Potential of Probiotics in Improving Gut Health

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Abstract

To maintain nutrition and health, presence of needful bacteria in the gut plays a crucial role. When there is condition like imbalance in human natural microflora, mostly in the gut results in ill conditions known as dysbiosis. Recent advance study on the human gut suggests that misbalance of microbial flora may result in predisposition to different disease phenotypes. The use of probiotics as mediators in health and diseases has been raised in recent years. The human gut has the ability to act as home to over 100–1000 species of microbes, where the internal environment is modulated, which plays an important role in host health. In this chapter, we have tried to explain some of the applications of probiotics on the human as well as animal gut and how they are beneficial. Points such as probiotics and its current value in the market, gut microbiota and its effect on the immune system, and several diseases are explained. Information related to microorganisms and their role is encoded.

Keywords

Ecobiotics · Gut microbiota · Immunomodulation · Intestinal diseases · Probiotics

21.1 Introduction

Joshua Lederberg introduced the concept of human microbiome to scientific community. Probiotic is modern era's phrase, and it is going to play an important role in the effect of human as well as animal health with the help of bacterial associations.

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The symbiotic connection between the human host and its bacterial residents has obtained extensive research interest in recent years. These bacteria are predominately showing their presence in the gastrointestinal system with their mutual genomes, known as the gut microbiome (Marchesi and Ravel 2015). Based on published literature and their positive results advice that in the human host homeostasis, health, and disease, there is an important role of gut microbiome. Some of the positive result of research associated with appetite, GIT function, and immune responses (Thaiss et al. 2016) are well documented. This chapter tries to explain collected current knowledge and research in probiotics in gut health. Metchnikoff in the early 1990s revealed probiotics in scientific circumstances as moderation of floral diversity in animal and human bodies and substitute harmful microbes with useful ones. Afterwards, Henry Tissier observed that the stool of children suffering from diarrhea contains less concentration of particular bacteria compared to the stool of healthy children. He also suggested oral administration of live organism that is *Bifidobacterium* to patients with diarrhea. Modern definition of probiotics is a viable mixed or mono bacteria culture when its application is done to man or animal helps to maintain and improve properties of indigenous flora is given by Havenaar and Huisin't Veld (1992). In the year 2000, Government of Argentina has requested to food and agriculture expert panel for evaluation of health and nutritional properties of probiotics. After that grammatically corrected definition of probiotics is "living microorganism, when administered in required amounts, gives benefit on health of host" (Hill et al. 2014). It can also define as probiotics as substitute of microorganisms in host to which play an important role in enhancing measurable health outcomes. In 2017, updated definition of probiotics exists as "a substrate that is selectively utilized by host microorganism conforming benefit to health". The main cause for dysbiosis is when there is disturbance or changes in collection of bacteria, bacteria, and viruses which help to form gut microbiota, threat to gut integrity is imposed by normal microbial homeostasis. Until now, for healthy gut exact number of microbes require is not found or defined. Microbes play an important role in maintaining regulatory and metabolic networks. Shaping of the gut epithelium is also mostly depending upon the microbiota present in the gut (Sender et al. 2016). *Streptococcus*, *Clostridium*, *Lactobacillus*, and *Bifidobacterium* are currently the major strains used as probiotics, but in recent study in culturomics and metagenomics related to disease lead to increase knowledge related to microbial composition and their role in health benefit (Fig. 21.1).

21.2 Probiotics: Current Importance and Future

It is better to select probiotic strains for the preparation of products based upon the evidence of phenotype. In recent years, there has been an increased use of probiotics as a medicine to treat diseases and maintain better health. This condition leads due to evidence of effect of gut microbiota on their effect on health. Current consideration gives rise with industries and academia to do research and develop probiotics with success along with develop technologies. There is expansion of global market related to probiotics. Recently, there is still a need to study the interaction of

