

Review

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Review

# A New Therapeutic Approach Utilizes Probiotics, Prebiotics, Synbiotics, Postbiotics, and Gut Microbiota

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**Abstract:** Recent advancements in gut microbiome research have highlighted the complex interplay between gut microbiota and various physiological and pathological processes, showing that gut microbiota plays a vital role in human health and disease. Imbalances in the gut microbiota, known as dysbiosis, have been associated with a range of health conditions, including gastrointestinal disorders, metabolic diseases, etc. In response to these findings, probiotics, prebiotics, synbiotics, and postbiotics have emerged as a promising therapeutic strategy to modulate gut microbiota composition and functionality. This review paper explores the latest research on how gut microbiota impacts host physiology, immune responses, and overall well-being. Furthermore, the paper delves into the therapeutic potential of probiotics, postbiotics, prebiotics, and synbiotics in therapeutic applications and curing various diseases. The paper also addresses the challenges and opportunities in the field, highlighting the need for personalized approaches to probiotic therapy and the importance of considering factors such as strain specificity, dosing, and safety. Overall, this review aims to provide a comprehensive overview of the evolving landscape of gut microbiota and probiotics, prebiotics, synbiotics, and postbiotics as novel therapeutic agents. It underscores the potential of harnessing the gut microbiome to improve health, prevent diseases, and complement traditional medical interventions. As research in this field continues to expand, a deeper understanding of the gut microbiota and probiotics, prebiotics, synbiotics, and postbiotics promises new avenues for preventive and therapeutic healthcare strategies.

**Keywords:** gut microbiome; probiotics; prebiotics; synbiotics; and postbiotics

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## Introduction:

Antibiotics discoveries drastically changed human health related events which saved many lives of people and revolutionized the drug industries but nowadays according to the WHO, AMR (Antibiotic resistance) threatens the effective prevention and treatment of the ever increasing range of infections caused by bacteria, viruses and fungus. Nowadays people are concerned about the medicine's side effects and they are moving to natural products for disease therapy which are considered safe and less costly. This increased scientific curiosity about natural products, probiotics, various polyphenols etc as therapy for infections. Natural products have been the most successful source of potential drug leads in recent times. Maintaining the balance of the gut microbiome are the key points for promoting human health. Growing evidence has demonstrated that by manipulating gut microbiota through probiotics, evaluating human health and preventing or treating various illnesses. 'Gut microbiota' is the collection of bacteria, archaea and eukarya which may be possibly

colonizing in the gastrointestinal tract, co-evolved with the host over thousands of years to form an tangled and unanimous beneficial relationship. Variation in the diversity or structure of the gut microbiome is termed as dysbiosis, Dysbiosis affects various pathways, resulting in countless disorders. According to the results from experimental studies and clinical trials, probiotics, prebiotics, symbiotics, and post biotics (PPSP) have shown alleviated effects on many diseases such as Obesity, Type 2 diabetes Mellitus, and other Metabolic diseases [92].

Various scientific reports point to the health benefits of using probiotics, prebiotics, synbiotic, and post biotics (PPSP) [1]. Probiotics promote health by reviving native gut microbiota, host immunity, cholesterol reduction and several other functions, whereas post biotics which is made of their metabolites such as bacteriocins, lactic acid and hydrogen peroxide secreted by these microorganisms can be of huge importance as antimicrobials against a vast range of pathogenic bacteria [2]. Prebiotics are generally several plants such as onion, asparagus, garlic, chicory, Jerusalem artichoke, oat and wheat which encourage the existing metabolic activities in the colon by stimulating bacterial growth in the gut [3]. Synbiotics are the mixture of prebiotics and probiotics used for improvement of human or animal health [4].

Thus, scientific use of probiotics, postbiotics, prebiotics and synbiotics may be a safe and alternative therapeutics strategy. Further research into the procurement of new probiotic strains, the selection of probiotics and prebiotics for synbiotics, dose setting, safety of use, and clinical trials evidence the desired health effects is necessary. Therefore, there is a need for the update of knowledge in this field to explore future possibilities for application of probiotics in human and animal diseases. Hence, the aim of this review is to understand the gut microbiota role in health and dysbiosis in gut microbiota cause the disease, role in therapeutic approach and by using the nature-derived products such as probiotics, prebiotics, symbiotic, and post biotics (PPSP) and their possible applications for boosting the treatment or management of a variety of human diseases. The selection of probiotic strains, prebiotics with their dosages plays a critical role in obtaining a therapeutic effect.

