



# Health Benefits of Probiotic

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## Abstract

Probiotics are widely promoted for the prevention and treatment of a diverse range of health conditions. Their effectiveness is well-supported in some clinical situations, and they are commonly used by consumers and in clinical settings worldwide. When using probiotics continues to grow, it is crucial to comprehensively assess their risks and benefits. In this article, we evaluate the security of Probiotics and address areas of uncertainty related to their utilization.

While probiotics generally have a strong safety track record, caution is advisable when considering their use in specific patient groups, especially in preterm infants and individuals with weakened immune systems. Further study is necessary in these areas since there is inadequate understanding about the exact 2 processes by which probiotics work, suitable dose schedules, and possible interactions.

Additionally, it is crucial that note that different probiotic species can have varying properties, and their effects can be strain-specific. As a result, without validation from other research, it is inappropriate to extrapolate the results of one probiotic strain to others. Careful consideration of these aspects is required prior to prescribing probiotic supplements in clinical practice.

**Key Words-** Probiotics, Lactobacillus, Bifidobacterium, Escherichia, Enterococcus,

## Introduction

Probiotics originated about 1908, when Nobel winner Eli Metchnikoff hypothesised that Bulgarian peasants' longer life expectancies might be related to their intake of fermented milk products. The word "probiotic" was first used in 1965 by Lilly and Stillwell to refer to compounds that are produced by one organism but aid in the growth of another. Definition of the term "probiotics" by Marteau et al. (2002) as "preparations of microbes or elements of microorganisms that are beneficial to health and wellbeing."

Human beings maintain close associations with a vast array of microorganisms, which are present in the skin, in the oral cavity, and within the gastrointestinal tract. The gastrointestinal tract, with a surface area of over 400 square meters, hosts the highest concentration of commensal organisms. This places it second only to the respiratory tract in terms of total surface area within the body. The GIT hosts a diverse array of over 500 bacterial species, some of which play crucial roles in maintaining health. These roles encompass stimulating the immune system, safeguarding the host against harmful bacteria and viruses, and aiding in digestion. The gut

microbiota establishes soon after birth, remains relatively stable throughout one's life, and is indispensable for human well-being. When the gut microbiota is developing, interactions between this microflora and the host lead to the formation of a unique and distinct intestinal immune system. The main challenge for this host mucosal immune system is to distinguish between harmful pathogens and benign organisms, promoting protective immunity while preventing excessive inflammation that could harm the integrity of the GI mucosa.

Treatments include radiation, immunosuppressive medications, antibiotics, and other medical procedures may alter the gut flora's makeup. As a result, the introduction of advantageous bacterial species into the gastrointestinal system becomes a desirable strategy for reestablishing microbial equilibrium and averting illness.

The gastrointestinal tract contains around 500 distinct bacterial species, some of which are vital to overall health. These functions include boosting the immune system, protecting the host from dangerous germs and viruses, and facilitating digestion. Human health depends on the gut microbiota, which emerges soon after birth and is relatively stable throughout life. Interactions between the developing intestine microflora and the host result in the formation of a unique and distinct intestinal immune system. The capacity of the host's mucosal immune system to distinguish between infections that represent a threat and benign species, therefore encouraging protective immunity, is the main challenge it faces and preventing over-inflammation, which might jeopardize the mucosa of the gastrointestinal tract.

Treatments such as radiation therapy, immunosuppressive drugs, antibiotics, and other medical procedures might change the composition of the gut flora. As a result, reestablishing the microbial balance and averting illness through the introduction of advantageous bacterial species into the digestive system becomes a desirable alternative.[1]

## DEFINITION

The name "probiotics" originates from the Greek word "probiotics," which meaning "for life." As defined by the Food and Agriculture Organization, probiotics are "live microorganisms" that enhance the host's health when administered in enough amounts. (WHO) and the Food and Agriculture Organization (FAO) to a panel of experts. Probiotic formulations often contain bacterial species such Lactobacillus, Bifidobacterium, Escherichia, Enterococcus, Bacillus, and Streptococcus; Saccharomyces is one example of a fungus strain that has also been employed.

