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SHORT REVIEW

# Probiotics and Postbiotics: Exploring their Role as Antibiotic Alternatives and Health Enhancers

**Hijam Chandramani Singh[1], Hmangte Wendy Kom[1], Wankupar Wankhar[2], Surjya Loying[3], Manash Pratim Sarma[3], Rupesh Kumar[4] and Devabrata Saikia[3*]**

[1]Program of MLT, Assam down town University, Guwahati - 781026, Assam, India

[2]Department of Dialysis, Kaziranga University, Jorhat - 785006, Assam, India

[3]Program of Biotechnology, Faculty of Science, Assam down town University, Guwahati - 781026, Assam, India; devabrata.saikia@adtu.in

[4]Department of Biotechnology and MLT, The Assam Royal Global University, Guwahati, Assam, 781035, India

## Abstract

Probiotics are live microorganisms that, when administered in sufficient quantities, provide health benefits to the host. Probiotics have become essential components in supporting health and preventing diseases. Notably, *Bifidobacterium* and *Lactobacillus* strains have demonstrated remarkable efficacy in enhancing nutrient absorption, strengthening the immune system, and preventing infections. These beneficial microbes play a crucial role in maintaining gut health, detoxifying harmful compounds, and synthesizing essential nutrients like vitamin K, riboflavin, and folate. Probiotics have shown potential in preventing antibiotic-associated complications, managing gastrointestinal disorders, and reducing food intolerances. Furthermore, they have promising applications in agriculture and animal husbandry, reducing antibiotic usages and minimizing the risk of antibiotic resistance. Recently, probiotics-derived from inactive microorganisms and their bioactive compounds- have gained attention as safer and more stable alternatives to live probiotics. They offer similar health benefits, including immunomodulation, anti-inflammatory effects, and antioxidant properties, without the risks associated with live bacterial administration. Recently, postbiotics have emerged as bioactive formulations of inactivated microorganisms or their components, scientifically validated for their health benefits. Postbiotics also provide advantages in food processing, ensuring stability in products where probiotics may not survive. Despite their promising potential, issues like large-scale production, stability of formulation, and precise mechanisms of action remain under active investigation. This review article explores the multi-dimensional benefits of probiotics and postbiotics, focusing on their roles as alternatives to antibiotics, mechanisms of action, and applications in food and medicine. It also explores the challenges inherent in their development and utilization, emphasizing the significance of advancing research and clinical trials to unlock their full potential. Probiotics and postbiotics are promising weapons against antibiotic resistance and sustainable health practices, a natural, effective and innovative solution to many modern healthcare problems.

**Major Findings:** Probiotics have been shown to improve gut health, boost immunity and prevent microbial infections. Recently, postbiotics have emerged as safer alternatives with similar benefits. This short review compares the ways how probiotics and postbiotics reduce antibiotic use and support sustainable life.

**Keywords:** *Bifidobacterium*, Immune System, *Lactobacillus*, Probiotics, Postbiotics

## 1. Introduction

The term "Probiotic" was initially introduced by Werner Kollath in 1953[1]. It is derived from the Latin word "pro" which means "for" and the Greek word "biotic" meaning "bios" or "life"[2]. Probiotics are living microorganisms that have shown positive effects on human health. They played an important role for delivering potential health advantages probiotics, available in supplements or functional foods have become a cornerstone of

*Author for correspondence

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modern health-focused nutrition[3,4]. Probiotics have always been crucial constituent and commercial targets for providing potential health benefits. The Food and Agriculture Organization (FAO) and the World Health Organization (WHO) have characterized probiotics as viable microorganisms that, when given in sufficient amounts, provide health advantages to the host organisms[5]. In recent times, ongoing research on probiotic bacteria has paved the way for exploring their potential as promising adjunct treatments for various intestinal diseases[6].

