

# Commonly Asked Questions about Probiotics and the Potential Benefits for Your Health<sup>1</sup>

Fiona Desland, Lauren Christiansen, Mafuza Rahman, Karim Khan, Anastasia Potts, Claudio F. Gonzalez, and Graciela Lorca<sup>2</sup>

## What are probiotics?

Probiotics are defined as living microorganisms that cause health benefits for a treated host. These health benefits depend on the host consuming a sufficient amount of the microorganisms. Probiotics comprise a rapidly expanding area of research and development because they can be added to diets as a form of preventative health care.<sup>1</sup>

## What is the history of probiotics? How were they discovered?

Although people living before the Common Era (C.E.) did not know about the existence of probiotics, they used probiotics in fermented milk as feed supplements. While humans have consumed fermented milk for thousands of years, it was not until the 20th century that scientific research was conducted in order to determine the cause of the health benefits from consuming fermented milk products.

The man credited with introducing the idea of probiotics was the Nobel Prize winner Ilya Ilyich Mechnikov, a Russian microbiologist working at the Pasteur Institute in Paris. Mechnikov discovered the existence of lactic acid bacteria, including *Lactobacillus delbrueckii*, and their role in the fermentation of milk and production of yogurt. He then

correlated his observations of the long and healthy life span of the Bulgarian people with their consumption of these fermented milk products. Thus, he proposed that these fermenting bacteria had a positive impact on the microorganisms of the colon, as well as decreased toxicity in the colon.<sup>2</sup> Mechnikov's studies into the relationship between lactic acid bacteria and the health benefits of yogurt laid the foundations for the modern development of probiotics.

## What are the typical microorganisms used as probiotics?

The majority of the probiotic organisms belong to the obligate and facultative genera *Bifidobacterium* and *Lactobacillus*, respectively, with *Bifidobacterium* being the most predominant in the human intestine.<sup>3,4</sup> Organisms in these genera are gram-positive lactic acid producers.<sup>5</sup>

## What are some examples of probiotic foods?

Research over the past few decades has resulted in the development of a large number of food or dietary supplements that contain probiotics. Some examples of dairy

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2. Fiona Desland, undergraduate student, Department of Microbiology and Cell Science; Lauren Christiansen, undergraduate student, Department of Microbiology and Cell Science; Mafuza Rahman, undergraduate student, Department of Microbiology and Cell Science; Karim Kahn, undergraduate student, Department of Microbiology and Cell Science; Anastasia Potts, graduate student, Department of Microbiology and Cell Science, Genetics Institute; Claudio F. Gonzalez, assistant professor, Department of Microbiology and Cell Science, Genetics Institute; and Graciela Lorca, assistant professor, Department of Microbiology and Cell Science, Genetics Institute; Florida Cooperative Extension Service, Institute of Food and Agricultural Sciences, University of Florida, Gainesville, FL 32611.

probiotic foods are yogurt, acidophilus milk, certain cheeses, and buttermilk. Soy-based probiotic foods have also been developed. Miso, which is used in numerous dishes, and tempeh, an Indonesian meat substitute, are also probiotic foods. Vegetable products, such as pickled cabbage (i.e., sauerkraut, kimchi, curtido, and choucroute), brine pickles, and brine olives also contain probiotics, as long as they are not pasteurized. Numerous companies have added probiotics to food products that do not naturally contain them. For example, certain commercially available juices, cereals, and snack bars now contain probiotics.<sup>6</sup>

## How are probiotics being used in research today?

There has been a wide range of investigations into probiotics and their benefits for those with gastrointestinal diseases, such as bacterial or antibiotic-induced diarrhea, lactose intolerance, inflammatory bowel disease, and irritable bowel syndrome.<sup>7</sup> Recent research has even shown that as well as modulating the gut, probiotics can aid in the prevention of cancer.<sup>8,9</sup>

