Study Material for M.Sc. in Human Physiology of 2nd. Semester

Presented by Dilip K Nandi, Ph.D.

PREBIOTICS AND PROBIOTICS

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29.2.1 Introduction

The health benefits imparted by probiotics and prebiotics as well as synbiotics have been the subject of extensive research in the past few decades. These food supplements termed as functional foods have been demonstrated to alter, modify and reinstate the pre-existing intestinal flora. They also facilitate smooth functions of the intestinal environment. Most commonly used probiotic strains are: Bifidobacterium, Lactobacilli, S.boulardii, B. coagulans. Prebiotics like FOS, GOS, XOS, Inulin; fructans are the most commonly used fibers which when used together with probiotics are termed synbiotics and are ableto improve the viability of the probiotics. Now, we shall learn in details about of the prebiotics and probiotics.

Objectives

After going through this SML, you will be able to understand of the following contents:

Able to basic idea's about prebiotics and probiotics.

Able to understand about the characteristics and classification of prebiotics and Probiotics.

Able to know about the different potential probiotics.

How to utilise the prebiotics and probiotics in our body system?

Capable of exerting a beneficial effect on the prebiotics and probiotics.

To know about the details on different health preventive and promotive functions of prebiotics and probiotics.

29.2.2 Definition of Prebiotics

The prebiotics concept was introduced for the first time in 1995 by Glenn Gibson and Marcel Roberfroid. Prebiotic was described as "a non-digestible food ingredient that beneficially affects the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon, and thus improves host health". This definition was almost unchanged for more than 15 years. According to this definition, only a few compounds of the carbohydrate group, such as short and long chain _-fructans [FOS and inulin], lactulose, and GOS, can be classified as prebiotics.

In 2008, the 6th Meeting of the International Scientific Association of Probiotics and Prebiotics (ISAPP) defined "dietary prebiotics" as "a selectively fermented ingredient that results in specific changes in the composition and/or activity of the gastrointestinal microbiota, thus conferring benefit(s) upon host health".

29.2.3 Characteristics and classification of Prebiotics

The following criteria are used to classify a compound as a prebiotic: (i) it should be resistant toacidic pH of stomach, cannot be hydrolyzed by mammalian enzymes, and also should not be absorbed in the gastrointestinal tract, (ii) it can be fermented by intestinal microbiota, and (iii) the growth and/or activity of the intestinal bacteria can be selectively stimulated by this compound and this process improves host's health.

Although not all the prebiotics are carbohydrates, the following two criteria can be exploited to distinguish fiber from carbohydrate-derived prebiotics: (i) fibers are carbohydrates with a degree of polymerization (DP) equal or higher than 3 and (ii) endogenous enzymes in the small intestine cannot hydrolyze them. It should be taken into account that the fiber solubility or fermentability is not crucial.

There are many types of prebiotics. The majority of them is a subset of carbohydrate groups and is mostly oligosaccharide carbohydrates (OSCs). The relevant articles are mainly on OSCs, but there are also some pieces of evidence proving that prebiotics are not only carbohydrates.

Fructans

This category consists of inulin and fructo-oligosaccharide or oligofructose. Their structure is a linear chain of fructose with _(2!1) linkage. They usually have terminal glucose units with _(2!1) linkage. Inulin has DP of up to 60, while the DP of FOS is less than 10.

Previously, some studies implicated that fructans can stimulate lactic acid bacteria selectively. However, over recent years, there are some investigations showing that the chain length of fructans is an important criterion to determine which bacteria can ferment them. Therefore, other bacterial species can also be promoted directly or indirectly by fructans.

Galacto-Oligosaccharides

Galacto-oligosaccharides (GOS), the product of lactose extension, are classified into two subgroups:

(i) the GOS with excess galactose at C3, C4 or C6 and (ii) the GOS manufactured from lactose through enzymatic trans-glycosylation. The end product of this reaction is mainly a mixture of tri- to pentasaccharides with galactose in _(1!6), _(1!3), and _(1!4) linkages. This type of GOS is also termed as trans-galacto-oligosaccharides or TOS. GOSs can greatly stimulate Bifidobacteria and Lactobacilli. Bifidobacteria in infants have shown high incorporation with GOS. Enterobacteria, Bacteroidetes, and Firmicutes are also stimulated by GOS, but to a lesser extent than Bifidobacteria. There are some GOSs derived from lactulose, the isomer of lactose. This lactulose-derived GOSs are also considered as prebiotics. Besides these types of GOS, the other types are based on sucrose extension named raffinose family oligosaccharides (RFO). The effect of RFO on gut microbiota has not been elucidated yet.

Starch and Glucose-Derived Oligosaccharides

There is a kind of starch that is resistant to the upper gut digestion known as resistant starch (RS). RS can promote health by producing a high level of butyrate; so it has been suggested to be classified as a prebiotic. Various groups of Firmicutes show the highest incorporation with a high amount of RS. An in vitro study demonstrated that RS could also be degraded by Ruminococcus bromii, and Bifidobacterium adolescentis, and also to a lesser extent by Eubacterium rectale and Bacteroides thetaiotaomicron. However, in the mixed bacterial and fecal incubations, RS degradation is impossible in the absence of R. bromii. Polydextrose is a glucose-derived oligosaccharide. It consists of glucan with a lot of branches and glycosidic linkages. There is some evidence that it can stimulate Bifidobacteria, but it has not been confirmed yet.

