

THERAPEUTIC PROPERTIES OF PROBIOTICS

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Abstract

Probiotics are known to humans as foods having enormous health benefits. Apart from holding nutritional values, probiotics are also a good source of immunity for the consumers. The history of probiotic use is as old as 2000BC and still holds importance among daily human life. Use of probiotics in daily life can enhance the immunity of humans in a natural way and reduce the administration of synthetic drugs for common gastrointestinal disorders. Different species of microorganisms are employed as probiotics for their various roles. These can be usually seen in humans amongst the normal microflora and serve in different ways to the host. Species of *Lactobacillus*, *Lactococcus*, *Bifidobacterium*, *Enterococcus*, *Saccharomyces* *Streptococcus*, etc. are some common microorganisms used as probiotics. Most of these are a natural inhabitant of the human body and can be found in the gut, buccal cavity, vagina and other parts of the body.

Keywords: Probiotic, health benefits, common organism, safety guidelines

Introduction

The consumption of fermented processed foods by humans has been practiced for decades. These foods that contain a range of microorganism are known to hold plenty of health benefits to humans. These fermented foods were found to be probiotic in nature.^[1] In the present era, probiotic concept is not novel to the society. The first history for the use of probiotic dated back to 2000BC where man knew how to preserve milk for a long time without spoilage.^[2, 3]

Definition of probiotics

The interpretation of probiotic was by scientific approach, after Lilly and Stillwell (1965) coined the concept. The term probiotic evolved in 1974, and is currently one of the major commercial products on the market. In 1989, Fuller redefined probiotic as “a live microbial feed supplement

that beneficially affects the host animal by enhancing its microbial intestinal balance". Nevertheless, according to the FAO / WHO in 2002, the word probiotic is described as "living microorganism that provides health benefits when consumed in sufficient quantities".^[4] The term probiotics was derived from the Latin "pro" preposition, meaning "for" and the Greek word "biotic" meaning "bios" or "life". The minimum dose of probiotic as recommended is usually between 10^9 – 10^{11} CFU/ day.^[5]

At present people are using probiotics for two reasons; they are living organisms which provide nutrients to the host and they are able to fight against certain infections (mostly pathogenic organism causing gastrointestinal infection).^[6] Probiotics production is a multibillion dollar industry.^[7] Common food products which contain probiotics include yogurt, nutrition bar, cheese, ice-cream, cereals, infant's food, milk, curd. Apart from food products, probiotics are also known to be found in cosmetic products.^[1,4] Probiotics can also be widely consumed in the form of lyophilized tablets, only under a doctor's prescription for gastrointestinal problems.^[4]

History of probiotics

Emmanuel Karasu of Ottoman Salonica decided to send Isaac Carasso (nephew) back to Barcelona during Balkan time, which was the beginning of the 20th century. He found that a lot of people suffer from gastrointestinal disorder and recommended that they take yogurt for improved bowel health. He got a pure LAB strain from the Pasture Institute and started to produce yogurt using conventional methods.^[5] He later developed a company called "Dannon milk products" in America in 1942. While, in 1935, Dr. Shirota created "Yakult", a dietary supplement of probiotic drink that can be eaten orally. The name Yakult comes from the Esperanto word "yogurt".^[5] Table 1 indicates the probiotic history that existed.

