

Review Article

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Probiotics, Prebiotics, Synbiotics and its Health Benefits

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ABSTRACT

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Functional foods have become a part of an everyday diet and are demonstrated to offer potential health benefits beyond the widely accepted nutritional effects. Currently, the most important and frequently used functional food compounds are probiotics and prebiotics, or they are collectively known as ‘synbiotics’. Most commonly used probiotic strains are: *Bifidobacterium*, *Lactobacilli*, *S. boulardii*, *B. coagulans*. Prebiotics like Fructooligosacchaides (FOS), galacto-oligosaccharides (GOS), xyloseoligosaccharide (XOS), Inulin; fructans are the most commonly used fibers which when used together with probiotics are termed synbiotics and are able to improve the viability of the probiotics.

Introduction

Probiotics are defined as ‘live microorganisms which when administered in adequate amount confer health benefits to the host’ (FAO/WHO, 2002). Alternatively, probiotics have been defined as live microbial feed supplements that beneficially affect the host animal by improving its intestinal microbial balance (Fuller, 1989). Probiotics were originally used to improve the health of both animals and humans through the modulation of the intestinal microbiota. At present, several well-characterized strains of *Lactobacilli* and *Bifidobacteria* are available for human use to reduce the risk of

gastrointestinal (GI) infections or treat such infections (Salminen *et al.*, 2005). Some of the beneficial effects of probiotic consumption include improvement of intestinal health by the regulation of microbiota, and stimulation and development of the immune system, synthesizing and enhancing the bioavailability of nutrients, reducing symptoms of lactose intolerance, and reducing the risk of certain other diseases (Fig. 1–3) (Kumar *et al.*, 2009a, Kumar *et al.*, 2009b, Kumar *et al.*, 2010, Kumar *et al.*, 2011a, Kumar *et al.*, 2011b; Nagpal *et al.*, 2007, Nagpal *et al.*, 2010, Nagpal *et al.*, 2011; Yadav *et al.*, 2007a, Yadav *et al.*, 2007b, Yadav *et al.*, 2008). The primary clinical

interest in the application of probiotics has been in the prevention of and treatment for GI infections and diseases (Parvez *et al.*, 2006). Gut microbiota deviations have been associated with enhanced risk of specific diseases; therefore, modulation of an unbalanced indigenous microbiota forms the rationale of probiotic therapy (Turnbaugh *et al.*, 2006).

Also, the development of adjuvant or alternative therapies based on bacterial replacement is becoming important owing to the rapid emergence of antibiotic-resistant pathogenic strains and the adverse consequences of antibiotic therapies on the protective flora, which enhances the risk of infection (Forestier *et al.*, 2001).

However, the use of probiotics should be further investigated for their benefits and possible side effects, if any. As the knowledge about intestinal microbiota, nutrition, immunity, and genetics in health and disease has increased in the past years, such information could certainly help to develop new probiotic strains with disease-specific functions and could also facilitate the understanding of when to use probiotics and how they affect specific pathological states. However, it is important that the probiotic strains for human use should undergo animal studies followed by human clinical trials in order to authenticate the suitability, safety, and benefits of probiotics for human consumption and development of functional foods.

Functional foods

Functional foods are fortified or enriched during processing and then marketed as providing some benefit to consumers. Sometimes, additional complementary nutrients are added, such as Vitamin D to milk. Functional foods are “Ordinary food

that has components or ingredients added to give it a specific medical or physiological benefit, other than a purely nutritional effect”. All functional foods must meet three established requirements: Foods should be

Present in their naturally occurring form, rather than a capsule, tablet, or powder

Consumed in the diet as often as daily

Should regulate a biological process in hopes of preventing or controlling disease.

Functional foods as immune function

Immune function throughout life can be influenced by nutrition. Possible ingredients for the development of functional foods that could contribute to optimal immune response include the antioxidant vitamins, trace elements (e.g. zinc, copper and manganese), n-3 and n-6 PUFAs, l-arginine, nucleotides and nucleosides, probiotics, prebiotics and synbiotics.

Functional foods as gastrointestinal health

The GI tract is an obvious target for the development of functional foods because it acts as an interface between the diet and all other metabolic functions.

GI function depends on an appropriate balance of healthy bacteria to prevent the invasion of harmful bacteria. One of the most promising areas for the development of functional foods lies in the use of ingredients to modify the composition and metabolic activity of the gut microflora:

Probiotics;

Prebiotics;

Synbiotics (mixtures of probiotics and prebiotics).

