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Significance of prebiotics, probiotics and synbiotics as health potentiators

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Worldwide, the demand of synbiotic foods is growing rapidly due to the increased awareness of the consumers for their health. Synbiotic describes synergism or synergistic relationship. It is a supplement that contains both a prebiotic and probiotic component working together to improve the 'friendly flora' of the human intestine. Fermented milk products e.g. yoghurt and kefir are considered to be synbiotic products since they supply the live bacteria and the food for live bacteria to survive. However, evidently not all fermented products promote symbiosis. The best synbiotic combinations currently available include bifidobacteria and fructo-oligosaccharides (FOS), *Lactobacillus* GG and inulins, bifidobacteria and lactobacilli with FOS or inulins and Lactowise – *Lactobacillus sporogenes* and Fenumannan. For many of the potential benefits of probiotics, research is limited and only preliminary results are available.

Key Words : Probiotics, Prebiotics, Synbiotics, Health benefits

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INTRODUCTION

A synbiotic product is a blend of prebiotic ingredient/s and probiotic culture in synergism or synergistic relationship. Synbiotic foods come under the category of functional foods *i.e.* the foods that contain one or more biologically active components which may beneficially affect one or more target functions in the body, beyond adequate nutritional effects, in a way that is relevant to either the state of well-being and health or the reduction of the risk of a disease (Diplock *et al*., 1999).

Synbiotic should reserve for products in which the prebiotic selectively favours the probiotic component. Before elaborating the health potential of synbiotic association in foods, the basic understanding of pre and probiotics is essential. Basically synbiotics are defined as, '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' (Gibson and Roberfroid, 1995). *Prebiotic* is a greek word which means *'before life' i.e.* a substance (usually an oligosaccharide) that cannot be digested but does promote the growth of beneficial bacteria (probiotics). *Probiotics* means '*for life'*, it is a substance that contains micro-organisms or bacteria that are beneficial to the host organism. From these two, a concept of *synbiotic* arises which means *'plus life' i.e.* it is a substance containing both a prebiotic and probiotic (Fig.1). The main reason for using a synbiotic food product is that a true probiotic culture, without its prebiotic support, does not survive well in the digestive system. To enhance viability, not only on the shelf but also in the colon, the product must allow for much greater attachment and growth rate for healthy bacteria to

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minimize the growth of harmful bacteria. Without necessary food source probiotics will be more intolerant to oxygen, low pH and temperature. In addition, the probiotic will have to compete against other bacteria that will take over if its specific food source is not available. Therefore, the benefits of synbiotics lie on the total health potential provided by probiotics and prebiotics.

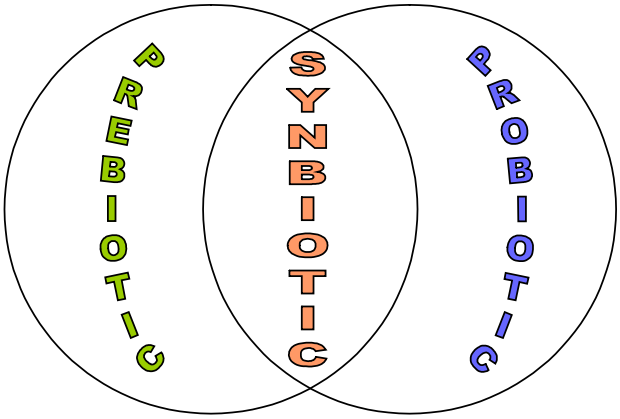

Fig. 1 : Interrelationship among pre, pro and synbiotics

Probiotics :

The history of Probiotics dates back as far as the first intake of fermented milks, over 2000 years ago. The scientific interest in this area boosted from the work of Metchinkoff (1907) to transform the toxic flora of large intestine into host-friendly colony of *Lactobacillus bulgaricus* (Hord, 2008). Probiotics basically are live micro-organisms thought to be beneficial to the host. According to the currently adopted definition by FAO/ WHO, probiotics are 'Live micro-organisms which when administered in adequate amounts confer a health benefit on the host animal by improving the intestinal microbial balance' (FAO, 2001). Lactic acid bacteria (LAB) and bifidobacteria are the most common types of microbes used as probiotics; but certain yeasts and bacilli may also be helpful as probiotics. Probiotics such as yoghurt, soy yoghurt or as dietary supplements are commonly consumed as part of fermented foods with specially added active live cultures.