Year	Event	Reference
1857–1864	LAB is considered to be spoiling species by Pasteur	8
1873	Lister isolated LAB from milk	9
1889	In Tissier's microbiological intestinal micro biota of breast-fed infants, <i>Bifidobacterium</i> was described when it was isolated and named bacterium, characterized by Y-formed morphs ("bifid")	10
1890	Ernst Moro an Austrian physician discovered <i>Lactobacillus acidophilus</i>	11
1900	Moro described <i>Bacillus acidophilus</i> and Metchnikoff tried first to find out The possible effect of these microbes on human health.	12,13
1906	Henry Tissier discovered <i>Bifidobacteria</i> organism	14
1907	<i>Bulgaricus</i> associated with health was described by Metchnikoff	15
1923	French scientist by name Henry Boulard discovered probiotic yeast <i>Saccharomyces boulardii</i>	16
1930	Shirota markets <i>Lactobacillus casei</i> isolate-based fermented milk.	17
1935	<i>Lactobacillus acidophilus</i> strains have been shown to be involved in human digestive tract implantations. Shirota Minoru develops probiotic yogurt drink	15
1953	The term probiotika was used by Kollath for active substances promoting health	18,19
1965	The word Probiotics has been identified by Lilley and Stillwell as microbes that stimulate the growth of other microorganisms	20
1989	Probiotics as beneficial microbial supplements was defined by Fuller	15
2001	FAO/WHO provide the definition of probiotics	21
2002	Probiotic officially recognized by the United Nations and the WHO as a living microorganism that has health benefits when	21

	administered in sufficient amounts for host health benefits	
2003	Genomic era: <i>Lactobacillus plantarum</i> , first genome sequence of a probiotic	22
2005	Relman catalogs gut microbiome using high-throughput 16S rRNA amplicon sequencing	23
2016	FDA / CBER Live Biotherapeutics Guidelines	24
2017	100 new candidates for next generation probiotics	25

Table 1: Milestones in the Discovery of Probiotics

Overview of Probiotic Study

Based on the definition of the word probiotics coined in 1974 and updated in 2002, there was a wide number of microorganisms isolated and known as probiotics. Such micro-organisms have been tested on humans and animals to treat different diseases and disorders. The probiotics are used in many varieties. Probiotics successfully produced should require stability in a variety of environmental conditions and survival in many different forms. There are many different methods available for screening the probiotic parameter. It is possible to select methods of isolation or their characterization, depending on the application of probiotics. [26, 27]

According to previous studies, the properties of the lactic acid bacteria (LAB) were. [15, 28, 29]

- They are non-toxic and non-pathogenic organisms.
- Genetically stable in all conditions.
- Bile resistance
- Capable of producing organic acids, hydrogen peroxide, antimicrobial substances (Bacteriocin).
- Have many clinical health benefits.
- Acid resistance
- Has susceptible to the production process like freezing, storage, concentration, recovery and distribution.

- Target specificity
- Accurate in taxonomical identification

Microorganism used as Probiotics

In order to select the strain for probiotic use, it must be indicative of microorganisms Generally Recognized as Safe (GRAS). A list of such microorganisms are shown in Table 2. These different ecological positions in the human gastrointestinal tract. *Lactobacilli* are natural intestinal inhabitants while *Bifidobacter* reside is in the colon. ^[30]

Sl. No.	Genus	Species	Reference
1.	<i>Lactobacillus</i>	<i>L. rhamnosus</i>	31, 32
		<i>L. acidophilus</i>	12, 33
		<i>L. plantarum</i>	34, 35
		<i>L. casei</i>	36, 37
		<i>L. delbrueckii</i>	38, 39
		<i>L. bulgaricus</i>	38, 39
		<i>L. brevis</i>	40, 41
		<i>L. johnsonii</i>	42, 43
		<i>L. fermentum</i>	44, 45
		<i>L. reuteri</i>	46, 47
		<i>L. pentosus</i>	48, 49
2.	<i>Bifidobacterium</i>	<i>B. infantis</i>	7, 50
		<i>B. animalis</i> subsp. <i>lactis</i>	51
		<i>B. bifidum</i>	52, 53
		<i>B. longum</i>	52, 54
		<i>B. breve</i>	55, 56
		<i>B. adolescentis</i>	57
3.	<i>Saccharomyces</i>	<i>S. boulardii</i>	58, 59
4.	<i>Lactococcus</i>	<i>L. lactis</i> subsp. <i>lactis</i>	60, 61
5.	<i>Enterococcus</i>	<i>E. durans</i>	62