Classification of functional foods

Functional foods are classified in to

Probiotic
Prebiotic
Synbiotic

Probiotic

Probiotic is a greek word which means "for life" and it is generally used to name the bacteria associated with the beneficial effects for the humans and animals. Live microorganisms that, when administered in adequate amounts, confer a health benefit on the host. Probiotics are living microorganisms which upon ingestion in sufficient numbers exert health benefits beyond basic nutrition. Probiotics are a viable microbial dietary supplement which uplifts the health of the host.

Probiotics are living microorganisms which include *Lactobacillus* species, *Bifidobacterium* species and yeasts. When ingested in certain amounts these have a positive impact on human health, by improvement of the balance of the intestinal microflora (MacFarlane and Cummings, 1999; Morelli *et al.*, 2003; Schrezenmeir and de Vrese, 2001). In fact, one of the oldest methods used to produce and preserve food was fermentation carried out by microorganisms, and cultured dairy products and soured milks were often used therapeutically. Recent controlled scientific investigation supports these traditional views, suggesting that probiotics are a valuable part of a healthy diet.

In the stomach, food is mixed with gastric juices, containing digestive enzymes and hydrochloric acid, producing the chyme. This goes to the small intestine, where more enzymes and bile are joined, to complete the

breakdown of dietary proteins, fats and sugars. Most nutrients are absorbed in the small intestine and the rest passes into the large intestine, or colon, where water and electrolytes are absorbed and fecal matter is expelled through the rectum. The gastrointestinal tract is a complex ecosystem, with a delicate balance between the intestinal microflora and the host. In the large intestine, microbes complete the digestion of any food components that were not digested in the small intestine, such as lactose in lactose intolerant people or some fibers resistant to the enzymes in the small intestine.

The intestinal microflora is important for the maturation of the immune system, the development of normal intestinal morphology and the maintenance of a balanced inflammatory response. On the other hand, the microflora reinforces the barrier function of the intestinal mucosa, thus preventing the attachment of pathogenic microorganisms and the entry of allergens. Moreover, some microorganisms may positively contribute to the body's requirements for certain vitamins.

The different probiotics include: *Bifidobacterium*, *Lactobacillus* (or lactic acid bacteria – LAB), *Lactococcus*, *Saccharomyces*, *Streptococcus thermophilus* and *Enterococcus*. Most of the presently available probiotics are bacteria, however, *Saccharomyces boulardii* is an example of a probiotic yeast.

Regarding the effects of probiotics on human health, it is important to recognize that different strains, species and genera of bacteria may have different effects, and therefore, the health benefits claimed for a certain probiotic may be dependent on the specific conditions tested. However, many studies claim that certain strains consumed at adequate levels positively influence human health, namely concerning diarrhea (van Niel

et al., 2002; Weizman *et al.*, 2005), antibiotics (Cremonini *et al.*, 2002; Johnston *et al.*, 2006), irritable bowel syndrome (Kajander *et al.*, 2005; Quigley and Flourie, 2007), inflammatory bowel disease (Ghosh *et al.*, 2004; Penner and Fedorak, 2005), lactose intolerance (de Vrese *et al.*, 2001; Pelletier *et al.*, 2001), hypertension (Parvez *et al.*, 2006; Sydoruk *et al.*, 2005), hepatic encephalopathy (de Santis *et al.*, 2000; Solga, 2003), cancer (Brown and Valiere, 2004; Donaldson, 2004; Parvez *et al.*, 2006), immune system (Brown and Valiere, 2004; Galdeano and Perdigon, 2006), vaginal infections (Brown and Valiere, 2004; Reid *et al.*, 2004), *Helicobacter pylori* (Nam *et al.*, 2002; Sgouras *et al.*, 2004), kidney stones (Azcarate-Peril *et al.*, 2006; Federici *et al.*, 2004), cholesterol (Liong and Shah, 2005; Pereira *et al.*, 2003), allergies and eczema (Isolauri *et al.*, 2000; Pohjavuori *et al.*, 2004).