The term 'probiotics' was first introduced by Kollath in 1953 (Hamilton-Miller, 2003). Contrasting antibiotics, probiotics were defined as microbiologically derived factors that stimulate the growth of other micro-organisms. In a very simple form one can understand that antibiotics may turn the immune system "off" while probiotics turns it back on "idle", and more able to quickly react to new infections (Science Daily, 2010). In 1989, Fuller suggested a definition of probiotics as, "a live microbial feed supplement which beneficially affects the host animal by improving its intestinal microbial balance" (Fuller, 1989). Probiotics are rapidly becoming a popular and important tool for preserving our natural health. Probiotics are living, health-promoting micro-organisms that are incorporated to flourish into various kinds of foods. The ability of probiotics to withstand the normal acidic conditions of the gastric juices and the bactericidal activity of the bile salts, as well as the production of lactic acid that inhibits the growth of other micro-organisms, allow them to be established in the intestinal tract (Catanzaro and Green, 1997). The reported health benefits of probiotics include boosting of the immune system, inhibition of the growth of pathogenic organisms, prevention of diarrhoea from various causes, prevention of cancer, reduction of the risk of inflammatory bowel movements, improvement of digestion of proteins and fats, synthesis of vitamins, detoxification and protection from toxins (Hobbs, 2000). Members of the genera *Lactobacillus*, *Bifidobacterium* and *Streptococcus* are the most common probiotics used in commercial fermented and non-fermented dairy products of today's market (Heller, 2001). Microbes considered to be beneficial to the human body include the genus names *Lactobacillus*, *Streptococcus*, *Bifidobacterium*, and *Saccharomyces* and more specifically the microbes *are Lactobacillus bulgaricus*, *Lactobacillus acidophilus*, *Lactobacillus casei*, *Lactobacillus rueteri*, *Streptococcus lactis*, *Streptococcus citrovorus*, *Bifobacterium bifidium*, *Saccharomyces boulardii* and others (Table 1).

Mechanism of probiotic action :

A healthy human gastrointestinal tract contains about 1.2 kg of bacteria and large numbers of yeasts (Abott, 2004). These native microbes in the gastrointestinal tract play an important role in the health and well-being of the host. The favourable effects of these bacteria may comprise inhibition of pathogens, stimulation of the immune system, help in digestion, synthesis of vitamins and drug metabolism. However, such defensive effects associated with these microbial flora last as long as a proper balance is maintained among the different microbes residing in the intestine.

Table 1 : Examples of common probiotics, prebiotics and synbiotics organism

Sr. No.	Component	Common examples
1.	Probiotics	(i) Lactobacilli *: L. acidophilus , L. casei, L. delbrueckii* subsp. *bulgaricus, L. reuteri, L. brevis, L. cellobiosus, L. curvatus, L. fermentum, L. plantarum,* Gram-positive cocci (ii) *Lactococcus lactis* subsp. *cremoris, Streptococcus salivarius* subsp. *thermophilus, Enterococcus faecium, S. diaacetylactis, S. intermedius* (iii) *Bifidobacteria: B. bifidum, B. adolescentis, B. animalis, B. infantis, B. longum, B. thermophilum*
	Market availability	Yakult – Danone, Proactive and Probiotic Curd – Mother Dairy, LC1 – Nestle, Actimal, Ski Biovita, Sveltesse optimisc 0%, Munch Bunch Drinky (UK), Muller Dairy, Orchard Maid (UK), Onken dairy, RowanGlen Dairy (UK) etc.
2.	Prebiotics	Fructo-oligosaccharides (FOS), galactooligosaccharides (GOS), soya-oligosaccharides, xylo-oligosaccharides, pyrodextrins, isomalto-oligosaccharides and lactulose.FOS (eg, oligofructose and neosugar)
	Market availability	Lactulose, Lactitol, Actilife (Zydus) health drink etc.
3.	Synbiotics	Bifidobacteria + FOS, Lactobacilli + lactitol, Bifidobacteria + GOS,
	Market availability	LactoWise (Gram positive, *Lactobacillus sporogenes* / *Bacillus coagulans* + Fenumannan) etc.

