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ROLE OF PROBIOTICS BEVERAGES IN HUMAN HEALTH: A REVIEW

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ABSTRACT

Probiotics, which means “for life”, have been used for centuries as natural components in health promoting food. They have a long history of association with dairy products because some of the same bacteria that are associated with fermented dairy products also make their home in different sites in the human body. Probiotics, live cells with different beneficiary characteristics, have been extensivelly studied and explored commercially in many different products in the world. Their benefits to human and animal health have been proven in hundreds of scientific research. Lactoba-cillus and Bifidobacterium are the main probiotic groups; however, there are reports on the probiotic potential of Pediococcus, Lactococcus, Bacillus and yeasts. Some of the identified probiotic strains exhibit powerful anti-inflammatory, antiallergic and other important pro-perties. Apart from that, the consumption of dairy and non-dairy products stimulates the immunity in different ways. Various food matrices have been used with probiotics, which are briefly documented. In this review, the history of probiotics, their application in the health and food areas and new trends in probiotic products and processes are presented.

KEYWORDS: Probiotics, intestinal microflora, probiotic production, food carriers, dairy products.

INTRODUCTION

The word ‘probiotic’ comes from Greek language ‘pro bios’ which means ‘for life’ opposed to ‘antibiotics’ which means ‘against life’. The history of probiotics began with the history of man by consuming fermented foods that is well known Greek and Romans consume very much.[1] In 1908 a Russian researcher Ellie Metchnikoff, who has a nobel prize, firstly proposed the beneficial effects of probiotic microorganisms on human health. Metchnikoff hypothesized that Bulgarians are healthy and long lived people because of the consumption of fermented milk products which consists of rod shaped bacteria (Lactobacillus spp.). Therefore, these bacteria affect the gut microflora positively and decrease the microbial toxic activity.[2]

The term ‘probiotic’ firstly used in 1965 by Lilly and Stillwell to describe substances which stimulate the growth of other microorganisms. After this year the word ‘probiotic’ was used in different meaning according to its mechanism and the affects on human health. The meaning was improved to the closest one we use today by Parker in 1974. Parker defined ‘probiotic’ as ‘substances and organisms which contribute to intestinal microbial balance’. In 1989, the meaning use today was improved by Fuller. Thus, probiotic is a live microbial supplement which affects host’s health positively by improving its intestinal microbial balance. Then this definition was broadened by Havenaar and Huis in’t Veld in 1992 including mono or mixed culture of live microorganisms which applied for animal and man.[3,4]

Probiotics are also challenging for the industrial applications. The probiotic concept is open to lots of different applications in a large variety of fields relevant for human and animal health. Probiotic products consist of different enzymes, vitamins, capsules or tablets and some fermented foods contain microorganisms which have beneficial effects on the health of host. They can contain one or several species of probiotic bacteria.[5,6] Most of products which destine human consumption are produced in fermented milk or given in powders or tablets. These capsules and tablets do not used for medicinal applications. They are just used as health supporting products. The oral consumption of probiotic microorganisms produces a protective effect on the gut flora.[7]

Lots of studies suggest that probiotics have beneficial effects on microbial disorders of the gut, but it is really difficult to show the clinical effects of such products. The probiotic preperations use for traveller’s diarrhoea, antibiotic associated diarrhoea and acute diarrhoea which is showned that they have positive therapeutic effect. Nevertheless, despite the promising evidence, the role of probiotics in human health as well as the safety of their application should be further investigated as the current knowledge of the characteristics that are necessary for their functionality in the gut is not complete.

Microorganisms applied in probiotic products

More than 400 bacterial species exit in human intestinal tract. It is an enormously complex ecosystem that includes both facultative anaerobic and anaerobic microorganisms.[8] The numbers of genera is nearly steady, because they each have their own growth niches. The composition of the gut microflora is constant but can be affected by some factors such as; age, diet, environment, stress and medication.[9] To have a healthy intestine the balance of the bacteria must be maintained but this is difficult as the lifestyles change.

