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Evaluating the Health Value of Probiotics

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ABSTRACT

Probiotics are defined as live microorganisms, which when administered in adequate amounts, confer a health benefit on the host. Probiotic bacteria have become increasingly popular during the last two decades as a result of the continuously expanding scientific evidence pointing to their beneficial effects on human health. As a result they have been applied as various products with the food industry having been very active in studying and promoting them. Health benefits have mainly been demonstrated for specific probiotic strains of the following genera: *Lactobacillus*, *Bifidobacterium*, *Saccharomyces*, *Enterococcus*, *Streptococcus*, *Pediococcus, Leuconostoc*, *Bacillus*, *Escherichia coli*. The human microbiota is getting a lot of attention today and research has already demonstrated that alteration of this microbiota may have far-reaching consequences. One of the possible routes for correcting dysbiosis is by consuming probiotics. The credibility of specific health claims of probiotics and their safety must be established through science-based clinical studies. As probiotic properties have been shown to be strain specific, accurate identification of particular strains is also very important. On the other hand, it is also demonstrated that the use of various probiotics for immune compromised patients or patients with a leaky gut has also yielded infections, sepsis, fungemia, bacteraemia. Although the vast majority of probiotics that are used today are generally regarded as safe and beneficial for healthy individuals, caution in selecting and monitoring of probiotics for patients is needed and complete consideration of risk-benefit ratio before prescribing is recommended. This review aims to evaluate the preventive and therapeutic effects of probiotics in various health condition and disease.
Keywords: Lactic-acid bacteria, *Lactobacillus*, *Bifidobacterium*, Probiotics, Microorganisms.

INTRODUCTION

Probiotics are microorganisms that contribute some form of health benefit to the host. They can be found in a variety of different foods. They are considered to be live microorganisms which when administered in adequate amounts confer a health benefit on the host. According to the World Health Organization, the successful growth of probiotic bacteria depends on indigestible carbohydrates that are available in thousands of diverse plants and fruits. Collectively the nutrients that probiotics require for "survival" are called prebiotics. The term synbiotic is used for the combination of probiotics and prebiotics. Probiotics are usually consumed in the form of fermented foods with active live cultures such as yogurt [1] [2] [3]. The most commonly used bacterial genera in probiotic food are *Lactobacillus* and *Bifidobacterium.*

Probiotics are believed to play very important roles in regulating correct intestinal function and digestion by balancing intestinal microflora. Probiotics act through diverse microflora. Probiotics act through diverse mechanisms that affect the microbiota. Molecular mechanism facilitates to identify immunomodulation property of probiotics. Traditionally, probiotics are considered to be related with gut health.

However, during the last decade, a rising number of established and proposed beneficial health effects of probiotic bacteria have been reported, including treatment or prevention of urogenital, oral and respiratory tract infections, and prevention or alleviation of allergies, regulation of brain function, atopic disease in infants and prevention of skin infection. These benefits further tend to increase with the development of more advanced research methods utilized in studying the microbe-host interactions [4]. The literature on the health benefits of probiotics has often focused on disease states using either animal models of such diseases or studies in human populations by clinical trial.

Microorganisms that Serve as Probiotics

Taking into consideration their definition the number of microbial species which may exert probiotic properties is impressive. As far as nutrition is concerned only the strains classified as lactic acid bacteria are of significance and among them the ones with the most important properties in an applied context are those belonging to the genera *Lactococcus* and *Bifidobacterium* [5] [6]. Lactic acid bacteria are Gram-positive, catalase-negative bacterial species able to produce lactic acid as main end-product of carbohydrate fermentation. The genus *Bifidobacterium* is therefore rather traditionally than phylogenetically listed among them as they use a separate metabolic pathway. Two other species playing an important role in the food industry, particularly dairy products, although not strictly considered as probiotics are *Streptococcus thermophilus* and *Lactococcus lactis*, two of the most commercially important lactic acid bacteria [7]. It is important to mention that since probiotic activities are strain related, strain identification is recommended in order to establish their suitability and performance for industrial application. This is achieved by a combination of phenotypic tests followed by genetic identification using molecular techniques like DNA/DNA hybridisation, 16SRNA sequencing, and so forth [8] [9].

Essential Properties of Probiotics

It is of utmost importance that the probiotic strain survives the site where it is presumed to be active. For maximum activity, the strain should be able to proliferate and colonize at this specific location. Besides, it should also be tolerated by the immune system. It should not be pathogenic, allergic, or mutagenic/carcinogenic [10]; [11]. Probiotics for human should be generally regarded as safe, with a proven low risk of inducing or being associated with the etiology of disease. The probiotic organisms should preferably be of human origin [12], must be able to survive and grow in the in vivo conditions of the desired site of administration, and thus must be able to tolerate low pH and high concentration of both conjugated and deconjugated bile acids. For successful application in foods, the probiotic used should also be technologically compatible with the food manufacturing process. In addition to that, the foods containing the probiotic bacteria must maintain the characteristic sensory attributes of the traditional food.

