

Role of probiotics in health and disease: A review

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Abstract

For some decades now, bacteria known as probiotics have been added to various foods because of their beneficial effects for human health. The mechanism of action of probiotics is related to their ability to compete with pathogenic microorganisms for adhesion sites, to antagonize these pathogens or to modulate the host's immune response. The potential application of probiotics includes prevention and treatment of various health conditions and diseases such as gastrointestinal infections, inflammatory bowel disease, lactose intolerance, allergies, urogenital infections, cystic fibrosis, various cancers, reduction of antibiotic side effects, in oral health such as prevention of dental caries, periodontal diseases and oral malodour and many other effects which are under investigation.

The results of many of these clinical investigations suggests that probiotics may be useful in preventing and treating various health conditions and diseases. However, many of these clinical studies require validation so as to apply these results to clinical realm. The role of clinical trials is instrumental in such investigations and in near future the results of such trials will decide the usefulness of probiotics in health and disease. This article strives to summarize the currently available data on the potential benefits of probiotics in health and disease.

Keywords: Bifidobacterium, Immunomodulation, Lactobacilli, Probiotics.

Introduction

Each day, every human being ingests a large number of living microorganisms, predominantly bacteria. Although these organisms are naturally present in food and water, they can also be deliberately added during the processing of foods such as sausages, cheese, yoghurt and fermented milk products. For several decades now, bacteria called probiotics have been

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added to some foods because of their beneficial effects for human health.^{1,2}

Endorsed by the Food and Agriculture Organization and the World Health Organization, the definition of probiotics, in 2001,³ describes them as live microorganisms which when administered in adequate amounts confer health benefits on the host. Commonly, most of the species ascribed as having probiotic properties belong to the genera *Lactobacillus* and *Bifidobacterium*. These bacteria are generally regarded as safe because they can reside in the human body causing no harm and, on the other hand, they are key microorganisms in milk fermentation and food preservation and used as such from the dawn of mankind.⁴

Probiotic strains are now widely used to give consumers a health benefit substantiated in a range of randomized clinical trials. The list of disease conditions that may benefit from bacteria includes systemic and infectious diseases such as acute diarrhoea and Crohns disease, cardiovascular disease, urogenital infections, oropharyngeal infections, cancers, food allergies, lactose intolerance, cystic fibrosis, reduction of antibiotic associated side effects, dental and oral disorders-prevention of dental caries, periodontal disease and treatment of oral malodour and this list tends to increase with the advent of more sophisticated research methods utilized in studying the microbe-host interactions.⁵

Over the years, the scientific interest to discover, asses and analyze species with probiotic properties has intensively grown. This article aims to summarize in the light of currently available literature about probiotics and their role in health and disease.

Historical Perspective:

The role of beneficial bacteria on human health stems from the work of the bacteriologist and Nobel Prize laureate Ilye Metchnikoff in the turn of 20th century. Studying longevity and general health of a Bulgarian population dwelling in the rhodopes mountains and fed basically on dairy products, the scientist introduced the idea that lactic acid bacteria in yogurt may neutralize

deleterious effects of gut pathogens thus extending life span. He further contributed to the adoption of the name of the species, *Lactobacillus bulgaricus*, one of the two essential yoghurt starter microorganisms. This also meant the birth of modern dairy industry.⁴

Mechanism of Action of Probiotics:

The mechanism of action of probiotic microorganisms can be explained by enhancement of the non-specific and specific immune response of the host, production of antimicrobial substances and competition with pathogens for binding sites. Further probiotics show adhesion and colonization (at least transitory) of the human body which may increase their retention time thus facilitating prolonged probiotic activity.⁵⁻⁷

Currently Used Probiotics:

The following microorganisms are commonly used as probiotics:

A. Bacteria:

i) *Lactobacillus*: *acidophilus*, *sporogenes*, *plantarum*, *rhamnosum*, *delbrueck*, *reuteri*, *fermentum*, *lactus*, *cellobiosus*, *brevis*. ii) *Bifidobacterium*: *bifidum*, *infantis*, *longum*, *thermophilum*, *animalis*. iii) *Streptococcus*: *lactis*, *cremoris*, *alivarius*, *intermedius*. iv) *Leuconostoc*. v) *Pediococcus*. vi) *Propionibacterium*. vii) *Bacillus*. viii) *Enterococcus*. ix) *E. faecium*.