Probiotics suppress the growth of pathogenic bacteria by limiting binding sites on mucosal epithelial cells and influencing the host immune response, thereby enhancing intestinal barrier integrity[7]. These entities are pivotal in the detoxification process of xenobiotics and environmental contaminants, metabolizing mycotoxins found in food, synthesizing essential nutrients such as vitamin K, riboflavin, and folate, and actively participating in the fermentation of undigested fiber in the colon[4,7,8].

The benefits of probiotics are linked to their ability to adjust gut microbiota, reduce nutritional intolerances (such as lactose intolerance), enhance the bioavailability of macro and micronutrients, and alleviate allergic reactions in susceptible individuals[9]. Numerous fermented foods contain active microbes that are genetically akin to probiotic strains. These foods enhance functional and nutritional properties by transforming substrates and producing bioactive, bioavailable end-products[10]. Probiotic strains commonly used are primarily from the *Bifidobacterium* and *Lactobacillus* genera, which deliver substantial health benefits through a range of mechanisms.

Probiotics can be consumed through their integration into foods and beverages, including both dairy and non-dairy options, or in the form of dietary supplements[11]. The food industry has incorporated them into a diverse array of products, including drinks, ice cream, yogurt, bread, and more. A key obstacle in the food industry regarding probiotics is their vulnerability to processing conditions and their sensitivity to Gastrointestinal (GI) stresses. Nevertheless, consumers continue to appreciate the health benefits associated with probiotic products[12].

Postbiotics is a newer concept that incorporates different products produced by probiotics which have health beneficial effects[13]. These products include short chain fatty acids, enzymes, bacteriocins, peptides *etc.* Unlike probiotics, postbiotics are non-living entity that overcomes the barriers faced by live probiotic bacteria during food processing and gastro-intestinal transit tolerance. This review aims to explore the health benefits, mechanism of action and commercial utilization of probiotics and postbiotics as potential alternatives to antibiotics.

## 2. Therapeutic Efficacy of Probiotics

Probiotics have gained significant attention as they are one of the most well-known beneficial bacteria. Bacterial strains from genera like *Pediococcus, Lactococcus, Enterococcus*, *Streptococcus, Propionibacterium*, and *Bacillus* are seen as strong contenders for qualifying as probiotics (as detailed in Table 1)[14,15].

## 3. Mechanism of Action of Probiotics

### 3.1 Competitive Exclusion of Pathogens

Probiotics can inhibit pathogenic bacteria by competing for adhesion sites on the intestinal mucosa, thereby preventing pathogens from colonizing the gut. For instance, *Lactobacillus rhamnosus* GG demonstrates strong adherence to the gut epithelium, effectively blocking the attachment of pathogens like *E. coli* and *Salmonella*[40]. Moreover, probiotics compete with pathogens for vital nutrients, depriving harmful bacteria of the resources needed for their growth and proliferation (in Figure 1).

### 3.2 Production of Antimicrobial Substances

Probiotics produce various antimicrobial compounds, such as bacteriocins, organic acids (*e.g.*, lactic acid, acetic acid), and hydrogen peroxide, that inhibit the growth of pathogenic bacteria. Bacteriocins are proteinaceous toxins produced by bacteria that can kill or inhibit closely related bacterial strains. For example, *Lactobacillus plantarum* produces plantaricin, a bacteriocin that is effective against a range of Gram-positive pathogens, including *Listeria monocytogenes*[41]. These antimicrobial substances create an unfavorable environment for pathogens, reducing their viability and virulence.