		<i>E. faecium</i>	63, 64
6.	<i>Streptococcus</i>	<i>S. thermophilus</i>	65, 66
7.	<i>Pediococcus</i>	<i>P. acidilactici</i>	67, 68
8.	<i>Leuconostoc</i>	<i>L. mesenteroides</i>	65, 69
9.	<i>Bacillus</i>	<i>B. coagulans</i>	42, 70, 71
		<i>B. subtilis</i>	42, 72
		<i>B. cereus</i>	42, 73
10.	<i>Escherichia</i>	<i>E. coli</i>	74,75

Table 2: A list of microorganisms employed in the production of probiotics

Lactobacillus species

Lactobacillus is a gram positive rod used as a probiotic in dairy products which is more prevalent microorganism. They are found in humans in oral micro flora, lower small intestine, colon, and vagina. They can live in acidic stomach conditions and are a large group of bacteria producing lactic acid. A few of these bacterial strains are pathogenic to the human host. ^[76] The first isolated strain of *lactobacillus* was *L. rhamnosus GG* discovered by Gorbach and Goldin in the year 1987 from the feces of a healthy human. This strain can survive in bile and acidic conditions obtained from the human host. ^[77]

L. acidophilus strains that are primarily used in the marketing of probiotics found in fermented dairy products and that are part of normal intestinal and vaginal micro-flora. Analysis of the literature found that these strains are capable of producing antimicrobials. ^[78] *L. casei* is a strain mostly used in the manufacture of dairy products such as cheese, fermented milk, yogurt etc. They develop lactic acid and are capable of increasing immune response, decreasing cholesterol levels, inhibiting intestinal pathogens and aversion to lactose. ^[79]

Bifidobacterium species

These species are purely anaerobic and gram positive. These are used in mixed fermentation reactions such as lactic and acetic acid production. These are present in the natural intestinal flora and used in the catabolism of dietary carbohydrates and vitamin synthesis in patients with diarrhea, used in immune stimulation, as anti-mutagens and anti-cholesterol agents, and most importantly, these can restore the immune system or boost immunity in children. [6]

Saccharomyces species

Saccharomyces boulardii is the only yeast strain used in production of probiotic commercial products. They help in stimulating the immune system during immunotherapy and are naturally resistant to antibiotics. [80]

Guidelines for Health Evaluation of Probiotics

Guidelines for assessing safety aspects of probiotic food products should be followed according to VKM Report 2014 .To commercialize the probiotic product, the mentioned parameters should be fulfilled completely. [21] The major guidelines for the safety assessments are illustrated in Figure 1.