B. Yeast and Moulds:

A. cerevisiae, *A. niger*, *A. oryzae*, *C. Pantolopesii*, *Sacharomyces boulardii*.

Table denotes the probiotics provided in food products throughout the world.⁸

Indications of Probiotics:

The following are the areas where probiotics may be indicated:

Rotavirus diarrhea, reduction of antibiotic-associated side effects, food allergies and lactose intolerance, atopic eczema, prevention of vaginitis, urogenital infections, irritable bowel syndrome, inflammatory bowel disease, cystic fibrosis, traveller's diarrhea, enhance oral vaccine administration, *H. pylori* infection, various cancers, oral and dental conditions such as dental Caries, periodontal diseases and oral malodour.

Prevention of Diseases:

Probiotics may selectively inhibit the growth of pathogenic bacteria. Probiotics like *S. faecalis*, *C. butyricum* and *B. mesentericus* promote the growth of *bifidobacterium* which selectively inhibits the growth of

Table: Probiotics that are used in various products in the world.

Probiotic Bacteria	Product	Country
<i>Bifidobacterium bifidum</i>	Infant Formula	Turkey
<i>B. breve</i>	Drink	Japan
<i>B. lactis</i>	Infant formula	Israel
	Drink	South Africa, Chile
<i>B. longum</i> SBT-2928	Milk	Japan
<i>B. longum</i> BB536	Milk	Japan
<i>B. sp</i>	Drink	UK
<i>L. acidophilus</i>	Yoghurt	Chile, USA
	Drink	UK
	Yoghurt Drink	Austria
<i>Lactobacillus acidophilus</i> 5	Yoghurt	UK
<i>L. acidophilus</i> 7	Drink	Austria
<i>L. acidophilus</i> NCFB 1748	Yoghurt	Denmark
<i>L. acidophilus</i> SBT-2062	Milk	Japan
<i>L. bulgaricus</i>	Drink	France, Austria
<i>L. casei</i> Shirota	Drink	Argentina, Australia, Belgium, Brazil, Brunei, China, Germany, Hong Kong, Indonesia, Japan, Korea, Luxembourg, Mexico, Netherlands, Philippines, Singapore, Taiwan, Thailand, Uruguay, UK, New York/USA
	USA	
<i>L. casei</i>	Drink	USA
	Yoghurt	France, Colorado-Arizona/USA
<i>L. helveticus</i>	Milk drink	Finland
	Drink	Iceland
<i>L. johnsonii</i> Lal	Yoghurt	Switzerland, Germany, Japan, Austria
<i>L. lactis</i> L1A	Yoghurt	Sweden
<i>L. plantarum</i> 299v	Fruit drink	Sweden
	Ice cream	Sweden
	Recovery drink	Sweden
	Oat mixture	Sweden
<i>L. reuteri</i>	Infant formula	Israel
	Cheese	Spain, Portugal, Finland
	Milk	Japan, Finland
	Yoghurt	USA, Finland
	Yoghurt drink	UK
	Ice cream	Finland
	Fruit drink	Finland
<i>L. rhamnose</i> ATCC53103	Yoghurt	Australia, Papua New Guinea, Indonesia

pathogenic bacteria and also produces glutamine that maintains mucosal integrity and enhances the protection of mucosal barrier.^{9,14}

Effectiveness in Controlling Various Types of Diarrhoea:

Studies have reported effectiveness of probiotics in treating diarrhoea of various nature, especially in

traveller's diarrhoea, antibiotic induced diarrhoea and diarrhoeal diseases in young children caused by rotavirus.^{11,12}

Effects on Mutations and Carcinogens:

Various pathogenic bacterias like E.coli [enterohaemorrhagic E. coli (EHEC) strain, extraintestinal E. coli (ExPEC)] and Clostridium perfringens are mutagenic and associated with the development of colorectal cancers.^{13,14} Probiotics such as bifidobacteria can selectively inhibit growth of these pathogenic bacterias and develop a favourable microenvironment which modulates the bacterial enzymes. Purified bifidobacteria has cell wall antitumour activities and induces activation of phagocytes to destroy growing tumour cells.^{13,14}

Irritable Bowel Syndrome (IBS):

The etiology of irritable bowel syndrome is not well understood. It is a multifactorial condition making it difficult to treat such patients. Hunter et al¹⁵ demonstrated a symptomatic improvement in patients with the use of Enterococcus faecium strain PR88 as oral probiotic. However further studies are needed to justify the role of probiotics in such cases.¹⁶

Probiotics and Food Allergies:

Probiotics have shown beneficial effects in patients with food allergies, their effects are due to additive action on immunologic and non-immunologic defense barriers of the gut. Lactobacilli modify the immunomodulatory properties of native food protein. Thus, probiotics influence the immune system by activating the lymphoid cells of the gastrointestinal lymphoid tissue.¹⁷⁻²⁰

Atopic Dermatitis and Probiotics:

Studies have been conducted to assess the role of probiotics in atopic disease. Kirjavainen PV et al reported an alleviation of atopic eczema and subjective symptoms in study population with oral supplementation of viable and heat inactivated probiotic bacteria.²¹

