Script

Probiotics and prebiotics

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1. Introduction

‘Let food be thy medicine and medicine be thy food’ the age old quote by Hippocrates, is certainly the tenet of today. With the growing interest of the self care and integrative medicine coupled with our health – embracing baby bromes population recognition of the link between diet and health has never been stronger. As a result, the market for fermented foods/products that promotes health beyond providing basic nutrition, is flourishing. With in the fermented foods, is the small but rapidly expanding arena of *Probiotics***.**

Probiotic as a term is a relatively new word meaning “for life” and it is currently used to describe a group of bacteria when administered in sufficient quantity, confer beneficial effects for humans and animals. The concept of probiotics dates back to 1908, when Noble Prize winner Eli Metchnikoff suggested that the long life of Bulgarian peasants resulted from their consumption of fermented milk products. The term "probiotic" was first used in 1965, by Lilly and Stillwell, to describe substances secreted by one organism which stimulate the growth of another. Probiotics are viable bacteria or their inactivated cells or cell wall components that have a beneficial effect on human health. However, the concept of probiotic bacteria is very old, and is associated with the consumption of fermented foods by human beings, for thousands of years. Since ancient times, man has made and eaten probiotic foods. The earliest types of probiotic food were cheeses and milks made by lactic acid bacterial (LAB) and fungal fermentation, and leavened bread fermented by yeasts fermentation. The main probiotic microorganisms used belong to the *Bifidobacterium* and *Lactobacillus* genera. Other bacteria and yeasts e.g. *Saccharomyces boulardii* have also been used.

In the modern ages, the concern to understand the importance and mechanisms of action of probiotic bacteria to exert their beneficial effects has been raised. In the early 1900s, Eli Metchnikoff, attributed the good health and longevity of Bulgarian peoples to their high consumption of fermented probiotic foods. He not only identified the health-giving bacteria used to ferment these foods, he also concluded that the general human being’s health is function of the balance between beneficial "good" probiotic bacteria and disease-causing “bad” bacteria in human gut. 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, and these “bifid” bacteria were abundant in healthy children. Also, Tissier found that these bifidobacteria are dominant in the gut flora of breast-fed babies. The isolated bacterium named *Bacillus bifidus*, and was later renamed to the genus *Bifidobacterium*. Accordingly, he suggested that these bacteria could be administered to patients with diarrhea to help restorea healthy gut flora. This claimed effect was due to bifidobacteria displacement of proteolytic bacteria causing the disease. The words of

Metchnikoff and Tissier were the first scientific suggestions about the probiotic use of bacteria.

However, In 1917, during sever shigellosis outbreak, the German professor Alfred Nissle isolated a nonpathogenic strain of *Escherichia coli* from the feces of a soldier who did not develop enterocolitis. Disorders of the intestinal tract were frequently treated with viable nonpathogenic bacteria to change or replace the intestinal microbiota. The *E. coli* strain Nissle 1917 is one of the few examples of a non-LAB probiotic. In 1989, Fuller, in order to point out the microbial nature of probiotics, redefined the word as "A live microbial feed supplement which beneficially affects the host animal by improving its intestinal balance". Another definition was proposed by Huis in't Veld "a viable mono or mixed culture of bacteria which, when applied to animal or man, beneficially affects the host by improving the properties of the indigenous flora". A more recent, but probably not the last definition is "live microorganisms, which when consumed in adequate amounts, confer a health effects on the host beyond inherent basic nutrition.

As investigations continued in the probiotic field, its concept has been expanded to include bacteria from intestinal origin beside those bacteria isolated from fermented dairy products. Nowadays, probiotic bacteria are available in a variety of food products, dietary supplements and drugs. Food products containing are almost dairy products – fluid milk and yogurt – due to the historical association of LAB with fermented milk. The most frequently used bacteria in these products include the *Lactobacillus* and *Bifidobacterium* species. Recently, new types of food products containing probiotic bacteria started to be introduced into the markets, including nondairy products, such as chocolate, cereals, beverages, fruits and vegetables products. In the near future wide range of non-traditional food products containing probiotic bacteria are expected to be introduced into the markets, as the researches in probiotic products development continue in both scientific and commercial centers around the world. Probiotic may be composed of a single bacterial strain or it may be a combination of two or more than two species as well. Probiotics can be in powder form, liquid form, gel, paste, granules and are generally available in the form of capsules, sachets, etc.