Other Oligosaccharides

Some oligosaccharides are originated from a polysaccharide known as pectin. This type of oligosaccharide is called pectic oligosaccharide (POS). They are based on the extension of galacturonic acid (homogalacturonan) or rhamnose (rhamnogalacturonan I). The carboxyl groups may be substituted with methyl esterification, and the structure can be acetylated at C2 or C3. Various types of sugars (e.g., arabinose, galactose, and xylose) or ferulic acid are linked to the side chains. Their structures vary significantly depending on the sources of POSs.

Non-Carbohydrate Oligosaccharides

Although carbohydrates are more likely to meet the criteria of prebiotics definition, there are some compounds that are not classified as carbohydrates but are recommended to be classified as prebiotics, such as cocoa-derived flavanols. In vivo and in vitro experiments demonstrate that flavanols can stimulate lactic acid bacteria.

29.2.4 Production of Prebiotics

Prebiotics play an important role in human health. They naturally exist in different dietary food products, including asparagus, sugar beet, garlic, chicory, onion, Jerusalem artichoke, wheat, honey, banana, barley, tomato, rye, soybean, human's and cow's milk, peas, beans, etc., and recently, seaweeds and microalgae. Because of their low concentration in foods, they are manufactured on industrial large scales. Some of the prebiotics are produced by using lactose, sucrose, and starch as raw material. Since most prebiotics are classified as GOS and FOS regarding industrial scale.

Mechanism of Action of Prebiotics

The gut microbiota community presents an extensive genetic potential involved in many metabolicfunctions, whose modulation may improve the health of the host. This modulation can be achieved through the use of prebiotics, which are short-chain carbohydrates with a degree of polymerization ofbetween two and about sixty and are non-digestible by human or animal digestive enzymes. Since prebiotics are not the only substances with an ability to alter the intestinal environment, the capacity of selective utilization differentiates prebiotics from other undigested dietary ingredients and compounds, such as antibiotics, minerals, and vitamins.

The presence of prebiotics in the diet usually found in fruits and vegetables may lead to numerous health benefits. Among the advantages of those prebiotics, the reduction of the blood-density lipoprotein level, the stimulation of the immunological system, the increased absorbability of calcium, the maintenance of correct intestinal pH value, and the low caloric value, among others, are worth mentioning.

Recent studies have suggested that mechanisms through which prebiotics confer benefits to the host (Figure 2) are mediated by microbial metabolic products, noting SCFAs, the promotion of ion and trace element absorption, such as that of calcium, iron, and magnesium, and the regulation of the immune system, increasing IgA production and modulating cytokine production.

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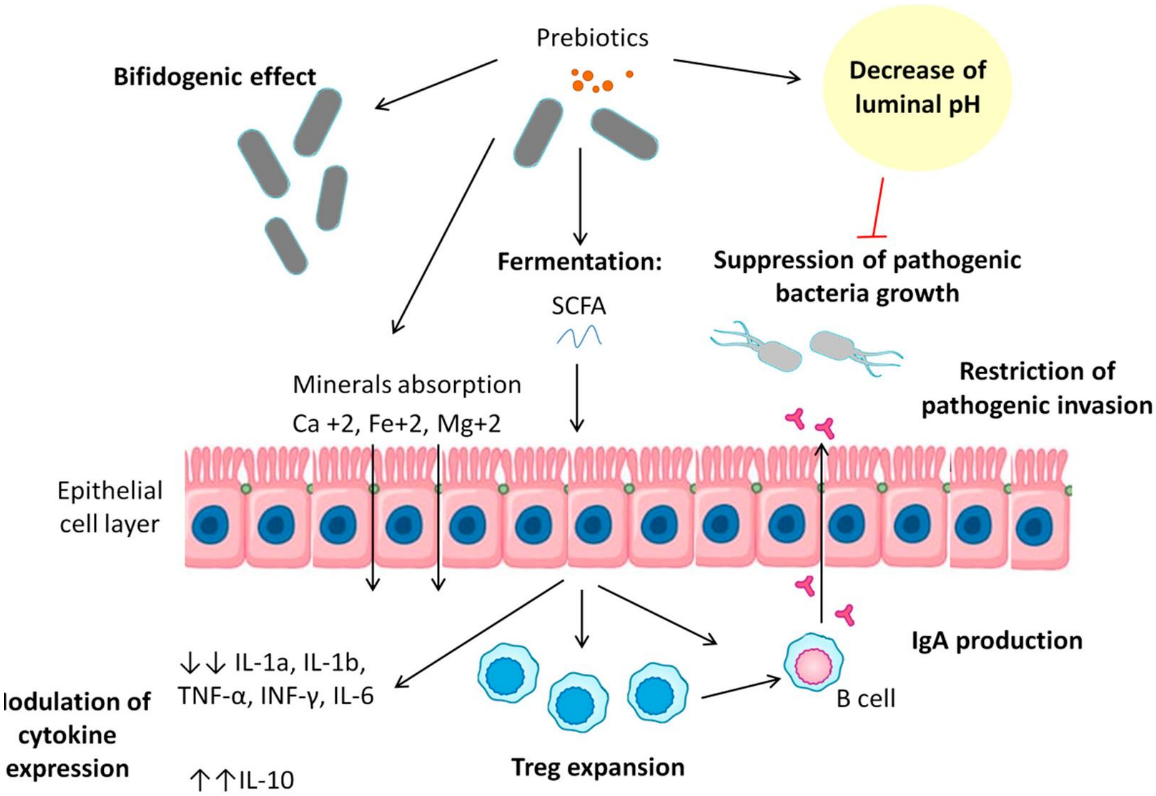