Probiotics and Vaccine Adjuvants:

Isolauri et al²² observed an increase in rotavirus specific IgM secreting cells when the children were given Lactobacillus GG as an adjuvant to an oral vaccine to rotavirus as compared to placebo on 8th post-vaccination day. LGG also increased IgA and IgM seroconversion when measured in paired sera measured prior to vaccination, and after 30 days of vaccination.²²

Probiotics and Urinary Tract Infections:

It has been known that lactobacilli has a preventive effect against urinary tract infection(UTI) in females.²³ Studies have shown that a two strain combination of distal urethral isolate L rhamnosus GR-1, selected primarily for its anti gram-negative activities and resistance to spermicide and L fermentum B-54 replaced more recently by RC-14, for anti gram-positive cocci activities and hydrogen peroxide production. Results from various studies indicate that the recurrence rate of UTI can be significantly reduced using one or two capsules vaginally per week for a year with no side effects or yeast infections.²³⁻²⁶

Blood Cholesterol Levels and Probiotics:

Probiotics have been reported to have cholesterol lowering properties in humans. The mechanism of action is that probiotics cause direct assimilation of lipids, convert them into other metabolites and end products, which affects synthesis of cholesterol. Many studies have been conducted but none of the studies had shown statistical significant changes in cholesterol levels.²⁷

Inflammatory Bowel Diseases:

Probiotics by their immunomodulatory and bowel flora manipulating properties, show a promising effect in treatment of chronic inflammatory bowel disease.²⁸ As only a few clinical trials are reported in the current indexed literature further studies are needed to evaluate the true place of probiotics within a treatment regimen for chronic inflammatory bowel disease.

Oral Health

Probiotics and Dental Caries:

Dental caries is a multifactorial disease of bacterial origin that is characterized by acid demineralization of the tooth enamel. To have a beneficial effect in limiting or preventing dental caries, a probiotic must be able to adhere to dental surfaces and integrate into the bacterial communities making up the dental biofilm. It must also compete with and antagonize the cariogenic bacteria and thus prevent their proliferation. Comelli and colleagues reported that of 23 bacterial strains used in the dairy industry, Streptococcus thermophilus and Lactobacillus lactis ssp. lactis were the only ones with the capacity to integrate into a biofilm present on a hydroxyapatite surface and to interfere with development of the cariogenic species Streptococcus sobrinus. More recently, it was demonstrated that isolates of W. cibaria had the capacity to inhibit, both in vitro and in

vivo, biofilm formation by *S. mutans* and to prevent proliferation of this bacterial strain.²⁹⁻³¹

Probiotics and Periodontal Diseases:

Periodontal disease is classified into 2 types: gingivitis and periodontitis. Gingivitis is characterized by inflammation limited to the unattached gingiva, whereas periodontitis is a progressive, destructive disease that affects all supporting tissues of the teeth, including the alveolar bone.³² Since the primary etiological factors for the development of periodontal disease are bacteria in supra- and subgingival biofilm, efforts for disease prevention and treatment are mainly focused on pathogen reduction and strengthening of the epithelial barrier, thus contributing to decreased susceptibility to infection. Probiotic bacteria, generally regarded as safe, may favour periodontal health if able to establish themselves in oral biofilm and inhibit pathogen growth and metabolism. Only few clinical studies outlining probiotic effectiveness in periodontal disease have been published.^{33,34} Therefore, data on probiotics with specific target periodontal structures are mainly from laboratory experiments. Patients with periodontal disease who used chewing gum or lozenges containing probiotics saw their periodontal status improve.

Halitosis:

Halitosis, foetor ex ore, 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 sulfur compounds (VSC) predominantly by Gram negative anaerobes residing in periodontal pockets and on the tongue dorsum.³⁵ It has been shown that bacteriotherapy can also improve this condition. The replacement of bacteria implicated in halitosis by colonization with probiotic bacterial strains from the indigenous oral microbiota of healthy humans may have potential application as adjuncts for the prevention and treatment of halitosis.³⁵

Conclusions

Probiotics represent a new area of research in medicine, the examination of the close relationships between food and health. Preliminary data obtained by various research laboratories have been encouraging, but numerous randomized clinical studies will be required to clearly establish the potential of probiotics in preventing and treating various diseases. Such studies will allow identification of the probiotics that are best suited to specific use, as well as the most appropriate vehicles: food products (cheese, milk, yoghurt) or

supplements (chewing gum, lozenges). The existence of probiotics in the indigenous microflora of humans warrants exploration because these bacteria offer the advantage of being perfectly adapted to the human oral ecosystem.

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