India is also fast emerging as a potential market for probiotics in food. The global probiotic market generated US $15.9 billion in 2008 and is expected to be worth US$ 32.6 billion by 2014 with a compound annual growth rate of 12.6% from 2009 to 2014. On the other hand the probiotic product industry in India was estimated to be around Rs 20.6 million with a projected annual growth rate of 22.6% until 2015.

2. Desirable probiotic properties

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 are

- Acid and bile tolerance which seems to be crucial for oral administration.
- 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.

- Antibiotic susceptibility/resistance profile, antibiotic resistance of the probiotic strains should be considered as it could be transferred to other species, although transfer from lactobacilli has been observed occasionally *in vivo* in diassociated animal models.
- Antimicrobial activity against pathogenic bacteria
- Resistance to Artificial Duodenum Juice as the probiotic cultures should resist the digestive system.
- Bile salt hydrolase activity
- The strains must be able to grow under manufacture and commercial conditions and should retain viability under normal storage conditions.
- Viability is by definition a prerequisite for probiotic functionality as it potentiates mechanisms such as adherence, reduction of gut permeability, and immunomodulation and constitutes an industrial challenge

3. Potential health benefits of Probiotics

Most of the potential benefits to be discussed will focus on those applicable to human health or nutrition.

- **Control of Growth of Undesirable Organisms in the Intestinal Tract**

  Lactobacillus acidophilus, *Lb. casei*, and species of *Bifidobacterium* can inhibit growth of undesirable microorganisms that might be encountered in the gastrointestinal tract. Most of the older reports dealing with this type of control focused on a therapeutic approach; in that cultured products made with these organisms were used to treat infections of various types. In recent years, several studies have shown the efficacy of certain probiotic organisms in controlling growth of undesirable microorganisms in the intestinal tract. Antimicrobial substances, mainly including bacteriocins, produced by probiotic bacteria have been implicated in recent publications as having a possible role in controlling intestinal pathogens.

- **Improvement of Immune Response**

  Enhancement of the body's immune response by consuming cells of certain lactobacilli increases resistance of the host to intestinal infections. Researchers in this area have suggested that this action involves activation of macrophages which in turn destroy pathogenic organisms in the body. It also has been suggested that consumption of these organisms is followed by secretion of components into the intestinal tract which are inhibitory toward certain of the foodborne pathogens. This enhancement of the immune system increases the host defense mechanisms and could be very important for control of foodborne illnesses. This may be a key explanation as to how certain probiotic microorganisms used as dietary adjuncts can exert control over intestinal infections.

- **Improvement of Lactose Digestion**

  People who lack the ability to digest lactose adequately are classified as lactose maldigestors. (In the past, terms such as ''lactose intolerance'' or ''lactose malabsorption'' have been used to describe this condition). The problem results from inadequate levels of β-galactosidase in the small intestine to hydrolyze ingested lactose adequately. Research has shown that the presence of viable starter cultures

such as probiotics can be beneficial to lactose maldigestors. This beneficial action results from presence of β -galactosidase in the bacterial cells. Apparently being inside the bacterial cells protects the enzyme during passage through the stomach so that it is present and active when yogurt reaches the small intestine. Once the probiotic culture reaches the small intestine, it interacts with bile, which increases permeability of the cells of these bacteria and enables the substrate to enter and be hydrolyzed.

