International Journal for Pharmaceutical Research Scholars (IJPRS)

V-2, I-4, 2013 ISSN No: 2277 - 7873

REVIEW ARTICLE

Understanding of Probiotics: A Review

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Manuscript No: IJPRS/V2/I4/00212, Received On: 24/11/2013, Accepted On: 30/11/2013

ABSTRACT

There is an increasing scientific and commercial interest in the use of beneficial microorganisms, or "probiotics," A probiotic is viable microbial dietary supplements that have been used for centuries because they beneficially affect the host through its effects in the intestinal tract. Similarly, prebiotics are non-digestible food ingredients that benefit the host by selectively stimulating the growth or activity of beneficial microorganisms that comprise part of the resident microbiota. Both probiotics and prebiotics are together called as synbiotics. Various bacterial genera most commonly used in probiotic preparations are Lactobacillus, Bifidobacterium, Escherichia, Enterococcus, Bacillus and Streptococcus. Some fungal strains belonging to Saccharomyces have also been used. This review focuses on the history, characteristics, mechanism of action, safety of probiotics and prebiotics. It subsequently describes the several beneficial properties of probiotic bacteria including prevention of intestinal infections, nutritional benefits, immunological effects, antibiotic associated diarrhea, prevention of hypercholesterolaemia, promote to digestion, active against pathogens, prevention of cancer, constipation, pancreatitis, allergies, pregnancy, urogenital infections and HIV, lactose intolerance, antioxidant effects, enhancement of mineral bioavailability, oral health and dental caries, halitosis, oral cavity, and other possible benefits.

KEYWORDS

Probiotics, Prebiotics, Beneficial properties, Antibiotic associated diarrhea, Immunological effects

INTRODUCTION

Probiotics are live microorganisms that when administered in adequate amounts confer a health benefit on the host and the term 'probiotic' was derived from the Greek word, meaning "for life".[1, 2] Probiotics are commonly isolated from human and animal intestinal tracts. However, dead bacteria, products derived from bacteria, or end products of bacterial growth also may impart certain benefits, but these derivatives are not considered to be probiotics because they are not alive when administered. Native bacteria are not probiotic until the bacteria are isolated, purified, and proved to have a health benefit when administered.[3] Probiotic bacteria should be safe for consumption, reach the intestines alive in large numbers, and impart specific health benefits to the host such as anti-mutagenic effects, anti-carcinogenic properties, improvement in lactose metabolism, reduction in serum cholesterol, and immune system stimulation. These bacteria should maintain the balance of the intestinal flora by altering favorably the gut environment in such a manner that the growths of friendly beneficial bacteria are promoted and harmful disease-causing

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organisms are inhibited. However, probiotics do not work the same in everyone. They may be more effective in older people than in younger ones since more mature bellies may have fewer good bacteria. There are also some evidences that genetic factors, that is, how much good and bad bacteria you have in your gut, can affect your reaction to the probiotics.[4, 5]

Because of the potential health benefits, probiotic organisms are increasingly being incorporated into a number of dairy foods. In addition, fermented functional foods with health benefits like Evolus® and Calpis®, have been introduced in the market, which are based on bioactive peptides released by probiotic organisms.[6] The emergence of antibiotic-resistant bacteria and natural ways of suppressing the growth of pathogens has contributed to the concept of 'probiotics'. Probiotic bacteria not only compete and suppress 'unhealthy fermentation' in human intestine, but also produce a number of beneficial health effects of their own.[7] Most commonly, Lactobacillus acidophilus, L. casei, Bifidobacterium bifidum, B. longum and the yeast Saccharomyces boulardii have been used as probiotics in humans.[8]

Recently, there is an increasing scientific and commercial interest in the use of beneficial microorganisms in the prevention and treatment of diseases. The use of microorganisms to restore or maintain health is the basis of probiotics which is one of the largest segments of the functional foods (FF) market. The global sales of probiotic supplements were predicted to rise 48% from $2.7bn in 2011 to $4bn in 2016.[9] Indeed, the market of probiotics and healthy food has great potential to grow, especially in Asia. However, the European market is now saturated, and growth of probiotic market is likely to occur mainly in non-dairy food areas and novel applications.[10]

History

The concept of probiotics evolved around 1900, when Nobel Prize-winning Elie Metchnikoff hypothesized that the long, healthy lives of Bulgarian peasants were the result of their consumption of fermented milk products and later he was convinced that yogurt contained the organisms necessary to protect the intestine from the damaging effects of other harmful bacteria.[11] At this time Henry Tissier, a French pediatrician, observed that children with diarrhea had in their stools a low number of bacteria characterized by a peculiar, Y shaped morphology while these "bifid" bacteria were, on the contrary, abundant in healthy children.[12] He suggested that these bacteria could be administered to patients with diarrhea help to restore a healthy gut flora. The works of Metchnikoff and Tissier were the first to make scientific suggestions about the probiotic use of bacteria, even if the word "probiotic" was not coined until 1960, to name substances produced by microorganisms which promoted the growth of other microorganisms.[13]