Figure-1: Mechanism of prebiotic action. These mechanisms include the production of microbial metabolic products, noting short-chain fatty acids (SCFAs), the promotion of ion and trace element absorption (such as that of calcium, iron, and magnesium), a decrease in luminal pH, and the regulation of the immune system (increasing IgA production and modulating cytokine production).

29.2.5 Health Benefits of Prebiotics

Prebiotics exert a remarkable influence on human health, which makes them alluring attractive agents to improve the quality of human life against cancer, vascular diseases, obesity, and mental disorders. There are many studies on the positive effects of prebiotics on human health; however, accurately designed long-term clinical trials and genomics investigations are needed to confirm the health claims. By determining the fundamental mechanisms of prebiotics, scientists would be able to formulate enhanced food supplements to ameliorate human health. The ability to normalize the composition of the gut microbiota by prebiotic dietary substances is an appealing procedure in the control and healing of some foremost disorders.

Irritable Bowel Syndrome and Crohn's Disease

There are a few studies about the effects of prebiotics on irritable bowel syndrome (IBS) and Crohn's disease. IBS is a gastrointestinal syndrome characterized by chronic abdominal pain and altered bowel habits in the absence of any organic cause. Crohn's disease is a type of chronic, relapsing inflammatory bowel disease (IBD), which can involve any part of the gastrointestinal tract from the mouth to the anus. It has been reported that in both IBS and Crohn's disease, the Bifidobacteria and Faecalibacterium prausnitzii population along with Bacteroides to Firmicutes ratio were decreased.

Colorectal Cancer

Colorectal cancer, ranked as the third most common malignancy worldwide, is a multi-step disease from genetic mutation to adenomatous polyps, which then leads to invasive and metastatic cancer. It has been demonstrated that prebiotics fermentation products, such as butyrate, could have protective effects against the risk of colorectal cancer, as well as its progression, via inducing apoptosis. In addition, a clinical trial demonstrated that symbiotic therapy (Lactobacillus rhamnosus and Bifidobacterium Lactis plus inulin) could reduce the risk of colorectal cancer by reducing the proliferation rate in colorectal, inducing colonic cells necrosis, which leads to improving the integrity and function of epithelial barrier.

Necrotizing Enterocolitis

Necrotizing enterocolitis (NEC) is a gastrointestinal emergency condition primarily in premature neonates, in which portions of the bowel undergo necrosis. It can lead to high morbidity and mortality rates. Since prebiotics, such as FOS and GOS, can stimulate the growth of gut microbiota (e.g., Bifidobacteria) and reduce the pathogenic bacteria in preterm infants. Moreover, SCFAs can improve feeding tolerance by enhancing both gastric emptying and bowel motility.

Prebiotics and the Immune System

Consuming prebiotics can improve immunity functions by increasing the population of protective microorganisms. Animal and human studies have shown that prebiotics can decrease the population of harmful bacteria by Lactobacilli and Bifidobacteria. For example, mannose can reduce colonization of pathogens by promoting mannose adhesion to Salmonella. Mannose binds to Salmonella via type 1 fimbriae (finger-like projections)q1. In addition, pathogens are not able to bind to the epithelium in the presence of OSCs. Prebiotics can also induce the expression of immunity molecules, especially cytokines. Interestingly, maternal prebiotics metabolites are able to cross the placenta and can affect the development of the fetal immune system. In 2010, Fugiwara et al. reported that FOS administration in a pregnant mouse model modified offspring microbiota, and consequently, their skin inflammation was attenuated. In contrast, Shadid et al. in a placebo-controlled, randomized, and double-blinded study demonstrated that bifidogenic effects of prebiotics supplementation in humans could not be transferred to the next generation. The details of well-known prebiotic effects on the immune systems are discussed below:

Oligofructose and inulin mixture: The mixture of oligofructans and inulin can improve antibody responses toward viral vaccines, such as influenza and measles.

FOS: Studies have shown the improvement of antibody response to influenza vaccine following FOS consumption. Moreover, the side effects of the influenza vaccine are reduced. Diarrhea-associated fever in infants is also reduced by this category of prebiotics. Apart from these, it can decrease the use of antibiotics, duration of disease, and the incidence of febrile seizures in infants fructans can up-regulate the level of interleukin 4 (IL-4) in serum, CD282+/TLR2+ myeloid dendritic cells, and a toll-like receptor 2-mediated immune response in healthy volunteers. In contrast, another study demonstrated that the salivary immunoglobulin A (IgA), immune cells in serum, and activation and proliferation of T cells and natural killer (NK) cells were not changed after consuming. It has been noted that FOS reduces the risk of some immune diseases in infants, such as atopic dermatitis. This type of prebiotic decreases the expression of IL-6 and phagocytosis inmonocytes and granulocytes.