### The Probiotics: A Dynamic Relationship with Gut Microbiota

**GUT MICROBIOTA:** In most people, the human gut is ruled by Bacteroides and Bacillota phyla which occupy approximately 90% of the entire bacteria abundance. In terms of human health outcomes, there are links between overall species diversity and gut microbiota ratio [5]. The distinction between various sections of the gut environment leads to differences in species density and distribution. The stomach has a highly acidic environment so having the limited diversity of the microbiota, inhabited by bacteria such as *Helicobacter pylori* [6]. Small intestinal pH rises as it has a unique and less diverse microbiota than large intestine [7]. In the colon, including the cecum and rectum, decreased pH, harsh anaerobic conditions made the condition to increase morbid stiffness the species such as *Bacteroides*, *Pseudomonadota*, and *Bacillota* which are usually found in the highest populations [9]. The following table shows the change in the pH, and microbiota load and various common species of microbiota in gut:

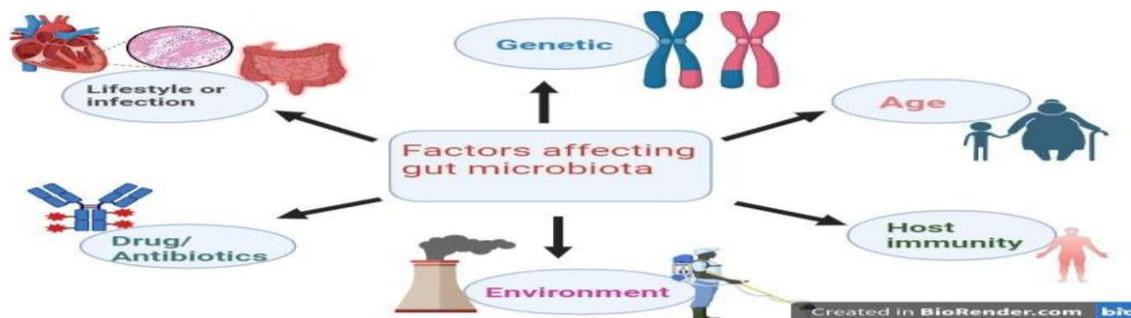
**Table 1.** The various gut parts having unique microbiota.

GUT	MICROBIOTA	pH	BACTERIAL LOAD	DIVERSITY	REFERENCE
Stomach	<i>Helicobacter</i>	Stomach (2-4)	~10 <sup>7</sup> CFU ml <sup>-1</sup> ,	limited diversity of gut microbiota	[6,7]
	<i>Streptococcus</i>				
	<i>Prevotella</i>				
Small intestine	<i>Streptococcaceae</i>	Duodenum (6)	~10 <sup>1</sup> - 10 <sup>3</sup> CFU ml <sup>-1</sup>	Unique and less diverse	[7,8]
	<i>Veillonellaceae</i>	Illium (7.5)	~10 <sup>4</sup> -10 <sup>7</sup> CFU ml <sup>-1</sup>		
	<i>Enterobacteriaceae</i>	Jejunum (7.5)	~10 <sup>4</sup> -10 <sup>7</sup> CFU ml <sup>-1</sup>		
large intestine	<i>Bacteroidaceae</i>	Caecum (7.4 to 6.3)	~10 <sup>11</sup> -10 <sup>12</sup> CFU ml <sup>-1</sup>	Abundant and diverse microbiota	[7,9]
	<i>Lachnospiraceae</i>				
	<i>Ruminococcaceae</i>				

**GUT MICROBIOTA DYSBIOSIS:** Dysbiosis disrupts the natural balance of the gut microbiome, known as eubiosis, and is characterized by changes in its composition and functioning. This includes

a decrease in diversity and a shift towards an imbalance of “healthy” and “less healthy” microbes. Dysbiosis is a broad term that encompasses various deviations from a healthy state [36]. Notably, the relative abundance of *Proteobacteria*, specifically *Escherichia coli* and *Klebsiella species*, has been found to increase in dysbiotic cases. While *Proteobacteria* typically make up less than 10% in healthy individuals, dysbiosis can lead to levels as high as 20-30%. Several methods have been proposed to identify dysbiosis, particularly in patients who have recurring *C. difficile* infections [37]. A measure which gives valuable insights into imbalances in gut bacteria, called the Microbiome Health Index (MHI), looks at the composition of bacteria in the Firmicutes, Bacteroidetes, and *Proteobacteria* groups.