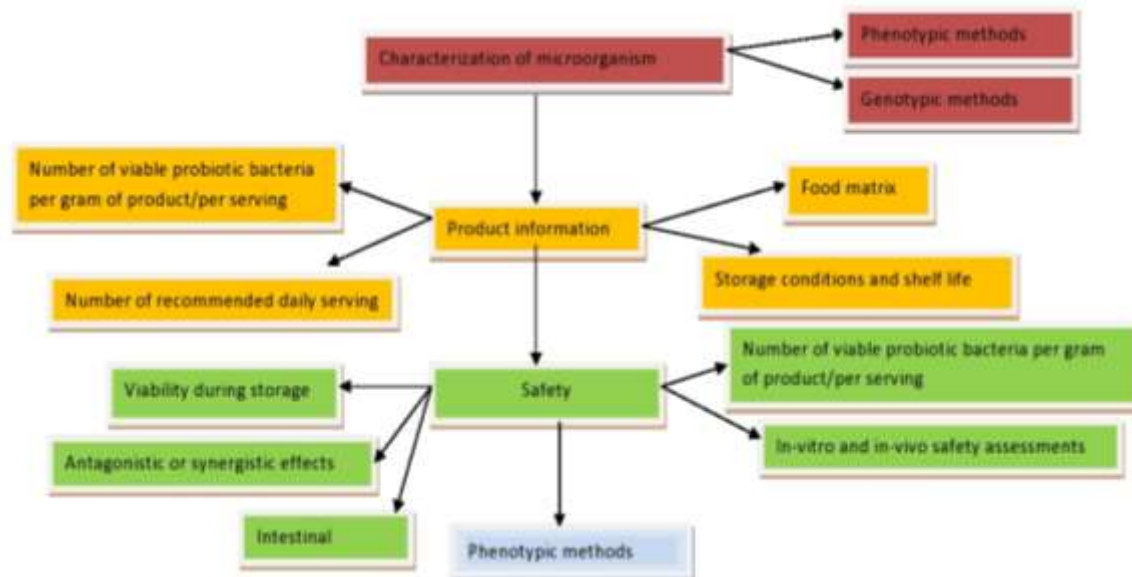


Figure 1: Guidelines and Parameters for Commercializing the Probiotic Product [21]

Major health benefits of probiotics

Probiotics are the microorganisms which are present in fermented products and have more beneficial effect on human health. This effect has been directly observed in the case of human being and strains and observed also using in-vitro models ^[6] like improving the normal microflora in the gut, improving intestine's immunological barrier functions of the intestinal inflammatory response. ^[81] Some of the health benefits are listed in Table 3.

Lactose intolerance

Approximately 75 percent of the world's adult population is currently suffering from lactose intolerance, which is a digestive condition caused by the inability to digest lactose. Lactose is a significant carbohydrate believed to be found in dairy products. People suffering from lactose intolerance do not produce the enzyme lactase, which usually digests lactose in the host gut. Common disorders caused by lactose intolerance are bloating, abdominal cramp, production of gas in stomach, diarrhea, vomiting and nausea. Suggesting yogurt as a food supplement to people suffering from lactose intolerance found to produce less hydrogen component in their breath when compared to patients consuming normal milk. ^[82]

Treatment for acute gastroenteritis

Rotavirus is the most common virus causing gastroenteritis among children worldwide. This virus enters the host and ruptures the small intestine epithelial cell and causes disorder in the intestine. Studies have shown that treating with probiotics helps to rebuild the ruptured epithelial layer in the small intestine caused due to such infection. ^[58]

Lowering of cholesterol levels

Research has shown that probiotics help to lower the total level of serum cholesterol and LDL. Probiotics can bind to cholesterol in intestine and does not allow fat absorption and also helps in producing bile acids, which can metabolize fat and cholesterol in the body. ^[83]

Treatment for urogenital infections

Urinary tract infection (UTI) caused by bacteria and fungi is most common in females worldwide. According to a survey, about 300 million cases of urogenital infections are reported annually. Probiotics can be used for treating the infection, as strains like *L. acidophilus* can lower the strains of *Candida* that causes vaginitis. [84]

Probiotic in prevention of dental caries

Pathogenic organisms present in the oral micro flora cause caries and increase acid tolerance. Studies have shown that the use of probiotics to replace carcinogenic bacteria in non-carcinogenic organisms will interact with the oral biofilm in which probiotics grow in chewing gum with Xylitol combination. [85]

Sl. No.	Major Health Benefits Using Probiotics	Reference
1.	Helps in maintaining the normal micro flora in the digestive system	86-88
2.	Helps in treating diarrhea	89-92
3.	Helps in improving mental health conditions	93-95
4.	Helps to reduce cholesterol (LDL), increases good cholesterol (HDL) and reduce blood pressure	96-99
5.	Helps to reduce allergies and eczema	100-101
6.	Helps in improving immune system	102-105
7.	Helps in reducing belly fat and lose weight	106-111

Table 3: Major Health Benefits of Probiotics

Role of probiotics in pharmaceutical companies

The use of probiotics in modern era helps to control and treat infections. Probiotics have become commercialized products due to their major health benefits based on which, different pharma companies manufacture probiotic drug using a cocktail of probiotic microorganism. According to the FDA working definition for probiotic is defined as they are live biotherapeutics which

include microorganism like bacteria and yeast. The probiotic strains used by different companies in formulation ^[112] are listed in Table 4.

