COLONCARE CAPSULES AND SACHETSTM - A BLEND OF PROBIOTICS, PREBIOTICS AND COLOSTRUM

Govind shukla*, Sharathkumar and Sampath kumar CJ

Product Manager, LACTONOVA INDIA, (makers of COLONCARE) Hyderabad

LACTONOVA INDIA, a Hyderabad based Indian multinational company founded in the year 2000, is a manufacturer and supplier of nutraceutical raw materials, ethical formulations, phytoneutrients, cosmeceuticals, minerals and specialty fine (comes under under the sub-category of products) chemicals. A vertically integrated bio-technology based research, manufacturing and marketing company. Lactonova India has R&D tie-ups and two patent pending molecules and 20 product registrations in the CIS countries. The company has manufacturing facilities in Hyderabad and Himachal Pradesh to cater to its own product manufacturing and to other companies across the country. The company leads in the manufacturing and sales Lycopene and other carotenoids in the country and has the distinction of launching many new molecules for the first time in India.

ABSTRACT
A probiotic is defined classically as a viable microbial dietary supplement that beneficially affects the host through its effects in the intestinal tract. This definition, however, was initially intended for use with animal feed products. For human nutrition, the following definition has been proposed: “a live microbial food ingredient that is beneficial to health” (1). A prebiotic is defined as “a nondigestible food ingredient that beneficially affects the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon” (2). Modification by prebiotics of the composition of the colonic microflora leads to the redominance of a few of the potentially health-promoting bacteria, especially, but not exclusively, lactobacilli and bifidobacteria. This article reviews the scientific data showing that probiotics and prebiotics may positively affect various physiologic functions in ways that will permit them now or in the future to be classified as functional foods for which health claims (of enhanced function or of reduction in disease risk) will be authorized.

Keywords: Probiotic, prebiotic, synbiotic, lactobacilli, bifidobacteria, inulin.

INTRODUCTION
A probiotic is a viable microbial dietary supplement that beneficially affects the host through its effects in the intestinal tract. Probiotics are widely used to prepare fermented dairy products such as yogurt or freeze-dried cultures. In the future, they may also be found in fermented vegetables and meats. Several health-related effects associated with the intake of probiotics, including alleviation of lactose intolerance and immune enhancement, have been reported in human studies. Some evidence suggests a role for probiotics in reducing the risk of rotavirus-induced diarrhea and colon cancer. Prebiotics are nondigestible food ingredients that benefit the host by selectively stimulating the growth or activity of one or a limited number of bacteria in the colon. The combination of probiotics and prebiotics in a synbiotic might improve the survival of the...
bacteria crossing the upper part of the gastrointestinal tract, thereby enhancing their effects in the large bowel. In addition, their effects might be additive or even synergistic. Probiotics are live microorganisms thought to be beneficial to the host organism. According to the currently adopted definition by FAO/WHO, probiotics are: “Live microorganisms which when administered in adequate amounts confer a health benefit on the host”.\(^1\) Lactic acid bacteria (LAB) and bifidobacteria are the most common types of microbes used as probiotics; but certain yeasts and bacilli may also be helpful. Probiotics are commonly consumed as part of fermented foods with specially added active live cultures; such as in yogurt, soy yogurt, or as dietary supplements.

Etymologically, the term appears to be a composite of the Latin preposition pro (“for”) and the Greek adjective βιωτικός (biotic), the latter deriving from the noun βίος (bios, “life”).\(^2\)

At the start of the 20th century, probiotics were thought to beneficially affect the host by improving its intestinal microbial balance, thus inhibiting pathogens and toxin producing bacteria.\(^3\) Today, specific health effects are being investigated and documented including alleviation of chronic intestinal inflammatory diseases,\(^4\) prevention and treatment of pathogen-induced diarrhea,\(^5\) urogenital infections,\(^6\) and atopic diseases.