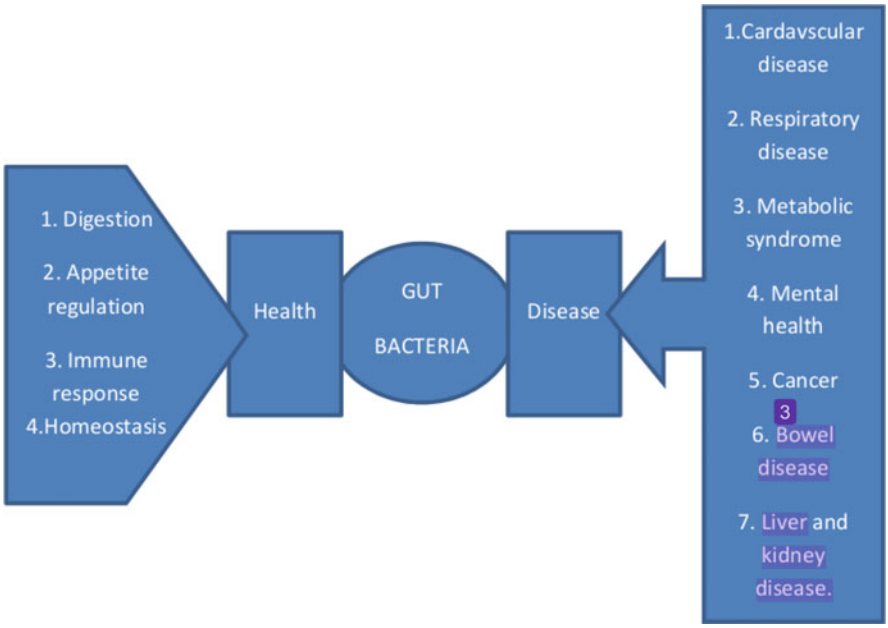


Fig. 21.1 A diagrammatic overview of the positive influence of gut bacteria

microbiota with supplementation. A more in-depth study of single and combined strains is to be done and ongoing. A lot of research is done related to probiotics, but health claim is yet to be done. Among the research activities done, near about 19,000 results have been found for literature survey (Chamberlain and Lau 2016). The National Institutes of Health funded project entitled "Human Microbiome Project (HMP1)" which was performed on 250 healthy volunteers. This project concluded that human microbiome is constituted between 3500 and 35,000 species (Morgan et al. 2013). In the human body, a lot of microorganisms are present, and microorganisms present at different sites vary in number. The sequence of amount of microorganisms present in oral and colonic cavity have large amount compared to vagina. Hadza in Tanzania in one survey it was found that diversity of GIT microorganisms in hunter-gatherer populations (Clemente et al. 2015). Among colorectal cancer, IBS, Crohn's disease, and obesity are observed in persons with a low diversity of microorganisms in the lower GIT (Mosca et al. 2016). In the biological basis and mechanisms of action of probiotics, with diverse biological functions and mechanisms apparent across different bacterial strains, it is important for researchers and probiotic product developers to understand the properties of each strain and apply these proactively to target a preferred physiological interaction/response. For example, it is likely to be important and beneficial for probiotic strains that exhibit anti-inflammatory properties to be applied to research in health conditions associated with an augmented inflammatory response (e.g., Crohn's disease). In clinical probiotic research, an early and consistent research focus on gastrointestinal diseases is

now resulting in inclusion of probiotics into evidence-based guidance for clinicians. Beyond the gut, the scope of clinical conditions amenable to probiotic management seems almost limitless. However, although the results from research in new indications, such as neurological pathologies, are very promising, a substantial amount of further work is required to provide healthcare providers with the confidence to embrace probiotics into regular practice. The probiotics industry is an ever-growing entity with continual expansion of products being taken to market. This has driven scientific research with the aspirations to uncover probiotic strains that provide conclusive evidence of improvements in health and disease outcomes. These opportunistic endpoints have not currently been met, evidenced by the fact that no certified health claims credited to probiotic products are currently in place. This is likely owing to the wide interpersonal variations in commensal bacteria as well as fundamental differences between probiotic strains. The further application of advanced omics technologies will provide an improved understanding of the complex host-bacteria interactions.

