

# A Study on the Usage of Probiotics as a Safer Antipyretic

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## Abstract

Most medicines and supplements which include probiotics have both expected clinical outcomes and unwanted side effects, which plays a major role when considering them as a mode of treatment. This review is an update about the advantages and disadvantages associated with the use of probiotics as part of a safe therapeutic armamentarium in health and other diseases. The advantages of probiotics run across multiple tissue systems in the body and has a wide age spectrum. Probiotics also promote cardiovascular health, accelerate recovery from the condition of antibiotic-associated diarrhoea, decrease the effect of necrotizing enterocolitis with reduced inflammation, and accelerate the healing of the wound. Probiotics also contribute in treating chronic diseases for patients with type 2 diabetes as well as patients with HIV/AIDS. Moreover, probiotics play an important role in the treatment and/or prevention of cancers, especially those of the colon and bladder. On the other hand, probiotics also mimic serious threats to immunocompromised, genetically predisposed bodies, children, and newborns. Using probiotics may lead to bacteremia, fungemia, or septicemia when consumed more. Also, probiotics are found as a causative agent for pneumonia and abdominal abscesses, increase platelet aggregation, and promote antibiotic resistance among others. A huge number of microorganisms inhabit the human gut and consequently cause a compound network of the interactions of those organisms with each other and within the host cells, which stresses the requirement of extra caution in the use of probiotics as treatment therapy.

**Keywords:** Probiotics, Prebiotics, Carcinoma, Bacteremia, *Lactobacillus*, Pathogens

## Introduction

'Probiotic' is a derived Greek word which means 'for life'. It is considered the opposite of the term antibiotics and has had different meanings over time. The Probiotic was first introduced in mid 1950s' by scientist Werner Kollath and was first used by Lilley and Stillwell in the year 1965 describing probiotics as a substance that are secreted by one microorganism mainly *Lacto bacillus* which stimulates the growth of another microorganism [1-3]. However in 1971, there was a different description of the word probiotics; as the tissue extracts which stimulates microbial growth and in 1974, scientist Parker defined Probiotics as "Organisms and substances which contribute to intestinal microbial balance" [4]. Probiotics is a field of study that is growing. A Medline search for the term "probiotics" turned up almost 1,000 publications, compared to 85 during the previous 25 years, indicating a huge increase in research in this area during the last 5 years [5]. This demonstrates the potential

significance of this nascent field, but much work has to be done to clarify what a probiotic is and which strains satisfy the criteria for true probiotic bacteria. Despite mounting clinical evidence of the probiotics' true benefits, the commercial front has not yet caught up. Unfortunately, many products labelled as "probiotic" aren't actually "probiotic" because they haven't been sufficiently identified, documented, made using appropriate manufacturing techniques, or clinically validated [6]. Nevertheless, many companies make claims that lead consumers to believe they are using reliable goods. To guarantee the validity and effectiveness of probiotic products, creating guidelines and norms is an essential first step. These recently developed standards and recommendations will be covered later [7].

## Methodology

For papers without a language constraint, PubMed, Medline, Google Scholar, Scopus, and UpToDate databases were

searched from 2010 to 2018. Reference lists, authors, reviews, comments, linked disorders, books, and meeting abstracts were also searched manually and in secondary. Probiotics AND bacteremia, cancer, *Lactobacillus*, opportunistic infections, microbiome, pregnancy, history, digestive system, oral health, side effects, inflammatory bowel disorders, irritable bowel syndrome, and colorectal cancer were the search phrases used to find this review paper. Initial search tactics were wide, followed by a focus on the relevant ailment. Using these search parameters, 150 articles were located, and 56 of them fit our review criteria. Each article was mined for data on research methodology, design, interventions, results, side effects, and treatments.