Probiotic bacteria also reinforce the intestinal walls by crowding out pathogenic organisms, thereby helping to prevent their attachment to where they can cause disease. Probiotic bacteria also stimulate antigen-specific and nonspecific immune responses. The ingestion of Lactobacilli is known to result in the reduction of faecal enzymes such as β-glucuronidase, azoreductase and nitroreductase in humans, which are capable of converting pro-carcinogens to carcinogens in the digestive tract. Thus, they lower the chances for tumour development

Probiotics associated health benefits :

Probiotics have become an important part of nutrition because our microbial populations have been altered by the use of antibiotics and other substances that are designed to kill germs and disease. It has been relatively recent that scientists have discovered more about the specific ways that these microbes improve our health. The beneficial bacteria that make up our gut flora have many functions in the body and are essential to our health. A search of medical journals finds a huge number of experiments and research articles on the benefits of probiotics. Amin *et al*. (2013) discussed microencapsulation as the future of probiotic culture. They are available in various forms as powder, liquid, gel/paste and capsule etc. (Suvarna and Boby, 2005). Some of these benefits include; enhancing bowel function, prevention of colon cancer, cholesterol lowering, lowering of blood pressure, improving immune function and reducing infections, reducing inflammation, improving mineral absorption, preventing growth of harmful bacteria, fighting off diseases like *candida* and exzema etc. (Fig. 2). Some potential benefits are illustrated as in Table 2.

Prebiotics :

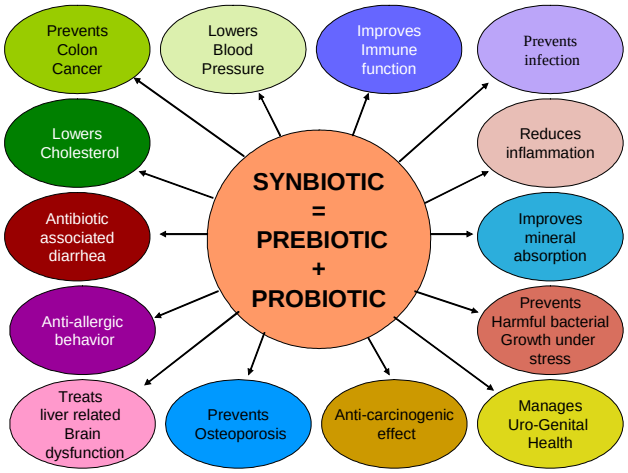

Fig. 2 : Associate health benefits of Pre, Pro and Synbiotics

A prebiotic was originally defined in 1995 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' (Gibson and Roberfroid, 1995). A more recent definition stated that 'A prebiotic is a selectively fermented ingredient that allows specific changes, both in the composition and/or activity in the gastrointestinal microbiota that confers benefits upon host wellbeing and health' (Gibson *et al*., 2004). The

Table 2 : Potential benefit

Sr. No.	Health benefits	References
1.	Managing lactose intolerance	Sanders, 2000
2.	Prevention of colon cancer	Wollowski *et al.*, 2001 and Brady *et al.*, 2000
3.	Lowering cholesterol	Sanders, 2000
4.	Lowering blood pressure	Sanders, 2000
5.	Improving immune function and preventing infections	Hatakka, 2001; Nase *et al.*, 2001; Reid *et al.*, 2003 and Ouwehand *et al.*, 2002
6.	Helicobacter pylori	Hamilton – Miller, 2003
7.	Antibiotic-associated diarrhoea (AAD)	D'Souza *et al.*, 2002; Cremonini *et al.*, 2002; Szajewska and Mrukowicz, 2005; Mcfarland, 2006; Szajewska *et al.*, 2006; Doron *et al.*, 2008; Surawicz, 2008 and Sazawal *et al.*, 2006
8.	Reducing inflammation	Reid *et al.*, 2003; Boyle *et al.*, 2008 and Braat *et al.*, 2004
9.	Improving mineral absorption	Famularo *et al.* (2001)
10.	Preventing harmful bacterial growth under stress	Hitti (2006)
11.	Irritable bowel syndrome and colitis	Whorwell *et al.* (2006) and Guyonnet *et al.*, 2007
12.	Managing urogenital health	Reid, 2001 and Famularo *et al.*, 2001
13.	Anti-microbial activities	Eduardo and Anne, 2003

principal concept associated with both these definitions is that the prebiotic has a selective effect on the microbiota that results in an improvement in health of the host.