Attributes and Benefits of Probiotics

It is now an established fact that the indigenous microbial communities is host specific, location specific, very complex in composition and has beneficial properties to the host. However, it is not precisely known which species of microorganisms play the principal part in these beneficial properties. Some of the major health attributes of probiotics are discussed below.

Antimicrobial properties

The intestinal microbial community is a complex ecosystem, and introducing new organisms into this highly competitive environment is difficult. Thus, organisms that can produce a product that inhibits the growth of existing organisms have a characteristic advantage [13]. The ability of probiotics to establish in the GI tract is enhanced by their ability to eliminate competitors. In different studies on humans and animals, beneficial microorganisms are used to improve the colonization resistance on body surfaces, such as GI, the urogenital, and the respiratory tract.

Bifidobacteria produce acetic and lactic acids in a molar ratio of 3:2 [14]. *Lactobacillus acidophilus* and *Lactobacillus casei* produce lactic acid as the main end product of fermentation. In addition to lactic and acetic acids, probiotic organisms produce other acids, such as hippuric and citric acid. Lactic acid bacteria also produce hydrogen peroxide, diacetyl, and bacteriocin as antimicrobial substances. These inhibitory substances create antagonistic environments for foodborne pathogens and spoilage organisms. Yoghurt bacteria are reported to produce bacteriocin against probiotic bacteria and vice versa [15].

Probiotics and Allergy

Recent evidence suggests that exposure to bacteria in early life may exhibit a protective role against allergy and in this context probiotics may provide safe alternative microbial stimulation needed for the developing immune system in infants. In the same time they improve mucosal barrier function, a property that is considered to contribute in moderating allergic response. The role of intestinal microbiota in allergy is supported by observations of their quantitative as well as qualitative differences among children and infants suffering from allergies and healthy ones, the former exhibiting colonization by a more adult-like type of microflora [16], [17], [18]. These probiotic effects seem to particularly involve food allergy and atopic dermatitis. The latter is a common chronic relapsing skin disorder of infancy and childhood with hereditary predisposition being an important component of its pathogenesis together with the individual's exposure to environmental allergens. A limited number of strains have been tested for their efficacy in the treatment and prevention of allergy in infants.

In a study involving breast fed infants suffering from atopic eczema *B. lactis* and *L. rhamnosus* GG were found to be effective in decreasing the eczema severity. Furthermore *L. rhamnosus* GG has been found successful in preventing the occurrence of atopic eczema in high risk infants, when supplied prenatally to selected mothers who had at least one first degree relative with atopic eczema, allergic rhinitis, or asthma [19]. Probiotics however have not been very successful in alleviating symptoms of asthma [20].

As far as food allergy is concerned, it is described as an immunologically mediated adverse reaction against dietary antigens leading to secondary intestinal inflammation and disturbances. The mechanisms of the immune modulating effect of *L. rhamnosus* GG are not entirely understood but seem to be related to the antigen's transport across the intestinal mucosa [21]. Recently the use of probiotic preparations in adults with milk hypersensitivity not lactose intolerance has been studied, concluding that certain strains may suppress the milk-induced inflammatory response and improve allergy symptoms. Nevertheless further study in the field is necessary [22], [23].

Anticarcinogenic properties

[24] reported that the introduction of *L. acidophilus* into the diet lowers the incidence of chemically induced colon tumors in rats. Later, the same authors also suggested that diet and antibiotics can lower the generation of carcinogens in the colon and reduce chemically induced tumors [25]. These effects appear to be mediated through the intestinal microbial communities. A possible mechanism for these anticancer effects relies on inhibiting intestinal bacterial enzymes that convert procarcinogens to more proximal carcinogens [26]. This approach can be expanded in the future by testing probiotics for their ability to inhibit the growth of organisms normally found in the flora that have high activities of enzymes such as b-glucuronidase [27], nitroreductase, azoreductase, and b-glycosidase or the capability for nitrosation.

The sixth most commonly diagnosed cancer in the world is hepatitis B virus. Consumption of foods, contaminated with aflatoxins, is also established causes of liver cancer. Aflatoxin B1 (AFB1) causes characteristic genetic changes in the p53 tumor suppressor gene and ras protooncogenes. Some probiotic bacterial strains have been successfully shown to bind and neutralize AFB1 in vivo and thus reduce the bioabsorption of the toxin from the gut [28] [29].