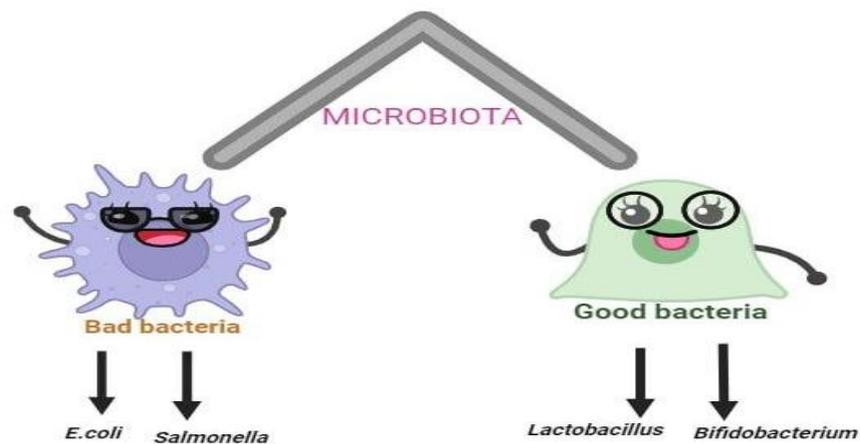
**FACTOR AFFECTING GUT MICROBIOTA WHICH LEADS TO DYSBIOSIS OF GUT MICROBIOTA:** A wide variety of factors such as genetics, age, diet, host immunity, environment, drugs, lifestyles or infections, (as shown in Figure 1) which together make the digestive system a complex ecosystem, dictate the composition and balance of gut microbiota [10]. Out of all, diet plays crucial in determining the availability of essential nutrients to various species of microorganisms [10,11]. A fiber-rich diet promotes the Beneficial bacteria, whereas an intake of highly processed food may facilitate the multiplication of bad bacteria in the gut indirectly.



**Figure 1.** Factors affecting gut microbiota.

Furthermore, there are several antibiotics that alter the natural balance and can cause dysbiosis leading to decreased biodiversity. Natural determinants, such as exercise, have been found to result in colonies of microorganisms which are more stable and diverse [93]. The gut microbiota composition, one of the factors that can be affected by environmental influences such as pollution, toxins and other external sources and cause the gut disturbance [12]. Another determinant age and host genetics, also influence susceptibility to specific disease. The initial colonization of the gut microbes is influenced by mode of delivery at birth (vaginal or cesarean section) and whether the infant was breastfed or formula-fed [11]. These factors clearly demonstrate how lifestyle is related to genes, surroundings, and microbial communities.

**DYSBIOSIS LEADS TO CLASSIFICATION OF BACTERIA IN GUT AS GOOD BACTERIA AND BAD BACTERIA:** The human microbiome, an intricate and complex network, can be divided into two main groups of bacteria: the good bacteria and bad bacteria. (as shown in Figure 2) The bad bacteria can pose a threat to the host, and the good bacteria plays vital for maintaining overall health. The group of bad bacteria or pathogenic strains have the potential to cause infection or disease and have the power to disrupt the delicate balance of the microbiota, resulting in various conditions such as infections, inflammation, and dysbiosis [36]. In contrast, the good bacteria, known as beneficial or commensal bacteria, are essential for numerous contributions to significant well-being of the host by aid in digestion, produce vital nutrients, and support the optimal functioning of the immune system.