The probiotics which are use to feed both man and animals are shown in the Table 1.

Table 1: Microorganisms applied in probiotic products.

Lactobacillus species	Bifidobacterium species	Others
L. acidophilus	B. bifidum	Enterococcus faecalis
L. rhamnosus	B. animalis	Enterococcus faecium
L. gasseri	B. breve	Streptococcus salivarus subsp.
L. casei	B. infantis	thermophilus
L. reuteri	B. longum	Lactococcus lactis subsp. lactis
L. delbrueckii subsp. bulgaricus	B. lactis	Lactococcus lactis subsp. cremoris
L. crispatus	B. adolascentis	Propionibacterium freudenreichii
L. plantarum		Pediococcus acidilactici
L. salivarus		Saccharomyces boulardii
L. johnsonii		Leuoconostoc mesenteroides
L. gallinarum		
L.plantarum		
L. fermentum		
L. helveticus		

The Effects of Probiotics on Health

There are lots of studies on searching the health benefits of fermented foods and probiotics. However, in most of these studies researchers did not use sufficient test subjects or they use microorganisms were not identified definitely.[10] So, while a number of reported effects have been only partially established, some can be regarded as well established and clinically well documented for specific strains. These health-related effects can be considered as in the below.[11]

- Managing lactose intolerance.
- Improving immune system.
- Prevention of colon cancer.
- Reduction of cholesterol and triacylglycerol plasma concentrations (weak evidence).
- Lowering blood pressure.
- Reducing inflammation.
- Reduction of allergic symptoms.
- Beneficial effects on mineral metabolism, particularly bone density and stability.
- Reduction of Helicobacter pylori infection.
- Suppression of pathogenic microorganisms (antimicrobial effect).
- Prevention of osteoporosis.
- Prevention of urogenital infections.

Lactose Intolerance

Most of human commonly non-Caucasians become lactose intolerant after weaning. These lactose intolerant people can not metabolize lactose due to the lack of essential enzyme β-galactosidase. When they consume milk or lactose-containing products, symptoms including abdominal pain, bloating, flatulence, cramping and diarrhoea ensue. If lactose passes through from the small intestine, it is converted to gas and acid in the large intestine by the colonic microflora. Also the presence of breath hydrogen is a signal for lactose maldigestion. The studies provide that the addition of certain starter cultures to milk products, allows the lactose intolerant people to consume those products without the usual rise of breath hydrogen or associated symptoms.[12,13]

The beneficial effects of probiotics on lactose intolerance are explained by two ways. One of them is lower lactose concentration in the fermented foods due to the high lactase activity of bacterial preparations used in the production. The other one is; increased lactase active lactase enzyme enters the small intestine with the fermented product or with the viable probiotic bacteria.

When the yogurt is compared with milk, cause the lactose is converted to lactic acid and the yogurt consist of bacterial β-galactosidase enzyme; it is suitable end beneficial to consume by lactose intolerants. Furthermore, the LAB which is used to produce yogurt, Lactobacillus bulgaricus and Streptococcus thermophilus, are not resistant to gastric acidity. Hence, the products with probiotic bacteria are more efficient for lactose intolerant human. It is thought that the major factor improves the digestibility by the hydrolyses of lactose is the bacterial enzyme β-galactosidase. Another factor is the slower gastric emptying of semi-solid milk products such as yogurt. So the β-galactosidase activity of probiotic strains and other lactic acid bacteria used in dairy products is really important.

β-galactosidase activity within probiotics varies in a huge range. It has to be considered both the enzyme activity of probiotic strain and the activity left in the final product for their use in lactose intolerant subjects.[14]

Immune System and Probiotics

The effects of immune system are promising. However, the mechanism is not well understood. Human studies have shown that probiotic bacteria can have positive effects on the immune system of their hosts.[15]

Several reserchers have studied on the effects of probiotics on immune system stimulation. Some in vitro and in vivo searchs have been carried out in mice and some with human. Data indicate that oral bacteriotherapy and living bacteria feeding in fermented milks supported the immune system against some pathogens. Probiotics affect the immune system in different ways such as; producing cytokines, stimulating macrophages, increasing secretory IgA concentrations. Some of these effects are related to adhesion while some of them are not.