GOS: Studies reported that GOS increased the blood level of interleukin 8 (IL-8), interleukin 10 (IL-10), and C-reactive protein in adults, but decreased IL-1.NK cells improves by consuming GOS. In infants, GOS reduces the risk of atopic dermatitis and eczema.

AOS (acidic oligosaccharides): The possibility of atopic dermatitis is reduced by AOS in low-risk infants.

Prebiotics and the Nervous System

The gastrointestinal tract is connected to the central nervous system through the “gut-brain axis”. For instance, administration of prebiotics in piglets decreases the gray matter in order to improve neural pruning. Gut microbiota affects the brain through three routes, including neural, endocrine, and immune pathways as given below.

I- Neural Pathway: The products of prebiotics fermentation can affect the brain by the vagus nerve [146]. Some prebiotics, such as FOS and GOS, have regulatory effects on brain-derived neurotrophic factors, neurotransmitters (e.g., d-serine), and synaptic proteins (e.g., synaptophysin and N-methyl-D-aspartate or NMDA receptor subunits).

II- Endocrine Pathway: Hypothalamic-pituitary-adrenal axis is a neuroendocrine pathway. The microbiome growth in mice can induce corticosterone and adrenocorticotropic hormone in an appropriate way. In addition, prebiotics act as a regulator of other hormones, such as plasma peptide YY.

III- Immune Pathway: As discussed before, prebiotics can affect different aspects of the immune system. Beside neurological functions, prebiotics are also capable of influencing mood, memory, learning, and some psychiatry disorders by changing the activity and/or composition of gut microbiota.

IV- Mood: Stress hormones are able to affect anxiety-related behaviors. It was demonstrated that the level of stress hormones (adrenocorticotropic hormone (ACTH) and corticosterone) increased in germ-free mice following exposure to controlled stress. After administrating Bifidobacterium infantis, corticosterone and ACTH reached normal levels.

Prebiotics and Skin

As mentioned in the previous sections, the consumption of prebiotics was shown to decrease the risk of development, as well as the severity of allergic skin diseases, such as atopic dermatitis. Upon metabolizing aromatic amino acids by gut microbes, some compounds, such as phenols, may be produced. These compounds are transferred into the skin. Phenols, such as p-cresol, may be toxic for patients with underlying kidney diseases. In women, consumption of GOS with or without probiotics, such as Bifidobacterium breve, can abolish the reduction of water and keratin caused by phenols.

Prebiotics and Cardiovascular System

According to the statistics, 30% of the deaths in the United States in 2013 were caused by cardiovascular diseases (CVD). The main reason for this growing trend is the alteration of people's lifestyles and eating habits. Therefore, many researchers have studied the influence of fibers and prebiotics consumption on CVD. However, the direct beneficial functions of prebiotics in this regard have not been demonstrated yet. In this section, we summarized some of the indirect effects of prebiotics on CVD. Prebiotics are able to lower the risk of CVD by reducing the inflammatory elements. Several investigations demonstrated an improvement in the lipid profile by consuming prebiotics. Russo et al. demonstrated that the consumption of inulin-enriched pasta with a formulation of 86% semolina, 11% inulin, and 3% durum wheat vital gluten decreased both TAG and lipogenesis in healthy individuals, rather than cholesterol level. In contrast, Frochen and Beylot reported that the consumption of 10 g/day inulin-type fructans for six months had no significant effects on lipogenesis in the liver of healthy subjects.

29.2.6 Definition of Probiotics

The term Probiotics is derived from a Greek word meaning "for life" and used to define living non-pathogenic organisms and their derived beneficial effects on hosts. The term Probiotics was first introduced by Vergin, when he was studying the detrimental effects of antibiotics and other microbial substances, on the gut microbial population. He observed that probiotika was favourable to the gut microflora. Probiotic were then redefined by Lilly and Stillwell as "A product produced by one microorganism stimulating the growth of another microorganism. Subsequently the term was further defined as Non-pathogenic microorganisms which when ingested, exert a positive influence on host's health or physiology by Fuller. The latest definition put forward by FDA and WHO jointly are live microorganisms when administered in adequate amounts confer a health benefit on the host. The guidelines make it necessary to perform the following activities:

1. Strain identification.

2. Functional characterization of the strain(s) for safety and probiotic attributes.

3. Validation of health benefits in human studies.

4. Honest, not misleading labeling of efficacy claims and content for the entire shelf life.

29.2.7 Characteristics and classification of Probiotics

Should not be hydrolyzed or absorbed in the upper part of G.I tract.

Should be a selective substrate for one or a limited number of potentially bacterial commercial to the colon culture protagonist.

Should be able to alter the colonic microflora towards a healthier composition or selectively stimulates the growth and or activity of intestinal bacteria associated with health and well being.

Should help increase the absorption of certain minerals such as calcium and magnesium.

Favourable effect on the immune system and provide improved resistance against infection.

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 bacteriocin 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

Probiotic Food Products

The range of food products containing probiotic strains is wide and still growing. The main products existing in the market are dairy-based ones including fermented milks, cheese, ice cream, buttermilk, milk powder, and yogurts, the latter accounting for the largest share of sales. Nondairy food applications include soy based products, nutrition bars, cereals, and a variety of juices as appropriate means of probiotic delivery to the consumer.