**Table1.** The therapeutic efficacy of probiotics in managing diverse health conditions

| Probiotic Microorganism | | Trial against Disease | Reference |
|---|---|---|---|
| **Gram-positive Bacteria** | | | |
| *Bifidobacterium* | *B. animalis*<br>*B. bifidum*<br>*B. thermophilus*<br>*B. longum*<br>*B. lactis* | Ulcerative colitis, antibiotic associated diarrhea, Chron's disease | 16-21 |
| *Bacillus* | *B. amyloliquefaciens*<br>*B. toyonensis*<br>*B. coagulans*<br>*B. subtilis* | Antioxidant activity, gastric conditions | 22-27 |
| *Lactobacillus* | *L. acidophilus*<br>*L. reuteri*<br>*L. casei*<br>*L. gallinarum*<br>*L. delbrueckii subsp. Bulgaricus*<br>*L. plantarum*<br>*L. brevis* | Allergic reactions,Hypercholesterolemia | 28-31 |
| *Enterococcus* | *E. faecium* | Enhanced production of bacteriocin | 32 |
| *Clostridium* | *C. butyricum* | Essential amino acid for the host | 28,33,34 |
| *Streptococcus* | *S. faecium*<br>*S. salivarius subsp. thermophilus* | Allergy | 31,17 |
| *Pedicoccus* | *P. acidilactici* | Cancer | 18 |
| *Lactococcus* | *L. lactis* | Ulcerative colitis | 35,36 |
| **Gram-negative Bacteria** | | | |
| *Escherichi* | *E. coli Nissle 1917* | Urinary tract infection, abdominal and pelvic infection | 37 |
| *Megasphaera* | *M. elsdenii* | Diarrheal | 38 |
| *Prevotella* | *P. bryantii* | Rheumatoid arthritis | 19 |
| **Yeast and Fungi** | | | |
| *Saccharomyces* | *S. boulardii*<br>*S. cerevisiae* | Diarrhea, Urinary tract infections | 31,39 |
| *Candida* | *C. pintolepesii* | *Fungal infection* | 17 |
| *Aspergillus* | *A. oryzae*<br>*A. niger* | *Fungi, allergic* | 17,19 |

## 3.3 Immune System Modulation

Probiotics enhance the host's immune response by enhancing the production of specific antibodies and stimulating both innate and adaptive immune cells. Probiotics like *Bifidobacterium* and *Lactobacillus* species can up regulate the production of secretory Immunoglobulin A (IgA), which essentially contributes to mucosal immunity by neutralizing pathogens and toxins[42]. Furthermore, certain probiotics can modulate cytokine production, shifting the immune response towards a more regulated and less inflammatory state, which is particularly beneficial in preventing infections and managing inflammatory diseases.

## 3.4 Probiotics as Alternatives to Antibiotics

The rampant overuse and misuse of antibiotics have led to a global rise in antibiotic resistance, posing a significant challenge to modern medicine. As antibiotic-resistant bacteria become more prevalent, the growing need for alternative approaches to prevent and treat