- **Anticarcinogenic Actions**

  Anticarcinogenic or antimutagenic activities have been reported for several cultures used to manufacture various fermented milk products. Some of the recent studies have involved products containing probiotic bacteria expected to survive and grow in the intestinal tract, whereas others have involved only bacteria used to manufacture the product and which are not normally expected to survive and grow in the intestinal tract. For instance, consumption of yogurt by mice inhibited development of certain tumors. This represents another potential health benefit for a cultured product without necessarily involving one of the traditional probiotic bacteria. In other studies involving human subjects, a culture of lactobacilli exhibited potential in controlling cancer of the colon. *Lactobacillus acidophilus, Lb. casei*, and *Lb. delbrueckii* subsp. *bulgaricus* are species most often mentioned as having potential to provide anticarcinogenic actions. However, the main effect may result indirectly through inhibiting growth of undesirable bacteria that form carcinogens in the large intestine. Thus, this may represent another benefit in being able to control growth of undesirable organisms in the gastrointestinal tract.

- **Control of Serum Cholesterol**

  In the 1970s, two studies were published that suggested organisms such as *Lb. acidophilus* can potentially reduce serum cholesterol levels in humans. One of these studies involved milk fermented with what was described as a ‘‘wild’’ strain of lactobacillus and then fed to a group of men on a high-cholesterol diet. In another study, cells of *Lb. acidophilus* added to infant formula reduced serum cholesterol in infants receiving the formula, whereas infants receiving the formula without cells of *Lb. acidophilus* exhibited increased serum cholesterol levels. Another activity of *Lb. acidophilus* that may be important is its ability to deconjugate bile acids. This provides yet another mechanism whereby ingested *Lb. acidophilus* might exert control of serum cholesterol levels.

4. Safety of probiotic bacteria

Safety considerations of probiotic bacteria are of high importance, as most probiotic bacteria are marketed in foodstuffs or feed supplements. The safety of these microbes has been confirmed through a long experience of safe use in food as starter cultures. Bacteria such as *Lactobacillus, Leuconostoc,* and *Pediococcus* species have long been involved in food processing throughout human history, and the ingestion of foods containing live or dead bacteria, and metabolites of these bacteria has taken place for many centuries. Generally, LAB are classified as generally recognized as safe (GRAS), and there were no reports of any harmful effects from the consumption of these bacteria through the long history of their use in the processing of many foods (i.e. fermented dairy, fermented vegetables …etc.). In an

epidemiological study of *Lactobacilli bacteremia* case reports, concluded that the increased usage of probiotic products of lactobacilli did not cause any increase in incidence or frequency of bacteremia in Finland. However, it was found that under certain conditions, some lactobacilli strains have been associated with adverse effects, such as rare cases of bacteremia. Ecologically, bifidobacteria are the predominant bacteria in the intestinal tract of breast-fed infants and are believed to contribute to the good health of infants. Until now, the safety of the bifidobacteria has not been questioned, as the reports of a harmful effect of these microbes on the host are very rare.

The concern of probiotic bacteria safety has been raised with the more recent use of intestinal isolates of bacteria delivered in high numbers to severely ill patients. Use of probiotic bacteria in ill persons is restricted to the strains and indications with proven efficacy. A multidisciplinary approach is necessary to assess the toxicological, immunological, gastroenterological, pathological, infectivity, the intrinsic properties of the microbes, virulence factors comprising metabolic activity, and microbiological effects of probiotic strains. Conventional toxicology and safety evaluation is not sufficient, since a probiotic is meant to survive and/or grow in human colon in order to benefit humans. Several methods have been developed for evaluation the safety of LAB through the use of in vitro studies, animal studies, and human clinical studies. Also, proposed studies on intrinsic properties and interactions between the host and probiotic bacteria can be used as means to assess the safety of probiotic bacteria. Evaluation of the acute, sub-acute and chronic toxicity of ingestion of extremely large quantities of probiotic bacteria should be carried out for all potential strains. Such assessment may not be necessary for strains with established documented use.

Thus, safety considerations of probiotic bacteria should include:

- Antibiotic resistance profiles.
- Infectivity in immune-compromised animal models
- Toxin production: probiotic bacteria must be tested for toxin production. One possible scheme for testing toxin production has been recommended by the European Union Scientific Committee on Animal Nutrition.
- Hemolytic activity.
- Metabolic activities (D-lactate, bile salt de-conjugation).
- Genetic and pathological side effects.
- Epidemiological surveillance of adverse incidents in consumers (post market).

