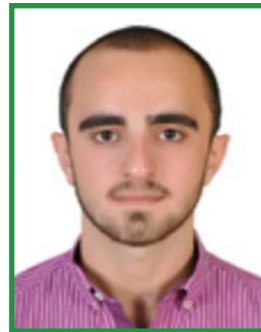


Probiotics: Bacteria Friendly To Our Health



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is good proof that probiotics help the body, there is still no good proof that taking probiotic pills does any good.¹

Health Canada has accepted the following bacterial species, when delivered in food at a level of 1×10^9 colony forming units (CFU) per serving, as probiotics for which nonstrain-specific claims might be made: Bifidobacterium (adolescentis, animalis, bifidum, breve and longum) and Lactobacillus (acidophilus, casei, fermentum, gasseri, johnsonii, paracasei, plantarum, rhamnosus and salivarius).³

Foods with Probiotics

Foods that contain natural probiotics include:

- Yogurt
- Kefir
- Aged cheeses
- Kimchi
- Sauerkraut
- Miso
- Tempeh
- Some soy beverages.

There are also products available which are probiotic-fortified such as juices, chocolates, flour and cereal.⁴



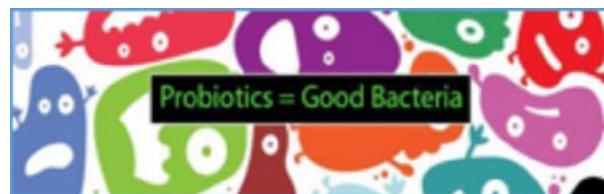
Probiotics vs. Prebiotics

A probiotic is a live, naturally-occurring microorganism that functions internally to promote health and well-being. A prebiotic is a non-digestible food ingredient (normally a carbohydrate) that beneficially affects the host by

What are Probiotics?

Probiotics are what many people call “friendly bacteria” or “good bacteria.” They are bacteria that live in the body and help it work well. Often probiotics help defend the body from infections caused by unfriendly bacteria or other germs.¹

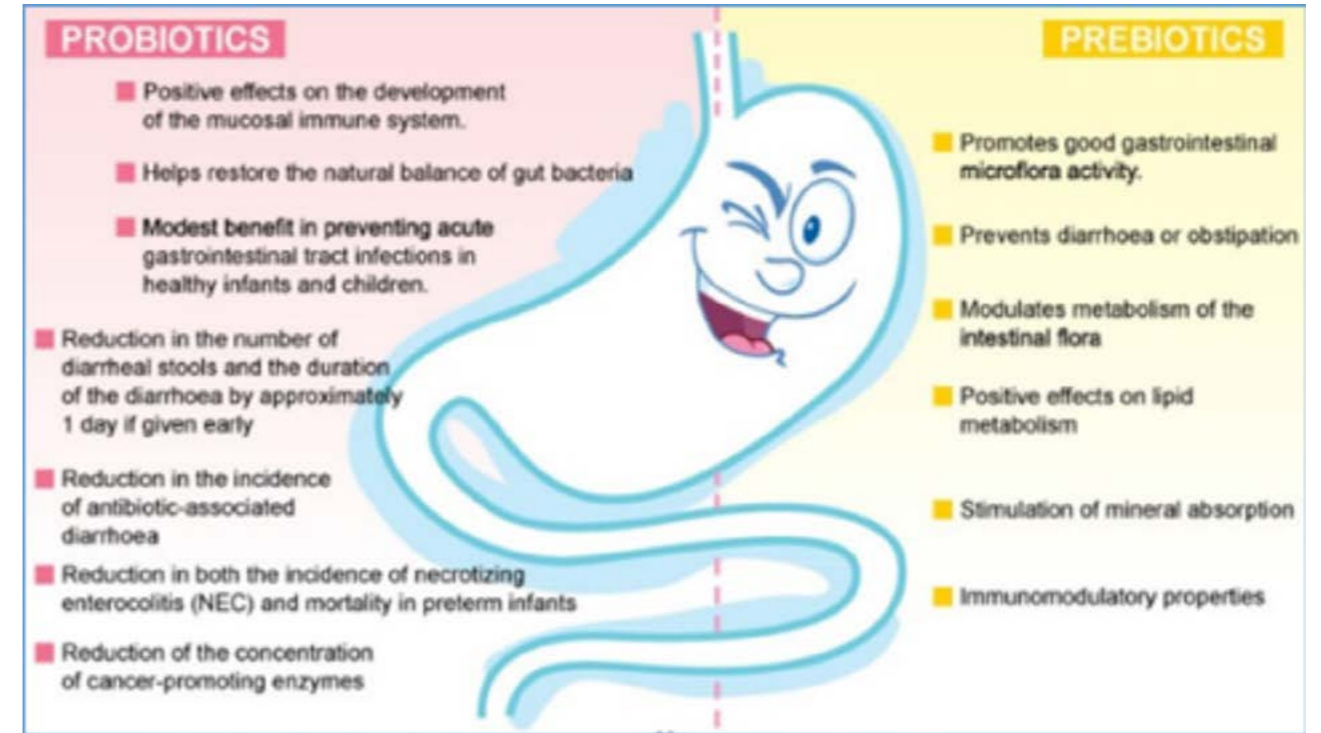
In 2001, the Food and Agriculture Organization of the United Nations (FAO) and the WHO debated the emerging field of probiotics and put the following definition of probiotics: “live microorganisms which when administered in adequate amounts confer a health benefit on the host”.²