**History**

The original observation of the positive role played by certain bacteria was first introduced by Russian scientist and Nobel laureate Élie Metchnikoff, who in the beginning of the 20th century suggested that it would be possible to modify the gut flora and to replace harmful microbes with useful microbes.\(^7\) Metchnikoff, at that time a professor at the Pasteur Institute in Paris, produced the notion that the aging process results from the activity of putrefactive (proteolytic) microbes producing toxic substances in the large bowel. Proteolytic bacteria such as clostridia, which are part of the normal gut flora, produce toxic substance including phenols, indoles and ammonia from the digestion of proteins. According to Metchnikoff these compounds were responsible for what he called “intestinal auto-intoxication”, which caused the physical changes associated with old age. It was at that time known that milk fermented with lactic-acid bacteria inhibits the growth of proteolytic bacteria because of the low pH produced by the fermentation of lactose. Metchnikoff had also observed that certain rural populations in Europe, for example in Bulgaria and the Russian steppes who lived largely on milk fermented by lactic-acid bacteria were exceptionally long lived. Based on these facts, Metchnikoff proposed that consumption of fermented milk would “seed” the intestine with harmless lactic-acid bacteria and decrease the intestinal pH and that this would suppress the growth of proteolytic bacteria. Metchnikoff himself introduced in his diet sour milk fermented with the bacteria he called “Bulgarian Bacillus” and found his health benefited. Friends in Paris soon followed his example and physicians began prescribing the sour milk diet for their patients.\(^8\)

*Bifidobacteria* were first isolated from a breast-fed infant by Henry Tissier who also worked at the Pasteur Institute. The isolated bacterium named *Bacillus bifidus communis*\(^9\) was later renamed to the genus *Bifidobacterium*. Tissier found that bifidobacteria are dominant in the gut flora of breast-fed babies and he observed clinical benefits from treating diarrhea in infants with bifidobacteria. The claimed effect was bifidobacterial displacement of proteolytic bacteria causing the disease.

During an outbreak of shigellosis in 1917, German professor Alfred Nissle isolated a strain of *Escherichia coli* from the feces of a soldier who was not affected by the disease.\(^1\) Methods of treating infectious diseases were needed at that time when antibiotics were not yet available, and Nissle used the *Escherichia coli* Nissle 1917 strain in acute gastrointestinal infectious salmonellosis and shigellosis. In 1920, Rettger demonstrated that Metchnikoff’s “Bulgarian Bacillus”, later called *Lactobacillus delbrueckii* subsp. *bulgaricus*, could not live in the human intestine,\(^1\) and the fermented food phenomena petered out. Metchnikoff’s theory was disputable (at this stage), and people doubted his theory of longevity. After Metchnikoff’s death in 1916, the centre of activity moved to the United States. It was reasoned that bacteria originating from the gut were more likely to produce the desired effect in the gut, and in 1935 certain strains of *Lactobacillus acidophilus* were found to be very active when implanted in the human digestive tract.\(^1\) Trials were carried out using this organism, and encouraging results were obtained especially in the relief of chronic constipation.
The term "probiotics" was first introduced in 1953 by Werner Kollath (see Hamilton-Miller et al. 2003). Contrasting antibiotics, probiotics were defined as microbially derived factors that stimulate the growth of other microorganisms. In 1989 Roy Fuller suggested a definition of probiotics which has been widely used: "A live microbial feed supplement which beneficially affects the host animal by improving its intestinal microbial balance." Fuller's definition emphasizes the requirement of viability for probiotics and introduces the aspect of a beneficial effect on the host.

In the following decades intestinal lactic acid bacterial species with alleged health beneficial properties have been introduced as probiotics, including Lactobacillus rhamnosus, Lactobacillus casei, and Lactobacillus johnsonii.

**Indications**

Experiments into the benefits of probiotic therapies suggest a range of potentially beneficial medicinal uses for probiotics. For many of the potential benefits, research is limited and only preliminary results are available. It should be noted that the effects described are not general effects of probiotics. Recent research on the molecular biology and genomics of Lactobacillus has focused on the interaction with the immune system, anticancer potential, and potential as a biotherapeutic agent in cases of antibiotic-associated diarrhoea, travellers' diarrhoea, pediatric diarrhoea, inflammatory bowel disease and irritable bowel syndrome.

All effects can only be attributed to the individual strain(s) tested. Testing of a supplement does not indicate benefit from any other strain of the same species, and testing does not indicate benefit from the whole group of LAB (or other probiotics).

**Diarrhea**

**Infectious**

Some probiotics have been shown to be beneficial in preventing and treating various forms of gastroenteritis. They reduce both the duration of illness and the frequency of stools. Fermented milk products (such as yogurt) also reduce the duration of symptoms.