A prebiotic is a non-viable food component that confers a health benefit on the host associated with modulation of the microbiota (FAO, 2007). Therefore, in simpler terms, prebiotics are food components that exert beneficial effects on the health of host via stimulating the growth and/or activity of probiotics. A prebiotic can be a fibre but all fibre need not be a prebiotic. It is a substance that can be characterized chemically and in most cases this will be a food grade component. Modulation deals with the sole presence or formulation of any component which changes the composition or activities of the microbiota in the target host. This mechanism might include fermentation, receptor blockage or others.

Common prebiotics in use include inulin, fructo-oligosaccharides (FOS), galacto-oligosaccharides (GOS), soya – oligosaccharides, xylo – oligosaccharides, pyrodextrins, isomalto-oligosaccharides and lactulose (Table 1). The majority of studies have so far focused on inulin, FOS and GOS (Macfarlane *et al*., 2008 and Aggett *et al*., 2005). These saccharides have now a long history of safe use and are generally regarded as safe, although there is some concern over increased gas production with some compounds, particularly when ingested in higher amounts during the first few days of intake.

The most prevalent forms of prebiotics are nutritionally classed as soluble fibre. To some extent, many forms of dietary fibre exhibit some level of prebiotic effect. Researchers now also focus on the distinction between short-chain, long-chain, and full-spectrum prebiotics. Short-chain prebiotics, e.g. oligofructose, contain 2-8 links per saccharide molecule, are typically fermented more quickly in the right-side of the colon providing nourishment to the bacteria in that area. Longer-chain prebiotics, e.g. inulin, contain 9-64 links per saccharide molecule; tend to be fermented more slowly, nourishing bacteria predominantly in the left-side colon.

Prebiotic action :

Probiotic bacteria are not normally found in the human intestine. They also do not colonize well when introduced and are eliminated quickly. Therefore, prebiotic foods are vital to encourage probiotic organisms to survive and thrive in the human gut. Beneficial bacteria must constantly be introduced in the diet and fed proper food to encourage them to adhere to the intestinal wall rather than passing through the digestive tract. The reason behind this is probiotic bacteria and the short-chain fatty acids (SCFAs) that are produced in vegetarian diet restrict the growth and activity of less beneficial species of microbes. In addition, the vegetarian intestinal tract discourages putrefactive and disease-causing bacteria and yeast because plant-based foods move out of the intestine more quickly than do animal products. This 'crowding out' of undesirable organisms, known as Competitive Exclusion, promotes better gut integrity and function,

increases immune system function and improves calcium absorption and cholesterol maintenance. In fact, most of the energy required by the colon is provided directly by SCFAs. In any condition when the colon does not have enough SCFAs to meets its energy requirements, this result in various 'starved bowel' disorders collectively known as IBS (Irritable Bowel Syndrome) or IBD (Irritable Bowel Disease). For sufferers, the most recommended prebiotics are lactosucrose, oligofructose, inulin, bran, psyllium, and germinated barley foodstuffs. Therefore, there are mounting scientific evidence that symbiotic relationship between prebiotics and probiotics significantly contributes to health.

Synbiotics :

The term synbiotic refers to nutritional supplements combining probiotics and prebiotics in a form of synergism. Synbiotics may be defined as the combination of probiotics (*the live bacteria*) and prebiotics (*the food components they live on*) (Fig. 1). The main reason for using a synbiotic is that; a true probiotic, without its prebiotic 'food source', does not survive well in the digestive system. Without such a necessary food source for the probiotic, it will have a greater intolerance for oxygen, low pH, and temperature. In addition, the probiotic will have to compete against other bacteria that will take over if its specific food source is not available. Therefore, a 'synbiotic' product makes for a better choice. Both work together in a synergistic way, more efficiently promoting the probiotics benefits.

Examples of some synbiotic combination are Bifidobacteria and fructo-oligosaccharides (FOS), *Lactobacillus rhamnosus* GG and inulins and Bifidobacteria or *Lactobacilli* with FOS or inulins or galacto-oligosaccharides (GOS), LactoWise (Gram positive, *Lactobacillus sporogenes / Bacillus coagulans* + Fenumannan) (Table 1).

Doses :

Typically, synbiotic products containing one to ten billion active cells are taken several times a week, if not daily. In cases where antibiotics have been taken, it is sometimes suggested that such a product be taken several times a day, preferably at least 30 minutes before meals (Table 3).

