

Probiotics for the prevention of AAD (Antibiotic-Associated Diarrhea)

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ABSTRACT

Probiotic-rich fermented foods have gained popularity as therapeutic choices with purported medical properties in a number of communities. We now understand the significance of microbial balance and how probiotics can correct imbalances. Probiotics have undergone testing for several therapeutic applications as the treatment of various diseases, preventing antibiotic-associated diarrhea (AAD), and preventing allergies, treating illnesses like *H. pylori* infection, irritable bowel syndrome, vaginitis, and neonates with necrotizing enterocolitis. The most common therapeutic use for probiotics has been for AAD, Up to 30% of individuals experience AAD, a typical adverse effect of antibiotic use. The rationale for utilising

probiotics for AAD is that they help restore a disturbed flora. Probiotics may promote intestinal health through a variety of mechanisms, including immune system enhancement, (ii) improvement of gut barrier integrity, (iii) production of antimicrobial substances, (iv) modulation of the gut microbiome, (v) increased water absorption, and (vi) reduction of opportunistic pathogens. The advantages of probiotics in treating AAD have been demonstrated in numerous randomized-controlled trials, including strain-specific trials using *Lactobacillus* and *Saccharomyces* and meta-analyses. Probiotics have been associated with some side effects, but overall, they are regarded as a secure and affordable preventative treatment option for AAD and other gastrointestinal illnesses.

Key Words: Probiotics; Antibiotic-Associated Diarrhea (AAD); Microbiome

INTRODUCTION

The probiotic market is expected to be worth \$15 billion USD annually and is expanding at an estimated 7% yearly rate. Probiotics are becoming increasingly popular, so understanding both the historical context and the contemporary state of human health applications are crucial for potential medical implications. The definition of probiotic is the Latin "pro" and Greek "bios," which originally meant "for life," was given by German physicist Werner Kollath.

Background

Scientists reported on the purported health advantages of consuming fermented milk products in the 1800s. The mode of action that brought about these advantages, nonetheless, persisted and was unclear. Louis Pasteur was successful in pinpointing the bacteria and yeast that cause fermentation, but he disregarded any potential health implications. Elie Metchnikoff followed in 1905. A Russian scientist who had collaborated with Pasteur connected the longevity of Bulgarians, not just because of the frequently consumed yogurt, but also because of the *Lactobacilli* presence in the colon and how they fe-

mented it. Then, in 1906, Henry Tissier identified *Bifidobacterium* from a baby and hypothesized that it may replace intestinal harmful bacterium. These hallmark discoveries catalyzed research into health-promoting and disease-fighting microbes in the next century. In 2001, an Expert Panel was created at the request of the Food and Agriculture Organization of the United Nations, and backed by the World Health Organization, to define probiotics as: "Live microorganisms which when administered in adequate amounts confer a health benefit on the host". The earliest probiotics were species-specific, such as those from the *Saccharomyces* or *Lactobacillus* genera.

Clinical use of Probiotics

Probiotics have undergone testing for several clinical applications. Probiotics are most frequently used in medicine to prevent antibiotic-related diarrhea. The management of pediatric acute diarrhea, the prevention of *H. pylori* infection the treatment of *H. pylori* infection, and allergies, irritable bowel syndrome, vaginitis, and necrotizing enterocolitis in newborns are among the conditions that are treated. However, the results of the clinical effectiveness of probiotics differ by

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probiotic strain and by indication.

ANTIBIOTIC-ASSOCIATED DIARRHEA

Due to the rising prevalence of AAD and the resulting pressure on the healthcare system, probiotic research is expanding for the treatment of AAD. Up to one-third of patients receiving antibiotic treatment experience AAD, a typical adverse effect of antibiotic use.

Mechanisms through which antibiotics cause diarrhea

1. Altering the diversity of gut bacteria: While antibiotics kill and target pathogens, they also impact the symbiotic bacteria integral to the gut microbiome. This decrease in bacterial diversity in the GI tract can drastically alter the immunological ecosystem. This puts the patient at greater risk of opportunistic infections and allows pathogens to competitively out-compete other bacteria.
2. Age of patient: While AAD can occur in any patient population, the pediatric population is particularly at risk. Since the infant microbiome is not fully developed, antibiotic use in this population can cause a longer, more drastic effect on the microbiome, including an increase in *Proteobacteria* and a decrease in the diversity of *Actinobacteria*.
3. Metabolic disturbances: The gut microbiome plays an important role in nutrition and metabolism. While most carbohydrates are absorbed in the small intestine, some carbohydrates are fermented by the bacteria and turned into Short-Chain Fatty Acids (SCFAs). When antibiotics kill and lyse these bacteria, excess amounts of non-absorbable carbohydrates remain in the gut. These non-absorbable carbohydrates pull in water by osmosis as they move toward the large intestine. This leads to the development of osmotic diarrhea.
4. Loss of colonization resistance: Colonization resistance is the ability of bacteria to prevent pathogenic microbes from invading. The gut microbiome regulates many metabolites including bile acids, carbohydrates, and amino acids. These metabolites help to defend against pathogens. One example is the regulation of *Clostridium difficile* through secondary bile acids. Secondary bile acids are produced by gut bacteria and inhibit *C. difficile* growth. Antibiotics destroy the gut microbiome, leading to the diminishment of secondary bile acids. This then allows *C. difficile* to flourish.