**Antibiotic associated**

Antibiotic-associated diarrhoea (AAD) results from an imbalance in the colonic microbiota caused by antibiotic therapy. Microbiota alteration changes carbohydrate metabolism with decreased short-chain fatty acid absorption and an osmotic diarrhea as a result. Another consequence of antibiotic therapy leading to diarrhea is overgrowth of potentially pathogenic organisms such as *Clostridium difficile*. The Culturelle product contains the strain Lactobacillus rhamnosus LGG, which studies indicate may reduce the risk of antibiotic associated diarrhea, improve stool consistency during antibiotic therapy and enhance the immune response after vaccination. Probiotic treatment can reduce the incidence and severity of AAD as indicated in several meta-analyses. However, further documentation of these findings through randomized, double blind, placebo-controlled trials are warranted.

**Lactose intolerance**

As lactic acid bacteria actively convert lactose into lactic acid, ingestion of certain active strains may help lactose intolerant individuals tolerate more lactose than they would have otherwise.

**Colon cancer**

In laboratory investigations, some strains of LAB (Lactobacillus bulgaricus) have demonstrated anti-mutagenic effects thought to be due to their ability to bind with heterocyclic amines, which are carcinogenic substances formed in cooked meat. Animal studies have demonstrated that some LAB can protect against colon cancer in rodents, though human data is limited and conflicting. Most human trials have found that the strains tested may exert anti-carcinogenic effects by decreasing the activity of an enzyme called β-glucuronidase (which can generate carcinogens in the digestive system). Lower rates of colon cancer among higher consumers of fermented dairy products have been observed in one population study.

**Cholesterol**

Animal studies have demonstrated the efficacy of a range of LAB to be able to lower serum cholesterol levels, presumably by breaking down bile in the gut, thus inhibiting its reabsorption (which enters the blood as cholesterol).
A meta-analysis that included five double blind trials examining the short term (2-8 weeks) effects of probiotic yoghurt on serum cholesterol levels found an overall decrease of 8.5 mg/dL (0.22 mmol/L) (~4% decrease) in total cholesterol concentration, and a decrease of 7.7 mg/dL (0.2 mmol/L) (~5% decrease) in serum LDL concentration. A slightly longer study evaluating the effect of probiotic yoghurt on twenty-nine subjects over six months found no statistically significant differences in total serum cholesterol or LDL values. However, the study did note a significant increase in serum HDL from 50 mg/dL (1.28 mmol/L) to 62 mg/dL (1.6 mmol/L) following treatment. This corresponds to an improvement of LDL/HDL ratio from 3.24 to 2.48, with a 95% confidence interval of ± 0.33. [33]

**Blood pressure**

Several small clinical trials have indicated that consumption of milk fermented with various strains of LAB may result in modest reductions in blood pressure. It is thought that this is due to the ACE inhibitor-like peptides produced during fermentation. [34]

**Immune function and infections**

LAB are thought to have several presumably beneficial effects on immune function. They may protect against pathogens by means of competitive inhibition (i.e., by competing for growth) and there is evidence to suggest that they may improve immune function by increasing the number of IgA-producing plasma cells, increasing or improving phagocytosis as well as increasing the proportion of T lymphocytes and Natural Killer cells. [35][36] Clinical trials have demonstrated that probiotics may decrease the incidence of respiratory tract infections and dental caries in children. [37] LAB foods and supplements have been shown to aid in the treatment and prevention of acute diarrhea, and in decreasing the severity and duration of rotavirus infections in children and travelers’ diarrhea in adults. [38][39]

A 2010 study suggested that the anecdotal benefits of probiotic therapies as beneficial for preventing secondary infections, a common complication of antibiotic therapy, may be because keeping the immune system primed by eating foods enhanced with “good” bacteria may help counteract the negative effects of sickness and antibiotics. It was thought that antibiotics may turn the immune system “off” while probiotics turns it back on “idle”, and more able to quickly react to new infections. [38]

**Helicobacter pylori**

LAB are also thought to aid in the treatment of *Helicobacter pylori* infections (which cause peptic ulcers) in adults when used in combination with standard medical treatments. [39]

**Inflammation**

LAB and supplements have been found to modulate inflammatory and hypersensitivity responses, an observation thought to be at least in part due to the regulation of cytokine function. [34] Clinical studies suggest that they can prevent reoccurrences of inflammatory bowel disease in adults, [34] as well as improve milk allergies. [40] They are not effective for treating bowel disease, a persistent skin inflammation. [41] How probiotics counteract immune system overactivity remains unclear, but a potential mechanism is desensitization of T lymphocytes, an important component of the immune system, towards pro-inflammatory stimuli. [42]

**Mineral absorption**

It is hypothesized that probiotic lactobacilli may help correct malabsorption of trace minerals, found particularly in those with diets high inphytate content from whole grains, nuts, and legumes. [43]