Sources of Probiotics

Probiotics get into your body on their own, so you can get benefits without doing or taking anything extra. But some people take pills that contain probiotics because they think the pills will help keep them healthy. Some people even take “pre-biotics,” which are pills that contain a form of food that probiotics like. The problem is, even though there

Figure 1 | Probiotics vs. prebiotics.



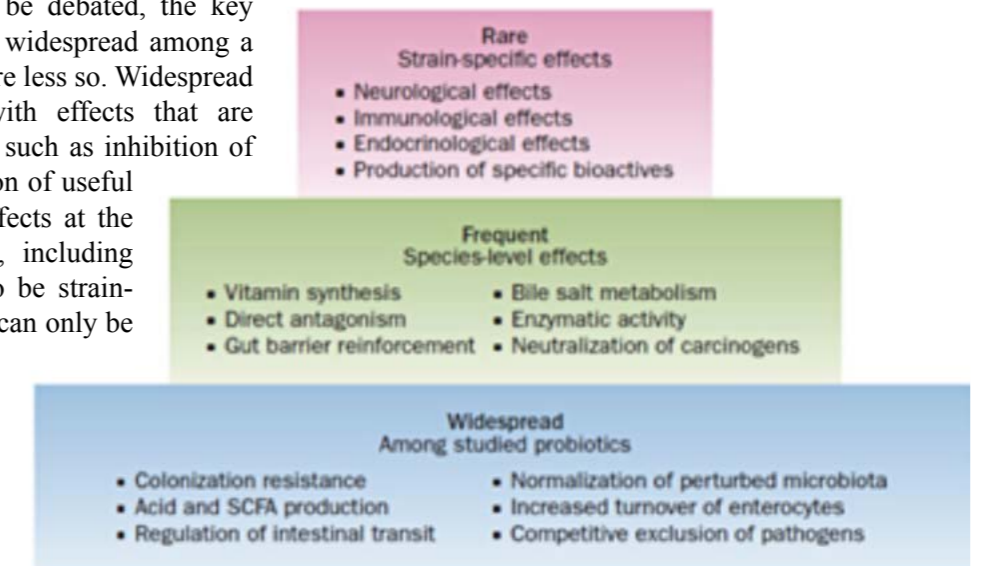
selectively stimulating the growth and/or activity of a limited number of bacteria in the colon. In other words: the prebiotic could be the food for the probiotic.

Underlying mechanisms

Figure 2 considers, in a general sense, the distribution of mechanisms of action among probiotic strains. Although specific attributions can be debated, the key point is that some mechanisms are widespread among a diversity of strains whereas others are less so. Widespread mechanisms can be associated with effects that are observed across taxonomic groups, such as inhibition of potential pathogens or the production of useful metabolites or enzymes.^{5,6} Other effects at the intestinal or extra intestinal level, including immune effects, are more likely to be strain-specific⁷ and claims of such benefit can only be made for strains or species in which the mechanistic basis has been demonstrated.^{8,9} In many cases, a given probiotic might exert several health-promoting effects. Although multiple mechanisms are often represented in a single strain, no

individual probiotic would be expected to have all the effects listed in Figure 2.

Figure 2 | Possible distribution of mechanisms among probiotics. Some mechanisms might be widespread among commonly studied probiotic genera; others might be frequently observed among most strains of a probiotic



species; others may be rare and present in only a few strains of a given species. Evidence is accumulating on a cross-section of probiotic strains that suggest some generalizations can be made beyond strain-specific effects.