Link-Amster examined whether eating fermented milk containing Lactobacillus acidophilus La1 and bifidobacteria could modulate the immune response in human. They give volunteers the test fermented milk over a period of three weeks during which attenuated Salmonella typhi Ty21a was administered to mimic an enteropathogenic infection. After three weeks, the specific serum IgA titre rise to S.typhi Ty21a in the test group was >4-fold and significantly higher ($p=0.04$) than in the control group which did not ate fermented foods but received S. typhi Ty21a. The total serum IgA increased. These results showed that LAB which Cn survive in the gastrointestinal tract can act as adjuvants to the humoral immune response.[16]

Perdigon et al.feed the mice with lactobacilli or yogurt and it stimulated macrophages and increased secretory IgA concentrations.[17] Also in a human trial Halpern feed human with 450 g of yogurt per day for 4 months and at the end a significant increase is observed in the production of γ-interferon.

Diarrhea

Diarrhea is many causes and many types so it is difficult to evaluate the effects of probiotics on diarrhea. But there are lots of searchs and evidence that probiotics have beneficial effects on some types of dierrhea. Diarrhea is a severe reason of children death in the worldwide and rotavirus is its common cause. In the treatment of rotavirus dierrhea, Lactobacillus GG is reported really effective. The best documented probiotic effect is shortened duration of rotavirus diarrhea using Lactobacillus GG. It has been given proof in several studies around the world by some researchers. Also Lactobacillus acidophilus LB1, Bifidobacterium lactis and Lactobacillus reuterii are reported to have beneficial effects on shortening the diarrhea. One of types of dierrhea is traveller's diarrhea (TD) which affects the healthy travellers not only in developing countries but also in Europe. Probiotics have beneficial effects in preventing some forms of TD. Some researcher evaluated the efficacy of Lactobacillus GG in preventing diarrhea in 820 people travelling from Finland to Turkey. Antibiotic therapy causes mild and severe outbreaks of diarrhea. The normal microflora may be suppresed during the microbial therapy and resulting with filling with pathogenic strains. The changes of microflora may also ancourage the resistant strains at least Clostridium difficile which is the reasan of antibiotic associated diarrhea (AAD). Several clinical trails have used Saccharomyces boulardii, Lactobacillus spp. and Bifidobacterium spp. in AAD.[18,19]

Probiotics which are able to restore and replace the normal flora should be used. Also they shoukd be used in high risk patients such as old, hospitalised or immunocompromised. Studies with Saccharomyces boulardii proved that Clostridium difficile concentraiton is decreased in the presence of Saccharomyces boulardii.[20]

Cancer

Epidemiological studies point out that if the consumption of saturated fats increases in the diet, the occurrence of colon cancer increases in Western World. Bacterial enzymes (β-glucornidase, nitroreductase and azoreductase) convert precarcinogens to active carcinogens in the colon. It is thought that probiotics could reduce the risk of cancer by decreasing the bacterial enzymes activity. Although the exact mechanism for the anti tumor action is not known, some suggestions have been proposed by McIntosh as follows:

1. Carcinogen/procarcinogen are suppressed by binding, blocking or removal.
2. Suppressing the growth of bacteria with enzyme activities that may convert the procarcinogens to carcinogens.
3. Changing the intestinal pH thus altering microflora activity and bile solubility.
4. Altering colonic transit time to remove fecal mutagens more efficiently.
5. Stimulating the immune system.[21]

There are in vitro and in vivo evidences not only from animal studies but also from human studies that probiotics have beneficial effects on suppression of cancer. Oral administration of lactic acid bacteria has been shown to reduce DNA damage caused by chemical carcinogens, in gastric and colonic mucosa in rats. The consumption of lactobacilli by healthy volunteers has been demonstrated to reduce the mutagenicity of urine and feaces associated with the ingestion of carcinogens in cooked meat. When it comes to epidemiological studies, they show an association between fermented dairy products and colorectal cancer. The consumption of a large quantity of dairy products especially fermented foods like yogurt and fermented milk with containing

Lactobacillus or Bifidobacterium may be related to a lower occurrence of colon cancer.[22,23] A number of studies have shown that predisposing factors (increases in enzyme activity that activate carcinogens, increase procarcinogenic chemicals within the colon or alter population of certain bacterial genera and species) are altered positively by consumption of certain probiotics.