Sl. No.	Drug Brand Name	Organism	Company Names
1.	Florajen	<i>Lactobacillus acidophilus</i>	Clarion brands
2.	Florajen3	<i>Bifidobacterium infantis</i> <i>Lactobacillus acidophilus</i>	Clarion brands
3.	Florajen Acidophilus	<i>Lactobacillus acidophilus</i>	Clarion brands
4.	Florajen4Kids	<i>Saccharomyces boulardii lyo</i>	Clarion brands
5.	VSL#3	<i>Bifidobacterium infantis</i> <i>Lactobacillus acidophilus</i> <i>Streptococcus thermophilus</i>	VSL Pharmaceuticals, Inc.
6.	Florastor	<i>Saccharomyces boulardii lyo</i>	Biocodex, Inc
7.	Acidophilus	<i>Lactobacillus acidophilus</i>	Novalife Healthcare
8.	Phillips Colon Health	<i>Bifidobacterium infantis</i> <i>Lactobacillus acidophilus</i>	Phillips Colon Health
9.	Bacid (LAC)	<i>Lactobacillus acidophilus</i>	Prestige Consumer Healthcare, Inc.
10.	BD Lactinex	<i>Lactobacillus acidophilus</i> <i>Lactobacillus bulgaricus</i>	Becton, Dickinson and Company
11.	Culturelle Digestive Health	<i>Lactobacillus rhamnosus gg</i>	Culturelle®
12.	Culturelle Health and Wellness	<i>Lactobacillus rhamnosus gg</i>	Culturelle®
13.	Flora-Q	<i>Lactobacillus acidophilus</i>	PharmaDerm A division o Fougera Pharmaceuticals Inc.
14.	Floranex	<i>Lactobacillus acidophilus</i> <i>lactobacillus bulgaricus</i>	Rising pharma

15.	Neoflora Veg 30Billion	<i>B. bifidum</i> <i>B. breve</i> <i>B. infantis</i> <i>B. lactis</i> <i>B. longum</i> <i>L. acidophilus</i> <i>L. casei</i> <i>L. fermentum</i> <i>L. gasseri</i> <i>L. paracasei</i> <i>L. plantarum</i> <i>L. reuteri</i> <i>L. rhamnosus</i> <i>L. salivarius</i> <i>S. boulardi</i> <i>S. thermophilus</i>	Novus Life Sciences Pvt. Ltd.
16.	Primadophilus Bifidus	<i>Bifidobacterium infantis</i> <i>Lactobacillus acidophilus</i>	Nature's Way
17.	Superdophilus	<i>Lactobacillus acidophilus</i>	Wellness resources
18.	Visbiome Extra Strength	<i>Bifidobacterium breve,</i> <i>Bifidobacterium longum,</i> <i>Bifidobacterium infantis</i> <i>Lactobacillus bulgaricus,</i> <i>Lactobacillus paracasei</i> <i>Lactobacillus acidophilus</i> <i>Lactobacillus plantarum,</i> <i>Streptococcus thermophilus</i>	ExeGi Pharm

Table 4: List of companies with their drug brands employing probiotic organisms

Conclusion

Probiotics play an important role in the present age where they are used in the food and pharmaceutical industries, the use of probiotics that improve the gut micro flora and provide immunity for the host they also have antimicrobial activity, and the use of probiotics worldwide as a therapeutic agent. Probiotics have a role to play in recognizing the connection between nutrition and health that has a major impact on consumer demand for food that is directly linked to nutritional value and has changed over time. Food is, therefore, defined as functional food that has psychological and mental health benefits to combat nutrition related diseases.

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