Among probiotics, Lactobacillus rhamnosus GG (LGG) attracted the first significant clinical interest. The conventional strain of Lactobacillus employed in dairy fermentation was unable to colonize the gastrointestinal tract. Thus, the ideal conditions for probiotics were met with the 1985 discovery of Lactobacillus rhamnosus strain GG. Through increasing the amount of IgA and other intestinal mucosa's immunoglobulin-secreting cells, which produce interferon, and improving antigen transport to lymphoid cells in Peyer's patches, Lactobacillus rhamnosus GG has been shown to have beneficial effects on intestinal immunity.

Contrarily, prebiotics are indigestible food components that enhance host health by favorably promoting the development and activity of certain microorganisms throughout the intestines. Prebiotics are dietary carbohydrates that are resistant to digestion in the upper gastrointestinal tract. They change the substrate that the preexisting microbial population can use, which changes the bacterial composition of the gut. Fructooligosaccharides, gluco-oligosaccharides, and inulin are a few examples. Synbiotics, which combine probiotics and prebiotics, increase the survival of gut bacteria to optimize their health effects.[2]

## SELECTION CRITERIA FOR PROBIOTICS

A probiotic strain aiming for success should possess several favorable traits to achieve its beneficial effects. The relevant selection criteria for potential probiotic microorganisms. Some of these criteria will be elaborated upon from a mechanistic perspective due to their overall significance. Depending on the specific desired outcome, additional properties may be necessary for a probiotic. It's worth noting that not all selection criteria must be met by a potential probiotic.

## production of Anti- microbial substances

Coaggregation is the process of microorganisms binding together, closely linked to adhesion. Some believe that probiotic microorganisms with the ability to coaggregate with potential pathogens might be more efficient in combating these pathogens. This is because they can generate antimicrobial substances in close proximity to the pathogens (Reid, McGroarty, Angotti & Cook, 1988).

Lactic acid bacteria (LAB), including many probiotics, have been observed to produce antimicrobial substances. The most common antimicrobial substances they produce are organic acids, particularly lactic and acetic acids. LAB also commonly produce hydrogen peroxide and carbon dioxide. When probiotic LAB remain metabolically active as they pass through the intestine, it's likely that they produce some of these substances. One indicator of this is the generation of organic acid, as evidenced by a drop in fecal pH following consumption of specific probiotic strains. However, it is uncertain whether other antimicrobial components like diacetyl, reuterin, pyroglutamic acid, and bacteriocins are produced under in vivo conditions. The intestine produces bacteriocins, but their usefulness has not yet been studied.

Nonetheless, there is some proof that the oral cavity creates and utilizes bacteriocins. A bacteriocin-producing *S. mutans* was shown by Hillman, Dzuback, and Andrews (1987) to lower the overall level of *S. mutans* and colonise healthy volunteers for at least a year following a single injection. Conversely, a strain with lower bacteriocin production colonized more slowly. When rats given daily doses of bacteriocin, the number of carious lesions significantly decreased in the rats fed a cariogenic diet. Similar results were found in human volunteers in good health (Ikeda, Koulourides, Kurita, Housch & Hirasawa, 1985). Although this has not yet been clinically proven, these results imply that bacteriocins may be generated and active in the intestine.[3]

## production technology

### Production of frozen and freeze-dried cultures

The foundation of all bacterial culture production lies in the creation of a culture bank, ensuring the safe preservation of the original pure strain. Typically, these strains are stored in one of three ways: deep-frozen in liquid nitrogen at  $-176^{\circ}\text{C}$ , in a freezer at  $-80^{\circ}\text{C}$ , or freeze-dried. Many ampoules of a particular strain, produced with few propagation steps, ideally concurrent with the strain's deposit, are contained in the cell bank. Ampoules must be produced under aseptic conditions to prevent contamination. This primary material serves as the basis for a stock culture, requiring only a few intermediate propagations. For instance, at Chr. Hansen, we maintain enough ampoules of primary material to last 50-100 years and stock cultures for 3-5 years of industrial use. Proper and precise coding and registration are essential at every stage to easily trace the origin of a culture, if needed.

In our project, all selected probiotic strains were deposited at Chr. Hansen and supplied to project partners in frozen ampoules.

### Milk fermentation.

Fermented milk product production was demonstrated using all strains as outlined in Probiotic strains were employed either as the sole starter or in conjunction with support cultures, which were added to expedite the acidification process. While two of these support cultures were yoghurt cultures with both *Lactobacillus delbrueckii* ssp. and *Streptococcus thermophilus* (St-20), one of the cultures exclusively contained *S. thermophilus. bulgaricus* (YC280 and YC380), all sourced from Chr. Hansen A/S in Denmark. These support cultures were introduced as an example of frozen pellet cultures.