**Bacterial growth under stress**

In a study done to see the effects of stress on intestinal flora, rats that were fed probiotics had little occurrence of harmful bacteria latched onto their intestines compared to rats that were fed sterile water. [44]

**Irritable bowel syndrome and colitis**

*B. infantis* 35624, sold as Align, was found to improve some symptoms of irritable bowel syndrome in women in a recent study. [45] Another probiotic bacterium, *Lactobacillus plantarum* 299v, was also found to be effective in reducing IBS symptoms. [46] Additionally, a probiotic formulation, VSL#3, was found to be safe in treating ulcerative colitis, though efficacy in the study was uncertain. [47] *Bifidobacterium animalis* DN-173 010 may help. [48] For maintenance of remission of ulcerative colitis, Mutaflor (E.coli Nissle 1917) there are 3 controlled, randomized, double blind clinical studies which have proven equivalence of Mutaflor and mesalazine (5-ASAs). [49]
Other
A study in 2004 testing the immune system of students given either milk or Actimel over a 6 week exam period (3 weeks of studying, 3 weeks of exams) tested 19 different biomarkers. Of these 19 biomarkers only 2 were shown to be different between the two groups, increased production of lymphocytes and increased production of CD56 cells. The tests were not blind and show that certain probiotic strains may have no overall effect on the immune system or on its ability.\cite{50}

A 2007 study at University College Cork in Ireland showed that a diet including milk fermented with \textit{Lactobacillus} bacteria prevented \textit{Salmonella} infection in pigs.\cite{51}

A 2007 clinical study at Imperial College London showed that preventive consumption of a commercially available probiotic drink containing \textit{L. casei} DN-114001, \textit{L. bulgaricus}, and \textit{S. thermophilus} can reduce the incidence of antibiotic-associated diarrhea and \textit{C difficile}-associated diarrhea.\cite{52}

The efficacy and safety of a daily dose of \textit{Lactobacillus acidophilus} CL1285 in the prevention of AAD was demonstrated by Montreal’s Maisonneuve-Rosemont Hospital, in a clinical study of hospitalized patients.\cite{53}

Current research is focusing on the molecular biology and genomics of \textit{Lactobacillus} and bifidobacteria. The application of modern whole genome approaches is providing insights into bifidobacterial evolution, while also revealing genetic functions that explain their presence in the particular ecological environment of the gastrointestinal tract.\cite{54,55}

Probiotics are used in industry to improve yields of pork and chicken production.\cite{56}

In some situations, such as where the person consuming probiotics is critically ill, probiotics could be harmful. In a therapeutic clinical trial conducted by the Dutch Pancreatitis Study Group, the consumption of a mixture of six probiotic bacteria increased the death rate of patients with predicted severe acute pancreatitis.\cite{57}

In a clinical trial conducted at the University of Western Australia, aimed at showing the effectiveness of probiotics in reducing childhood allergies, Dr Susan Prescott and her colleagues gave 178 children either a probiotic or a placebo for the first six months of their life. Those given the good bacteria were more likely to develop a sensitivity to allergens.\cite{58}

Some hospitals have reported treating \textit{Lactobacillus} septicaemia, which is a potentially fatal disease caused by the consumption of probiotics by people with lowered immune systems or who are already very ill.\cite{58,59}

There is no published evidence that probiotic supplements are able to replace the body’s natural flora when these have been killed off; indeed bacterial levels in feces disappear within days when supplementation ceases.\cite{60}

Side effects

In a therapeutic clinical trial conducted by the Dutch Pancreatitis Study Group, the consumption of a mixture of six probiotic bacteria increased the death rate of patients with predicted severe acute pancreatitis.\cite{57}

In a clinical trial conducted at the University of Western Australia, aimed at showing the effectiveness of probiotics in reducing childhood allergies, Dr Susan Prescott and her colleagues gave 178 children either a probiotic or a placebo for the first six months of their life. Those given the good bacteria were more likely to develop a sensitivity to allergens.\cite{58}

Some hospitals have reported treating \textit{Lactobacillus} septicaemia, which is a potentially fatal disease caused by the consumption of probiotics by people with lowered immune systems or who are already very ill.\cite{58,59}

There is no published evidence that probiotic supplements are able to replace the body’s natural flora when these have been killed off; indeed bacterial levels in feces disappear within days when supplementation ceases.\cite{60}

Recent studies indicate that probiotic products such as yogurts could be a cause for obesity trends.\cite{62}