**Figure 2.** Types of gut microbiota.

**Table 2.** Effect of probiotics on the various health condition and their possible mechanism of action:

Probiotics	Effect on health	Mechanism of action	Reference
<i>L. acidophilus</i> , <i>S. thermophilus</i> , <i>B. longum</i> , <i>L. rhamnosus</i> GG and <i>B.bifidum</i>	Inhibits Escherichia coli, Salmonella, Clostridium difficile and rotavirus that may cause diahrea	Production of organic acids, bacteriocins, hydrogen peroxide, carbon dioxide and diacetyl	[15]
<i>Lactobacillus acidophilus</i> and <i>Bifidobacterium infantis</i>	Inhibits Staphylococcus aureus, Salmonella typhimurium, Yersinia enterocolitica, Clostridium perfringens that may cause intestinal infection	Production of organic acids, bacteriocins and other primary metabolites, such as hydrogen peroxide, carbon dioxide and diacetyl	[14]
<i>B. longum</i> , <i>L. casei</i> Shirota, <i>L. acidophilus</i> , <i>Bifidobaterium spp.</i> and <i>L. rhamnosus</i> GG	Inhibits formation and proliferation of tumor	Inhibition of carcinogens and/or procarcinogens, inhibition of bacteria that convert procarcinogens to carcinogens, activation of the host's immune system, reduce the levels of faecal enzymes responsible for catalysing the conversion of carcinogenic amines	[16]
<i>L. acidophilus</i> and <i>Bifidobacterium spp.</i>	Inhibits Helicobacter pylori that Reduction of peptic ulcer, gastro-oesophageal reflux, nonulcer dyspepsia and gastric cancer	Production of acetic and lactic acids, bacteriocins etc	[17]
<i>L. rhamnosus</i> GG	Help to relieve intestinal inflammation and hypersensitivity reactions in infants with food allergies	Hydrolyse the complex casein to smaller peptides and amino acids and hence decrease the proliferation of	[18]

		mitogen-induced human lymphocytes	
<i>L. acidophilus</i>	Reduces cholesterol level	Assimilation of cholesterol and deconjugation of bile s	[19]

### Prebiotics: Nourishing the Gut Microbiota for Health

In 1995, prebiotics were defined by Gibson and Roberfroid as ‘non-digested food components that, through the stimulation of growth and/or activity of a single type or a limited amount of microorganisms residing in the gastrointestinal tract, improve the health condition of a host [20].

Recently, the definition has been updated by a panel of experts from International Scientific Association for Probiotics and Prebiotics (ISAPP) as “a substrate that is selectively utilized by host microorganisms conferring a health benefit” [38].

Prebiotics naturally occur in several plants such as onion, asparagus, garlic, chicory, oat and wheat which prompt the existing metabolic activities in the colon by stimulating bacterial growth in the gut [39].

There are different types of prebiotics:

Fructans: This consists of inulin and fructo-oligosaccharide or oligofructose [40].

Galacto - oligosaccharide: Galacto-oligosaccharides (GOS), the product of lactose extension, are categorized into two subgroups: (i) it with a excess galactose at C3, C4 or C6 and (ii) it manufactured from lactose through enzymatic trans-glycosylation. GOSs can greatly stimulate Bifidobacteria and Lactobacilli [41].

Starch and Glucose-Derived Oligosaccharides: There is a kind of starch that is resistant to the upper gut digestion known as resistant starch (RS). RS can promote health by producing a high level of butyrate(classified as prebiotic) [42].

Non carbohydrates oligosaccharides: There are some compounds that are not classified as carbohydrates but are recommended to be classified as prebiotics, such as cocoa-derived flavanols [43].

Uptaking prebiotics can improve immunity functions by increasing the population of protective microorganisms. Animal and human studies have shown that prebiotics can decrease the population of harmful bacteria by Lactobacilli and Bifidobacteria [44].