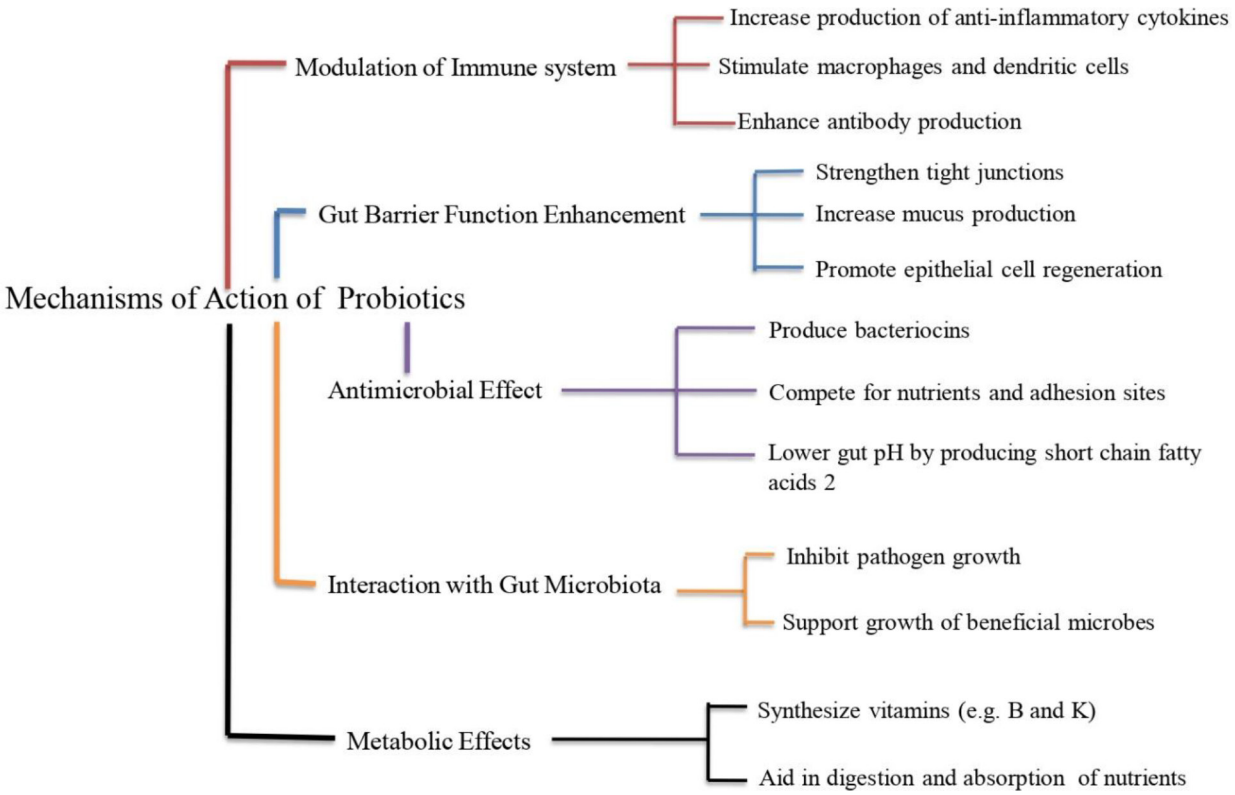



**Figure 1.** Mechanism of action of probiotics.

infections has become urgent. Probiotics, which are live microorganisms that confer health benefits when provided in sufficient quantities, have emerged as a promising alternative or adjunct to antibiotics. Probiotics, particularly Next-Generation Probiotics (NGPs), offer a range of mechanisms that can aid in preventing and treating infections while avoiding the promotion of antibiotic resistance. Probiotics function through multiple mechanisms, including modulating the gut microbiota, enhancing immune responses, competing with pathogens for nutrients and adhesion sites, and producing antimicrobial substances[43]. This multifaceted approach offers an effective strategy for controlling bacterial infections and promoting overall health. The following outlines the key mechanisms by which probiotics act as alternatives to antibiotics

### 3.5 Restoration of Gut Microbiota after Antibiotic Use

Antibiotic treatment often disrupts the gut microbiota, leading to dysbiosis and the overgrowth of pathogenic bacteria such as *Clostridioides difficile*. Probiotics can help restore the natural balance of the gut microbiota, reducing the risk of infections and complications associated with antibiotic use. For example, the use of *Saccharomyces boulardii*, a non-pathogenic yeast probiotic, has been shown to be effective in preventing antibiotic-associated diarrhea[44]. Probiotics role in restoring the gut microbiota can prevent the colonization and overgrowth of opportunistic pathogens, thereby reducing the need for additional antibiotic interventions.

## 4. Biofilm Disruption and Inhibition

Biofilms are diverse bacterial communities that attach to surfaces and are surrounded by a protective matrix, which makes them highly resistant to antibiotics. Certain probiotics, such as *Lactobacillus acidophilus* and *Lactobacillus reuteri*, have been shown to disrupt biofilms and inhibit their formation by producing biosurfactants and other anti-biofilm agents[45]. This ability to the ability to prevent biofilm formation is particularly important in clinical settings where biofilm-associated infections, such as those on medical implants and catheters, are common and challenging to treat.