The application of ''health promoting'' bacteria for therapeutic purposes has a long tradition in medicine; however, this so-called ''bacteriotherapy'' has long been considered to be a non-standard procedure whose efficacy has not yet been proved or is at most based on observation but not on clinical studies.[14] The successful introduction of probiotics to the market has helped and inspired research in this area to a huge extent. In recent years, there has been a great increase in the number of clinical studies in which the prevention, alleviation, or therapy of diseases has been scientifically investigated not only to find evidence for a health claim for a target group of ''healthy consumers'' but also to test the medicinal (preventive and therapeutic) application of probiotics.[15]

Characteristics of Ideal Probiotics

Following are the features of a good probiotic.[16]

- It should be isolated from the same species as its intended host.
- It should be a strain, which is capable of exerting a beneficial effect on the host, e.g. increased growth or resistance to disease.
- It should be non- pathogenic and non-toxic.

Table 1: Microorganisms considered as probiotics

Lactobacillus	Bifidobacterium	Other lactic acid bacteria	Non-lactic acid bacteria
L. acidophilus	*B. adolescentis*	*Enterococcus faecalis*[1]	*Bacillus cereus* var. *toyoi*[1]
L. casei	*B. animalis*	*E. faecium*	*Escherichia coli* strain
L. crispatus	*B. bifidum*	*Lactococcus lactis*[3]	*Propionibacterium*
L. gallinarum[1]	*B. breve*	*Leuconostoc* mesenteroides	*Saccharomyces*
L. gasseri	*B. infantis*	*Pediococcus acidilactici*[3]	*S. boulardii*
L. johnsonii	*B. lactis*[2]	*Sporolactobacillus inulinus*[1]	
L. paracasei	*B. longum*	*Streptococcus thermophilus*[3]	
L. plantarum			
L. reuteri			
L. rhamnosus			

[1] Mainly used for animals.
[2] Recently reclassified as *B. animalis* subsp. *lactis*.[20]
[3] Little is known about probiotic properties.

- It should be present as viable cells, preferably in large numbers.
- It should be capable of surviving and metabolizing in the gut environment e.g. resistance to low pH, organic acids and bile.
- On storage, large number of viable bacteria must be able to survive prolonged periods.

The list of such microorganisms continues to grow and includes strains of Lactobacillus species, Bifidobacterium species, other lactic acid bacteria; Non-lactic acid bacteria are given in the Table 1.17.[19]

Mechanism of Action

The scientific evidence is based on a limited number of *in vivo* studies and deductions from well founded in vitro studies that have involved adults and children with intestinal disorders.[21] Strain information should be reported with each clinical and microbiological study because even closely related probiotic strains may have different clinical effects. This information may have important implications both for assessing and planning future studies. So, the main mechanisms whereby probiotics exert protective or therapeutic effects are incompletely understood. Some authors include colonization resistance or competitive inhibition with pathogenic bacteria, effects on barrier function, antagonism through the production of antimicrobial substances (acids, hydrogen peroxide and bacteriocins) and modulation of the immune system.[22,23] These mechanisms vary according to the specific strain or a combination of strains used, the presence of prebiotics and the condition that is being treated the patient. Probiotic microorganisms compete with pathogens for nutrients and physical space.[24-26]

Some bacteria can inhibit and prevent the colonization by pathogenic microorganisms by means of a mechanism of steric obstruction or blocking of specific receptors.[27] L. plantarum have been shown to competitively inhibit the attachment of enteropathogenic E. coli 0157H7 to HT-29 human colonic cancer cells.[28] The effect of probiotics may be classified in three modes of action: (i) Probiotics have a direct

effect on other microorganisms, commensal and/or pathogenic ones. This principle is in many cases of importance for the prevention and therapy of infections and restoration of the microbial equilibrium. (ii) Probiotics also might be able to modulate the host's defenses including the innate as well as the acquired immune system. This mode of action is most likely important for the prevention and therapy of infectious diseases but also for the treatment of chronic inflammation. (iii) Probiotic effects may be based on actions affecting microbial products like toxins, host products e.g. bile salts and food ingredients.[29]

Safety of Probiotics

Probiotics are increasingly being used by consumers for their various health benefits and in healthy individuals probiotics are safe to be used. So, the absolute essence of probiotics to be considered as safe is the absence of pathogenicity and infectivity. Safety criteria for successful probiotics have been well defined in several studies.[30, 31] However, the probiotics are viable microorganisms, and therefore it is feasible that they could infect the host. First selection criteria mentioned that a probiotic supplement have to be generally regarded as safe microorganisms.[1,22] Species of Lactobacillus or Bifidobacterium are normal residents of the gastrointestinal and/or vaginal microbiota and do not display infectivity or toxicity. The risk of infection with these microorganisms is lower.[26, 32]