Types of Probiotics

Probiotics may contain a variety of microorganisms. The most common are bacteria that belong to groups called *Lactobacillus* and *Bifidobacterium*. Other bacteria may also be used as probiotics, and so may yeasts such as *Saccharomyces boulardii*.

Taking into consideration their definition the number of microbial species which may exert probiotic properties is impressive. Some of the most important representatives are listed below.

Microorganisms considered as probiotics

***Lactobacillus* species**

L. acidophilus
L. casei
L. crispatus
*L. g*allinarum
L. gasseri
L. johnsonii
L. paracasei
L. plantarum
L. reuteri
L. rhamnosus

***Bifidobacterium* species**

B. adolescentis
B. animalis
B. breve
B. lactis
B. longum
B. bifidum
B. infantis

Other lactic acid bacteria

Enterococcus aecium
Streptococcus thermophilus
Lactococcus lactis

Nonlactic acid bacteria

Escherichia coli strain nissle
Saccharomyces cerevisiae
S. boulardii

As far as nutrition is concerned only the strains classified as lactic acid bacteria are of significance and among them the ones with the most important properties in an applied context are those belonging to the genera Lactococcus and Bifidobacterium. Lactic acid bacteria are Gram-positive, catalase-negative bacterial species able to produce lactic acid as main end-product of carbohydrate fermentation.Two other species playing an important role in the food industry, particularly dairy products, although not strictly considered as probiotics are Streptococcus thermophilus and Lactococcus lactis, two of the most commercially important lactic acid bacteria.

29.2.8 Properties of Probiotics

In order for a potential probiotic strain to be able to exert its beneficial effects, it is expected to exhibit certain desirable properties. The ones currently determined by in vitro tests are

(i) acid and bile tolerance which seems to be crucial for oral administration,

(ii) adhesion to mucosal and epithelial surfaces, an important property for successful immune modulation, competitive exclusion of pathogens, as well as prevention of pathogen adhesion and colonisation,

(iii) antimicrobial activity against pathogenic bacteria,

(iv) bile salt hydrolase activity.

Nevertheless, the value of these parameters is still under debate as there are matters of relevance, in vivo and in vitro discrepancies, and lack of standardization of operating procedures to be considered. As there are no specific parameters essential to all probiotic applications, the best approach to establish a strain's properties is target population and target physiologic function specific studies. As far as the final product is concerned, the probiotic dose levels should be based on the ones found to be efficacious in human studies and the colony forming units per gram of product is an important parameter. Although the information about the minimum effective concentrations is still insufficient, it is generally accepted that probiotic products.

29.2.9 Mechanisms of Probiotic Activity

Probiotics have various mechanisms of action although the exact manner in which they exert their effects is still not fully elucidated. These range from bacteriocin and short chain fatty acid production, lowering of gut pH, and nutrient competition to stimulation of mucosal barrier function and immunomodulation. The latter in particular has been the subject of numerous studies and there is considerable evidence that probiotics influence several aspects of the acquired and innate immune response by inducing phagocytosis and IgA secretion, modifying T-cell responses, enhancing Th1 responses, and attenuating Th2 responses.