## 5. Use in Animal Husbandry to Reduce Antibiotic Use

The agricultural sector, particularly animal husbandry, has been a significant contributor to the overuse of antibiotics, which has further fueled antibiotic resistance. Probiotics have been investigated as an alternative to antibiotics in livestock to promote growth, improve feed efficiency, and prevent infections. For instance, *Bacillus subtilis* and *Enterococcus faecium* have been used as feed additives in poultry and swine to reduce enteric infections and enhance growth performance[46]. This approach not only reduces the reliance on antibiotics in agriculture but also minimizes the risk of transmitting antibiotic-resistant bacteria from animals to humans.

## 6. Preventing and Treating Gastrointestinal Infections

Probiotics have shown promise in preventing and managing various gastrointestinal infections, including those caused by *Helicobacter pylori, C. difficil*e, and *Salmonella* spp. For instance, combining probiotics with standard antibiotic therapy for *H. pylori* infection can improve eradication rates and reduce side effects, such as antibiotic-associated diarrhea[47]. Similarly, probiotics like *L. rhamnosus* GG have been used to prevent recurrent *C. difficile* infections by restoring gut microbial balance.

## 7. Prevention of Respiratory Infections

Probiotics have been investigated as preventive approach against respiratory infections. Certain strains, such as *Lactobacillus casei* and *L. reuteri*, have been demonstrated to lower the incidence and severity of upper respiratory tract infections in both children and adults, by modulating the immune response and boosting mucosal immunity[48].

## 8. Prevention of Urinary Tract Infections (UTIs)

Probiotics like *Lactobacillus crispatus* have been studied for their potential to prevent recurrent urinary tract infections, especially in women. These probiotics help maintain a healthy vaginal microbiota through the production of lactic acid, which reduces the pH and inhibits the colonization of uropathogens like *E. coli*[49].

## 9. Probiotics and Oral Health

Probiotics are also being considered for preventing oral infections such as dental caries, gingivitis, and periodontitis. Probiotic strains like *L. reuteri* and *Streptococcus salivarius* have shown potential in reducing pathogenic bacterial load in the oral cavity and maintaining oral health[50].

## 10. Postprobiotics

The term "postbiotic" was selected by the panel as a combination of "biotic" which means "related to or derived from living organisms" with the prefix "post" which means "after". The combination of these terms suggests the idea of "after life" meaning non-living organisms. The idea that non-living microorganisms can contribute to health promotion or preservation is not a new one and numerous terms have been employed to describe these substances. A postbiotic is described as a product that offers a health advantage for the host organism and is made from inactive microorganisms or their components. A number of other related terms have also been employed, parapsychobiotics, paraprobiotics, ghost probiotic, metabiotics, tyndallized probiotics and bacterial lysates[51-61]. Postbiotics are specially inactivated microbial cells that have been linked to proven health benefits. They may contain metabolites or other biological components. It is crucial to note that vaccinations and refined microbial metabolites are not regarded as postbiotics. To be considered a postbiotic, an organism does not need to be a probiotic in the first place. A postbiotics health advantages must be validated in the target host, which can include people, pets, livestock, and other pertinent populations. Postbiotics work on host surfaces including the oral cavity, gut, skin, and urogenital tract or nasopharynx; their effects are not limited to the gut. Injectables do not meet the criteria for postbiotics. It is also crucial that postbiotics are safe for the purposes for which they are designed.

### 10.1 Postbiotics Safety and Health Issues

Postbiotics are likely to have a more favorable safety profile compared to probiotics, as they contain

microorganisms that are no longer-replicating bacteria. This eliminates the risk of fungaemia or bacteraemia, which are extremely rare but can happen while using probiotics[62]. Lipopolysaccharides from Gram-negative bacteria can trigger toxic shock and sepsis when endotoxin A is released from dead cells. A safety evaluation tailored to each postbiotic's intended use is crucial before application[63].

