

# Probiotics: Friendly Microbes For Better Health

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## Abstract

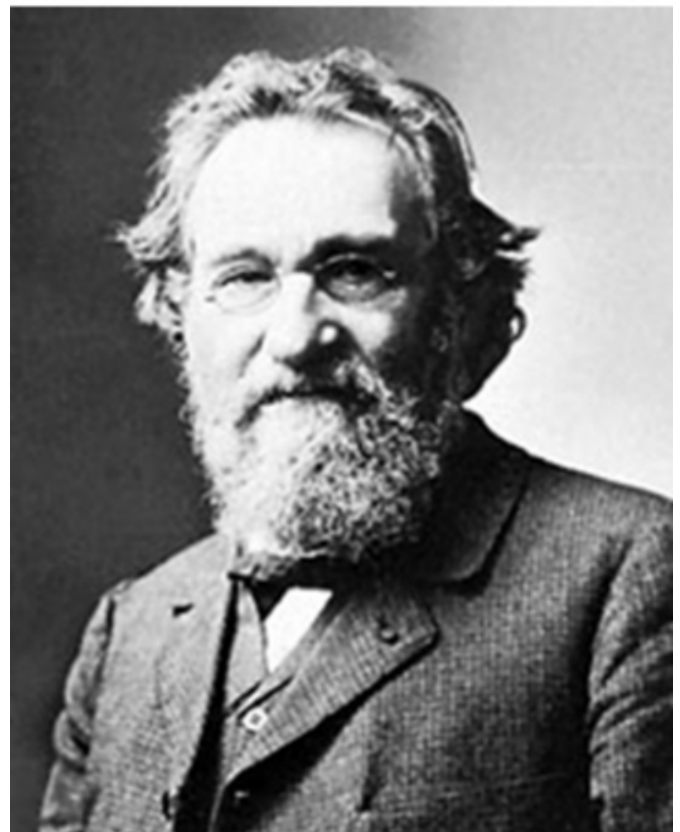
Microorganisms have been used for hundreds of years by our ancestors in various food and beverages, and in the last decades have undergone clinical research for their ability to prevent and cure a variety of diseases. In recent years, novel insights have been gained into the role of bacterial micro flora in health and disease. Natural flora manipulation by probiotic bacteria has been investigated in human and experimental inflammatory bowel disease. Various probiotic species have shown promise in the treatment of ulcerative colitis, Crohn's disease and pouchitis in small studies; although a clear clinical benefit remains to be established. Probiotics may also have antimicrobial, immunomodulatory, anticarcinogenic, antiallergic, antidiarrheal and antioxidant properties. The various mechanisms include chelation of metallic ions, scavenging of reactive organs species, and reduction of bacterial activity. The probiotics that are marketed as nutritional supplements and used in foods, such as yogurt, are principally the bifidobacteria species and the lactobacillus species. This article discusses the information on the health benefits of probiotics.

## INTRODUCTION

Probiotics are normally bacteria and other microorganisms that have beneficial effects on the human and animal health. According to Fuller, a probiotic is a live microbial food supplement that beneficially affects the host animal or human by improving the intestinal microbial balance. In the context of the humans it also includes fermented food products, e.g. yogurt, curd, and lyophilized bacteria etc. Originally the term was used to denote microorganisms promoting the growth of other microorganisms but has now been extended to refer to viable microorganisms that promote or support a beneficial balance of the autochthonous microbial population of the gastrointestinal tract. Such organisms need not necessarily be constant inhabitants of the GI tract, but they should have beneficial effect on the general and health status of man and animal. According to WHO, probiotics are the 'live microorganisms which when administered in adequate amounts confer a health benefit on the host.' In recent years, probiotics have been given a more precise definition as mono or mixed cultures of live microorganisms which, when applied to animal or man, beneficially affect the host by improving the properties of the indigenous microflora. <sup>1,2</sup>

Figure 1

Ellie Metchnikoff



The term probiotic was derived from the Greek word, meaning for life. This term was first introduced in 1953 by Kollath. The concept of probiotics is very ancient. The first recorded probiotic was fermented milk for human consumption. After that, probiotics became popular with animal nutrition. The role of fermented milk in human diet was known even in Vedic times. In the late 19<sup>th</sup> century, microbiologists identified microflora in the gastrointestinal tracts of the healthy individuals that differed from those found in diseased individuals. The original observation of the positive role of these bacteria can be credited to the pioneering work of Metchnikoff from Pasteur Institute in the early 1900s. He suggested that these beneficial bacteria could be administered with a view to replacing harmful microbes with useful ones. <sup>3,4</sup> Metchnikoff studied the phenomenon of an incredible amount of people in Bulgaria living to be over 100 years old. He attributed their health and longevity to a microbe in the widely eaten Bulgarian yogurt, and he named the yogurt culturing microbe after the Bulgarians - *Lactobacillus Bulgaricus*.