Probiotic foods for improved gastrointestinal health

Probiotics are the well-known means to target the GI microbes with proven disease preventing/curing attributes. Viable probiotic bacteria such as *Lactobacilli* and *Bifidobacteria* can survive in sufficient numbers to assist the GI tract to become metabolically active. Their therapeutic effects have been confirmed in clinical trials and they have been utilized effectively in formulation of certain functional and nutritional foods. Probiotics primarily targets immune system through exerting anti-microbial activity, enhancing the proliferation of immune-defense cells, regulating certain metabolic enzymes and inhibiting the degenerative processes. The exact mechanisms related to beneficial effects of probiotics vary with target group and microorganisms. The food products which assist in improving the GI health are also termed as “colonic foods” and include probiotics, prebiotics and synbiotics.

Advantages of probiotic foods

- Produce lactic acid- lowers the pH of intestines and inhibiting bacterial villains such as Clostridium, Salmonella, Shigella, E. coli, etc.
- Decreases the production of a variety of toxic or carcinogenic metabolites.
- Aid absorption of minerals, especially calcium, due to increased intestinal acidity.
- Production of β -D galactosidase enzymes that break down lactose.
- Produce a wide range of antimicrobial substances acidophilin and bacitracin etc. help to control pathogenic bacteria.
- Produce vitamins (especially Vitamin B and vitamin k
- Act as barriers to prevent harmful bacteria from colonizing the intestines Cont.

Potential health benefits of probiotics include

- Reduced incidence or severity of GI infections;
- Alleviation of lactose intolerance;
- Overall improvement in gut function, including reduction in constipation as well as diarrhoea.

Probiotics display numerous health benefits beyond providing basic nutritional value. Probiotics have been used in fermented food products for centuries. However, nowadays it has been claimed that probiotics can serve a dual function by their potentially importing health benefits. The health benefit of fermented foods may be further enhanced by supplementation of *Lactobacillus* and *Bifidobacterium* species (Shah, 2000). *L. acidophilus*, *Bifidobacterium* spp. and *L. casei* species are the most used probiotic cultures with established human health in dairy products, whereas the yeast *Saccharomyces cerevisiae* and some *E. coli*

and *Bacillus* species are also used as probiotics.

There is increasing evidence in favour of the claims of beneficial effects attributed to probiotics, including improvement of intestinal health, enhancement of the immune response, reduction of serum cholesterol, and cancer prevention. Several studies have documented probiotic effects on a variety of gastrointestinal and extra intestinal disorders, including prevention and alleviation symptoms of traveler's diarrhea and antibiotic associated diarrhea, inflammatory bowel disease (Marteau *et al.*, 2002), lactose intolerance (de Vrese *et al.*, 2001), protection against intestinal infections (Reid *et al.*, 2001), and irritable bowel syndrome. Some probiotics have also been investigated in relation to reducing prevalence of atopic eczema later in life (Gueimonde *et al.*, 2006), vaginal infections, and immune enhancement (Isolauri *et al.*, 2001), contributing to the inactivation of pathogens in the gut, rheumatoid arthritis, improving the immune response of in healthy elderly people (Ibrahim *et al.*, 2010), and liver cirrhosis.

In addition, probiotics are intended to assist the body's naturally occurring gut microbiota. Some probiotic preparations have been used to prevent diarrhea caused by antibiotics, or as part of the treatment for antibiotic-related dysbiosis. Although there is some clinical evidence for the role of probiotics in lowering cholesterol but the results are conflicting.

Probiotics have a promising inhibitory effect on oral pathogens especially in childhood but this may not necessarily lead to improved oral health (Twetman and Steckslen-Blicks, 2008). Antigenotoxicity, antimutagenicity and anticarcinogenicity are important potential functional properties of probiotics, which have been reported recently. Observational data suggest that consumption of fermented

dairy products is associated with a lower prevalence of colon cancer, which is suggested that probiotics are capable of decreasing the risk of cancer by inhibition of carcinogens and pro-carcinogens, inhibition of bacteria capable of converting procarcinogens to carcinogens (Vasiljevic and Shah, 2008).

Allergy prevention and recovery

Experimental evidence indicates that probiotics are effective in treating atopic eczema in infants. It has also been shown that the incidence of allergies in infants with a high risk of allergy can be halved with the consumption of certain probiotics by their mothers when pregnant and by the infant after birth. It is thought that consumption of probiotics helps to form a normally functioning immune system, preventing allergies (Ouwehand, 2007).