5. Prebiotics

Food (or feed) ingredients that are not digestible by humans (or livestock) that might provide benefit to the consumer by stimulating growth or activity of bacteria in the gastrointestinal tract are considered to be potential prebiotics. The large intestine is the most often considered sight of action for these substances, although they could have some impact on microorganisms in the small intestine.

For the most part, these prebiotic compounds contain oligosaccharides, which are not normally digested in the gastrointestinal tract except by resident bacteria. Theoretically, any dietary component reaching the large intestine undigested could be a potential prebiotic. However, oligosaccharides are most often considered and have received most attention as prebiotics. Oligosaccharides that have been considered as prebiotics include fructo-oligosaccharides, gluco-oligosaccharides, galacto-oligosaccharides, transgalacto-

oligosaccharides, isomalto-oligosaccharides, xylo-oligosaccharides, and soybean oligosaccharides. Inulin-type fructo-oligosaccharides have been the ones most investigated as prebiotics. Much of the focus has been on their ability to enhance growth of *Bifidobacterium* species. These bacteria can hydrolyze such oligosaccharides and use them as an energy source to support their growth. They use them in preference to other complex carbohydrates such as starch. Fermentation of these soluble fibers in the large intestine results in production of short-chain fatty acids, primarily acetic, propionic, and butyric acids. These fatty acids are important to the host in lipid metabolism.

Inulin is extracted from chicory roots with hot water. Partial hydrolysis of this extract yields fructo-oligosaccharides, sometimes referred to as fructans. These fructans are considered bifidogenic and increase growth of *Bifidobacterium* species in the intestinal tract, primarily in the large intestine. Galacto-oligosaccharides have a similar effect. Enhancing growth of this group of beneficial bacteria should improve their ability to exert an antagonistic action toward undesirable intestinal microorganisms such as pathogens. This should result in reduced shedding of intestinal pathogens by both humans and livestock when prebiotics are included in the diet.

Fructo-oligosaccharides in animal diets reportedly decrease the amount of fecal putrefactive compounds released, which implies an alteration in the intestinal microflora. This may be important in control of odors from livestock wastes.

Synbiotics

Recently progressive studies in the field of probiotics and prebiotics introduced a new terminology such as synbiotics. It is nothing but the synergy between probiotic and prebiotic effect in the GI tract or in other words, synbiotics is the usage of both probiotics and prebiotics in combinations. Indeed synbiotic combinations are considered to have more beneficial effects on human health than probiotics or prebiotics alone. Recent studies established that synbiotics improve the intestinal microbial environment and activate host immune function, leading to prevention of bacterial translocation. Administration of synbiotics as a food supplement is safe, simple, and convenient. Therefore, characterizing a new and novel synbiotic combination would find multifaceted use in disease prophylaxis and management for human use.

Conclusion

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 and animal health. Much of the clinical probiotic research has been aimed at infantile, antibiotic-related and traveller's diarrhoea. The non-pathogenic organisms used as probiotics consist of a wide variety of species and subspecies, and the ability to adhere, colonise and modulate the human gastrointestinal system is not a universal property. *Lactobacillus* and *Bifidobacterium* are the main probiotic groups; however, there are reports on the probiotic potential of yeasts. Some of the identified probiotic strains exhibit anti-inflammatory, anti-allergic and other important properties. Besides, the consumption of dairy and non- -dairy products stimulates the immunity in different ways.

Prebiotics, particularly oligosaccharides, apparently can be used alone to modify the intestinal flora, particularly in the large intestine. Since prebiotics tend to enhance growth of

Bifidobacterium species in the intestine, a product containing a prebiotic and a selected strain of *Bifidobacterium* species could enhance beneficial effects for the host. This might improve the control of intestinal pathogens or bacteria that create malodors in livestock waste.