**Table 3.** Effect of prebiotics on the various health condition and their possible mechanism of action:.

Prebiotics	Impact on health	Mechanism of action	Reference
Isomalto-oligosaccharides (IMO) from miso, soy sauce and honey	Local and systemic Th-1-like immune response and regulation of immune function, balancing the dysbiosis of gut microbiota	<i>Bifidobacterium</i> and the <i>Bacteroides</i> groups are able to utilize IMO	[21]
Inulin from chicory roots	promotes healthy gut	Stimulate the growth of <i>Bifidobacterium</i>	[22]
Xylooligosaccharides (XOS) from fruits, bamboo shoots, vegetables, honey,	promotes healthy gut	<i>B. adolescentis</i> utilizes xylobiose and xylotriose, whereas <i>L. lactis</i> , <i>L. rhamnosus</i> and <i>L. plantarum</i> utilize oat $\beta$ -galactooligosaccharides	[23]

### Synbiotics: Synergistic Effects For Enhanced Health Benefits

Synbiotics refer to a mixture of prebiotics and probiotics for improvement of human or animal health. In synbiotic food products, probiotic bacteria selectively utilize the prebiotics as substrate for

their growth. According to the International Scientific Association for Probiotics and Prebiotics, synbiotics are of two types, complementary and synergistic [45]. A complementary synbiotic consists of a probiotic and a prebiotic together confers one or more health benefits but do not require co-dependent functions. A synergistic synbiotic contains a substrate that is selectively utilized by co-administered microorganism [46].

A synbiotic product beneficially affects the host in improving the survival and implantation of live microbial dietary supplements in the gastrointestinal tract. This is obtained by selectively stimulating the growth and/or activating the metabolism of one or a limited number of health-promoting bacteria. Because the word "synbiotics" alludes to synergism, this term should be reserved for products in which the prebiotic compounds selectively favor the probiotic organisms. Synbiotics were developed to overcome possible survival difficulties for probiotics. It appears that the rationale to use synbiotics is based on observations showing the improvement of survival of the probiotic bacteria during the passage through the upper intestinal tract. A more efficient implantation in the colon as well as a stimulating effect of the growth of probiotics and ubiquitous bacteria contribute to maintaining the intestinal homeostasis and a healthy body [48].

Several factors like pH, H<sub>2</sub>O<sub>2</sub>, organic acids, oxygen, moisture stress etc. have been claimed to affect the viability of probiotics especially in dairy products like yogurts [47].

The probiotic strains used in synbiotic formulations include *Lactobacilli*, *Bifidobacteria spp*, *S. boulardii*, *B. coagulans* etc., while the major prebiotics used comprise of oligosaccharides like fructooligosaccharide [42] (FOS), GOS and xylose oligosaccharide (XOS), inulin, prebiotics from natural sources like chicory and yacon roots, etc [49].

The health benefits claimed by synbiotics consumption by humans include: Increased levels of Lactobacilli and Bifidobacteria and balanced gut microbiota, Improvement of liver function in cirrhotic patients. Other benefits includes improvement of immunomodulating ability, prevention of bacterial translocation and reduced incidences of nosocomial infections in surgical patients, etc [50].

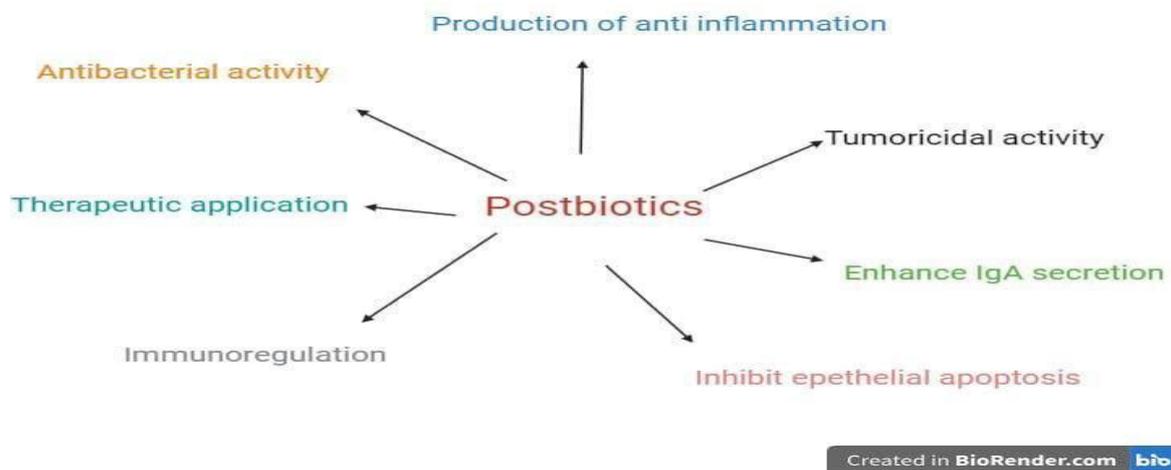
**Table 4.** Synbiotics effects on the various health condition and their possible mechanism of action:.