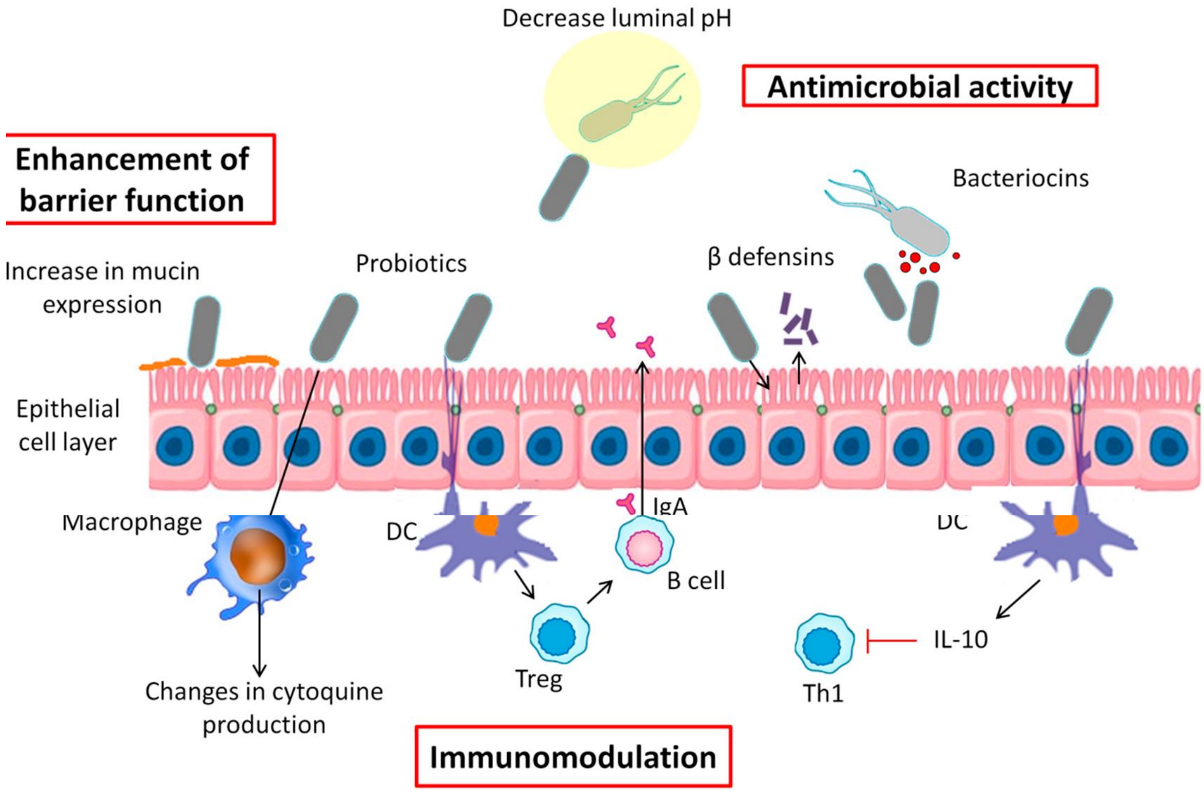


Figure-2: A schematic diagram about potential mechanisms whereby probiotic bacteria might perform within the intestine. These mechanisms include antagonistic effects on various microorganisms,competitive adherence to the mucosa and epithelium (antimicrobial activity), increased mucus production and enhanced barrier integrity (enhancement of barrier function), and modulation ofthe human immune system (immunomodulation).

29.2.10 Health Benefits of 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. These health properties are strain specific and are impacted by the various mechanisms mentioned above. While some of the health benefits are well documented others require additional studies in order to be established. In fact, there is substantial evidence to support probiotic use in the treatment of acute diarrhoeal diseases, prevention of antibiotic-associated diarrhoea, and improvement of lactose metabolism, but there is insufficient evidence to recommend them for use in other clinical conditions.

Antibiotic-Associated Diarrhoea

Mild or severe episodes of diarrhoea are common side effects of antibiotic therapy as the normal microflora tends to be suppressed, encouraging the overgrowth of opportunistic or pathogenic strains. The spectrum may range from diarrhea without mucosal abnormality to pseudomembranous colitis. The latter is a severe form of antibiotic-associated diarrhoea (caused by Clostridium difficile, cytotoxic strains of which may emerge after antibiotic use). The name of the condition is derived from the plaque-like adhesion of fibrinopurulent material to the damaged mucosal layer and it is characterized by diarrhoea, abdominal distention, vomiting, fever, and leukocytosis and if untreated might lead to complications such as toxic megacolon and perforation. Treatment with probiotics has been used in clinical practice with L. rhamnosus and S. boulardii being administered. Several studies that have been carried out suggest that probiotic use is associated with a reduced risk of antibiotic-associated diarrhoea. A recent meta-analysis evaluating the available evidence on probiotics for the prevention and treatment of antibiotic-associated diarrhoea concluded that probiotic administration- (namely, L. rhamnosus, L. casei, and the yeast S. boulardii, as these are the probiotics predominantly included in the majority of trials) is associated with a reduced risk of the condition.

Infectious Diarrhoea

Treatment and prevention of infectious diarrhoea are probably the most widely accepted health benefits of probiotic microorganisms. Rotavirus is the most common cause of acute infantile diarrhoea in the world and a significant cause of infant mortality. The virus replicates in the highly differentiated absorptive columnar cells of the small intestinal epithelium and the normal microflora seems to play an important role in the host response to the infection, as it has been shown that absorption of antigens is more enhanced in germ-free than in normal mice. Probiotic supplementation of infant formulas has been aimed both at the prevention of rotaviral infections and the treatment of established disease. Well-controlled clinical studies have shown that probiotics such as L. rhamnosus GG, L. reuteri, L. casei Shirota, and B. animalis Bb12 can shorten the duration of acute rotavirus diarrhoea with the strongest evidence pointing to the effectiveness of L. rhamnosus GG and B. animalis Bb12.The proposed mechanisms include competitive blockage of receptor site signals regulating secretory and motility defences, enhancement of the immune response, and production of substances that directly inactivate the viral particles. In addition to rotavirus infection there is evidence that certain food as well as nonfood probiotic strains can inhibit the growth and adhesion of a range of diarrhoeal syndromes. The benefit of probiotics such as L. reuteri, L. rhamnosus GG, L. casei, and S. boulardii in reducing the duration of acute diarrhoea in children has been demonstrated. For example, in a prospective, randomized, controlled French study conducted among children in day.

Lactose Intolerance

Lactose intolerance is a genetically determined beta-galactosidase deficiency resulting in the inability to hydrolyse lactose into the monosaccharides glucose and galactose. Upon reaching the large bowel the undigested lactose is degraded by bacterial enzymes leading to osmotic diarrhoea. Acquired, usually reversible, causes of beta-galactosidase deficiency include pelvic radiotherapy which damages the mucosa, as well as infection with rotavirus which infects lactase producing cells, and short bowel syndrome. Lactoseintolerant individuals develop diarrhoea, abdominal discomfort, and fatulence after consumption of milk or milk products. Although conventional yoghurt preparations, using S. thermophilus and L. delbrueckii ssp. Bulgaricus, are even more effective in this direction, partly because of higher betagalactosidase activity, improvement of lactose metabolism is a claimed health benefit attributed to probiotics and seems to involve certain strains more than others and in specific concentrations. Terefore and as certain individuals have responded positively to probiotic supplementation, clinicians should consider it as a therapeutic alternative.