However, this is contested as the link to obesity and other health related issue with yogurt may link to its dairy attributes.\cite{63,64,65}

Probiotics are used in industry to improve yields of pork and chicken production.\cite{56}

<table>
<thead>
<tr>
<th>Strain</th>
<th>Potential effect in humans</th>
</tr>
</thead>
<tbody>
<tr>
<td>\textit{Bacillus coagulans}</td>
<td>Improves abdominal pain and bloating in IBS patients.\cite{67} Increases immune response to viral challenge.\cite{66}</td>
</tr>
</tbody>
</table>

168
<table>
<thead>
<tr>
<th><strong>Bifidobacterium infantis</strong></th>
<th>Shown to improve symptoms of IBS. [77]</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lactobacillus acidophilus</strong></td>
<td>Shown to reduce the side effects of antibiotic therapy. [76]</td>
</tr>
<tr>
<td><strong>Lactobacillus casei</strong></td>
<td>Human studies have shown that L. casei alone or in combinations has a beneficial effect within gastrointestinal health.</td>
</tr>
<tr>
<td><strong>Lactobacillus paracasei</strong></td>
<td>Diarrhea prevention and mitigation in children</td>
</tr>
<tr>
<td><strong>Lactococcus lactis</strong></td>
<td>Immune stimulation, improves digestive health, reduces antibiotic-associated diarrhoea [76]</td>
</tr>
<tr>
<td><strong>Lactobacillus rhamnosus</strong></td>
<td>Immune stimulation, improves digestive health, reduces antibiotic-associated diarrhoea [76]</td>
</tr>
<tr>
<td><strong>Bifidobacterium animalis</strong></td>
<td>Human studies have shown that Bifidobacterium animalis has a beneficial effect within gastrointestinal health and immune health. [69]</td>
</tr>
<tr>
<td><strong>Bifidobacterium infantis</strong></td>
<td>Showed significant improvement for abdominal pain/discomfort, bloating/distention, and bowel movement difficulty. [71]</td>
</tr>
<tr>
<td><strong>Lactobacillus casei</strong></td>
<td>Protects against Salmonella typhimurium in mice. Uses prebiotics for improved colonization. Reduces inflammation in an allergy model. Reduces the severity of H. pylori infection of the stomach mucosa. Inhibits pathogenic bacteria, including H. pylori, monocytogenes, E. coli, and Salmonella typhimurium. Survives in the conditions of the gastro-intestinal tract. Adheres to human intestinal cell</td>
</tr>
<tr>
<td><strong>Lactobacillus casei</strong></td>
<td>Human studies have shown that LA has a beneficial effect within gastrointestinal health.</td>
</tr>
<tr>
<td><strong>Lactobacillus paracasei</strong></td>
<td>Diarrhea prevention and mitigation in children</td>
</tr>
<tr>
<td><strong>Lactobacillus johnsonii</strong></td>
<td>Reduces incidences of H pylori-caused gastritis and reduces inflammation [79]</td>
</tr>
<tr>
<td><strong>Lactobacillus rhamnosus</strong></td>
<td>Immune stimulation, improves digestive health, reduces antibiotic-associated diarrhoea [76]</td>
</tr>
<tr>
<td><strong>Lactobacillus rhamnosus</strong></td>
<td>Diarrhea prevention and mitigation in children, [76][79] eradication of H. pylori infection, [80] amelioration of gingivitis, [81] general illness prevention in children [82] and adults [83]</td>
</tr>
</tbody>
</table>
### Prebiotics

Prebiotics are non-digestible food ingredients that stimulate the growth and/or activity of bacteria in the digestive system in ways claimed to be beneficial to health. They were first identified and named by Marcel Roberfroid in 1995. As a functional food component, prebiotics, like probiotics, are conceptually intermediate between foods and drugs. Depending on the jurisdiction, they typically receive an intermediate level of regulatory scrutiny, in particular of the health claims made concerning them. Typically, prebiotics are carbohydrates (such as oligosaccharides), but the definition may include non-carbohydrates. The most prevalent forms of prebiotics are nutritionally classed as soluble fiber. To some extent, many forms of dietary fiber exhibit some level of prebiotic effect.

Roberfroid offered a refined definition in the 2007 Journal of Nutrition stating: "A prebiotic is a selectively fermented ingredient that allows specific changes, both in the composition and/or activity in the gastrointestinal microbiota that confer benefits upon host well-being and health."