Symbiotics	Impact on health	Mechanism of action	Reference
<i>L. acidophilus</i> , <i>L. rhamnosus</i> , <i>B. bifidum</i> , <i>B. longum</i> , <i>E. faecium</i> and FOS	Changes in anthropometric measurements that may cure obesity	Decrease in TC, LDL-C and total oxidative stress serum levels	[24]
Oral synbiotic preparation containing <i>L. plantarum</i> and FOS	Significant reduction in sepsis and lower respiratory tract infections that may lower sepsis in early infancy	Promotes growth of <i>L. plantarum</i> ATCC202195	[25]
<i>L. rhamnosus</i> GG, <i>B. lactis</i> Bb12 and inulin	Increase in probiotics in stools and decrease in <i>Clostridium perfringens</i> led to increase in the IL2 in polypectomies patients that may reduce cancer	Increases production of interferon- $\gamma$	[26]
<i>L. rhamnosus</i> CGMCC1.3724 and inulin	Weight loss that may decrease obesity	Reduction in leptin increase in Lachnospiraceae	[27]
Curd containing <i>B. longum</i> and fructooligosaccharide (FOS)	Reduces cardiovascular risk factors, metabolic syndrome prevalence and markers of insulin resistance in elderly patients	Increase in good bacteria	[29]

<i>L. plantarum</i> La-5, <i>B. animalis</i> subsp. <i>lactis</i> BB-12 and dietary fibres	Improvement in the IBS score and satisfaction in bowel movement reported	Increase in good bacteria	[28]
Food products containing <i>B. animalis</i> and amylose corn starch	promotes gut health	Promote the growth of bifidobacteria	[30]

### Postbiotics: Unveiling the Potential of Microbiome Metabolites

The concept of postbiotics is based on the observation that the beneficial effects (as shown in Figure 3) of the microbiota are mediated by the secretion of various metabolites. However, its precise definition remains under discussion. According to Tsilingiri et al. Postbiotics include any substance released by or produced through the metabolic activity of the microorganism, which exerts a beneficial effect on the host, directly or indirectly. For the purposes of this article, we assume that postbiotics include all substances of bacterial or fungal origin that confer beneficial effect to the host and do not meet the definition of a probiotic and are not exclusively of a prebiotic nature [51].



**Figure 3.** Various beneficial effects of postbiotics.

**Mechanisms of action of postbiotics:** Postbiotics display pleiotropic properties. Due to the induction of differentiation of T regulatory lymphocytes and synthesis of anti-inflammatory cytokines, postbiotics restore the imbalance between two major arms of the immune system represented by Th1 and Th2 lymphocytes [52]. The balance between Th1 and Th2 lymphocytes is vital for immunoregulation, and its disturbance causes various immune diseases, including atopic disorders. Antibacterial activity is probably mediated by postbiotics' impact on the molecular structure of enterocytes, which results in sealing the intestinal barrier. "Statin-like" activity of postbiotics and its future therapeutic application in metabolic and related diseases is highly anticipated [53].

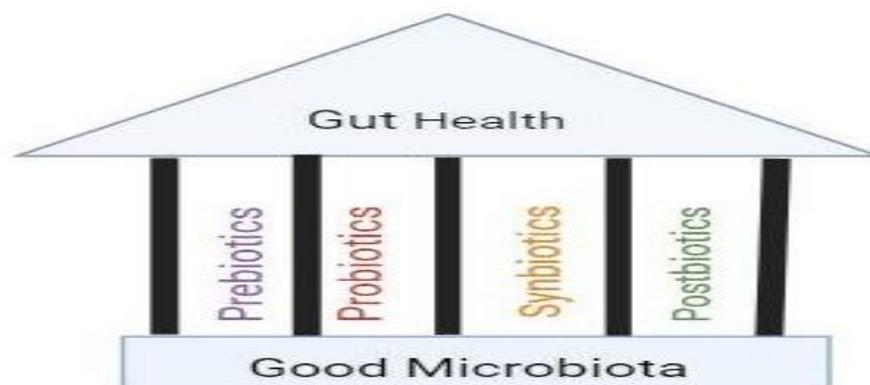
**Table 5.** Effect of postbiotics on the various health condition and disease.