Probiotics are safe for using in healthy people, but should be used with caution in high risk cases such as: people with immune compromise and premature infants. Current WHO/FAO guidelines recommend that, before using probiotic strains, a number of parameters should be evaluated to prevent health damages, including antibiotic susceptibility patterns, toxin production, metabolic and haemolytic activities, infectivity in immunocompromised animal models, side-effects and adverse incidents in humans.[9,33] Most stringent studies have to be completed for genetically modified strains intended for human consumption before commercialization.[34, 35]

Prebiotics

Prebiotics are non-digestible or low-digestible food ingredients that benefit the host organism by selectively stimulating the growth or activity of one or a limited number of probiotic bacteria in the colon. It is a substance that modifies the composition of the colonic microflora in such a way that a few of the potential health-promoting bacteria (especially, but not exclusively, lactobacilli and bifidobacteria) become predominant.[36] This role is played by fermentable carbohydrates, which are not digested or poorly digested in the small intestine and stimulate, preferentially, the growth of bifidobacteria and some Gram-positive bacteria, belonging to the probiotic bacteria. Complex carbohydrates pass through the small intestine to the lower gut where they become available for some colonic bacteria but are not utilized by the majority of the bacteria present in the colon. Lactulose, galactooligosaccharides, fructooligosaccharides, inulin and its hydrolysates, maltooligosaccharides, and resistant starch are prebiotics commonly used in human nutrition. The main end products of carbohydrate metabolism are short-chained fatty acids, namely acetate, butyrate and propionate, which are further used by the host organism as an energy source. In practice, the most common oligosaccharides are inulin and its hydrolysates and oligofructans.[37]

They can be found in chicory, topinambuco, onion, garlic, asparagus, artichoke, leek, bananas, tomatoes and many other plants. Oligosaccharides comprise glycosides that contain between three to ten sugar moieties. However, disaccharides are also included in this group. The degree of oligosaccharide polymerization is of importance. Usually, food-grade oligosaccharides are mixtures of saccharides with a different degree of polymerization.[38]

Prebiotic oligosaccharides can be produced in three different ways: by extraction of plant materials, microbiological synthesis or

enzymatic synthesis and enzymatic hydrolysis of polysaccharides.[39] The majority of prebiotic oligosaccharides are produced on the industrial scale and are widely available in the market. In practice, combined mixtures of probiotic and prebiotic that beneficially affects the host by improving the survival and establishment of live microbial dietary supplements in the gastrointestinal tract. It may selectively stimulate growth by activating the metabolism of one or a limited number of health-promoting bacteria. It is clear that both probiotics and prebiotics (both probiotics and prebiotics are together called as synbiotics) are able to modify the internal microbial composition towards a potentially healthier community. This approach offers much potential in the prophylactic management of gastrointestinal disease (such as inhibition of pathogens, bowel cancer prevention) and more systematic effects (e.g. reduction in blood lipids, hormonal regulation). Before health claims for probiotics, prebiotics and synbiotics can be made, more corroborative studies are required to associate changes in gut bacterial populations with physiological aspects in humans. In addition, a better understanding of how probiotics and prebiotics cause changes in the microbial community structure is essential.[40, 41]

Beneficial Properties of Probiotics

Nowadays, consumers are aware about the link among lifestyle, diet and good health, which explains the emerging demand for products that are able to enhance health beyond providing basic nutrition. There are several beneficial properties of probiotics are shown in Figure 1 and discussed as follows:

Prevention of Intestinal Infections

Lactobacillus acidophilus and bifidobacteria exert antagonistic effects on the growth of pathogens such as *Staphylococcus aureus, Salmonella typhimurium, Yersinia enterocolitica* and *Clostridium perfringens*. Probiotic bacteria enhance resistance against intestinal pathogens via antimicrobial mechanisms. These include competitive colonization and production of organic acids such as lactic and acetic acids, bacteriocins and other primary metabolites, such as hydrogen peroxide, carbon dioxide and diacetyl.[42] By competitive colonization, probiotic bacteria inhibit the adhesion of gastrointestinal pathogens to the intestinal mucosa.[43] Production of organic acids, such as lactic and acetic acids, by probiotic bacteria lowers intestinal pH and thereby inhibits the growth of pathogens. These organic acids also increase peristalsis, thereby indirectly removing pathogens by accelerating their rate of transit through the intestine.[44] Hydrogen peroxide produced by lactobacilli may function through the lactoperoxidase-thiocyanate system, in which hydrogen peroxide oxidizes the thiocyanate to release hydrocyanic acid, which is detrimental to food-borne pathogens. Carbon dioxide and diacetyl synthesized by lactic acid bacteria inhibit the growth of pathogens.[42] Numerous bacteriocins, such as nisin, acidophilin, acidolin, lactobacillin, lactocidin and lactolin, have been reported to be produced by lactobacilli. Bacteriocins are active against a wide range of food-borne pathogens, depending on their specificity.[41, 45]