Additionally, in his 2007 revisit of Prebiotics, Roberfroid stated that only two particular fructooligosaccharides fully meet this definition: oligofructose and inulin. Other authorities also classify galactooligosaccharides (GOS) as prebiotics. Mannan Oligosaccharides (MOS) have been termed as prebiotics but would more correctly be termed immunosaccharides.

Researchers now also focus on the distinction between short-chain, long-chain, and full-spectrum prebiotics. "short-chain" prebiotics, e.g. oligofructose, contain 2-8 links per saccharide molecule, are typically fermented more quickly in the right-side of the colon providing nourishment to the bacteria in that area. Longer-chain prebiotics, e.g. Inulin, contain 9-64 links per saccharide molecule, and tend to be fermented more slowly, nourishing bacteria predominantly in the left-side colon. Full-spectrum prebiotics provide the full range of molecular link-lengths from 2-64 links per molecule, and nourish bacteria throughout the colon, e.g. Oligofructose-Enriched Inulin (OEI). The majority of research done on prebiotics is based on full-spectrum prebiotics, typically using OEI as the research substance.

### Function

The prebiotic definition does not emphasize a specific bacterial group. Generally, however, it is assumed that a prebiotic should increase the number and/or activity of bifidobacteria and lactic acid bacteria. The importance of the bifidobacteria and the lactic acid bacteria (AKA lactobacillus or LABs) is that these groups of bacteria have several beneficial effects on the host, especially in terms of improving digestion (including enhancing mineral absorption) and the

<table>
<thead>
<tr>
<th><strong>Saccharomyces boulardii</strong></th>
<th>Protects against antibiotic-associated diarrhoea and infections of Clostridium difficile and other clostridial species; helps treat acute diarrhoea in adults &amp; children.(^{84,85,86})</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>tested as mixture:</strong></td>
<td><strong>Lactobacillus rhamnosus</strong> &amp; <strong>Lactobacillus</strong></td>
</tr>
<tr>
<td></td>
<td>Oral ingestion results in vaginal colonisation and prevention of vaginitis.(^{87})</td>
</tr>
<tr>
<td><strong>tested as mixture:</strong></td>
<td><strong>Lactobacillus acidophilus</strong> &amp; <strong>Bifidobacterium bifidum</strong></td>
</tr>
<tr>
<td></td>
<td>Reduction of C. difficile–associated disease [1].</td>
</tr>
<tr>
<td><strong>tested as mixture:</strong></td>
<td><strong>Lactobacillus acidophilus</strong> &amp; <strong>Lactobacillus casei</strong></td>
</tr>
<tr>
<td></td>
<td>Improves digestive health. Prevents Antibiotic Associated Diarrhea (AAD) and Clostridium difficile.(^{88})</td>
</tr>
<tr>
<td></td>
<td><a href="http://example.com">In vitro inhibition of <em>Listeria monocytogenes</em> and <em>L. innocua</em></a> and <em>Escherichia coli</em>, <em>Staphylococcus aureus</em>, <em>Enterococcus faecalis</em>and <em>Enterococcus faecium</em>.(^{90})</td>
</tr>
<tr>
<td></td>
<td>Reduction of symptoms of lactose intolerance and immune stimulation.(^{89})</td>
</tr>
<tr>
<td><strong>Lactobacillus plantarum</strong></td>
<td></td>
</tr>
<tr>
<td><strong>&amp; Lactobacillus paracasei</strong></td>
<td>Reduces the risk of acquiring common cold infections.(^{90})</td>
</tr>
</tbody>
</table>

Prebiotics are non-digestible food ingredients that stimulate the growth and/or activity of bacteria in the digestive system in ways claimed to be beneficial to health. They were first identified and named by Marcel Roberfroid in 1995. As a functional food component, prebiotics, like probiotics, are conceptually intermediate between foods and drugs. Depending on the jurisdiction, they typically receive an intermediate level of regulatory scrutiny, in particular of the health claims made concerning them. Typically, prebiotics are carbohydrates (such as oligosaccharides), but the definition may include non-carbohydrates. The most prevalent forms of prebiotics are nutritionally classed as soluble fiber. To some extent, many forms of dietary fiber exhibit some level of prebiotic effect.

Roberfroid offered a refined definition in the 2007 Journal of Nutrition stating: "A prebiotic is a selectively fermented ingredient that allows specific changes, both in the composition and/or activity in the gastrointestinal microbiota that confer benefits upon host well-being and health."