Probiotics and Allergy

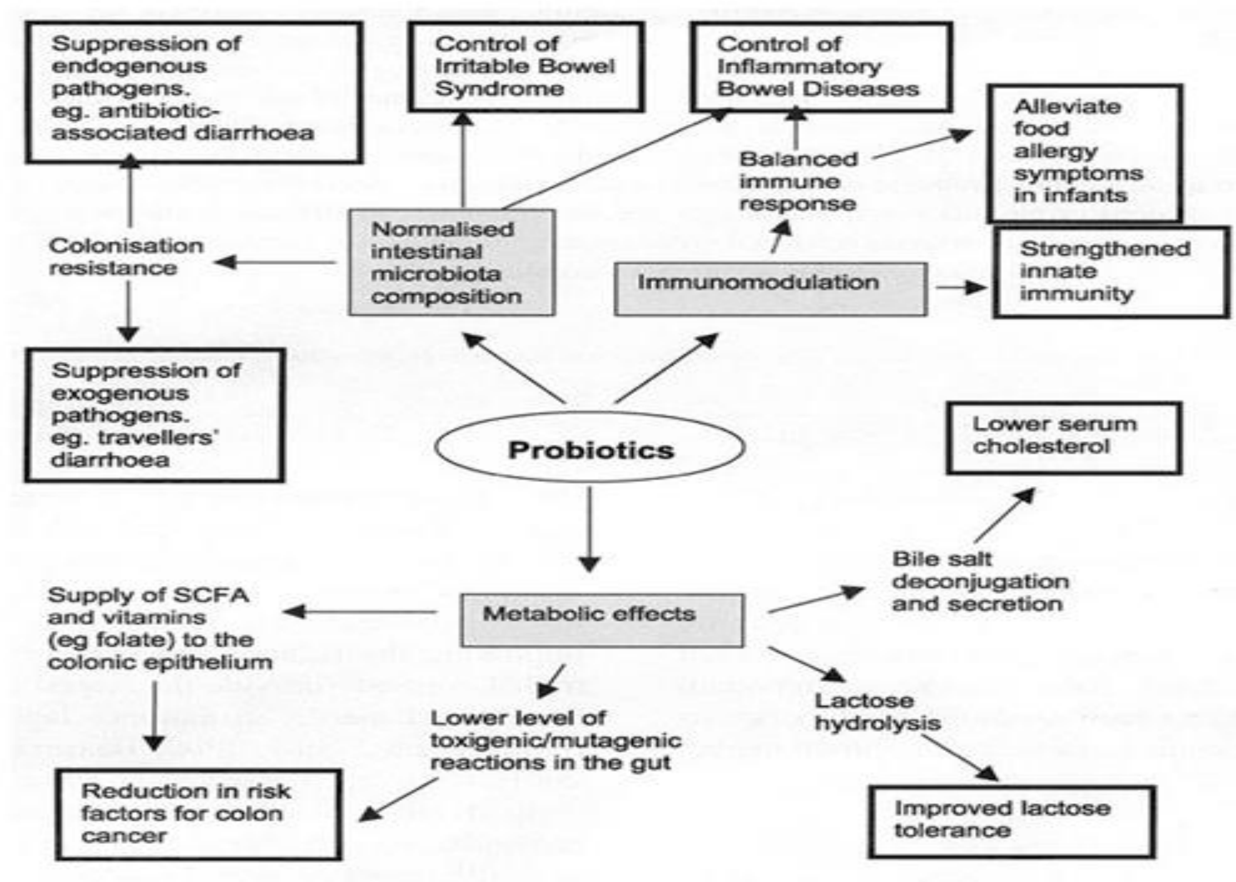
Recent evidence suggests that exposure to bacteria in early life may exhibit a protective role against allergy and in this context probiotics may provide safe alternative microbial stimulation needed for the developing immune system in infants. In the same time they improve mucosal barrier function, a property that is considered to contribute in moderating allergic response. The role of intestinal microbiota in allergy is supported by observations of their quantitative as well as qualitative differences among children and infants suffering from allergies and healthy ones, the former exhibiting colonization by a more adult-like type of microflora. These probiotic effects seem to particularly involve food allergy and atopic dermatitis. The latter is a common chronic relapsing skin disorder of infancy and childhood with hereditary predisposition being an important component of its pathogenesis together with the individual’s exposure to environmental allergens. A limited number of strains have been tested for their efficacy in the treatment and prevention of allergy in infants. In a recent study of breast fed infants suffering from atopic eczema B. lactis and L. rhamnosus GG were found to be effective in decreasing the eczema severity. Furthermore L. rhamnosus GG has been found successful in preventing the occurrence of atopic eczema in high risk infants, when supplied prenatally to selected mothers who had at least one first degree relative with atopic eczema, allergic rhinitis, or asthma.