The probiotic MRS broth was used to culture bacteria. at  $37^{\circ}\text{C}$  for 16-18 hours, then concentrated through centrifugation and subsequently utilized at concentrations ranging from  $4 \times 10^6$  to  $2.5 \times 10^7$  colony-forming units per milliliter for inoculating the milk. When used in conjunction with the yogurt culture YC280, the probiotic strains were introduced as an example of freeze-dried cultures.

Selective analysis of the probiotic counts was conducted as follows:

Bacterial counts for *L. delbrueckii* ssp. *bulgaricus* were made on MRS-agar at 5.4 pH, whereas *S. thermophilus* counts were determined using M17-agar.

*L. paracasei* F19 could be selectively distinguished from *L. delbrueckii* ssp. *bulgaricus* based on colony morphology.

For other probiotic organisms, *L. salivarius* UCC118 was enumerated using MRS containing 250 mg/ml rifampicin, *Lactobacillus rhamnosus* GG with MRS featuring 50 mg/ml vancomycin, Bi@dobacterium BB12 with MRS containing 0.5 mg/ml dichloxacillin, 1 mg/ml LiCl, and 0.5 mg/ml cysteine hydrochloride, *L. johnsonii* La1 with minimal nutrient agar (MNA) containing 0.5% salicin, and both *L. crispatus* MU5 and M247 with MRS containing 0.3% oxgall.

The fermented products were analyzed for potential contamination with Enterobacteriaceae group bacteria using the NMKL method on the day of production. Additionally, they were checked for yeast and mold contamination on a weekly basis throughout their shelf life, following the procedure outlined in reference.[4]

## Human use

### Infantile colic

Colic, characterized by incessant crying for over 3 hours a day, on more than 3 days per week, lasting beyond 3 weeks in an otherwise healthy child (Johnson et al. 2015), is a prevalent and challenging condition to manage. Traditional medical approaches have proven ineffective for colic (Johnson et al. 2015). Although the exact cause of colic is still unknown, up to 20% of babies can have it (Sung et al. 2014). Research suggests that diet and the intestinal microbiome may be contributing factors, as colicky infants often exhibit reduced levels of lactobacilli in their gut microbiota (Savino et al. 2004, 2005). These preliminary results sparked research on the effect of probiotics on colic.

Among the probiotics studied, *L. reuteri* 17938 stands out as the most extensively examined strain for treating colic in infants. In what is regarded as the highest level of evidence, a thorough meta-analysis based on individual participant data (Riley et al. 2010) examined four double-blind trials including 345 colicky infants (174 getting *L. reuteri* 17938 and 171 receiving a placebo). The outcomes demonstrated a statistically significant decrease in the amount of time spent sobbing per day [by 25.4 minutes (95% CI: -47.3, -3.5)], with a success rate of 28% in the probiotic group and 9% in the placebo group following *L. reuteri* 17938 treatment. This indicates that it is effective, as indicated by a Number Needed to Treat (NNT) of 4. Importantly, no adverse events were associated with *L. reuteri* 17938 treatment (Sung et al. 2018). It's worth noting that this effect was only observed in breastfed infants.[6,11,12,13]

### Eczema

Atopic eczema is an inflammatory skin condition characterized by itching, redness, and thick, scaly skin (Berke et al. 2012). It often co-occurs with other atopic conditions like allergic rhinitis and asthma, with an estimated 30% of children with atopic dermatitis eventually developing asthma (Spergel 2010). According to a meta-analysis of research, probiotics can lower an infant's risk of developing eczema. When taken by pregnant women during the last trimester (relative risk (RR) = 0.71; 95% CI: 0.60–0.84), breastfeeding mothers (RR = 0.57; 95% CI: 0.47–0.69), or given to infants (RR = 0.80; 95% CI: 0.68–0.94) (Cuello-Garcia et al. 2015). These findings led the World Allergy Organization (WAO) to assemble a panel to create evidence-based recommendations on probiotics for allergy prevention (Fiocchi et al. 2015). Probiotic usage is advised in three separate scenarios by the WAO panel: (1) pregnant women who are at a high risk of having allergies in their progeny; (2) nursing mothers of babies who are more susceptible to allergies; and (3) probiotic usage in babies who are highly susceptible. While acknowledging the need for more research due to existing data limitations, the WAO and the meta-analysis recognize the potential benefits outweigh the minimal risks, justifying their recommendations.[9]