Abbreviation: SCFA, short-chain fatty acid.
Health benefits of probiotics

Mechanisms for the benefits of probiotics are incompletely understood. However, four general benefits have been described^{10,11}:

1. Suppression of growth or epithelial binding/invasion by pathogenic bacteria¹².
2. Improvement of intestinal barrier function¹³⁻¹⁵.
3. Modulation of the immune system. Several probiotic species or their products induce protective cytokines, including IL-10 and TGF-beta, and suppress proinflammatory cytokines, such as TNF, in the mucosa of patients with pouchitis, ulcerative colitis, and Crohn disease, in murine experimental colitis, and in isolated splenocytes^{17,12,15,18-22}. *S. boulardii* limited the migration of T-helper 1 cells in inflamed colon tissue in a mouse model of inflammatory bowel disease²³.
4. Modulation of pain perception. Some *Lactobacillus* strains appear to induce expression of micro-opioid and cannabinoid receptors in intestinal epithelial cells and mediate analgesic functions in the gut in a manner similar to the effects of morphine²⁴.

Effects of probiotics have been noted in the following health conditions:

- **Pouchitis:** Data from small controlled trials suggest a benefit from VSL#3 (bifidobacterium and lactobacillus) in the primary and secondary prevention of pouchitis. Thus, it is a reasonable option in addition to standard medical therapy, although long-term efficacy is uncertain.²⁵
- **Ulcerative colitis:** A benefit of probiotics in ulcerative colitis remains unproven, but *E. coli* as shown by Nissle 1917 promise in maintaining remission and could be considered as an alternative in patients intolerant or resistant to 5-ASA preparations. No other probiotic preparation has been validated for this indication. VSL#3 may have some efficacy in treating active disease as an adjunctive approach.^{26,27}
- **Crohn disease:** A benefit of probiotics in Crohn disease remains unproven.²⁸
- **Diarrhea:** It is suggested to use probiotics in adults and children with presumed infectious diarrheal illness (Grade 2B). If probiotics are used, treatment should consist of regimens with *Lactobacillus* GG and *S. boulardii*.²⁹⁻³⁵ A 2010 review from the Cochrane

Collaboration concluded that probiotics shorten episodes of acute infectious diarrhea. In addition, in 2011, a Health Canada monograph stated that products containing certain probiotics (such as *Lactobacillus rhamnosus* GG) help manage acute infectious diarrhea and antibiotic-associated diarrhea.¹⁶ A 2012 research review published in the *Journal of the American Medical Association (JAMA)* reported that probiotics reduced the risk of antibiotic-associated diarrhea by 42 percent—but many of the studies had flaws, so these findings should be interpreted with caution. Moreover, a 2013 Cochrane review of 23 trials also concluded that probiotics may be effective for preventing antibiotic-related diarrheas. However, the largest and best-designed study to date, published in the *Lancet* in 2013, found that probiotics were no better than a placebo in preventing diarrhea in older people taking antibiotics.¹⁶

• **Constipation:** A few small randomized controlled trial suggest improvement in defecation frequency and stool consistency in patients with chronic constipation³⁶⁻⁴⁰. However, larger studies are needed before probiotics can be routinely recommended in the management of severe chronic constipation⁴¹

• **Irritable Bowel Syndrome:** More convincing evidence of a benefit of probiotics for irritable bowel syndrome is accumulating, although there is still considerable disagreement as to which agent or group of probiotics is most beneficial and which patient subgroups should be targeted. One product that has some research behind it for irritable bowel conditions is VSL#3, a combination of eight different probiotic strains, to be used under a doctor’s supervision. ¹⁶ A definitive therapeutic role remains unproven and needs to be further investigated in defined patient subsets.⁴²⁻⁴⁶

• **Lactose intolerance:** A benefit of probiotics for lactose intolerance remains unproven.⁴⁷

• **Hepatic encephalopathy:** Initial studies were associated with an improvement in hepatic encephalopathy. However, a large meta-analysis has shown no demonstrable benefit with regard to clinically relevant outcomes (eg, mortality and quality of life).

• **Allergy:** A definitive role of probiotics for allergic conditions remains unproven, although initial results in studies of children with a variety of preparations for atopic dermatitis are promising.

• **Immunity and colds/flu:** There is a close connection between the bacteria in your colon and the immune system—and probiotics have been linked to enhanced immune responses (such as to flu vaccines). Several

studies, including one published in 2012 in the *British Journal of Nutrition*, have found that certain probiotic strains boost measures of immune response—but whether this translates into any clinical benefits is uncertain. Studies have been inconsistent, for example, as to whether taking probiotics will actually curb colds and other upper respiratory infections. A 2011 Cochrane review concluded that probiotics may help prevent such infections, though there were limitations in the studies and no data presented for older people.¹⁶

• **Weight loss:** There is little published clinical work showing that probiotics will help promote weight loss, as some manufacturers claim or imply. A study in the *European Journal of Clinical Nutrition* in 2011 found that people who drank fermented milk with a particular strain of *Lactobacillus gasseri* for 12 weeks had a reduction in abdominal fat and body weight, compared to those consuming a control drink. Another study, published in the *Journal of Functional Foods* in November 2012, found that people who consumed yogurt containing two “novel” strains of probiotics experienced small losses in body fat, but no changes in body weight.¹⁶

• **Oral health:** In addition to the microflora that resides in the large intestine, bacteria populate the mouth as well. An increasing number of probiotic lozenges and gums are thus being promoted for.