### Diarrhea

The most prominent use of probiotic treatment has been for various types of diarrhea, including infectious, traveler's, antibiotic- or virus-induced diarrhea.<sup>4</sup> Approximately 80% of the cases of traveler's diarrhea are caused by pathogens in the *Enterobacteriaceae* family, which includes *Escherichia*, *Shigella*, and *Salmonella* species.<sup>10</sup> Results from studies using different species of *Lactobacillus* showed varied results in the reduction of diarrhea, dependent upon the specific strain as well as the geographic region in which the subjects resided.<sup>4,10</sup> For example, one study recorded a 15.6% decrease in diarrhea incidence in a group of travelers going to one location (in comparison to a placebo group), while no significant effect was seen when these tourists traveled to another destination.<sup>10</sup> These differences may be accounted for by such variables as strain, travel history, and method of administration.<sup>4</sup>

The most convincing results of probiotic use have been reported in the treatment of children with antibiotic-induced nosocomial infections and virus-mediated diarrhea. Rotavirus accounts for about 45% of these viral diarrhea cases.<sup>4,10</sup> Treatment with probiotic strains has been shown to decrease rotavirus shedding as well as increase rotavirus-specific antibodies.<sup>11</sup> The same trend in attenuation of the severity of the diarrheal symptoms could be seen after supplementing antibiotic treatments with probiotics.<sup>4</sup>

Although these studies are promising, there is a lack of consistency in the results. For this reason, probiotics cannot be definitively recommended for the treatment of diarrhea.

### Lactose Intolerance

Lactose intolerance refers to the inability to digest the sugar lactose. This widespread condition greatly affects the diets of people who suffer from it, as lactose is a milk sugar that is present in all dairy products. Except for those of northern European descent, most people do not produce lactase, the enzyme responsible for the degradation of lactose. Lactose intolerant individuals who ingest milk and other lactose-containing products often experience symptoms such as diarrhea, flatulence, bloating, and abdominal pain. These indicators of lactose intolerance are usually caused by the fermentation and consumption of lactose by microbes residing in the large intestine. By-products of the fermentation include gases and other products that result in the aforementioned symptoms.<sup>12</sup>

Lactic acid bacteria are now being used as natural treatments for lactose intolerance. The species of lactic acid bacteria most often employed are *Lactobacillus acidophilus*, *Lactobacillus bulgaricus*, *Streptococcus salivarius*, *Lactobacillus reuteri*, *Lactobacillus plantarum*, and *Streptococcus thermophilus*. These species of bacteria break down lactose during milk fermentation and/or in the large intestine, resulting in short fatty acid chains and other products that are then absorbed by the host. These bacteria, which are often added to other products (i.e., milk, yogurt, etc.) or ingested as a dietary supplement, have had mixed results in reducing the symptoms of lactose intolerance. While less than half of participants in numerous studies experienced fewer symptoms, probiotics show promise in the treatment of lactose intolerance.<sup>12</sup>

### Inflammatory Bowel Diseases

Inflammatory bowel diseases (IBDs) are a group of diseases that cause pain and inflammation in the gastrointestinal tract, primarily the small intestine and the colon. Crohn's disease and ulcerative colitis are the two most common inflammatory bowel diseases. They are regarded as types of autoimmune disorders in which intestinal immune cells attack self-tissue, resulting in painful intestinal inflammation. Symptoms include bloody diarrhea, abdominal pain, and fever. Though the specific causes of IBDs are unknown, a genetic component may be partially responsible. There is no known cure for these diseases, though patients often undergo surgery to remove diseased tissue or take anti-inflammatory drugs to ease the inflammation. Pouchitis is another painful IBD-related condition that is often

the result of colon surgery performed to treat ulcerative colitis.<sup>13</sup> During the surgery, a small pouch is formed from the small intestine for the storage of waste. Pouchitis occurs when this pouch becomes infected with bacteria, resulting in painful inflammation and other symptoms similar to ulcerative colitis and Crohn's disease. Many research groups are investigating the role of probiotics in the treatment and prevention of IBDs because, though the exact cause of these pathologies remains a mystery, they are thought to be related to disturbances or abnormal host responses to the microbial flora living in the intestines.<sup>13</sup>