Nutritional Benefits

The action microorganism during the preparation of cultured foods or in the digestive tracts has been shown to improve the quantity, availability and digestibility of some dietary nutrients. Fermentation of food with lactic acid bacteria increases folic acid in yoghurt, bifidus milk and kefir, sour cream containing approximately twenty times more folic acid than milk. Lactic acid bacteria are known to release various enzymes into the intestinal lumen that exert synergistic effects on digestion. The bacterial enzymatic hydrolysis may enhance the bioavailability of protein and fat,[46] and increase the production of free amino acids. Short chain fatty acids (SCFA) such as lactic acid, propionic acid and butyric acid also produced by lactic acid bacteria when absorbed these SCFAs contribute to the available energy pool of the host and may protect against the pathological changes into the colonic mucosa.[47]

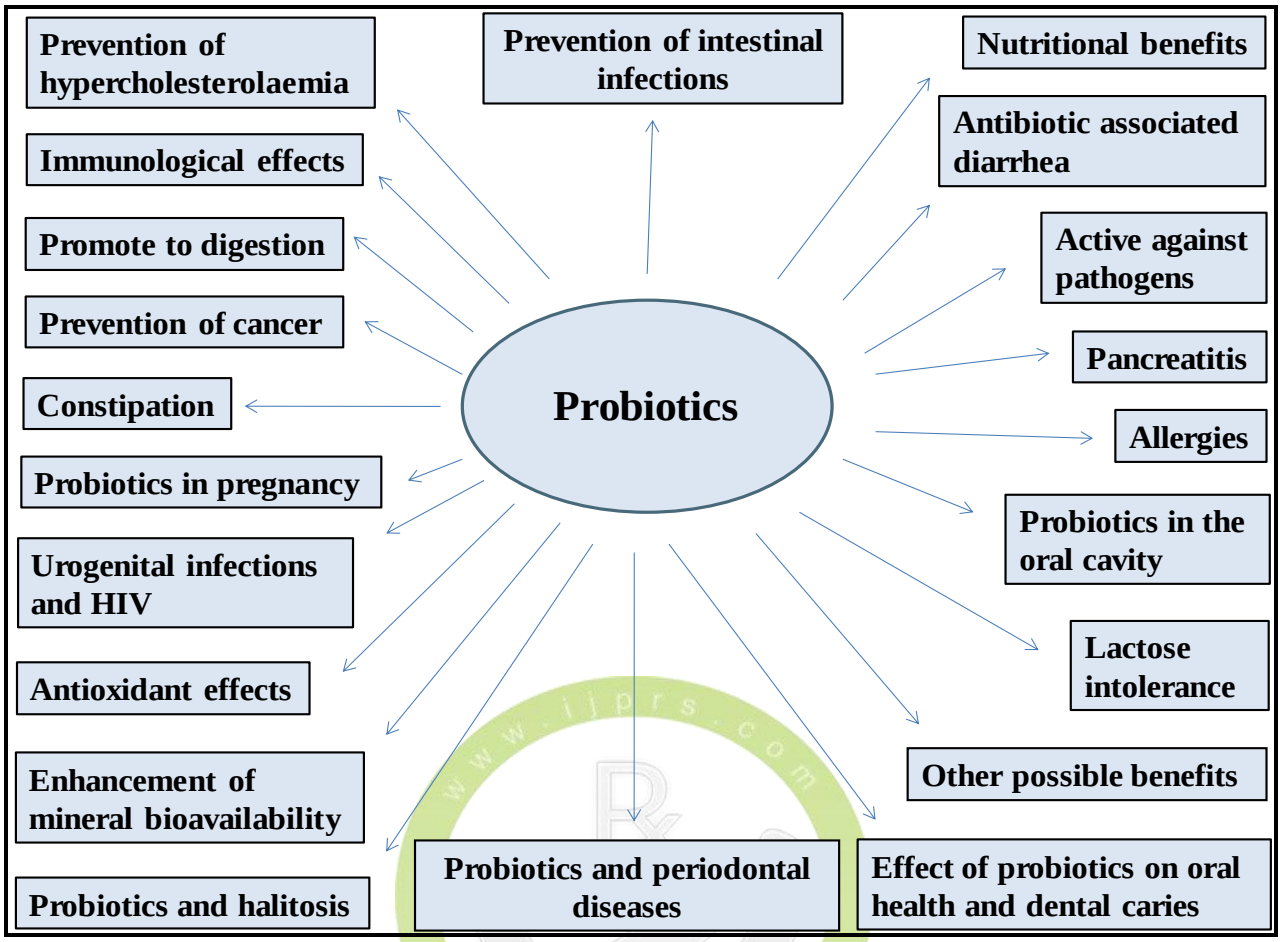

Figure 1: Beneficial properties of probiotics

Immunological Effects

The immune system is highly complex with various biological processes involved, and the various factors influencing its efficacy. During human ageing, a diminution of the immune response occurs, leaving elderly more prone to infections.[48] It is well known that a variety of dietary antigens and commercial and pathogenic microorganisms can cross the gut mucosal barrier and cause disease or stimulate the immune response. Gill has reported that there is sufficient evidence to suggest that lactic acid bacteria exert their immunity enhancing effects by augmenting both non-specific (e.g. phagocyte function, NK cell activity) and specific (e.g. antibody production, cytokinase production, lymphocyte proliferation, delayed-type hypersensitivity) host immune responses.[49] Kaila et al. have found that an enhancement of the circulating IgA antibody secreting cell response was observed in infants supplemented with a strain of *L. casei* and was related to prevention of diarrhoea in the study group compared with a control group.[50] An enhancement in the non-specific immune phagocytic activity of granulocyte populations in the blood of human volunteers after consumption of *L. acidophilus* and *B. bifidum* has been documented.[51] When given in adequate numbers, probiotic bacteria can attach to enterocytes and prevent binding of pathogens by a process of competitive exclusion. Attachment of probiotic bacteria to receptors on the cell surface of intestinal epithelial cells can activate signaling processes leading to the synthesis of cytokines that affect the function of mucosal lymphocytes. Many of these receptors, such as glycosphingolipids and mannosylated glycoproteins, are already being exploited by enteric pathogens. In a sense, probiotic bacteria

can act as de novo vaccines, with the capability to modulate immune responses to a higher plane of competence, thereby arming the immune system to better deal with incoming pathogens. The ability of probiotic bacteria to modulate immunity and to improve the microbial balance of commensal enteric microorganisms offers the consumer a more biologically effective alternative to better health than the consumption of therapeutic drugs.[41]