21.3 Gut Microbiota and Their Effect on Human Health

Since the project named as Human Microbiome Project (HMP) exists, a lot of study has been published related to the composition of microbiota in the human gut along with analysis of normal and diseased persons. There was also one study performed in which fecal study of two twins was performed in which characterization of fecal microbial community for obesity and leanness was carried out. The result of study concluded with sharing of an identifiable core set and pathways in human microbiome and it was observed that person with changes in microbiota at the phylum level having obesity problem. Metagenomic analysis study was also performed, and its study revealed that microbial biomarkers of obesity take part in lipid, amino acid, and carbohydrate metabolism. A recent metatranscriptomic analysis determined the distribution of functional roles of human fecal microbiota. This study demonstrated the distribution of Clusters of Orthologous Groups (COGs) categories across each of the 10 metatranscriptomes (A, B, C, D, E, F, K, L, N, and O) that were sequenced. The following are activities related to human health in which gut microbiota plays an important role: energy production and conservation, amino acid transport and metabolism, nucleotide transport and metabolism, carbohydrate transport and metabolism, transcription, cell mobility, defense mechanism, signal transduction mechanism, etc. Luminal conversion by intestinal microbes may play an important role in host-microbiota interactions. Orally consumed nutrients may be converted by intestinal microbes into bioactive compounds that could affect the health of the host and the intestinal microbiota (GABA, gamma-aminobutyric acid; SCFAs, short-chain fatty acids). Probiotics may manipulate intestinal microbial communities and suppress growth of pathogens by inducing the host's production of β-defensin and IgA. Probiotics may be able to fortify the intestinal barrier by maintaining tight junctions and inducing mucin production. Probiotic-mediated immunomodulation may occur through mediation of cytokine secretion through

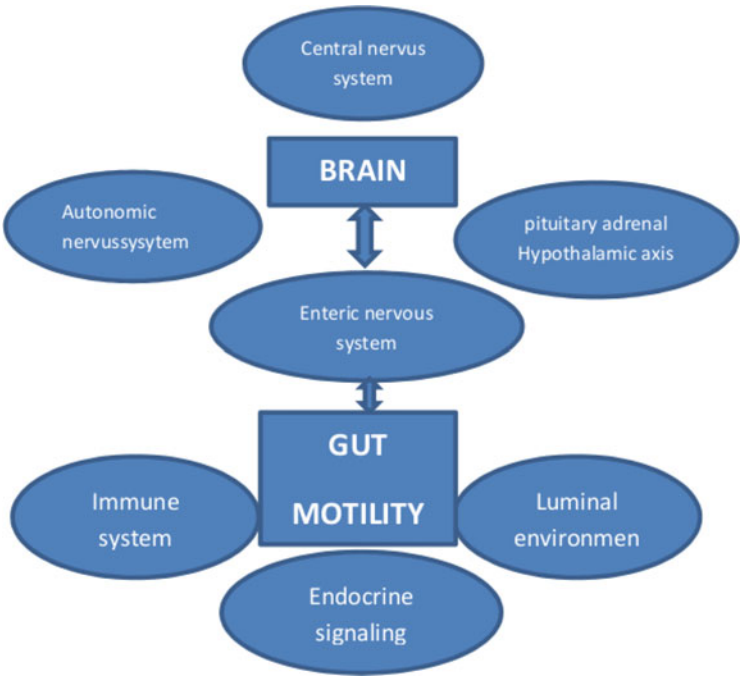


Fig. 21.2 Factors that control gut motility, the gut luminal environment

signaling pathways such as NFκB and MAPKs, which can also affect proliferation and differentiation of immune cells (such as T cells) or epithelial cells. Gut motility and nociception may be modulated through regulation of pain receptor expression and secretion of neurotransmitters (APRIL, a proliferation-inducing ligand; HSP, heat shock protein; IEC, intestinal epithelial cell; Ig, immunoglobulin; MAPK, mitogen-activated protein kinase; NFκB, nuclear factor-kappaB; pIgR, polymeric immunoglobulin receptor; STAT, signal transducer and activator of transcription; Treg, T regulatory cell) (Fig. 21.2).