Because of the lack of truly effective pharmaceutical drugs to treat IBDs, many patients are seeking alternative treatments and preventative measures in the form of probiotics and other dietary supplements. Many studies are currently being conducted around the world to determine if probiotics are effective at preventing, treating, and reducing the risk of relapse of IBDs. One previous study investigated the potential of the probiotic *Lactobacillus GG* to prevent the appearance of recurrent lesions after surgery in Crohn's disease patients. However, the results of this study were inconclusive with respect to the probiotic's therapeutic effect.<sup>10</sup> Many early IBD probiotic studies suffered from too small sample sizes and insufficient monitoring times. As with many other studies involving probiotics, there is currently not enough scientific evidence to support the claim that they are beneficial in the treatment and prevention of IBDs. However, as scientists continue to research probiotics, answers regarding their effectiveness with respect to IBDs are not far off. Numerous efforts are also currently being performed on the microbiota of healthy individuals in order to identify potential "probiotic" species that are absent in IBD patients.

## Irritable Bowel Syndrome

IBS or irritable bowel syndrome is a disorder of the lower intestinal tract. It causes a disturbance of bowel movements accompanied by symptoms of abdominal pain, bloating, gas, diarrhea, and constipation. It is estimated that about 10%–20% of the world's population of all ages suffer from symptoms associated with IBS.<sup>14</sup> Although there is no cure for IBS, medications along with dietary changes can often help reduce the symptoms with varying degrees of success among individuals. In recent studies, probiotics were found to be associated with improvement in global IBS symptoms compared to a placebo.<sup>15</sup>

## Cancer

Results from a study using *Bifidobacterium infantis* and *Bifidobacterium bifidum* showed that they were able to

inhibit the proliferation of the breast cancer cell line MCF7 by producing anti-mutagenic compounds.<sup>9</sup> A similar study using *L. acidophilus* and *Bifidobacterium longum* showed binding and neutralization of the liver carcinogen AFB1.<sup>16</sup> The anti-carcinogenic effects of probiotics can be attributed to their role in hindering carcinogen-producing microorganisms, altering tumor differentiation processes, and resisting mutations.

Current research also suggests that probiotics are particularly effective in the prevention of colon carcinogenesis.<sup>8</sup> One study showed a 25%–50% inhibition of carcinogen-induced pre-cancerous colon lesions in rats fed strains of *B. longum* in their diet. Another study showed that administration of *B. longum* completely suppressed colon tumors induced by the carcinogen, 2-amino-3-methyl-3H imidazo (4,5-f) quinoline, which can be found in the human diet.<sup>16</sup> In addition to animal models, studies in humans have also been conducted, with one showing that the consumption of lactobacilli by healthy individuals reduced the mutagenicity of urine and feces connected to the ingestion of carcinogens found in cooked meat.<sup>16, 17</sup>

There is still a lot to be learned regarding which species of probiotic bacteria have protective effects and the mechanisms by which they work. In addition, more studies need to be conducted in humans before it can be proven that probiotics have therapeutic effectiveness to reduce the risk of cancer.

## What are the suggested mechanisms by which probiotics produce their beneficial effects?

Some proposed mechanisms include the following:

- Production of anti-tumor and anti-mutagenic compounds;<sup>8, 19</sup>
- Stimulation of mucus production and intestinal motility in the host;<sup>4, 11</sup>
- Adhesion to intestinal epithelial cells, thus providing a physical barrier against the colonization of pathogens;<sup>20</sup> colonization of pathogens is also reduced due to production of antibacterial chemicals, such as peroxide and bacteriocins;<sup>4, 11</sup>
- Strengthening of the immune system by stimulating macrophages to produce anti-inflammatory factors, such as the cytokines interferon- $\gamma$ , IL-1b and TNF- $\alpha$ .<sup>4, 19, 21</sup>

For example, *Streptococcus thermophilus* is a probiotic that produces a large amount of folate, a DNA-repairing compound, which seems to play a role in this anti-inflammatory response.<sup>21</sup> In addition, probiotics can stimulate the release of IgA, which aids in preventing pathogenic bacteria from penetrating the mucosa.<sup>11</sup>