The clinical use of postbiotics has been restricted by challenges related to delivery and formulation. However, these issues are being addressed, and there is anticipation for the potential demonstrated by basic science into practical clinical use. Although the exact mechanisms remain unclear, *in vitro* studies have demonstrated the antibacterial, anti-inflammatory, immunomodulatory, anti-proliferative, and antioxidant properties of postbiotics. This indicates that these bioactive compounds may contribute to improving human health.

### 10.2 Postbiotics in Adults

Short-Chain Fatty Acids (SCFAs), which are products of microbiota-diet interactions, have been evaluated in clinical trials with humans, showing some promising outcomes. Butyrate enemas have been tested in clinical trials for the treatment of ulcerative colitis, including both cohort studies and open-label trials, with participant counts ranging from 10 to 47. Additionally, they have been used to a limited extent for radiation proctosigmoiditis in Randomized Controlled Trials (RCTs) that included 15 to 166 participants, and for visceral hypersensitivity in an RCT involving 11 healthy volunteers[64-66].

Additionally, postbiotics to foods has many advantages for food processing and sales. They can be included in foods where probiotics usually don't survive well, which helps grow the market for these types of foods. Postbiotics are safer and more stable for use in food and pharmaceuticals than the live bacteria they come from because they don't need to be viable for large-scale production or consumption[13]. Adjustments in processing conditions or scaling up production can cause structural changes and variations in the physiological effects of postbiotics, which can make large-scale industrial production challenging. This is true even though it is possible to synthesise these substances on a small scale or in a laboratory[67].

## 11. Challenges of Using Probiotics

While probiotics show great promise as alternatives to antibiotics, several challenges must be overcome to fully realize their potential. These challenges include ensuring strain-specific efficacy and safety, maintaining stability during storage and administration, and unraveling the complex interactions between probiotics, pathogens, and the host. Additionally, large-scale, well-designed clinical trials are essential to establish standardized guidelines for probiotic use in managing various infections[68].

The rapid advancement of microbiome research has paved the way for Next-Generation Probiotics (NGPs) and engineered probiotics, which offer even more targeted and effective alternatives to traditional antibiotics. These innovations hold the potential to develop custom-tailored probiotics based on an individual's microbiome profile, marking a significant step forward in precision medicine[69].

Probiotics present a sustainable and compelling alternative to antibiotics, addressing the escalating problem of antibiotic resistance while offering safe and effective solutions for infection prevention and treatment. As our understanding of the human microbiome deepens and new probiotic strains and technologies emerge, probiotics are poised to play a pivotal role in the future of infection management and overall health maintenance[70].

## 12. Conclusion

Probiotics present a compelling alternative to traditional antibiotics, addressing the growing issue of antibiotic resistance while offering various health benefits. Probiotics have proven effective in inhibiting pathogenic bacteria, boosting immune responses, and restoring gut microbiota post-antibiotic treatment, emphasizing their potential in preventing and managing infections. Probiotics have shown promise in managing infections and reducing biofilm formation, a key challenge in medical treatments. Their use in agriculture reduces antibiotic reliance in animal husbandry, lowering the risk of antibiotic-resistant bacteria transmission to humans. Probiotics enhance nutrient bioavailability, alleviate food intolerances, and support gut health, making them essential in functional foods. Postbiotics,

derived from inactive microorganisms, provide a safer, more stable alternative to live probiotics, offering health benefits without the risks. However, challenges like strain-specific efficacy, stability during processing, and scalability in production persist. Further research, particularly large-scale clinical trials, is needed to establish guidelines and unlock the full potential of probiotics and postbiotics in healthcare, agriculture, and the food industry, potentially revolutionizing medicine through sustainable, natural approaches.

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## 14. Author Contribution

**Hijam Chandramani Singh:** Writing-original draft, conceptualization, formal analysis. Hmangte Wendy Kom and Wankupar Wankhar: Writing-original draft, formal analysis. Surjya Loying, Rupesh Kumar and Manash Pratim Sarma: Validation, writing-review and editing. **Devabrata Saikia**: Supervision, validation, writing-review and editing. All authors have read and agreed to the published version of the manuscript.

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