### Probiotics As a Safer Antipyretic

Probiotics are non-pathogenic living microorganisms that comprise certain mutualistic bacteria that, when given to the host in the proper amount, can bestow health-promoting and disease-preventing qualities [8]. Probiotics must be accurately defined, refined to remain viable during their shelf life in a formulation, and have at least one successful human study to demonstrate their effectiveness and safety [9]. Lactic acid bacteria, comprising several strains of *Lactobacillus*, *Bifidobacterium*, *Streptococcus*, and *Enterococcus*, make up the majority of probiotics [10]. Of these, *Lactobacillus* and *Bifidobacterium* may be found in various fermented milk products as well as being sold commercially as nutraceuticals or functional foods. *L. acidophilus* LA14, a probiotic lactic acid bacterium, increases the beneficial bacteria in the gut, reduces opportunistic infections there, breaks down oxalates, produces bacteriocin, and improves immunological response [11-13]. Because they are popular nutraceuticals that are often regarded as safe and well-tolerated, probiotic dietary supplements may be a cutting-edge treatment approach for treating acetaminophen (APAP) toxicity. *L. acidophilus* LA14 has been demonstrated to have hepatoprotective properties in rats with an acute APAP overdose [14]. A drop in IL-1 levels in sera was another indication of how the probiotic reduced the hepatic inflammation brought on by APAP [15]. Furthermore, *L. acidophilus* LA14 treatment significantly decreased nuclear shrinkage in hepatocytes, inflammatory cell infiltration, and hepatic hemorrhage caused by APAP, according to liver

sections [16].

### Infection Control

The mechanisms by which probiotics function are still poorly understood and there are still many open research concerns. Probiotics do, however, play a part in modifying gut pH, preventing infections by producing antimicrobial compounds, competing for nutrients, growth factors, and pathogen binding and receptor sites, activating immunomodulatory cells, and producing lactase [17]. The most important characteristic of probiotics is that they have been demonstrated to be affordable, safe, and effective at preventing microbial diseases [18]. According to the World Health Organization in 1994, probiotics are thought to be the second-most important immune defense mechanism when commonly prescribed antibiotics stop working owing to antibiotic resistance. "Microbial interference therapy" refers to the use of probiotics to address antibiotic resistance [19].

### How Probiotics Reduce the Duration of Diarrhea

There have been several proposed mechanisms for how *Lactobacilli* reduce rotavirus diarrhea, but none of them have been shown, and they all have drawbacks [20]. Initially, *Lactobacilli* link to receptors and prevent the virus from sticking and invading by connecting to them through competitive inhibition of receptor sites [21]. This theory may hold water if there was evidence of specialized receptor competition. Patients normally experience diarrhea for at least 12 hours by the time a probiotic is administered [21]. Mature enterocytes have already been infected by the virus in the middle and upper regions of the small intestinal villi. Fluid and glucose absorption is decreased when the virus and/or its enterotoxin, NSP4, interfere with the transfer of fluid and electrolytes [22]. The secretory reflexes may have been set off by the toxin, resulting in fluid loss from secretory epithelia and diarrhea. It is uncertain if such suppression would reduce diarrhea; at most, the viral attachment might benefit from competitive exclusion afterward [23]. If *Lactobacilli* competed in any manner with the toxin or peptides produced by villous endocrine cells, the chain of events that causes diarrhea may be prevented [24].

**Table 1. Claimed health benefits of probiotic microorganisms.**

Genus	Species	Health benefits
<i>Lactobacillus</i>	<i>L. rhamnosus</i>	Viral-associated pulmonary damage reduction [25]
	<i>L. plantarum</i>	Antifungal activities and reduction in irritable bowel movements [26]
	<i>L. reuteri</i>	Reduction in diarrhea associated episodes in children [27]
<i>Bifidobacterium</i>	<i>B. longum</i>	Effective in gastrointestinal disease treatment [28] and allergic sensitization [29]

<i>Lactococcus</i>	<i>L. lactis subsp. Lactis</i>	Adhesion of epithelial cells [30], antimicrobial activity against <i>C. difficile</i> sp. [31]
<i>Enterococcus</i>	<i>E. durans</i>	Antibiotic and antioxidant activity [32], Anti-inflammatory activity [33]
<i>Streptococcus</i>	<i>S. thermophilus</i>	Reduction in enterocolitis in preterm infants [34,35]
<i>Bacillus</i>	<i>B. coagulans</i>	Prevention of caries [36], treatment of bacterial vaginosis [37]
<i>Escherichia</i>	<i>E. coli Nissle 1917</i>	Treatment of constipation [37], prevention of ocular disease [38], reduction in intestinal colonization [39]