Additionally, in his 2007 revisit of Prebiotics, Roberfroid stated that only two particular fructooligosaccharides fully meet this definition: oligofructose and inulin. Other authorities also classify galactooligosaccharides (GOS) as prebiotics. Mannan Oligosaccharides (MOS) have been termed as prebiotics but would more correctly be termed immunosaccharides.

Researchers now also focus on the distinction between short-chain, long-chain, and full-spectrum prebiotics. "short-chain" prebiotics, e.g. oligofructose, contain 2-8 links per saccharide molecule, are typically fermented more quickly in the right-side of the colon providing nourishment to the bacteria in that area. Longer-chain prebiotics, e.g. Inulin, contain 9-64 links per saccharide molecule, and tend to be fermented more slowly, nourishing bacteria predominantly in the left-side colon. Full-spectrum prebiotics provide the full range of molecular link-lengths from 2-64 links per molecule, and nourish bacteria throughout the colon, e.g. Oligofructose-Enriched Inulin (OEI). The majority of research done on prebiotics is based on full-spectrum prebiotics, typically using OEI as the research substance.

### Function

The prebiotic definition does not emphasize a specific bacterial group. Generally, however, it is assumed that a prebiotic should increase the number and/or activity of bifidobacteria and lactic acid bacteria. The importance of the bifidobacteria and the lactic acid bacteria (AKA lactobacillus or LABs) is that these groups of bacteria have several beneficial effects on the host, especially in terms of improving digestion (including enhancing mineral absorption) and the
effectiveness and intrinsic strength of the immune system.\[^{100}\] A product that stimulates bifidobacteria is considered a bifidogenic factor. Some prebiotics may thus also act as a bifidogenic factor and vice versa, but the two concepts are not identical.\[^{101}\]

**Sources**

Traditional dietary sources of prebiotics include soybeans, inulin sources (such as Jerusalem artichoke, jicama, and chicory root), raw oats, unrefined wheat, unrefined barley and yacon. Some of the oligosaccharides that naturally occur in breast milk are believed to play an important role in the development of a healthy immune system in infants. It is becoming more common to properly distinguish between prebiotic substances and the food that contains them. References to almonds, honey and other foods (most commonly in promotional materials from growers of those foods) as "a prebiotic" are not accurate. No plant or food is a prebiotic: Wheat, honey and many other foods contain prebiotics to a greater or lesser extent, ranging from fairly large portions (chicory root, Jerusalem artichoke) to only trace quantities (thousands of other plant-based foods). Referring to a food as "a prebiotic" is no more accurate than calling a food "a vitamin."

<table>
<thead>
<tr>
<th>Top 10 Foods Containing Prebiotics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Food</td>
</tr>
<tr>
<td>Raw Chicory Root</td>
</tr>
<tr>
<td>Raw Jerusalem Artichoke</td>
</tr>
<tr>
<td>Raw Dandelion Greens</td>
</tr>
<tr>
<td>Raw Garlic</td>
</tr>
<tr>
<td>Raw Leek</td>
</tr>
<tr>
<td>Raw Onion</td>
</tr>
<tr>
<td>Cooked Onion</td>
</tr>
<tr>
<td>Raw Asparagus</td>
</tr>
<tr>
<td>Raw Wheat bran</td>
</tr>
<tr>
<td>Whole Wheat flour, Cooked</td>
</tr>
<tr>
<td>Raw Banana</td>
</tr>
</tbody>
</table>

Genetically engineering plants for the production of inulins has also become more prevalent\[^{103}\][\(^{104}\)], despite the still limited insight into the immunological mechanisms activated by such food supplementation.\[^{105}\]

**Effects**

Studies have demonstrated positive effects on calcium and other mineral absorption,\[^{106}\] immune system effectiveness,\[^{107}\] bowel pH, reduction of colorectal cancer risk,\[^{108}\] inflammatory bowel disorders (Crohn's Disease and Ulcerative Colitis),\[^{109}\] Hypertension (high blood pressure),\[^{110}\] and Recent human trials have reinforced the role of Prebiotics in preventing and possibly stopping early stage colon cancer.\[^{111}\] It has been argued that many of these health effects emanate from increased production of short-chain fatty acids (SCFA) by the stimulated beneficial bacteria. Thus food supplements specifically enhancing the growth of SCFA producing intestinal bacteria (such as clostridia and bacteroides species) are widely recognized to be beneficial.