Cholesterol Reduction

Lots of researchers proposed that probiotics have cholesterol reduction effects. However, the mechanism of this effect could not been explained definitely. There are two hypotheses trying to explain the mechanism. One of them is that bacteria may bind or incorporate cholesterol directly into the cell membrane. The other one is, bile salt hydrolysis enzymes deconjugate the bile salts which are more likely to be exerted resulting in increased cholesterol breakdown.

A study on the reduction of cholesterol was showed that Lactobacillus reuteri CRL 1098 decreased total cholesterol by 38% when it is given to mice for 7 days in the rate of 104 cells/day. This dose of Lactobacillus reuteri caused a 40% reduction in triglycerides and a 20% increase in the ratio of high density lipoprotein to low density lipoprotein without bacterial translocation of the native microflora into the spleen and liver.[24]

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.[25,26]

Probiotics and 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.[27,28]

Nondairy food applications include soy based products, nutrition bars, cereals, and a variety of juices as appropriate means of probiotic delivery to the consumer.[29,30] The factors that must be addressed in evaluating the effectiveness of the incorporation of the probiotic strains into such products are, besides safety, the compatibility of the product with the microorganism and the maintenance of its viability through food processing, packaging, and storage conditions. The product's pH for instance is a significant factor determining the incorporated probiotic's survival and growth, and this is one of the reasons why soft cheeses seem to have a number of advantages over yoghurt as delivery systems for viable probiotics to the gastrointestinal tract.[31,32] Current technological innovations provide ways to overcome probiotic stability and viability issues offering new options for their incorporation in new media and subsequent satisfaction of the increasing consumer demand. Microencapsulation technologies have been developed to protect the bacteria from damage caused by external environment. By the introduction of a straw delivery system containing a dry form of the probiotic bacterium beverage manufacturers can now provide it to the consumer. In addition, viable spores of a spore forming probiotic are available in the market offering advantages during processing. In the same time, the potential of lantibiotics'—substances with antimicrobial properties—production by bifidobacteria is being explored in order to be applied in the food area.[33,34]

Dairy products

In the production of probiotics an important factor is the food substrate. Besides buffering the bacteria through the stomach, it may contain functional ingre- dients that interact with the probiotics, altering their ac-tivities. Fat content, type of protein, carbohydrates and pH can affect probiotic growth and survival. Dairy products are especially considered as ideal vehicle for delivering probiotic bacteria to the human gastrointestinal tract. The matrices used most frequently are cheese, yoghurt, ice cream and other dairy products.[35,36]

The most common means to incorporate probiotics to fermented milk include: (i) addition of probiotics to-gether with the starter cultures (DVI culture); (ii) the production of two batches separately, one containing the probiotic microorganism in milk to achieve a high con-centration of viable cells and another with starter cul-tures. When the fermentation stages are completed, the batches are mixed; (iii) the use of a probiotic microorga-nism as a starter culture. In this situation, the time of fermentation is generally higher than traditional proces-ses using non-probiotic starter cultures.[37] In this respect, it is necessary to consider the supplementation of the culture medium and the production conditions (e.g. incubation temperatures), since metabolites pro-duced by probiotics can lead to off-flavours.[38,39] In addition, the probiotic strains must be compatible with starter cultures, since the latter could produce inhibitory substances that damage the probiotics.[40]