Henry Tissier also from the same institute was the first to isolate a *Bifidobacterium*. He isolated the bacterium from a breast fed infant and named it *Bacillus bifidus communis*. This bacterium was later renamed *Bifidobacterium bifidum*. Tissier showed that bifidobacteria are predominant in the flora of breast fed babies, and he recommended administration of bifidobacteria to infants suffering from diarrhea. The mechanism claimed was that bifidobacteria would displace the proteolytic bacteria that cause the disease. <sup>5</sup> German professor Alfred Nissle, in 1917 isolated a strain of *Escherichia coli* from the feces of a First World War soldier who did not develop enterocolitis during a severe outbreak of shigellosis. In those days antibiotics were not yet discovered. Nissle used the strain with considerable success in acute cases of infectious intestinal disease like Shigellosis and Salmonellosis. *Escherichia coli* Nissle 1917 is still in use and is one of the few examples of a non-LAB probiotic. <sup>6</sup> In the 1960s the dairy industry began to promote fermented milk products containing *Lactobacillus acidophilus*. In subsequent decades other *Lactobacillus* species have been introduced including *Lactobacillus reuteri*, *Lactobacillus helveticus*, *Lactobacillus casei* and *Lactobacillus rhamnosus*, because they are intestinal species with beneficial properties. <sup>7,8</sup>

**Figure 2**



Courtesy: Jarrow Formulas

### TYPES OF PROBIOTICS

Probiotics can be in powder form, liquid form, gel, paste, granules or available in the form of capsules, sachets, etc (Figure 1). Probiotics can be bacteria, moulds, yeast. But most probiotics are bacteria. Among bacteria, lactic acid bacteria are more popular. *Lactobacillus acidophilus*, *L. casei*, *L. lactis*, *L. helveticus*, *L. salivarius*, *L. plantrum*, *L. bulgaricus*, *L. rhamnosus*, *L. johnsonii*, *L. reuteri*, *L. fermentum*, *L. delbrueckii*, *Streptococcus thermophilus*, *Enterococcus faecium*, *E. faecalis*, *Bifidobacterium bifidum*, *B. breve*, *B. longum* and *Saccharomyces boulardii* are commonly used bacterial probiotics. A probiotic may be made out of a single bacterial strain or it may be a consortium as well. Eg. LB17 “live” probiotic contains 17 strains of lactic bacteria (10 *Lactobacillus* + 2 *Bifidobacterium*), digestive enzymes, amino acids, vitamins and minerals. Recent evidence suggests that probiotic effects are strain-specific which means a beneficial effect produced by one strain cannot be assumed to be provided by another strain, even when it belongs to the same species. <sup>9</sup>

**Figure 3**

Picture 1: Different Dosage forms of Probiotics



**Figure 4**

Table 1: Examples of commercially using probiotics

Sl.	Strain	Brand	Manufacturer	Therapeutic use
1	<i>Lactobacillus casei</i> F19	Cultura	Arla food	Improves digestive health, immune stimulation, reduces antibiotic-associated diarrhoea, induces satiety, metabolizes body fat, and reduces weight gain.
2	<i>Lactobacillus casei</i> Shirota	Yakult	Yakult	Maintenance of gut flora, immune modulation, bowel habits and constipation.
3	<i>Lactobacillus rhamnosus</i> LB21	Verum	Normejerier	Immune stimulation, improves digestive health, reduces antibiotic-associated diarrhoea
4	<i>Bifidobacterium lactis</i> HN019 (DR10)	Howaru Bifido	Danisco	Immune stimulation
5	<i>Escherichia coli</i> Nissle 1917	Mutaflor	Ardeypharm	Immune stimulation
6	<i>Lactobacillus helveticus</i> R0052 <i>Lactobacillus rhamnosus</i> R0011	A'Biotica	Institut Rosell	prevents diarrhoea in children, prevents upset stomachs for patients on antibiotics, active against <i>Helicobacter pylori</i> .
7	<i>Lactobacillus rhamnosus</i> GR1 <i>Lactobacillus reuteri</i> RC14	Fem-Dophilus	Jarrow FORMULAS	Help to maintain or restore healthy vaginal flora that are important in maintaining vaginal health and support the health of the urinary tract.