Antibiotic Associated Diarrhea

Antibiotics are used to kill off harmful bacteria that cause infections in the human body. Unfortunately, the good bacteria in the gut are often also killed as well, which can lead to antibiotic-associated diarrhea (AAD). A severe form of AAD is caused by *Clostridium difficile*, a harmful bacterium that is common in clinical settings. Advanced age is one of the risk factors for developing *C. difficile* associated diarrhea (CDAD) during antibiotic treatment and intensive care unit (ICU) patients with CDAD have a high mortality.[52] AAD is one of the best established areas in probiotics research. Two strains, *Saccharomyces boulardii* and *L rhamnosus* GG, are the most studied strains and have been found effective in lowering the risk of AAD by about two thirds.[53] The use of probiotics in diarrhea is a wide and controversial field. Different types of diarrhea including antibiotic associated diarrhea can benefit from probiotic use in its prevention, treatment or recovery. It has been suggested that probiotics which are able to restore and replace the normal flora should be used. In particular, probiotics should be used in high risk patients such as the elderly, hospitalized or immunocompromised. Several clinical trials have used *S. boulardii*, *Lactobacillus* spp. and *Bifidobacterium* spp. in antibiotic associated diarrhea.[54]

Prevention of Hypercholesterolaemia

There is preliminary evidence that use of probiotic lactobacilli and metabolic by-products potentially confer benefits to the heart, including prevention and therapy of various ischemic heart syndromes and lowering serum cholesterol. Khedkar et al. have concluded that there is insufficient evidence that supplementation of the diet with fermented milks (yoghurt) has a beneficial hypocholesterolemic effect.[55] *Lactobacillus acidophilus* deconjugates bile acids into free acids that are excreted more rapidly from the intestinal tract than are conjugated bile acids. Because free bile salts are excreted from the body, the synthesis of new bile acids from cholesterol can reduce the total cholesterol concentration in the body. Isolates of *L. acidophilus* from the human intestinal material are better able to assimilate cholesterol and actively deconjugate bile salts than commercially used cultures of *L. acidophilus*.[56] However, the assimilation of cholesterol may be due to coprecipitation of cholesterol with bile acids at low pH.[41]

Promote to Digestion

Most lactic acid probiotic bacteria are capable of metabolizing a variety of carbohydrates, including lactose. Some LAB species also secrete proteolytic and lipolytic enzymes that facilitate digestion of proteins and fats. People who produce inadequate amounts of stomach acid and cannot activate the proteolytic enzyme pepsin and individuals with pancreatic insufficiency deficient in pancreatic proteases and lipases all benefit from dietary supplementation with probiotics. Enhanced protein digestion often benefits people with allergies due to increased gut permeability defects by reducing the ability of large proteins to cross the intestinal barrier, enter the bloodstream, and trigger immune responses.[57]