21.4 Probiotics as Nutritional Aid for Human

In the twentieth century, Elie Metchnikoff proposed the concept of probiotics, which means "for life." According to him, as we get older, essential microbes in our gut decrease, and this can be prevented by taking beneficial bacteria orally, and our health can be improved (Metchnikoff 1908). Every person wants good health and happy life and good food quality; in accordance to this, there has been increasing demand in requirement of probiotics as nutritional aid in the past few years. The increasing demand of probiotics is seen along with food and meals (Markova and Sheveleva 2014). Foodstuff consists of beneficial bacterial culture which is added

during the manufacturing process. Most of these products are manufactured in the form of frozen powder (Saarela et al. 2000). Most of the time, production of acetic acid as secondary metabolites during production of *Bifidobacterium* results in change in taste during fermentation and storage. It is necessary to get assured that foodstuff not get adversely affected due to culture inoculation. After preparation of probiotics, packing material used in it and its storage condition are the two main crucial steps. Until now, with positive result, more than 500 promising probiotic food supplements are in the market. Most of the probiotic foods include fermented cereals, fruits, vegetables, and meat foodstuff that are gaining popularity among consumers. The most successful examples are cheese and dips, mayonnaise, edible spreads, ice cream, milk, juices, oat, etc. (Ranadheera et al. 2017).

21.5 Probiotics in Constipation and Gastric Motility

Constipation is the most common problem seen in persons in our community which is mostly result in problem of gastric motility. While studying the effects of probiotics on humans as well as animals, there have been promising and positive results seen. Only problem of uncertainty related to mode of action of probiotics on gut motility and constipation. The immune system, nervous system function, bile acid mechanism, and mucus secretion are vital factors to gut motility, and imbalance or dysfunction related to these factors results in gut motility. The use of certain probiotic strains can help in modifying the gut luminal environment and provide a benefit for patients with constipation and motility (Dimidi et al. 2017). The central nervous system, the immune system, and the enteric nervous system are some of the factors that affect gut motility, and disturbance in these factors results in constipation (Tables 21.1 and 21.2).

21.6 Implications of Probiotics on the Maternal-Neonatal Interface: Gut Microbiota, Immunomodulation, and Autoimmunity

Treatment of autoimmune disease is also done with probiotics; it is possible by rebalancing dysbiosis inducing changes in the immune system. Autoimmune disease can also occur during pregnancy, and it is concerned with both mother and child. In literature, probiotics have obtained a lot of significance same with marketing. Microbiota significantly get changed in the mother's GIT, and it can be balanced with the help of probiotics, but interaction between probiotics changes during the period of pregnancy, and normal condition is not clearly observed. There is existing evidence that gut microbiota in the mother's GIT influences the offspring's microbiota and directly affects the health of neonates. Microbiota are directly gets

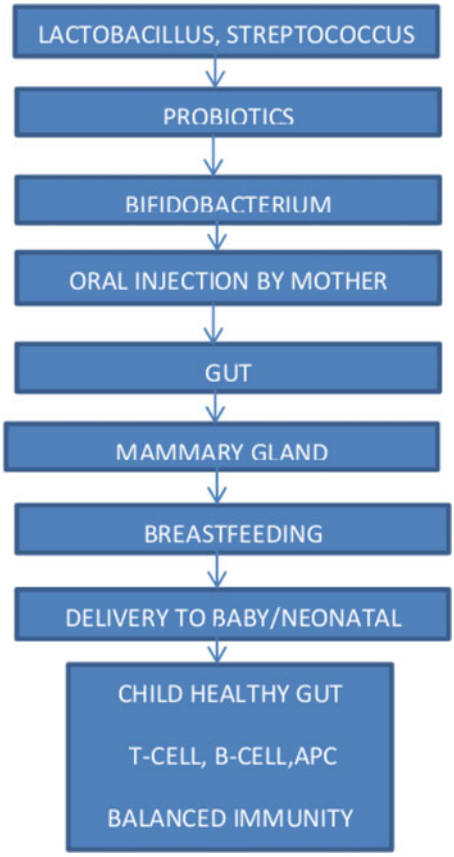
Table 21.1 Recommendations for use of probiotics in childhood intestinal diseases

