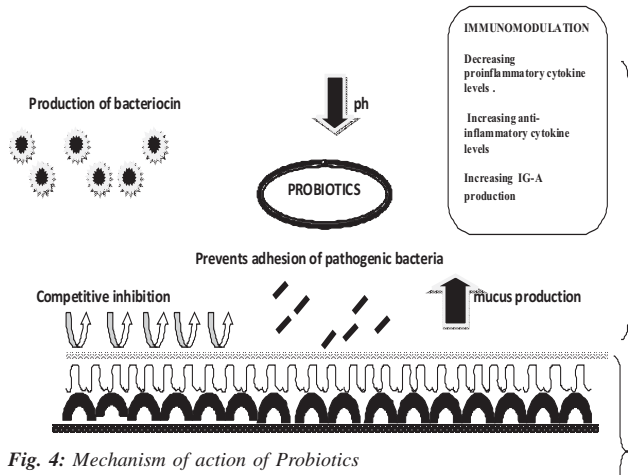


Fig. 4: Mechanism of action of Probiotics

FUTURE OUTLOOK AND CONCLUSION

The health promoting benefits and efficacy of Probiotics has been demonstrated in many models of gastrointestinal disease. Fermented milks, cheese, enriched yoghurt; yoghurt-like products are the commonly used probiotic food preparation. They are also marketed as capsules, and powders. In future, they are expected to be found in fermented vegetables and meats.

Probiotics seem to have beneficial effects in some diarrheal and inflammatory conditions in the gastrointestinal tract, where there seems to be an imbalance between 'good' and 'bad' bacteria. Until now, only a few small studies have been undertaken to define the role of Probiotics in clinical practice, the results of which are encouraging. The advantage of these products includes ease of administration, low cost, and good safety profiles.

The mechanisms of action, the optimal regimen – such as dose, strain(s), vehicle and frequency of administration and the duration of

probiotic treatment are not known. The quality control of the commercialised probiotic food supplements, the exactness of the label and the indications need to be improved. More research on pharmacodynamic and pharmacokinetic aspects is also needed. Safety should be better assessed in pre-term, immunodeficient and immunocompetent individuals for any risk of overstimulation (or modification) of the immune system in susceptible subjects. The establishment of standards of identity for probiotic-containing food products will serve to accelerate their development and availability.

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