Active against Pathogens

In the intestinal tract, a delicate balance constantly needs to be maintained between beneficial and pathogenic organisms. A variety of factors can shift the intestinal microflora balance in favor of pathogens. These factors include antibiotics, immunosuppressants, stress, aging, poor diet, excessive alcohol intake, environmental pollutants, and infections. Many studies have confirmed that probiotics promote a more favorable balance of intestinal

microflora by reducing populations of harmful microorganisms. Probiotics accomplish this task primarily by producing substances toxic to pathogenic organisms such as lactic acid, acetic acid, formic acid, hydrogen peroxide, and bacteriocins. Long-term, a re-established a healthy balance may reduce the risk of a variety of chronic degenerative or immunologically-mediated diseases.[58]

Prevention of Cancer

The consumption of probiotics and or prebiotics may have several antimutagenic effects. There is some preliminary evidence that the probiotic microorganisms can prevent or delay the onset of certain cancers. This stems from the knowledge that members of the gut microflora can produce carcinogens such as nitrosamines. Biochemical effects of probiotic bacteria include the reduction of faecal enzymes that can convert procarcinogens to carcinogens in the gastrointestinal system.[41] Therefore, administration of lactobacilli and bifidobacteria could theoretically modify the flora leading to decreased β- glucuronidase and carcinogen levels.[59] Morotomi has reported that *L. casei* shirota strain as a lactic acid bacterium has increasing potential for cancer chemoprevention.[60] *In vitro* studies with *L. rhamnosus* GG and bifidobacteria and an *in vivo* study using *L. rhamnosus* strains GG and LC-705 as well as *Propionibacterium* sp. showed a decrease in availability of carcinogenic aflatoxin in the lumen. Some probiotic bacteria produce butyric acid and this molecule can influence the rate of apoptosis in enterocytes and can also act as an anticarcinogen by neutralizing the activity of mutagens such as 4-nitroquinoline-N′-oxide, 2-nitrofluorene and benzopyrene.[61, 62]

Constipation

Although constipation affects all age groups while it is a particular concern in older people, particularly in those with chronic illness and those who live in nursing homes. Acute bouts of constipation can occur because of illness or dietary alterations, whereas the onset of chronic constipation usually occurs earlier in life and often deteriorates with age. The symptom experience can range from a mild, acute event that is remedied with a shift in fluid and dietary intake to a chronic condition that requires daily interventions with mixed results.[63] The composition of the fecal flora changes with age, most markedly by a fall in numbers of bifidobacteria.[64]It has been assumed that the probiotic microorganisms may have the potential to alleviate constipation by changing the gut flora. While it is still not clear whether this a cause or the effect of constipation, it is known that changes in intestinal flora can alter intestinal motility, and the short chain fatty acids produced by probiotic bacteria (by bifidobacteria, in particular) have an important effect on transit time.[65] A logical approach to relieving constipation is thus to increase the numbers of bifidobacteria, a strategy tried using prebiotics as well as probiotics.[66]

Pancreatitis

Pancreatic necrosis and associated pancreatic infection are determinants of poor outcome in patients with severe acute pancreatitis. Colonization of the lower gastrointestinal tract and oropharynx with gram-negative organisms often precede contamination of the inflamed pancreas. Human studies in which patients with acute pancreatitis received *the L. plantarum* 299v showed a decrease in occurrence of pancreatic infection/abscess and a shorter hospital stay.[67, 68] these human findings were supported by trials of probiotics (*L. plantarum* 299v and *S. boulardii*) in animal models of acute pancreatitis in which intestinal microbial translocation was reduced.[69]

Allergies

Intestinal microflora can contribute to the processing of food antigens in the gut resulting in food hypersensitivity, of which atopic disease is a manifestation. Probiotics may exert a beneficial effect on allergic reaction by improving the structure of potential antigens, reduce their immunogenicity, reduce intestinal permeability and the generation of proinflammatory cytokines that are elevated in patients with a variety of allergic disorders. There are a number of studies that evaluated

probiotics in allergic conditions including rhinitis, atopic dermatitis and food allergy.[69, 70]

Moreover, the ability of probiotics to reduce the symptoms of food allergy was noted over 20 years ago. Since then, several well-designed studies have indicated that supplementation with specific probiotic strains are effective for atopic disorders. In infants with atopic eczema and cow's milk allergy, a whey formula supplemented with *L. rhamnosus* GG was shown to significantly improve clinical symptoms and markers of intestinal inflammation. In children with atopic dermatitis, a combination of *L. rhamnosus* and *L. reuteri* proved beneficial. Consumption of these select *Lactobacillus* probiotics down-regulates over-expressed immune responses.[47]