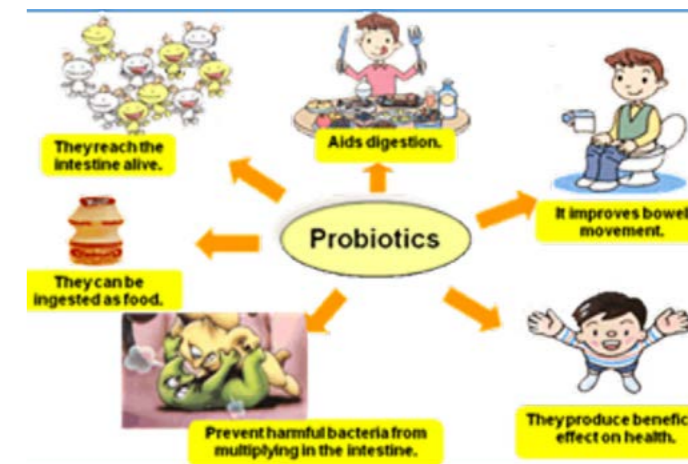
• **Oral health:** There is preliminary evidence that certain strains may have some benefits in reducing periodontal disease, throat infections and bad breath., but commercial products may not have the same strains and formulations as those tested in published studies. These products are not expected to replace brushing and flossing.¹⁶

• **Other uses:** Many other claims are made for probiotics—that they lower blood pressure and cholesterol, alleviate skin conditions like eczema, treat ulcers and urinary tract infections, improve vaginal health, prevent colon cancer, ease anxiety and depression and ward off traveler’s diarrhea. Good evidence to support these claims is lacking.¹⁶

Probiotics in Yogurt

Whether yogurt and other fermented dairy products (such as kefir) provide probiotic health benefits is debatable, but they are excellent foods, high in protein and calcium. The voluntary “Live and Active Culture” seal from the National Yogurt Association is the best assurance that a certain number of bacteria were present at the time of manufacture—though this may not mean much since many

may have perished since. And note that the Food and Drug Administration (FDA) has not approved the seal. Also, be aware that yogurts that are heat-treated after fermentation do not contain live organisms.¹⁶



Should I eat yogurt with “active cultures”?

Yogurt products that have “active cultures” have probiotics in them. If you like yogurt and can digest it normally, there is probably no harm in eating it. It is possible that eating yogurt will help your digestion and help keep you healthy. If nothing else, low-fat yogurt can be a part of a healthy diet.¹

If you are lactose intolerant, you’ll probably have less of a problem with yogurt than milk, because the live bacteria will have digested some of the lactose (milk sugar).¹⁶

Important Questions And Facts

• Do probiotic pills help improve health?

A few studies have hinted that probiotic pills might improve health, but scientists say there is not enough proof to say for sure. They think more research is needed.¹

• Should I take probiotic pills?

No. You should not take probiotics, unless your doctor or nurse tells you to. There is no proven benefit of taking probiotic pills.¹

• What are the downsides to taking probiotics?

Probiotics are not regulated by the US Food and Drug Administration (the FDA) the way standard medicines are. The companies that package probiotics don’t have to prove that the ingredients listed on the label are actually in the bottle. In the end, you could buy a bottle that does not have what you think it has, so you could lose money (Some probiotic pills are expensive) 1. Even if you do find pills that contain what you think they do, there is a small chance the pills could do you harm. In particular, people



with weak immune systems (for example, people on chemotherapy for cancer) should be extra careful. That's because probiotics could cause an infection. 1

- Several probiotic preparations have promises in preventing or treating various health conditions. However, most studies have been small, and many have important methodologic limitations, making it difficult to make unequivocal conclusions regarding efficacy, especially when compared with proven therapies. Furthermore, considerable differences exist in composition, doses, and biologic activity between various commercial preparations, so that results with one preparation cannot be applied to all probiotic preparations. Finally, costs to the patient may be considerable since no preparation is FDA approved and most are not reimbursed by insurers. Enthusiasm for probiotics has outpaced the scientific evidence. Large, well-designed multicenter controlled clinical trials are needed to clarify the role of specific probiotics in different well-defined patient populations.

- The decision to use a probiotic rests mostly upon the degree of anticipated benefit, available alternatives, the clarity of the available data in showing a benefit, costs and patient preferences. No probiotic strategy is currently considered to represent either the standard of care or primary treatment for any of the conditions described above.

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