Diseases	Probiotics	Treatment/ prevention	References
Helicobacter pylori infection	*L. casei* DN-114001	Treatment	Cameron et al. (2017)
Inflammatory bowel disease	VSL#32	Treatment	Cameron et al. (2017)
Infantile colic	*L. reuteri* DSM 17938	Treatment	Cameron et al. (2017)
Functional intestinal disorders (IBS)	*L. rhamnosus* GG *L. reuteri* DSM 17938	Treatment	Cameron et al. (2017)
Traveler's diarrhea	*S. boulardii*	Prevention	Cameron et al. (2017)
Nosocomial diarrhea	*L. rhamnosus* GG *B. lactis* Bb12+ *S. thermophilus*	Prevention	Cameron et al. (2017)
Acute gastroenteritis	*S. boulardii*, *L. rhamnosus GG*, Indian Dahi	Treatment	Cameron et al. (2017)
Clostridium difficile-associated diarrhea	*S. boulardii*	Prevention	Cameron et al. (2017)
Antibiotic-associated diarrhea	*S. boulardii*; *L. rhamnosus* GG, *B. lactis* Bb12 + *S. thermophilus*, *L. rhamnosus* strains E/N, Oxy and Pen	Prevention	Cameron et al. (2017)

influence on the immune system. Dysbiosis directly results in immune dysregulation and autoimmunity. Probiotics are considered safe during pregnancy (Brianna Swartwout et al. 2018).

Table 21.2 List of probiotic strains and their potential effects

Probiotic strain	Features	Potential effect	References
Wheat bran	Arabinoxylan oligosaccharides	Increases *Bifidobacterium* levels relative to total fecal microbiota and reduces colonic protein fermentation	Kleessen et al. (2007)
Yacon root	Fructooligosaccharides (FOS) and inulin	Improves the growth of *Bifidobacterium* in the colon, enhances mineral absorption and gastrointestinal metabolism, and plays a role in the regulation of serum cholesterol	Kim et al. (2009)
Chicory root	Inulin	Potential substrate for gut bacteria, helps in increasing bile production	Barszcz et al. (2016)
Dandelion greens	Inulin	Diuretic, antioxidant, and cholesterol-lowering effects	Samal et al. (2012)
Jerusalem artichoke	Inulin, high in thiamine and potassium	Potential substrate for gut bacteria and promotes proper muscle function	Ning et al. (2018)
Garlic	Inulin and fructooligosaccharides (FOS)	Increases the growth of *Bifidobacterium* and reduces the growth of disease-promoting bacteria	Kolida et al. (2002)
Oats	Beta-glucan	Reduces serum cholesterol and LDL cholesterol	Delaney et al. (2004)
Apples	Pectin	Increases the population of butyrate- and beta-glucuronidase-producing Clostridiales	Delaney et al. (2004)



Flow chat for beneficial effect of probiotics for mother and offspring

21.7 Probiotics for Animals' Gut Health

For proper absorption and digestion of dietary nutrients, the gut should remain always healthy, which helps inefficiency of animals. Presence of balance microbiota that is healthy micro-ecosystem will definitely result in healthy gut. When probiotics administered to animals in adequate amounts will result in conformation of healthy gut. Animals eat a lot of things, so probiotics can result into reduction of diarrhea-like condition and act as antitoxin. There is lots of literature survey and research have been done in conditions of animals where antibiotics are also ban for some treatments where these probiotics can play an active role. Lots of research has been done and going on related to safety issue of probiotics and there has been positive result coming out (Huang et al. 2019) (Table 21.3).

Table 21.3 List of microorganisms used as probiotics for animals

Genus	Species	References
Aspergillus	*A. oryzae*; *A. niger*	Yirga (2015), Bajagai et al. (2016)
Bacillus	*B. licheniformis* *B. megaterium* *B. mesentericus*	Yirga (2015), Bajagai et al. (2016)
Streptococcus	*S. intermedius* *S. salivarius* subsp. *thermophilus*	Pollmann et al. (1980), Azizpour et al. (2009)
Lactococcus	*L. lactis*	Azizpour et al. (2009)
Saccharomyces	*S. boulardii* *S. cerevisiae*	Bajagai et al. (2016)
Prevotella	*P. bryantii*	Bajagai et al. (2016)
Lactobacillus	*L. acidophilus* *L. amylovorus*	Yirga (2015), Bajagai et al. (2016)

21.8 Safety of Probiotics

Does it overstimulate the host immune system, does it cause sensitization of human sensitive areas, has it any association with infection, does it harbor transferable antibiotic gene, does it produce emesis after administration, and can it be identified at the strain level are some of the questions which arise during safety concern of probiotics.