Treatment of peptic ulcers

Helicobacter pylori are a pathogenic bacterium that causes peptic ulcers and other gastric problems. *Helicobacter pylori* are normally treated with antibiotics. This treatment is expensive and has negative side effects. The consumption of probiotics with antibiotics is thought to be the most effective and safest treatment (Lesbros-Pantoflickova *et al.*, 2007).

Diarrhea

Evidence indicates that probiotic bacteria in foods can help prevent and treat diarrhea in children. Rotavirus infections are a common cause of diarrhea in children. In clinical trials, infected children who consumed probiotic fermented milk had lower rates of diarrhea. Probiotic treatments have also been used to effectively treat antibiotic associated diarrhea (Agrawal, 2005)

Blood pressure regulation

Milk is fermented by bacteria and the protein in the milk is hydrolyzed into smaller peptides. The peptides are absorbed in the small intestine. Consumption of these peptides in milk and yogurt has been shown in clinical studies to lower blood pressure in some individuals (Jauhiainen and Korpela, 2007).

Regularity

The consumption of probiotics reduces the transit time for the movement of wastes through the intestines. This results in reduced constipation and may help prevent colon cancer. Prebiotics also decrease transit time through the intestines because they are a form of fiber (Dempsters, 2007).

Reduction of infection

Probiotics and prebiotics have been shown to reduce infections in sick and postoperative patients. Because the use of antibiotics reduces the population of intestinal bacteria, using probiotics and prebiotics to repopulate the digestive tract, ensures the presence of a healthy n of good bacteria to prevent infection (Agrawal, 2005).

Lactose digestion

Individuals with lactose intolerance are missing important digestive enzyme, lactase. Probiotic bacteria make the lactase enzyme and consumption of these bacteria can help lactose digestion (Stanton *et al.*, 2001).

Immune function

Consumption of probiotics can enhance natural immune functions (Agrawal, 2005).

Cancer prevention

Probiotics have been shown, *in vitro* and in animal studies, to prevent cancer by reducing

DNA damage by carcinogens (Stanton *et al.*, 2001).

Lowering cholesterol

A range of LAB able to break down bile in the gut, thus inhibiting its reabsorption (which enters the blood as cholesterol).

Prebiotics

A prebiotic is a non-digestible component which beneficially affects the host by selectively stimulating the growth and/or activity of one or a limited number of colonic bacteria, thereby improving the health of the host. The term prebiotic is applied to non digestible food ingredients that may have a positive impact by the improvement of the intestinal flora. Prebiotics are mostly oligosaccharides, which stimulate selectively the growth of bifidobacteria, being therefore referred to as bifidogenic factors. These include: fructooligosaccharides, inulins, isomalto-oligosaccharides, lactilol, lactosucrose, lactulose, pyrodextrins, soy oligosaccharides, transgalactooligosaccharides and xylo-oligosaccharides. The positive effects of prebiotics include antimicrobial, anticarcinogenic, hypo-lipidemic, glucosemodulatory and anti-osteoporotic activities. They may be used for the treatment of constipation, hepatic encephalopathy and inflammatory bowel disease. They can protect against some intestinal pathogens and may exert favorable lipid effects as well as have some benefit in diabetes mellitus. Besides, prebiotics also have a very important role in improving mineral absorption and balance, for instance, they may enhance the colonic absorption of some minerals.

Prebiotics, non-digestible food components that can stimulate growth and/or modify the metabolic activity of specific bacterial species already present in the gut, might also improve

gut health. They are also being evaluated for beneficial effects on the immune system and the potential to reduce risk of colon cancer. Their ability to increase production of short chain fatty acids in the colon is associated with increased absorption of minerals such as calcium and magnesium. Examples: inulin, garlic, onions, chicory root, Asparagus, whole wheat, rye, barley.

Commonly known prebiotics are:

Oligofructose

Inulin

Galacto-oligosaccharides

Lactulose

Breast milk oligosaccharides

Lactulose is a synthetic disaccharide used as a drug for the treatment of constipation and hepatic encephalopathy. The prebiotic oligofructose is found naturally in many foods, such as wheat, onions, bananas, honey, garlic, and leeks. Oligofructose can also be isolated from chicory root or synthesized enzymatically from sucrose. Fermentation of oligofructose in the colon results in a large number of physiologic effects, including:

Increasing the numbers of bifidobacteria in the colon

Increasing calcium absorption

Increasing fecal weight

Shortening gastrointestinal transit time

Possibly, lowering blood lipid levels

The increase in colonic bifidobacteria has been assumed to benefit human health by producing compounds to inhibit potential pathogens, by reducing blood ammonia levels, and by producing vitamins and digestive enzymes.