- Reducing the concentration of genotoxic substances and the activities of cancer-promoting enzymes, such as  $\beta$ -glucuronidase and nitroreductase. This is characterized by alteration of the microflora in the gut to increase the number of commensal bacteria in comparison to pathogenic bacteria (i.e., increasing *Bifidobacteria* and *Lactobacillus* species). In addition, if the carcinogenic compounds are formed, it has been reported that some probiotic bacteria are able to either absorb or bind to these compounds.
- Decreasing the gut pH, which allows for increased host absorption of minerals such as calcium and iron.<sup>4, 19, 21, 22</sup>
- Production of short chain fatty acids and other protective metabolites.<sup>11</sup> Studies with butyrate, a commonly produced fatty acid chain, have shown inhibition in the development of cancer cells as well as promotion of cancer cell death.<sup>8, 22</sup>

Although all are generally accepted as possibilities, these mechanisms cannot be considered actualities yet, due to variability of the results gathered thus far.

## What are prebiotics and what is their connection to probiotics?

Prebiotics are food components that aid the host by promoting the composition or activity of a limited number of beneficial intestinal microbes, including that of probiotics. Some resemble dietary fibers in that they are not hydrolyzed in the intestine, but instead act as substrates for fermentation by the microflora. The only prebiotics in use today are non-digestible, bifidogenic oligosaccharides such as inulin, oligofructose, galactooligosaccharides, and lactulose.<sup>4</sup>

The particular beneficial effects associated with prebiotics are indirect ones, as prebiotics simply stimulate the growth of particular beneficial members of the microflora. As a result, beneficial effects such as prevention of diarrhea and cancer are observed. Because of this indirect manner of action, measuring the beneficial contribution of prebiotics is difficult.

Synbiotics are a combination of probiotics and prebiotics. When used, they create a synergistic effect, which is an effect greater than a simple additive effect of either one used alone.<sup>4</sup>

## What are some of the future implications of probiotics?

There is evidence supporting the beneficial effects of probiotics in many clinical situations. However, there are many factors that contribute to the effectiveness of these microbes on the health of the individual, and so it has been difficult to determine the concrete mechanisms behind their beneficial effects. The efficacy of probiotics depends on an individual's age and eating and living habits; the strength of the hosts' immune system; and the dosage of probiotics given.<sup>4</sup> In addition, the effects of probiotics can vary depending on the combination of the strains of bacteria used (using a single strain or a combination of multiple strains of bacteria).<sup>4</sup> This variation is attributable to each strain having its own specific effects, which can also vary depending on the particular host environment in which it resides. All of these discrepancies will require population-specific studies to be conducted to further evaluate these variations and to provide a more definitive answer to what is the best treatment for the desired application.

With the field of bioinformatics becoming ever more popular, genomic comparisons can be utilized to uncover the similarities and differences among various probiotic species and strains. With this, as well as the utilization of new genetic technology, some of the direct mechanism(s) of the beneficial effects of probiotics will likely soon be revealed. In addition, these new tools will be used to develop improved strains, potentially leading to a more personalized "prescription" for users of probiotics.<sup>2</sup>

Aside from these implications, there have been new points of action in probiotic use that are now being considered. Although probiotics are available in most of the major industrialized nations, distribution is lacking in those nations with high-risk populations that may benefit from probiotics.<sup>2</sup> Future efforts should be made by governments and nonprofit organizations alike to make these products more broadly available in areas where their beneficial effects, particularly in the treatment of diarrheal diseases, could provide a great deal of relief.

## For the Consumer: Frequently Asked Questions

### Should I take probiotics? Are they safe?

Because probiotics are “friendly” bacteria that naturally exist in the digestive tract, there are no major risks associated with their use. Probiotics promote the growth of good bacteria while discouraging the growth of harmful microorganisms. Minor side effects of probiotics may include gas or bloating. However, some patients can have adverse reactions to probiotics because of allergies or interactions of the probiotic with other medications/supplements. Elderly people, newborns, and those with weak immune systems may also experience potential adverse reactions to probiotics.<sup>23</sup> If a patient is considering taking probiotics, he/she should first consult his/her doctor to ensure that there are no risks of harmful drug interactions or other adverse side effects.