Probiotics in Pregnancy

Good nutrition during pregnancy improves the chances of having a healthy baby who will be at lower risk of diseases later in life. Bacterial vaginosis has been suggested as a factor that increases risk of preterm labour and infant mortality and probiotics been shown to decrease risk of bacterial vaginosis and maintain normal lactobacilli vaginal flora.[71] In animal studies, these strains were found to be safe during pregnancy and to enhance the health of mothers and newborns.[72] Another area of interest is the use of probiotics in pregnancy is to prevent allergic reactions. Studies using *L. rhamnosus* GG and *B. lactis* BB12 has shown that atopic dermatitis, a condition that causes severe skin rashes in up to 15% of babies, can be prevented in 50% of cases if mothers ingest probiotics during pregnancy and newborns ingest them during the first 6 months of life. Probiotics during pregnancy also have an excellent safety record.[73-75]

Urogenital Infections and HIV

Among women producing estrogen or receiving estrogen supplementation, the largest part of the vaginal flora consists of lactobacilli, which possesses antimicrobial properties that regulate urogenital microbiota. Genitourinary infections in women are often characterized by an alteration in the local flora from the predominance of lactobacilli to coliform uropathogens as a result of hormone deficiency, sexual activity, contraceptive measures, and other factors.[76] Bacterial vaginosis, yeast vaginitis and recurrent urinary tract infections (UTIs) are common urogenital problems. In the complex vaginal environment, bacteria of the lactobacilli group are the predominant microorganisms in healthy pre-menopausal women and play an important protective role by limiting growth of pathogenic microorganisms.[77, 78] When lactobacilli are reduced, eliminated or replaced by pathogenic species, the host has an increased susceptibility to urinary tract infections (UTIs), genital tract infections (GTIs), bacterial vaginosis (BV), vulvovaginal candidiasis (VVC), and infection by *N. gonorrhoeae* or *Trichomonas vaginalis*.[79, 80] Evidence from the available studies also suggests that probiotics can be beneficial for preventing recurrent UTIs in women. The use of probiotics per se and mainly lactobacilli has received greater attention as an alternative, inexpensive and natural remedy to restore and maintain the genitourinary health.[81, 82] The prevention or resolution of bacterial vaginosis is particularly important in women at risk of human immunodeficiency virus (HIV) infection. Studies have shown that women with bacterial vaginosis (no lactobacilli) are at significantly increased risk of HIV.[69] Thus treatment of bacterial vaginosis and promotion of vaginal lactobacilli may reduce a woman's risk of acquiring HIV-1, gonorrhea and trichomoniasis. A recent publication has shown that a human vaginal probiotic strain (*Lactobacillus reuteri* RC-14) can express potent functional viral inhibitors which may potentially lower the sexual transmission of HIV.[83]

Lactose Intolerance

When the small intestine doesn't make enough of lactase—the enzyme needed to digest lactose, the sugar in milk and dairy products. Bloating, stomach cramps, flatulence and diarrhea are the result of lactose intolerance. Two-thirds of the world's population suffers from lactose intolerance, with the highest numbers in Asia

and Africa.[84] Probiotic bacteria such as *L. acidophilus* and bifidobacteria produce β-D-galactosidase, which autodigests lactose and improve tolerance to lactose. The increased tolerance for dairy products containing cultures could be due to intra-intestinal digestion of lactose by β-D-galactosidase released from cultures.[41]

Antioxidant Effects

Normal body metabolism produces free radicals especially the free radicals from oxygen. If these free radicals are not neutralized quickly enough, they can cause death of cells through oxidation of enzymes, proteins and lipids. Free radicals induced cellular damage can lead to cancer, heart disease and other serious illnesses. Bacteria like *Lactobacillus delbrueckii* ssp. *bulgaricus* and *Streptococcus thermophilus* some found in yoghurt can successfully entrap reactive forms of oxygen (hydrogen peroxide and hydroxyl radical). Researchers are working on milk bacteria to be used as an antioxidant food supplement because milk bacteria can eliminate oxygen free radicals, and also in view of the fact that some lactobacilli have an antioxidant effect in GI tract.[85]

Enhancement of Mineral Bioavailability

Mineral absorption requires an acidic medium, especially when the minerals are in the form of inorganic salts. Stomach acid is usually sufficient to dissolve mineral salts, but when stomach acid is inadequate mineral salts may not fully dissociate. LAB aid mineral absorption via the production of acidic microenvironments adjacent to the intestinal lining and by generating SCFA that donate protons necessary for mineral absorption, Animal studies have demonstrated that LAB, especially in the presence of a probiotic growth factor like inulin, increase intestinal absorption of calcium, magnesium, potassium and zinc.[86]

Effect of Probiotics on Oral Health and Dental Caries

Streptococcus mutans is the main microorganism involved in causation of dental caries. Probiotics can reduce the risk for a high *S. mutans* level occurrence. Bacteria administered as probiotics compete with cariogenic microbes for adhesion sites as well as for nutrients and growth factors leading to reduced levels of *S. mutans* in oral cavity.[87, 88]