Future directions for synbiotics :

Functional foods containing synbiotics should be developed by keeping in mind the specific functional characteristics associated with targeting specific groups of individuals, e.g. infants, children, elderly people, and for people suffering from diseases like diabetes and lactose intolerance etc. Members of the genera *Lactobacillus*, *Bifidobacterium* and *Streptococcus* are the most common probiotics used in commercial fermented and non-fermented dairy products today (Heller, 2001). With the recognition and endorsement by the United Nations and World Health Organization, the call that 'Efforts should be made to make synbiotic products more widely available, especially for relief work and populations at high risk of morbidity and mortality is yet to be ratified by government agencies and multinational probiotic companies. The success of probiotics in recent times, fueled by failure of pharmaceutical agents (antibiotics, statins, anti-inflammatories), consumer demands for natural products and scientific validity of the concept, has led to the entrance of products onto the market that are not close to meeting the standards (i) The origin of the probiotic strain is not relevant if it confers a health benefit. (ii) Strains should be specific using DNA-DNA hybridization or the equivalent molecular method. (iii) Each strain should have a number

Table 3 : Health benefits of Synbiotics

Sr. No.	Health benefits	References
1.	Antimicrobial activities	Eduardo and Amne, 2003
2.	Anticarcinogenic effect	Holzapfel and Schillinger, 2002; Gallaher *et al.,* 1996 and Tannock, 1999
3.	Antidiarrhoeal aspects	Saavedra and Bauman, 1994
4.	Antiallergeic behaviour	Kirjavainen *et al.,* 2003
5.	Osteoporosis prevention	Zubillaga *et al.,* 2001; Holzapfel and Schillinger 2002 and Ouwehand *et al.,* 1999
6.	Reduced risk of heart disease	Tannock, 1999
7.	Regulates the immune system	Perdigon *et al.,* 2002
8.	Nutrient synthesis and bioavailability	Friend and Shahani 1984; Shahani and Chandan, 1979
9.	Digestion	Friend and Shahani 1984; Shahani and Chandan, 1979

or letter designation (iv) New strains and products should be proven safe in human studies if designated as probiotics (v) Clear labeling is recommended when a strain used for patients with a leaky gut or at risk of blood born infection.(vi) Carefully designed, sized, placebo-controlled, statistically significant human efficacy or effectiveness studies are required to prove that probiotic strains in their product formulation confer specific disease reduction or clinical treatment benefits. (vii) Regulatory agencies need to develop new criteria that allow food and dietary supplement products to make health claims that are informative and useful for consumers, and that can be substantiated by appropriately designed and completed clinical studies set by the FAO/WHO. Severe research and trials from scientists, physicians and consumers are needed to force these issues, and determine the depth and limitations of probiotics, and their mechanism of action. When knowledge of human-bacteria genomics, nutrigenomics, proteomics and metabolomics emerges and becomes intertwined; the mechanisms and functionality of probiotics will become uncovered. Genetic technology will equally lead to the development of new strains and with the combination of basic and industry-based research, personalized probiotic products will eventually get to the consumer in the near future. Genetic analysis and modification of probiotics can lead to the development of new probiotics with beneficial health effects. New and cheaper sources of prebiotics and probiotics should be generated, for example from waste agriculture biomass (*i.e.* residues from plant, animal and microbial processing) and by using lactose from inexpensive whey feedstocks. There is potential for *in situ* manufacture of prebiotics during food processing operations. This might, for example involve the enzymatic modification or acid hydrolysis of various carbohydrates and polysaccharides during food processing. Better analytical methods should be developed, which can identify novel prebiotic oligosaccharides in foods; ideally, these should have good reproducibility, reliability and should not involve expensive, specialist analytical equipment. Technology now seems to be available for the expansion of new ranges of foods and drinks containing synbiotics, which can provide the industry with better prospects and an opportunity for growth. The use of synbiotics in food in critical care is promising; however, they should be administered carefully and cautiously and only on the basis of strong scientific evidences.

Conclusion :

Worldwide, the demand of consumption of synbiotic foods is growing rapidly due to the increased awareness of the consumers for their positive effects on health. Synbiotics shows 1 plus 1 does not always equal to 2, it is 1 plus 1 equal to 3 or more as their combination of pre- probiotic shows potential synergistic health benefits. This shows a synbiotic product should be considered as a 'functional food' rather than some obscure chemistry formulation. For many of the potential benefits of probiotics research is limited and only preliminary results are available. After going through various studies authors recommended that caution should be exercised when administering probiotic supplements to immuno compromised individuals or patients who have a compromised intestinal barrier. It is also noted that the issue of synbiotics should be addressed by a separate Technical Committee.

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