While research does clearly demonstrate that prebiotics lead to increased production of these SCFA’s,\[^{112}\] more research is required to establish a direct causal connection. It has been argued that prebiotics are beneficial to Crohn's Disease through production of SCFAs to nourish the colon walls, and beneficial to Ulcerative Colitis through reduction of Hydrogen Sulfide gas due to reduction of sulfate-producing bacteria, which do not thrive in the slightly acidic environment SCFAs create.

The immediate addition of substantial quantities of prebiotics to the diet may result in a temporary increase in gas, bloating or bowel movement. It has been argued that chronically low consumption of prebiotic-containing foods in the typical Western diet may exaggerate this effect.

Human colonic bacteria substrates are relatively stable. Production of SCFA and fermentation quality are reduced during long-term diets of low fiber intake.\[^{113}\] Until bacterial flora are gradually established to habituate or
restore intestinal tone, nutrient absorption will be impaired and colonic transit time temporarily increased with an immediate addition of higher prebiotic intake.[114]

REFERENCES


19. "Does yogurt decrease acute diarrhoeal symptoms in children with acute gastroenteritis".


48. Kruis, W; Fric, P; Pokrotniak, J; Lukás, M; Fixa, B; Kascák, M; Kamm, MA; Weismueller, J et al. (November, 2004). "Maintaining remission of ulcerative colitis with the probiotic Escherichia coli Nissle 1917 is as effective as with standard mesalazine". Gut 53(11): 1617–
23. doi:10.1136/gut.2003.037747. PM C 1774300. PMID 15479682.
54. Les yaourts font-ils grossir?
57. "So-called 'friendly' bacteria may be dangerous, according to new research - so which should you be taking?". Daily Mail. 29 January 2008.
58. "Gut Reactions programme 3". BBC.


71. http://www.optibacprobiotics.co.uk/images/engelbrektsson%202009%20probio%20reuteri%20r%20antibiotic%20therapy%20for%20daily%20wellbeing%20extra%20probiotic.pdf


73. "Lactobacillus johnsonii La1 Attenuates Helicobacter pylori-Associated Gastritis and Reduces Levels of Proinflammatory Chemokines in C57BL/6 Mice". December 12, 2005.


86. Millette, M; Luquet, FM; Lacroix, M (March 2007). "In vitro growth control of selected pathogens by Lactobacillus acidophilus- and Lactobacillus casei-fermented milk". Letters of Applied


93. Angelo Pietro Femia, Cristina Luceri, Piero Dolaro, Augusto Giannini1, Annibale Biggeri2, Maddalena Salvadori, Yvonne Clune3, Kevin J. Collins3, Milena Paglierani4 and Giovanna Caderni5; Antitumorigenic activity of the prebiotic inulin enriched with oligofructose in combination with the probiotics Lactobacillus rhamnosus and Bifidobacterium lactis on azoxymethane-induced colon carcinogenesis in ratsCarcinogenesis, Vol. 23, No. 11, 1953-1960, November 2002


96. MAHA TAHIRI, 1 JEAN C. TRESSOL, 1 JOSIANE ARNAUD, 2 FRANCIS BORNET, 3 CORINNE BOUTEOULOU-DEMANGE, 4 CHRISTINE FEILLET-COUDRAY, 1 VÉRONIQUE DUCROS, 2 DENISE PÉPIN, 5 FRED BROUNS, 3,6 ANNE M. ROUSSEL, 2 YVES RAYSSIGUIER, 1 CHARLES COUDRAY1; Five-Week Intake of Short-Chain Fructo-Oligosaccharides Increases Intestinal Absorption and Status of Magnesium in Postmenopausal Women Journal of Bone and Mineral Research, Journal of Bone and Mineral Research November 2001:16:2152-216


99. Food-Info.net Wageningen University

100. a Alanna J. Moshfegh2, James E. Friday, Joseph P. Goldman and Jaspreet K. Chug Ahuja, Presence of Inulin and Oligofructose in the Diets of Americans, Journal of Nutrition. 1999;129:1407S-1411S.


105. Lomax AR, Calder PC. Prebiotics, immune function, infection and inflammation: a review of the evidence. Institute of Human Nutrition, School of Medicine, University of Southampton, Trematra Road, Southampton, UK.


108. Antihypertensive Properties of Plant-Based Prebiotics: Siok-Koon Yeo, Lay-Gaik Ooi, Ting-Jin Lim, and Min-Tze Liong* School of Industrial Technology, Universiti Sains Malaysia, 11800 Penang, Malaysia


110. Macfarlane S et al; Prebiotics in the gastrointestinal tract Aliment Pharmacol Ther. 2006; 24(5): P-701-14;