Functions of prebiotics

Prebiotics reach the colon without being digested because of their chemical nature. A

part of the material is not digested by pancreatic and small-bowel enzymes in the human gut and therefore, reaches the large bowel. The whole length of human gut is occupied by microorganisms with population numbers and species distribution characteristics of specific region of guts (Macfarlane and Macfarlane, 1997). In the gut the relatively more stable colonies are in large intestines than smaller intestines because the transit time in small intestines is faster (4-6 h) than large intestines (48-70 h) in adults (Macfarlane and Gibson, 1994). The pH and relatively low absorptive state of colon further supports large microbial colonisation and growth (O'Sullivan, 1996). Due to this microflora, the colon has the ability to undertake complex hydrolytic digestive functions (Cummings and Macfarlane, 1991). This involves breakdown of dietary components, complex carbohydrates and some proteins that are not hydrolysed or absorbed in the upper digestion tract. The colonic microflora derives their food from the undigested food e.g., nondigestible oligosaccharides, dietary fibre, and undigested protein. They also get their substrates from the mucin: the main glycoprotein constituent of the mucus. Therefore, any undigested food that reaches the colon e.g., nondigested carbohydrates, some peptides and proteins, certain lipids is a source of prebiotics (Mussatto and Mancilha, 2007). Prebiotics have been suggested of having various health benefits on humans. It acts as a substrate for the useful gut microorganisms.

Synbiotics

The term synbiotic is used for products that contain both probiotics and prebiotics, and which take advantage of the addition of beneficial bacteria as well as the encouragement of beneficial bacterial growth. The best synbiotic combinations currently available include bifidobacteria and fructo-

oligosaccharides (FOS), *Lactobacillus* GG and inulins, and bifidobacteria and lactobacilli with FOS or inulins.

When Gibson introduced the concept of prebiotics he speculated as to the additional benefits if prebiotics were combined with probiotics to form what he termed as Synbiotics (DeVrese and Schrezenmeir, 2008). A synbiotic product beneficially affects the host in improving the survival and implantation of live microbial dietary supplements in the gastrointestinal tract by selectively stimulating the growth and/or activating the metabolism of one or a limited number of healthpromoting bacteria. Because the word “synbiotics” alludes to synergism, this term should be reserved for products in

which the prebiotic compound(s) selectively favor the probiotic organism(s) (Cencic and Chingwaru 2010). Synbiotics were developed to overcome possible survival difficulties for probiotics. It appears that the rationale to use synbiotics, is based on observations showing the improvement of survival of the probiotic bacteria during the passage through the upper intestinal tract. A more efficient implantation in the colon as well as a stimulating effect of the growth of probiotics and ubiquitous bacteria contribute to maintain the intestinal homeostasis and a healthy body (Peña 2007). Several factors like pH, H₂O₂, organic acids, oxygen, moisture stress etc. have been claimed to affect the viability of probiotics especially in dairy products like yogurts (Romeo *et al.*, 2010) (Table 1 and 2).

Table.1 Probiotic microorganisms

Lactobacillus species	Bifidobacterium species	Others
<i>L. acidophilus</i>	<i>B. adolescentis</i>	<i>Bacillus cereus</i>
<i>L. amylovorus</i>	<i>B. animalis</i>	<i>Clostridium botyricum</i>
<i>L. brevis</i>	<i>B. breve</i>	<i>Enterococcus faecalis</i> ^a
<i>L. casei</i>	<i>B. bifidum</i>	<i>Enterococcus faecium</i> ^a
<i>L. rhamnosus</i>	<i>B. infantis</i>	<i>Escherichia coli</i>
<i>L. crispatus</i>	<i>B. lactis</i>	<i>Lactococcus lactis subsp. cremoriss</i>
<i>L. delbrueckii subsp. Bulgaricus</i>	<i>B. longum</i>	<i>Lactococcus lactis subsp. Lactis</i>
<i>L. fermentum</i>		<i>Leuconostoc mesenteroides subsp. Dextranicum</i>
<i>L. gasseri</i>		<i>Pediococcus acidilactici</i>
<i>L. helveticus</i>		<i>Propionibacterium freudenreichii</i> ^a
<i>L. johnsonii</i>		<i>Saccharomyces boulardii</i>
<i>L. lactis</i>		<i>Streptococcus salivarius subsp. Thermophiles</i>
<i>L. paracasei</i>		<i>Sporolactobacillus inulinus</i> ^a
<i>L. plantarum</i>		
<i>L. reuteri</i>		
<i>L. salivarius</i>		
<i>L. gallinarum</i> ^a		