Addition of probiotic *Bifidobacterium longum* to the diet of rats has been shown to exert a strong antitumor activity on colonic mucosa by reducing the expression level of ras-p21 expression and cell proliferation [30]. Lactobacillus GG administration determined the up- and down regulation of 334 and 92 genes, respectively, by affecting the expression of genes involved in immune response and inflammation [transforming growth factor beta (TGF-b) and tumor necrosis factor (TNF) family members, cytokines, nitric oxide synthase 1, defensin alpha-1], apoptosis, cell growth and cell differentiation (cyclins and caspases, oncogenes), cell–cell signaling (intracellular adhesion molecules and integrins), cell adhesion (cadherins), signal transcription and transduction [31]. Probiotics have also been found by several researchers to decrease fecal concentrations of enzymes (glycosidase, B-glucuronidase, azoreductase, and nitroreductase) and secondary bile salts and reduce the absorption of harmful mutagens that may contribute to colon carcinogenesis [3]. Normal intestinal flora can influence carcinogenesis by producing enzymes (glycosidase, B-glucuronidase, azoreductase, and nitroreductase) that transform precarcinogens into active carcinogens [3]; [4]. *Lactobacillus acidophilus and L. casei* supplementation in humans helped to decrease the levels of these enzymes [8].

In mice, these bacterial enzymes were suppressed with the administration of Lactobacillus GG [11]. Several mechanisms have been proposed as to how lactic acid bacteria may inhibit colon cancer, which includes enhancing the host's immune response, altering the metabolic activity of the intestinal microbial communities, binding and degrading carcinogens, producing antimutagenic compounds, and altering the physiochemical conditions in the colon [21]; [22]. Oral administration of LAB has been shown to effectively reduce DNA damage, induced by chemical carcinogens, in gastric and colonic mucosa in rats [29].

Metabolically active L. acidophilus cells, as well as an acetone extract of the culture, prevented MNNG-induced DNA damage, while heat-treated L. acidophilus was not antigenotoxic. Azomethane-induced colon tumor development was also suppressed with a decrease in colonic mucosal cell proliferation and tumor ornithine decarboxylase and ras-p21 activities [7]. There was a report on the antitumorigenic activity of the prebiotic inulin, enriched with oligofructose, in combination with the probiotics Lactobacillus rhamnosus and Bifidobacterium lactis in the azoxymethane (AOM)-induced colon carcinogenesis rat model [15]. Other lactic acid bacteria have also shown the ability to lower the risk of colon cancer; however, the relationship between enzyme activity and cancer risk needs further investigation.

Infectious Diarrhoea

Treatment and prevention of infectious diarrhoea are probably the most widely accepted health benefits of probiotic microorganisms. Rotavirus is the most common cause of acute infantile diarrhoea in the world and a significant cause of infant mortality. The virus replicates in the highly differentiated absorptive columnar cells of the small intestinal epithelium and the normal microflora seems to play an important role in the host response to the infection, as it has been shown that absorption of antigens is more enhanced in germ-free than in normal mice [25]. Probiotic supplementation of infant formulas has been aimed both at the prevention of rotaviral infections and the treatment of established disease. Well-controlled clinical studies have shown that probiotics such as *L. rhamnosus* GG, *L. reuteri*, *L. casei* Shirota, and *B. animalis* Bb12 can shorten the duration of acute rotavirus diarrhoea with the strongest evidence pointing to the effectiveness of *L. rhamnosus* GG and *B. animalis* Bb12 [31].

The proposed mechanisms include competitive blockage of receptor site signals regulating secretory and motility defences, enhancement of the immune response, and production of substances that directly inactivate the viral particles. In addition to rotavirus infection there is evidence that certain food as well as nonfood probiotic strains can inhibit the growth and adhesion of a range of diarrhoeal syndromes. The benefit of probiotics such as *L. reuteri*, *L.*

rhamnosus GG, *L. casei*, and *S. boulardii* in reducing the duration of acute diarrhoea in children has been demonstrated, [7], [8]. For example, in a prospective, randomized, controlled French study conducted among children in day care, the administered probiotic yoghurt product containing *L. casei* shortened the mean duration of diarrhea significantly compared to the conventional one [4].
Several studies have investigated the efficacy of probiotics in the prevention of travellers' diarrhoea in adults. Although results are quite contradictory, due to differences in study populations, type of probiotic being investigated, applied doses, as well as trip destination and traveller compliance, *L. rhamnosus* GG, *S. boulardii*, *L. acidophilus,* and *B. bifidum* seem to exhibit significant efficacy [13]. Furthermore, numerous animal studies have indicated an inhibitory effect of probiotics against enteropathogens mainly through the production of bacteriocins [4]

CONCLUSION

In conclusion, information obtained from the *in vivo* and *in vitro* studies showed probiotics are suitable option for treatment and prevention of diseases without side effects. Probiotics have been reported to be effective in improving the insulin resistance. Beneficial effects on blood glucose levels are considered as one of the reasons in improving insulin resistance. Probiotic have positive effects on oxidative stress, metabolic lipid profile and high sensitivity C-reactive protein in T2DM patients.

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