**CHARACTERISTICS OF EFFECTIVE PROBIOTICS**

An effective probiotic must have features like exert a beneficial effect, non-pathogenic and non-toxic, contain large number of viable cells, capable of surviving and metabolizing in the gut, remain viable during storage and use, good sensory properties and isolated from the same species. Probiotics have manifold beneficial effects, if used properly. Major health effects of Probiotics ones include stimulation of lactose metabolism, improvement of digestion , suppression of various cancers, resistance to infectious diseases, reduction in serum cholesterol level and stimulation of immunity in the GI tract.

**THERAPEUTIC USAGE**

Probiotics have been used as growth promoters, for lactose intolerance, antitumour<sup>10</sup> and anticholestrolaemic effects<sup>11</sup> . Probiotics have been extensively studied under in vitro and in vivo conditions. The main fields of research with respect to probiotics are heart diseases, allergic reaction, cancer, diarrhoea, etc. The use of probiotics resulting in alleviation of lactose intolerance due to increased concentration of b-galactosidase in the small intestine, relief from constipation by increased bowel function, antitumour activities due to inhibition of tumour cells, destruction of carcinogens etc. have been well documented. Gastrointestinal benefits of probiotic food supplements have been well documented.<sup>12,13</sup> New research indicates it also benefits the whole body. For example, lactobacillus found in curd is intended to assist the body's naturally occurring intestinal flora to re-establish

themselves. They are recommended by doctors and nutritionists, after a course of antibiotics, or as part of the treatment for gut related candidiasis, a fungal infection.<sup>14,15</sup> Intestinal infections caused by *Escherichia coli*, *Campylobacter fetus* subsp. *jejuni*, *Clostridium perfringens* and *C. Botulinum* were reduced in the presence of *Lactobacillus* supplements<sup>1</sup> . The *Lactobacillus* has shown promising results and *Bifidobacterium longum* has been successfully used to reduce the after-effects of antibiotic therapy There have been claims that probiotics strengthen the immune system to combat allergies, excessive alcohol intake, stress, exposure to toxic substances and other diseases. The immune system's normal response to infection is rapid and effective. However, it may occasionally cause inflammation and damage to healthy tissue.<sup>16,17</sup>

Various probiotic species have shown promise in the treatment of ulcerative colitis and Crohn's disease in small studies although a clear clinical benefit remains to be established. Prevention of relapse is more thoroughly documented than the treatment of active disease. The following are illustrative controlled trials: The combination of a prebiotic (food intended to promote the growth of certain bacteria in the intestines) and a probiotic ( *Bifidobacterium longum* ) was associated with improvement in histologic scores and immune activation in a one-month randomized controlled trial.<sup>18</sup> *Lactobacillus GG* appeared to be more effective than standard treatment involving mesalazine in prolonging relapse-free time but did not influence relapse rates in patients with quiescent ulcerative colitis.<sup>19</sup> Patients with active colonic CD were treated with prednisolone on a standard schedule and were also randomized to receive *E. coli* (Nissle 1917) or placebo for one year. Patients in the two groups had similar rates of remission but patients treated with prednisolone and *E. coli* had fewer relapses than patients in the placebo group.<sup>20</sup>

Past research has shown that the probiotic *Bifidobacterium infantis* (BI) 35624 can positively impact the body's immune defence, and this most recent data suggests that its benefits are not restricted to the gastrointestinal tract. The study - whose report appeared in the August issue of the Public Library of Science (PLoS) Pathogens - examined the effect of BI-35624 on immunity to *Salmonella*, harmful bacteria that can cause intestinal infections and trigger the body's inflammatory response. BI-35624, a probiotic strain isolated from healthy human gastrointestinal tract, was administered to mice in freeze-dried powder at least three weeks prior to salmonella infection. They showed dramatically increased

numbers of certain immune cells that control the immune system response to harmful pathogens, in this case *Salmonella*. Additionally, data show increased numbers of T-regulatory cells, or cells that suppress inflammatory disease in a wide range of autoimmune diseases. Administration of BI-35624 resulted in the induction of these cells, which protected the host from excessive inflammation during the course of infection.