### Other Miscellaneous Advantages of Probiotics

Probiotic usage in human and animal health has also been reported to offer other benefits. According to *in vivo* data, the probiotic *Lactobacillus rhamnosus* GG (LGG) has specific effects on mucosal physiology that speed up wound healing [40]. These effects are brought on by the previously established secretion of the proteins P40 and P75, which regulate epidermal growth factor receptor signaling. Moreover, the anti-infective and anti-inflammatory properties of probiotics can reduce the risk of infection while speeding up the healing of wounds. Probiotics have a specific place in the local management of chronic wounds in diabetes patients [41]. Probiotics begin to treat diabetic wounds by entering the dermis through the intercellular lipid matrix. They trigger the type 1 transmembrane protein toll-like receptors (TLRs), which have been discovered to be key signaling receptors for pathogen-associated molecular patterns, inside the dermis (PAMPs) [42]. The mouth, nasal cavity, keratinocytes, and Langerhans cells are only a few epithelia that have TLRs. Via the TLRs, probiotic-derived bioactivities (PDBs) promote the production of beta-defensin proteins ( $\beta$ -defensins) [43].

The  $\beta$ -defensins antibacterial and anti-inflammatory properties boost the skin's immune system. Moreover, TLRs are essential for the upregulation of collagen and elastin, a rise in cellular respiration, and an enhancement of the skin's clarity, texture, and overall appearance [44]. Gram-positive pathogens like *Staphylococcus aureus* and *Enterococcus* as well as Gram-negative bacteria like *E. coli* are prominent sources of bacterial infection in diabetic foot ulcers [45]. Lipoteichoic acid (LTA), produced by these bacteria, has been discovered to be a TLR 2 ligand. The inflammatory response of the bacterial membrane lipoproteins is mediated by TLR 2 [46]. The host recognizes PAMPs, or bacteria's components, and regulates cellular processes. Hence, it has been established that TLR 2 is crucial for the host's defenses against the microbes [47].

Probiotics and pathogens compete for attachment sites on the host cell's surface [48]. This binding may cause the host cells to produce anti-inflammatory cytokines, reducing inflammation at the tissue's surface. Probiotics can also secrete several antimicrobials that can either inhibit the spread of illnesses or eradicate them [49]. Probiotics can immunomodulate, which increases overall body immunity. During the same process, probiotics reacts with APC (Antigen

Presenting cells) (macrophages and dendritic cells), which are essential for healing wounds and developing scars [50]. A 90% decrease in the size of chronic leg ulcers was observed in 43% of individuals with diabetes and 50% of non-diabetic patients after the 30 days of topical treatment with *L. plantarum*. A significant decrease in colony-forming units was also observed after 5 days [51].

Several types of research have shown that strains of *Lactobacilli* are very effective in preventing antibiotic-associated diarrhea [52]. *Lactobacilli* species are easily available in the form of probiotics because of their crucial properties such as higher tolerance to hydrochloric acid and bile juice along with having the capability to adhere to the surfaces of the intestine and can also tolerate low pH [53,54]. Results show that *Lactobacillus rhamnosus* CRL1505 has been effective in reducing pulmonary damage due to viral infections by blocking the protein chains [25]. In a recently published meta-analysis, it has shown that probiotic stains were safe and effective in reducing urinary tract infections in adult women [55].

### Conclusion and Future Research

In conclusion, because bacteria make up a significant physical portion of the gastrointestinal tract and other places, it is crucial that professionals recognize their existence and deliberately evaluate what role they may play in health and disease. Probiotics must be well documented to be used as therapeutic or health maintenance treatments. This includes the strain(s), product formulation, and mechanisms of action. The vast array of microbial species found in the gut must be further understood to employ probiotic strains in a way that makes sense given their interactions with host cells and one another. It's only that people are just now realizing how important microbes have always been to the human body.

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