^a mainly applied in animals

Table.2 Probiotic foods

Probiotic foods	Prebiotic foods	Vegan sources
Yogurt (plain, no added sugar, active cultures) buttermilk acidophilus milk Kefir Tempeh Kimchi Sauerkraut Kombucha Pickles Miso Dark chocolate Sourdough bread cheese (aged) cottage cheese fermented meats fermented vegetables fermented grains kombucha kvass lassi natto raw vinegars sour cream	Garlic Onions Leeks Asparagus Bananas Barley Oats Apples Flaxseeds Wheat Bran Artichokes Berries Black beans Cherries Dandelion greens Chicory root Chickpeas Eggplant Endive Honey Legumes Lentils Mangoes Oatmeal Peas Pears Quinoa Tomatoes White beans Whole grains	Coconut water kefir Live cultured nondairy yogurt (coconut, soy) Pickled or fermented fruits and vegetables Kombucha tea Tempeh

Fig.1 Functions of probiotics

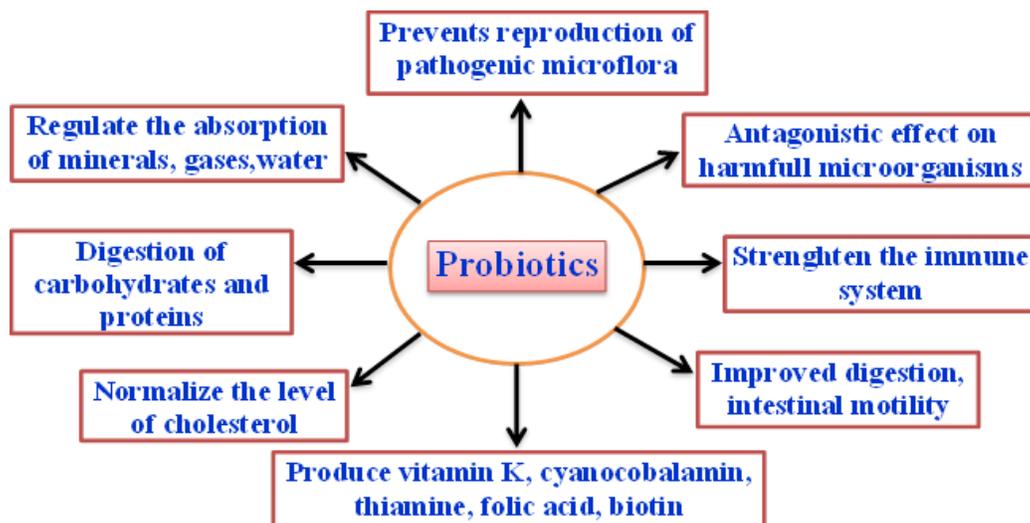


Fig.2 Health attributes of probiotics

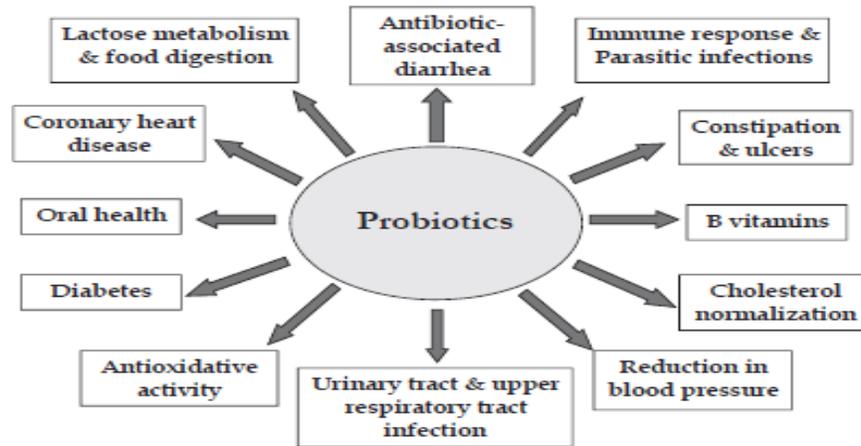
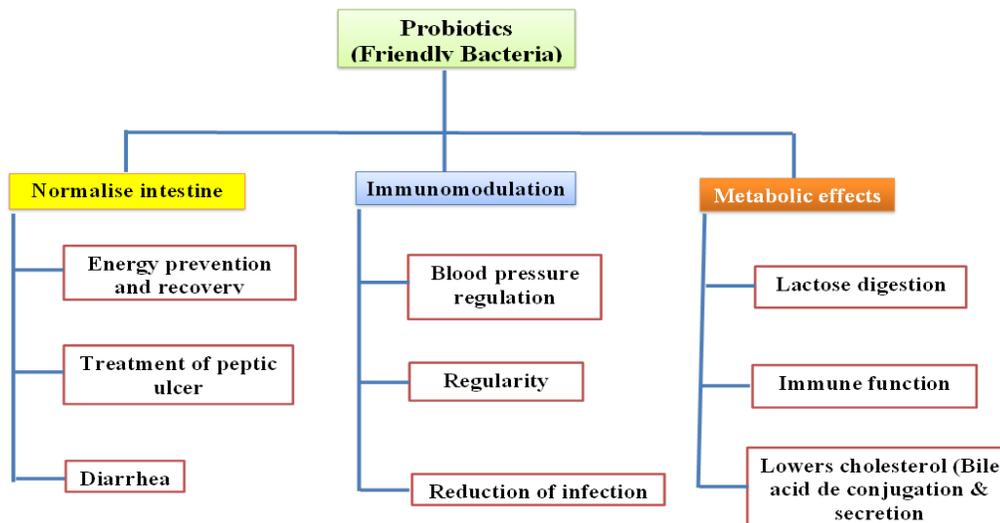


Fig.3 Health benefits of probiotics



The probiotic strains used in synbiotic formulations include *Lactobacilli*, *Bifidobacteria spp*, *S. boulardii*, *B. coagulans* etc., while the major prebiotics used comprise of oligosaccharides like fructooligosaccharide (FOS), GOS and xyloseoligosaccharide (XOS), inulin, prebiotics from natural sources like chicory and yacon roots, etc. The health benefits claimed by synbiotics consumption by humans include: 1) Increased levels of lactobacilli and bifidobacteria and balanced gut microbiota, 2) Improvement of liver function in cirrhotic patients, 3) Improvement

of immunomodulating ability, 4) Prevention of bacterial translocation and reduced incidences of nosocomial infections in surgical patients, etc. (Zhang *et al.*, 2010).

Health benefits of probiotics, probiotics and synbiotics

The most important and documented beneficial effects of probiotics include the prevention of diarrhea, constipation, changes in bile salt conjugation, enhancement of antibacterial activity, anti-inflammatory.