Studies have shown that absence or depletion of *Lactobacillus* in vagina is one of the main reasons for BV infections and these results in significantly increased risk of HIV as well as gonorrhoea, chlamydia and Herpes simplex viral infections. <sup>15</sup>

## **MECHANISM OF ACTION**

Mechanisms for the benefits of probiotics are incompletely understood. Generally probiotics have multiple modes of action. They are given below

1. Suppression of growth or epithelial binding / invasion by pathogenic bacteria
2. They colonize and adhere to the colon and reinforce the barrier function of the intestinal mucosa helping in the management of intestinal infection and food allergies.
3. They secrete antimicrobial substances called bacteriocins.
4. They increase the levels of circulating immunoglobulins especially immunoglobulin A in infants infested with rotavirus.
5. They enhance the nonspecific immunophagocytic activity of circulating blood granulocytes.
6. They potentiate intestinal immune response to viral infection.
7. They increase the frequency of interferon gamma and producing peripheral blood monocytes.
8. They secrete certain proteolytic enzymes which digest the bacterial toxins.
9. They alter the initiation and or promotional events of the chemically induced tumors by binding to the chemical carcinogen.

Several theories exist regarding modulation of the immune

system by probiotic preparations. These include stimulation of protective cytokines including interleukin (IL)-10 and transforming growth factor (TGF) and suppression of pro-inflammatory cytokines such as tumor necrosis factor (TNF) in the mucosa of patients with pouchitis and Crohn's disease (CD). *Saccharomyces boulardii* may limit the migration of T-helper 1 (TH1) cells in inflamed colon tissue in inflammatory bowel disease (IBD) in experimental studies. <sup>21</sup>

The effectiveness of probiotics is related to their ability to survive in the acidic environment of the stomach and the alkaline conditions in the duodenum, as well as their ability to adhere to the intestinal mucosa of the colon and to colonize the colon. Typical doses of probiotics range from one to ten billion colony forming units (CFU), to be taken a few times a week, to maintain their effect on the microecology. The microorganisms need to be alive when they are consumed and therefore maintaining suitable conditions for their storage and transport before consumption is important. In general, probiotics are well tolerated and do not have any serious side effect, except for flatulence and constipation. <sup>22</sup>

## **CURRENT STATUS OF PROBIOTICS IN INDIA**

In India, only sporulating *Lactobacilli* are produced and they are prescribed with some of the antibiotic preparations. Here probiotics are often used as veterinary and poultry feed supplements. This requirement is also met by importing probiotics from other countries. It is rarely used for human beings – *Sporolac*, *Saccharomyces boulardii* and yogurt (*L. bulgaricus* + *L. thermophilus*) are the most common ones. *Sporolac* is manufactured using *Sporolactobacilli*. *Lactobacilli* solution is an example of a probiotic, usually given to paediatric patients in India. The latest and recent addition to the list of probiotics in India is ViBact which is made up of genetically modified *Bacillus mesentericus*. This acts as an alternate to B-complex capsules.

## **CONCLUSION**

Probiotics are gaining importance because of the innumerable benefits, e.g. treating lactose intolerance, hypercholesterol problem, cardiac diseases and managing cardiac problems like atherosclerosis and arteriosclerosis. Today probiotics are available in a variety of food products and supplements. With the current focus on disease prevention and the quest for optimal health at all ages, the probiotics market potential is enormous. Health professionals are in an ideal position to help and guide their clients toward appropriate prophylactic and therapeutic uses

of probiotics that deliver the desired beneficial health effects. In recent years, there has been an upsurge in research in probiotics as well as growing commercial interest in the probiotic food concept. This increased research has resulted in significant advances in our understanding and ability to characterize specific probiotic organisms, which has resulted in an increasing amount of evidence indicating health benefits by consumption of food containing probiotics.

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