21.9 Modulation of Brain Function via the Gut-Brain Axis

Via the gut-brain axis, probiotics show their action, and it involves multiple routes. Blood circulation, immune system, and humoral pathway are involved in brain functions and influence was observed between stress person and normal person (Okada et al. 2010). Probiotics play an important role in maintaining homeostasis of the neuroendocrine and immune system by preventing disturbance of gut microbiota. It was found in one study that medical student who was under stress used to administer *Lactobacillus casei* to get suppress stress-related problems. Daily intake of *Lactobacillus gasseri* CP2305 has ability to reduce stress-related problems (Nishida et al. 1859). Stress, sociability, cognitive function, anxiety, depression, and autism are some of the problems which are associated due to shifts in gut microbiota diversity. Most of the time, age factor also can be considered in the unbalance of gut microbiota. Diet is also the most considered factor in gut microbiota. SCFAs are neuroactive metabolites of microbiota which constitute flow of information (Oleskin and Shenderov 2019). Brain-Derived Neurotropic Factor (BDNF) is maintained by butyrate which levels and neurogenesis in the hippocampus and improves behavior by reducing depression where bacterium known as *Clostridium butyricum* MIYAIRI 588 has been active role in butyrate production (Kim et al. 2009). In addition,

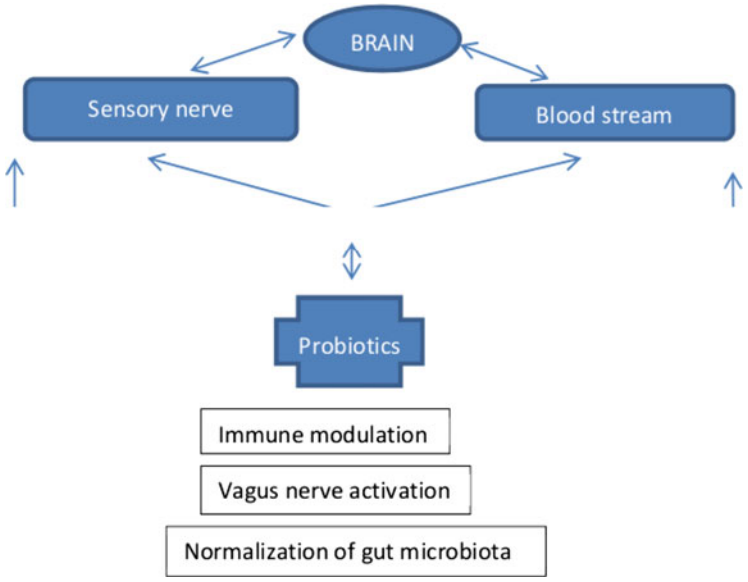


Fig. 21.3 Modulation of brain function via the gut-brain axis

mucosal barrier plays an important role in signaling pathway of microbiota-gut-brain interactions (Fig. 21.3).

21.10 The Feature Ahead of Probiotics, Ecobiotics

It is observed that decrease of infection in developing nations and increasing risk of allergic reaction and autoimmune diseases seen in developing countries (Liao and Nyachoti 2017). Most of the time, main reason for decrease in number of microbial content due to administration of broad spectrum an antibiotic, encountering of pathogen *Clostridium difficile* occurs. This pathogen colonizes in the large intestine. It results in diarrhea to life-threatening complications such as pseudomembranous colitis (PMC), toxic megacolon, and colonic perforation (Bartlett et al. 1978). In the USA, most healthcare associated problem is infection of *C. difficile* treated with antibiotics such as vancomycin, metronidazole, and fidaxomicin. There is alternative treatment comes in occurrence known as fecal microbiota transplantation (FMT) has risen in prominence during the recent past (Van Nood et al. 2013). Techniques are very efficient but there was always risk when we transfer unknown pathogen, it needs to insert healthy microbiota in the gut. Recently, developers are trying to develop an alternative method for FMT known as ecobiotics. Ecobiotics involve therapeutic dose formulations delivered orally based on gut ecology. And the clinical efficiency of this concept has also been seen. Seres Health plans (SER) also grant permission for trials ecobiotics alternative for FMT in *C. difficile* infection. Many of

the microbe-related therapies can be used in the treatment of diseases related to the gut (Khanna et al. 2016).

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