Furthermore, they also contribute to the synthesis of nutrients and improve their bioavailability; some probiotics are known to exert anti-oxidative activity in the form of intact cells or lysates. Probiotics have also demonstrated their inherent effects in alleviating symptoms of allergy, cancer, AIDS, respiratory and urinary tract infections. There are stray reports on their beneficial effects on aging, fatigue, autism, osteoporosis, obesity and type 2 diabetes (Harish and Varghese 2006).

Probiotics beneficial effects

Production of inhibitory substances like H₂O₂, bacteriocins, organic acids, etc.,
Blocking of adhesion sites for pathogenic bacteria.
Competition with the pathogenic bacteria for nutrients,
Degradation of toxins as well as the blocking of toxin receptors,
Modulation of immune responses.

In conclusions this review probiotics, prebiotics and synbiotics have been discussed with respect to the systemic effects they exert on the host's health, metabolism and immune system. Probiotics, prebiotics and synbiotics have systemic effects on the host's health metabolism and immune system. Utilization of prebiotics by probiotics should be a pre-requisite for symbiotic selection, in order to maintain a good synergy between the two and maximize the beneficial effects. Probiotics can turn many health benefits to the human, animals, and plants. Applications of probiotics hold many challenges. Probiotics have shown remarkable health benefits to human in a way that their utilization may reduce the use of antibiotics for treatment of diseases such as traveler's diarrhea reducing the risks of antibiotics resistance and other health problems related to microbiota imbalances. Lastly, it is an urging need to

establish international standards to regulate probiotics and prebiotics products and functional health claim on the label to ensure product effectiveness and safety.

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