ROLE PROBIOTICS IN PREVENTING ANTIBIOTIC-ASSOCIATED DIARRHEA

There are many different strains of probiotics on the market, many of which have undefined advantages. Numerous probiotic strains have undergone testing. The most extensively researched probiotic genera are *Lactobacillus*, *Saccharomyces*, and *Bifidobacterium*. The idea behind utilizing probiotics to treat digestive issues is that they can help restore a healthy balance to an unbalanced flora. Probiotics may enhance gut health through a variety of methods are:

1. Boosting immunity: While the exact mechanism is still unknown, probiotic bacteria have been shown to boost the humoral immune response by increasing the numbers of IgM-, IgG-, and IgA-secreting cells. They also stimulate nonspecific immune responses such as activating macrophages.
2. Increasing gut barrier integrity: The intestinal barrier is a heterogeneous system composed of a mucus layer, epithelium, and the underlying lamina propria. These create a physical barrier to gut microbes using multi-protein complexes called tight junctions. When the tight junctions are compromised, epithelium permeability increases, causing a leaky gut. A leaky gut is responsible for the development of many gastrointestinal conditions, such as irritable bowel syndrome, irritable bowel disease, and celiac disease. Probiotics can upregulate ZO-1 and occludin protein synthesis, thus protecting the integrity of the gut barrier.
3. Producing antimicrobial substances: Probiotics produce a variety of substances that can be inhibitory to both gram-positive and gram-negative bacteria. These substances include hydrogen peroxide, bacteriocins, and organic acids. This can not only reduce the number of pathogenic bacteria but can also alter bacterial metabolism and limit toxin production.
4. Modulating the gut microbiome: Probiotic use has been shown to re-equilibrate gut microbiome dysbiosis. Dysbiosis can occur when a patient is exposed to severe conditions such as prolonged antibiotic therapy, intense physical stress, and chronic illness. Probiotics metabolize complex carbohydrates and produce lactic acid and short-chain fatty acids. This reduces bacterial translocation, improves tight junction integrity, and stimulates mucin production.
5. Increasing water absorption: Aquaporins are water-channel membrane proteins expressed in many tissues with AQP1, 3, 4, and 8 mostly expressed in the colon. Pathogenic bacteria can disrupt these proteins, increase the water content in stool, and lead to dehydration. Probiotics have been shown to increase the expression of aquaporins and thus increase water absorption in the colon.

CURRENT CLINICAL PRACTICE OF USING PROBIOTICS IN AAD

At present, there is no consensus across the globe regarding the recommendation for the clinical use of probiotics for AAD. This emphasizes the urgent need for further research and the effective distribution of information as it emerges. A global panel of experts (World Gastroenterology Organization; WGO) reviewed the literature and made several evidence-based recommendations for the use of probiotics for various disease conditions. They suggested that there is evidence to support that certain probiotics are effective for the prevention of AAD in adult and pediatric patient populations. The Canadian Agency for Drugs and Technologies in Health (CADT-

H) carried out an evaluation of probiotics for AAD in the pediatric population. A strong recommendation was made for the use of *L. rhamnosus* GG and *S. boulardii* for preventing AAD in children, while the use of *B. clausii* as a single probiotic was not recommended. The Canadian Pediatric Society recommended that physicians should consider advising the use of probiotics for AAD, but should be aware of the small risks of invasive infections with certain strains, especially while treating immunocompromised patients. They also recommended that the federal government should require probiotics manufacturers to provide accurate and de-

-tailed labels and maintain the high quality of the products.

CONCLUSIONS

Research on microbial administration to modulate the human microbiome and improve health has been increasing at a rapid rate since probiotics were officially defined. The potential to alter these microbial ecosystems offers great hope for new preventative treatment options for antibiotic-associated diarrhea and other gastrointestinal disorders. However, the practical guidelines for probiotic use that provide strain-specific and diseasespecific recommendations are sparse.