## Inflammatory bowel diseases

In Western nations, inflammatory bowel disorders (IBD), such as Crohn's disease and ulcerative colitis (UC), are more prevalent due to a combination of factors including diet, inheritance, and environment (Friedman & Blumberg, 2014). Moreover, receiving antibiotics as a baby appears to considerably raise the chance of developing IBD (Friedman & Blumberg, 2014). As a result of the apparent relationship between the microbiome, nutrition, and IBD, dietary modifications and probiotic supplements are being considered as possible therapies.

Interestingly, traditional medicines are employed for both UC and Crohn's disease. However, trials testing probiotics as a treatment for Crohn's disease have consistently yielded negative results, as observed in the Bourreille et al. (2013) trial. On the other hand, some beneficial trials using various probiotic products/strains in UC patients have been conducted; these studies mostly used VSL#3 and E. coli Nissle 1917 (Floch et al., 2015). Number Needed to Treat (NNT) was 4, with a remission rate of 44.6% in the VSL#3 group and 25.1% in the placebo group, according to a metaanalysis of 319 UC patients receiving VSL#3 or a placebo (Cordina et al., 2011; Mardini & Grigorian, 2014). VSL#3 is now included in the formulary of some UK hospitals and prescribed by certain gastroenterologists as an adjunctive treatment for UC, although it is not yet standard practice in the UK.[8,14,18]

## Antibiotic-associated diarrhoea and Clostridium difficile infection

Antibiotics are frequently prescribed in UK hospitals and, in addition to treating infections, they can disrupt the gut's microbiota, potentially causing antibiotic-associated diarrhea (AAD). More alarmingly, this disruption can lower resistance to opportunistic pathogens like Clostridium difficile, leading to C. difficile infection. In the UK, this infection causes around 30 deaths annually and can be quite serious or deadly. Research indicates that concomitant use of probiotics and antibiotics can lower the frequency of AAD and C. difficile-associated diarrhea (AAD). For example, the probiotic Saccharomyces boulardii significantly reduced the risk of AAD in patients treated with antibiotics. Some large-scale studies have shown a significant reduction in CDAD risk when probiotics are co-prescribed with antibiotics. But there's still a lot to learn about the best time, length, composition, and dosage of probiotics to lower the risk of CDAD. Some trials have shown mixed results, but it's worth noting that administering probiotics appears safe. While some UK hospitals have implemented co-prescribing probiotics with antibiotics, it's not yet standard practice.[7,10,15,17]

## Applications:

1. Dietary chemical metabolism in the gut lumen
  - a. digestion of lactose
  - b. Metabolic lipids
  - c. Oxalate metabolism
  - d. Gut microbiota composition and metabolic markers
  - e. Phenobiotics and xenobiotics
  - f. Food ingredients that are indigestible
  - g. Liver and gastrointestinal mucosa metabolic activity
2. Dysfunctional bowel disease:

- a.Crohn's disease
- b.Colitis ulcerative
- c.Pouchitis
- d.Sensitive intestinal syndrome
- e.allergies-related illnesses
- f.Atopic dermatitis, eczema
- g.Rhinitis caused by allergies
- h.Inhalation

### 3.Reduction of infection risk factors

- a.diarrhea caused by infection (acute and antibiotic-associated)
- b.diarrhea caused by travelers
- c.Necrotizing infantile enterocolitis
- d.The Helicobacter pylori
- e.infections of the respiratory tract (in adults and children)
- f.infection of the throat, nose, and ears
- g.Infectious outcomes in patients undergoing surgery[16,19]

## Conclusion

The supplied text's conclusion stresses how crucial it is to carefully weigh the advantages and disadvantages of probiotics. Probiotics are usually regarded as safe, yet in certain patient groups, vigilance is urged. It is also noted that different probiotic strains and species can have differing effects; therefore extrapolating results should be done cautiously. To fully comprehend the specific workings of probiotics and any possible interactions, more research is required. Prior to giving probiotic supplements, these aspects must be thoroughly assessed. The article also briefly discusses the probiotics' historical background and potential health benefits.[20]

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