Probiotics and Cardiovascular diseases

Mann and Spoerry were the first to suggest the possible effects of probiotic consumption on lipid metabolism. They reported the reduction of cholesterol lowering effects of fermented milks and lactic acid bacteria. L. bulgaricus, L. reuteri, B. coagulans are some of the probiotic strains with reported hypocholerolemic effects. Studies in humans with L. acidophilus L1 milk, demonstrated a significant reduction in serum cholesterol.The hypocholesterolemic effect by probiotics could be due to 1) Decrease in hydroxyl-methyl-glutaryl-Coenzyme-A reductase in liver 2) A significant conversion of cholesterol into bile acids. Furthermore, enzymatic deconjugation of bile acids is also possible by the enzyme of probiotics. 3) Cholesterol may be removed by probiotics by incorporation into the cellular membranes during growth. In vivo studies are needed to verify such claims which are based on in vitro studies.

Cancer and Probiotics

There is evidence that probiotic bacteria are dietary components that may play role in decreasing cancer incidence. The exact mechanisms are under investigation, but studies have demonstrated that certain members of *Lactobacillus* and *Bifidobacterium* spp. decrease the levels of carcinogenetic enzymes produced by colonic flora through normalization of intestinal permeability and microflora balance as well as production of antimutagenic organic acids and enhancement of the host’s immune system. L. acidophilus is known to prolong the induction of colon tumors.



Proposed health benefits stemming from probiotic consumption.

29.2.11 Summary

The health benefits imparted by probiotics and prebiotics have been the subject of extensive research in the past few decades. These food supplements termed as functional foods have been demonstrated to alter, modify and reinstate the pre-existing intestinal flora. They also facilitate smooth functions of the intestinal environment. Most commonly used probiotic strains are: Bifidobacterium, Lactobacilli, S.boulardii, B. coagulans. Prebiotics like FOS, GOS, 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. This SLM focuses on composition and roles of Probiotics and Prebiotics in human health. Furthermore, additional health benefits like immune-modulation, cancer prevention, inflammatory bowel disease etc. are also discussed.

29.2.12 Glossary

Probiotics: live microorganisms that, when administered in adequate amounts, confer a health benefit to the host.

Live Biotherapeutic Product (LBP): a biological product that contains live organisms; is applicable to the prevention, treatment or cure of a disease or condition of human beings; and is not a vaccine.

Next-Generation Probiotic (NGP): live microorganisms identified on the basis of comparative microbiota analyses that, when administered in adequate amounts, confer a health benefit on the host.

Prebiotic: a non-digestible compound that, through its metabolization by microorganisms in the gut, modulates composition and/or activity of the gut microbiota, thus conferring a beneficial physiological effect on the host.

Synbiotic/Symbiotic: mixtures of probiotics and prebiotics that beneficially affect the host by improving the survival and implantation of live microbial dietary supplements in the gastrointestinal tract, by selectively stimulating the growth and/or by activating the metabolism of one or a limited number of health-promoting bacteria, thus improving host welfare.

Pharmabiotics: bacterial cells of human origin, or their products, with a proven pharmacological role in health or disease.

Post-biotics: non-viable bacterial products or metabolic products from microorganisms that have biologic activity in the host.

Paraprobiotic/ghost probiotics/inactivated probiotics: non-viable microbial cells (intact or broken) or crude cell extracts which when administered (orally or topically) in adequate amounts, confer a benefit to the human or animal consumer.

Probioceuticals/probiotaceuticals: probiotic derived factors.

Biogenic: products made by or of life forms including secretions and metabolites.

Non-digestible oligosaccharides: oligomeric carbohydrates which are resistant to hydrolyzed by colonic bacteria.

29.2.13 Self Assessment Questions

1. "All prebiotics and probiotics are functional foods, but all functional foods are not prebiotics and probiotics"-Justify the statement.
2. Define symbiotic / symbiotic.
3. What is Lactose Intolerance?
4. Give examples of few probiotics and prebiotics Indian foods.
5. Enlist the characteristics of prebiotics and probiotics.
6. What is the possible mechanism by which probiotics act?
7. Describe the physiological three effects of prebiotics.
8. What are the Properties for potential of Probiotics?
9. What is Necrotizing Enterocolitis?

29.2.14 References

1. FAO/WHO, *Report on Joint FAO/WHO Expert Consultation on Evaluation of Health and Nutritional Properties of Probiotics in Food Including Powder Milk with Live Lactic Acid Bacteria*, 2001.

2. Watson RR, Preedy VR, Bioactive foods in promoting health: probiotics and prebiotics. Academic Press, 2010.

3. Webb GP Dietary supplements and functional foods. John Wiley and Sons, 2011.

4. Vasudha S and Mishra H N. (2013). Non dairy probiotic beverages. *International Food Research Journal* 20(1): 7–15.

5. Vyas U and Ranganathan N. (2012). Probiotics, prebiotics, and synbiotics: Gut and beyond. *Gastroenterology Research and Practice* 2012: 1–16.

6. Nutrition Science By B.Srilashmi

7.. Food Theory and Applications by B.E.Brooker.

8. Foods: Facts and Principles by Shakuntala and Shadaksharaswami

9. Essentials of Food and Nutrition by M.Swaminathan.

10. Food Micobiology and Biotechnology By B.D.Singh.