Probiotics and Halitosis

Halitosis or bad breath is a condition affecting comparatively large section of the population. Bad breath in the oral cavity is mainly ascribed to the production of volatile sulphur compounds (VSC) predominantly by gram-negative anaerobes residing in periodontal pockets and on the dorsal surface of tongue. The replacement of bacteria implicated in halitosis by colonization with probiotic bacterial strains may have potential application as adjuncts for the prevention and treatment of halitosis. A definite inhibitory effect on the production of volatile sulfur compounds (VSC) by *F. nucleatum* was observed after ingestion of *Weissella cibaria* both *in vitro* and *in vivo* studies. In children, a marked reduction in the levels of H2S and CH3SH was registered after gargling with *W. cibaria* containing rinse. The possible mechanism in the VSC reduction is the hydrogen peroxide generated by *W. cibaria* that inhibits the proliferation of *F. nucleatum*. *Streptococcus salivarius*, also a possible candidate for an oral probiotic, has demonstrated inhibitory effects on the VSC by competing for colonization sites with species causing an increase in levels of VSC. Although various probiotic products are marketed for both mouth and gut associated halitosis, their efficacy demands more clinical studies.[88, 89]

Probiotics in the Oral Cavity

An essential requirement for a microorganism to be an oral probiotic is its ability to adhere and colonize surfaces in the oral cavity. Microorganisms generally considered as probiotics may not have oral cavity as their inherent habitat and, subsequently, their possibility to confer benefit on oral health is then questionable. Studies suggest that lactobacilli as members of the resident oral microflora could play an important role in the micro-ecological balance in the oral cavity. The

studies further demonstrated that Lactobacilli strains with probiotic properties may indeed be found in the oral cavity. Yet, there is no evidence whether these Lactobacilli strains were detected due to the frequent consumption of dairy products leading to temporary colonization only, or if the oral environment is their permanent habitat.[90]

Probiotics and Periodontal Diseases

Mucosal immune responses may be invoked by probiotic immunization. Studies of adhesion molecules have shown that superficial cell layers of the gingiva can be affected and can be stimulated to enhance the presence of potent immune cells. Regulation of microflora composition (e.g. by probiotics and prebiotics) may offer the possibility to influence the development of mucosal and systemic immunity, but it can also play a role in the prevention and treatment of diseases such as periodontitis.[91] Probiotic Bifidobacterium species reduced gingival and periodontal inflammation.[92]A decrease in gum bleeding and reduced gingivitis has been observed with the application of *L. reuteri*.[93, 94] Probiotic strains included in periodontal dressings at optimal concentration of 10^8 cfu/ml were shown to diminish the number of the most frequently isolated periodontal pathogens: *Bacteroides* sp., *Actinomyces* sp. and *S. intermedius*, and also *C. albicans*.[95]

Other Possible Benefits

The list of benefits mediated by probiotics is not limited to the ones mentioned so far and includes a range of promising effects that require however further studies in order to be substantiated includes from probiotic consumption may benefit hypertension[18, 19], illness-related weight-loss[96], reducing recurrence of bladder cancer[97], collagenous colitis[98], and alcohol-induced liver damage.[99] Studies suggest that probiotic bacteria produce small amounts of vitamins[100], favoring calcium absorption[101], restore fertility to the agricultural soil, used to eliminate the odor in waste-water systems, also used in the animal and poultry industry to prevent the disease-foods.[70] Probiotics are marketed as either pastes or powders are commonly given to young foals, horses being in competition, and these products are defined as live microbial feed supplements.[102] Probiotics have shown a reduction of post- liver transplant infective complications[103], and also helps in colonic involvement in Stevens-Johnson syndrome.[104] In addition, many other potential benefits of probiotics remain inconclusive and controversial at present.

CONCLUSION

Probiotics are live non-pathogenic microorganisms administered to improve microbial balance, particularly in the gastrointestinal tract. Normalization of the properties of unbalanced indigenous microflora of the intestinal tract by ingestion of specific strains of the healthy microflora forms the rationale of probiotic therapy. Probiotic, prebiotic, and synbiotic treatment is still in its infancy but is rapidly moving into the mainstream. Therefore the field of probiotics, prebiotics and synbiotics may potentially open a new branch of science. Probiotics have been extensively studied and explored commercially in many different products in the world. Recent studies have suggested that probiotics have demonstrated beneficial effects to human as well as animal health. Probiotics exert their beneficial effects through various mechanisms, including lowering intestinal pH, decreasing colonization and invasion by pathogenic organisms, and modifying the host immune response. Today probiotics are gaining importance because of the numerous benefits. Therefore, researchers should focus on understanding the mechanisms of health-promoting effects of probiotic cultures for the safe future of probiotics.

ACKNOWLEDGEMENT

The authors express their sincere thanks to Professor S. Srivastava, Department of Genetics, University of Delhi South Campus, New Delhi for suggestion and guidance.

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