Consumers must also be careful to buy probiotics from well-established, reputable companies whose products meet quality standards, such as those outlined by the Food and Agriculture Organization and the World Health Organization. In fact, the nonprofit organization ISAPP (the International Scientific Association for Probiotics and Prebiotics) was recently formed as a way to improve standards for research associated with probiotics and prebiotics, particularly in association with strain designation, effectiveness, and safety.<sup>2</sup>

### What constitutes a “good” probiotic?

Because probiotics are considered “dietary supplements,” they are not regulated as drugs by the FDA. Unlike drugs, their safety and efficacy does not have to be proven through numerous clinical trials and laboratory testing in order to be sold. Therefore, it is very important for individuals to do research on the probiotics and the companies that sell them. This will help ensure that they are buying high quality and safe probiotics that will possess the beneficial properties shown in the literature. While risk of contamination is a serious problem, another concern is that the consumer is not getting viable probiotics. One study demonstrated that only 4 of 13 products (31%) were in accordance with label claims.<sup>24</sup>

When looking at probiotic products, the consumer should look at the number of viable organisms that the product contains. Anything less than 1 billion organisms per gram is not sufficient as a therapeutic dosage.<sup>24</sup> Consumers should also be aware of the product’s expiration date and storage requirements. For instance, does the product need to be

refrigerated? For most probiotics, refrigeration is very important in ensuring that the product contains the right amount of viable organisms. Most experts recommend probiotics that are in a refrigerated powder form. Powder capsules can also be effective, though the number of viable organisms is often substantially reduced. Also, the strain and type of probiotic is important when attempting to achieve the maximum therapeutic response. The most important strains are members of *L. acidophilus*, *B. bifidum*, *L. bulgaricus*, and *S. thermophilus*.<sup>25</sup> The strain of bacterium used needs to be able to withstand the acidic conditions of the digestive system to reach the intestines in order to be effective.

### How much should I take?

The optimal dosage of probiotics highly depends on the type of probiotic taken, as well as the individual patient. A therapeutic dosage is usually considered between 5–10 grams per day.<sup>23</sup> However, a patient should consult his/her doctor and/or nutritionist and follow the directions on the probiotic’s packaging to achieve the maximum therapeutic effect. Aside from taking probiotics in powder or capsule form, people can also increase their probiotic intakes by eating probiotic-rich foods. Particularly, dairy products like yogurt and kefir are good sources of probiotics. According to a study done by Shahani and Ayebo, the consumption of large amounts of dairy products such as yogurt that contain probiotics like *Lactobacillus* or *Bifidobacterium* may be related to a lower incidence of colon cancer.<sup>18</sup>

### Can I use probiotics as a viable and more natural treatment option?

While conventional modern medicine dominates treatment of disease in today’s society, alternative medicine has become increasingly popular because some patients desire more natural remedies for disease instead of relying on pharmaceutical drug treatments.

Although research on the health benefits of probiotics is not always consistent, it seems that patients may find it worthwhile to try using probiotics because of the potential benefits and limited risk. Because probiotics have minimal side effects, it would be in a patient’s best interest to include probiotics in his/her diet. By supplementing the concentration of beneficial bacteria in their gut, individuals will be able to reap any potential benefits associated with probiotics for the prevention and treatment of cancer and intestinal diseases. Overall, for the average individual, it seems that the benefits outweigh the risks.

## Did You Know...?

- In a survey conducted on approximately 500 people in 2007 by the International Food Information Council, 58% were aware of potential digestive health benefits of probiotics; 54% were aware of potential immune system health benefits of probiotics; about 40% were already consuming products containing probiotics; and 45%–48% were likely or somewhat likely to consume such products.<sup>26</sup>
- The first industrially produced yogurt was developed according to the theories of Mechnikov to help children suffering from diarrhea and was sold in pharmacies.<sup>4</sup>
- Probiotic products taken by mouth as a dietary supplement are manufactured and regulated as foods, not drugs.<sup>1</sup>

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