Yoghurts with high fat content showed inhibitory effects against probiotic cultures, particularly B. bifidum BBI. The supplementation with vitamins (e.g. as-corbic acid) has been reported to improve the viability of L. acidophilus in yoghurts. The addition of sub-stances such as whey protein may also enhance the via-bility of some probiotics, probably due to their buffering property. In addition, the employment of prebiotics in yoghurt formulations could stimulate the growth and activity of probiotics. In this regard, fructooligossacha-rides showed to be most effective in maintaining the probiotic viability.[41]

The utilization of probiotics in the cheese elabora-tion presents some challenges: low moisture content; presence of salt; starter cultures competing for nutrients and developing acid and flavour during the maturation stage; extended storage (over 3 months), which can in-fluence biochemical activities, redox potential, and alter the cheese structure. Moreover, probiotics should sur-vive the entire shelf life of the cheese, not produce meta-bolites that affect the cheese quality and the starter cul-ture activities, and also, they should be able to grow in starter culture media (e.g. whey-based and phage inhi-bitory media). Several studied reported that Turkish white brined, Feta-type, Ched-dar, Philippine white soft, Edam, Emmental, Domiati, Ras, Herrgård cheese, Quarg, and cheese-based dips can be compared with yoghurts in delivering probiotics.

The proteolytic patterns can be influenced by the addition of probiotic strains.[42] As dairy starter adjuncts has lead to high concen-tration of free amino acids by a secondary proteolysis during ripening, and this was reduced when the cheese was stored at 4 ^{o}C. It was found that all probiotic strains survived the manufacturing process and produced a level of acetic acid higher than the control Cheddar cheese.

Other vehicles that could be used to deliver probiotics are ice cream and frozen dairy desserts. These products have the advantage to be stored at low temperatures, which makes them less exposed to abusive temperatures having higher viability at the time of consumption.[43] Besides, they are consumed by people of all ages and are composed of milk proteins, fat and lactose as well as other compounds that are required for bacterial growth. However, some probiotic species showed a decrease in the viability during the manufacture and freezing of ice cream. Some prebiotics could be used to improve the characteristics of the probiotic ice creams. Inulin de-monstrated to be beneficial to the firmness, melting pro-perties and dripping time of the ice creams.[44] Be-sides, the inulin level in ice cream enhanced the viability of L. acidophilus and B. lactis. The addition of oligo-fructose in low-fat ice cream also improved the survival of L. acidophilus La-5 and B. animalis ssp. lactis Bb-12 during storage at –18 °C for 90 days. However, to efficiently produce probiotic ice cream, it is important to select oxygen-resistant strains since the incorporation of air (overrun) in the mixture occurs in the production process, which is harmful to microaerophilic and an-aerobic strains such as Lactobacillus sp. and Bifidobacter-ium sp. This type of challenge can be resolved by the use of microencapsulation technique. As an alternative, aerated dairy dessert (e.g. chocolate mousse) has also been used as a potential agent to deliver probiotics.

Safety

In theory, probiotics may be responsible for four types of side effects in susceptible individuals: systemic infections, deleterious metabolic activities, excessive im-mune stimulation, and gene transfer.[45] In practice, however, lactobacilli and bifidobacteria (and probiotics based on these organisms) are extremely rare causes of infections in humans.[46,47] This lack of pathogenicity extends across all age groups and also to immunocom-promised individuals.

Traditional dairy strains of lactic acid bacteria (LAB) have a long history of safe use. LAB, including different species of Lactobacillus and Enterococcus, have been con-sumed daily since humans started to use fermented milk as food. Probiotic species such as Lactobacillus acidophilus have been safely used for more than 70 years. However, the safety aspects always have to be considered and possible adverse effects should be continuously evalu-ated, as illustrated by recent literature. Members of the genera Lactococcus and Lactobacillus are most commonly given the GRAS status, whilst members of the genera Streptococcus, Enterococcus and some other genera of LAB are considered opportunistic pathogens.[48,49]

The safety of probiotics has been considered in re-views and clinical reports which have drawn attention to isolate cases of human bacteraemia.[50,51] Available data indicate that no harmful effects have been observed in controlled clinical studies with lactobacilli and bifidobacteria.

Three approaches can be used to assess the safety of a probiotic strain: studies on the intrinsic properties of the strain, studies on the pharmacokinetics of the strain (survival, activity in the intestine, dose–response relation-ships, faecal and mucosal recovery) and studies search-ing for interactions between the strain and the host.

The Joint FAO/WHO Expert Consultation on Evalu-ation of Health and Nutritional Properties of Probiotics in Food Including Powder Milk with Live Lactic Acid Bacteria recognized the need for guidelines to set out a systematic approach for the evaluation of probiotics in food in order to substantiate the health claims. Conse-quently, a Working Group was convened by FAO/WHO to generate guidelines and recommend criteria and meth-odology for the evaluation of probiotics, and to identify and define what data need to be available to accurately substantiate health claims. The aims of the Working Group were to identify and outline the minimum requirements needed for probiotic status. Then, guidelines were pre-pared in 2002 to meet this objective. These guidelines are available in: Joint FAO/WHO Working Group Re-port on Drafting Guidelines for the Evaluation of Pro-biotics in Food.[52]

New Trends in Probiotic Products and Processing

In general, consumer's understanding of the poten-tial benefits of foods containing viable bacteria/probiotics is poor, particularly in the countries without a tradition of cultured/sour dairy products. There are many barriers to communicating messages about probiotics and the role of diet in the gut flora modulation. However, in the countries where there have been well planned educatio-nal programmes among consumers and health profes-sionals, the degree of awareness has increased.[53] In the future, health claims may help inform consumers of the potential benefits, but it is crucial that appropriate communication guidelines are adhered to and that all claims are scientifically substantiated.

As it was presented by several scientific publications on probiotics has doubled in the past three years and this recent interest[54] has been further stimulated by several factors: (i) exciting scien-tific and clinical findings using well documented pro-biotic organisms; (ii) concerns over limitations and side effects of pharmaceutical agents; and (iii) consumer's de-mand for natural products. The key to the future of pro-biotics will be the establishment of a consensus on product regulation, including enforcement of guidelines and stand-ards, appropriate clinical studies that define strengths and limitations of products, and basic science studies that uncover the mechanisms of action of strains. Be-sides, the molecular elucidation of the probiotic actions in vivo will help to identify true probiotics and select the most suitable ones for the prevention and/or treatment of a certain illness. In fact, not only new probiotic food must be developed, but the study and develop-ment of new medications to combat diseases should be continously performed.

CONCLUSION

There is scientific evidence supporting the incorporation of probiotics in nutrition as a means of derivation of health benefits. This evidence seems adequate concerning the prevention and treatment of certain conditions while simply promising or even controversial when it comes to others. The best documented effects include bowel disorders such as lactose intolerance, antibiotic-associated diarrhoea and infectious diarrhoea, and allergy, and emerging evidence accumulates concerning their potential role in various other conditions.[55] In the same time as relevant consumer awareness grows, such products are becoming increasingly popular and tend to represent one of the largest functional food markets. Dairy products, particularly yoghurt, continue to be the most important vehicles for delivery of probiotic bacteria to the consumer with the nondairy sector continuously evolving as well, as a result of food technology advances and the growing demand. A virtuous circle is therefore created: as the range of new products with improved sensory appeal widens, consumer acceptance increases and the food industry invests more on this growing market by development of new processes and products.[56] Nevertheless, the development of probiotics for human consumption is still in its infancy. Further research, in the form of controlled human studies, is needed to determine which probiotics and which dosages are associated with the greatest efficacy and for which patients, as well as to demonstrate their safety and limitations. In addition, the regulatory status of probiotics as food components needs to be established on an international level with emphasis on efficacy, safety, and validation of health claims on food labels.[57,58] There is no doubt that we will witness a significant increase in the role of probiotics in nutrition and medicine over the next decade and while their application in the prevention and treatment of various disorders should be considered by medical professionals and promoted by the food industry, this should be done with skepticism and respect to the consumer.

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