Postbiotics (microorganism)	Impact on health	Disease	Reference
Lysates of <i>Methylococcus capsulatus</i> Bath (McB)	Improve glucose regulation, reduce body and liver fat, and diminish hepatic immune infiltration	Non-alcoholic fatty liver disease (NAFLD)	[88]
Extracellular vesicles ( <i>Lactobacillus animalis</i> )	Increase angiogenesis, augment osteogenesis, and reduce cell apoptosis	Osteonecrosis of the femoral head (ONFH)	[89]

Outer membrane vesicles (OMVs) of <i>Bacteroides thetaiotaomicron</i>	Direct a balanced immune response to constituents of the microbiota locally and systemically	Inflammation disease (IBD)	bowel	[89]
Short-chain fatty acid (SCFA) butyrate	Repress HK2 expression via histone deacetylase 8 (HDAC8) and reduce mitochondrial respiration	Colitis		[90]

### Therapeutic Applications: Harnessing The Power of Probiotics, Prebiotics, Synbiotics, And Postbiotics (Ppsp) in Microbiome Modulation

The documented and most significant benefits of probiotics include their ability to prevent diarrhea and constipation, alter bile salt conjugation, enhance antibacterial activity and reduce inflammation. Additionally probiotics aid in nutrient synthesis and improve the body's absorption of them. In some cases probiotics have been found to possess antioxidant properties when consumed in intact cell form or as lysates. Alongside these benefits probiotics have shown potential in alleviating symptoms of Allergy, Cancer, AIDS, Respiratory and Urinary Tract Infections there have been isolated studies suggesting that probiotics may also have a positive impact on Aging, Fatigue, Autism, Osteoporosis, Obesity and Type 2 Diabetes. Numerous mechanisms have been proposed to explain these beneficial effects including the production of inhibitory substances [54].



**Figure 4.** Effect of PPSP in elevating good microbiota and promoting gut health.

**Table 6.** Effect of PPSP in elevating good microbiota and promoting gut health.

Disease	ppsp	Functions	Reference
Diarrhea	oral rehydration and probiotics	<i>S.boulevardii</i> , <i>L.rhamnosus</i> GG, <i>L.fermentum</i> , <i>L.acidophilus</i> , in bile salt conjugation enhancement of antibacterial activity, antiinflammatory	[31,55–59]
Irritable bowel syndrome	bowel probiotics and prebiotics	probiotics: <i>L.rhamnosus</i> , <i>B.infantis</i> , <i>B.breve</i> Bb99 prebiotics: Soluble, non-viscous fibers, such as partially hydrolyzed guar gum	Modulate the gut microbiota, improve stool frequency, improve transit time and improve stool consistency [32,60–63]
Inflammatory bowel disorder (Ulcerative Colitis (UC), Crohn's Disease (CD))	probiotics	<i>S.boulevardii</i> , <i>L.casei</i> , <i>Bifidobacterium bifidum</i> pouchitis. Probiotics: <i>S. boulandii</i> , <i>Lactobacillus casei</i> , <i>Bifidobacterium bifidum</i> for UC; general benefits for CD; probiotic mixes for pouchitis	Balance the intestinal homeostasis, induce remission in IBD, inhibit epithelium attachment [33,64–68]

Lactose intolerance	probiotics	probiotics: <i>L.acidophilus</i> , <i>L.casei shirota</i> , <i>Bifidobacterium Yakult</i> , <i>L.helveticus</i>	Modulation of mucin production, enhance Ig A secretion by a GALT, production of SCFA [69]
Cardiovascular disease	probiotics, prebiotics and synbiotics	<i>L.bulgaricus</i> , <i>L.reuteri</i> , <i>B.coagulans</i> , <i>L.acidophilus</i> prebiotics: <i>Inulin can enhance hypocholesterolemic activity.</i> synbiotics1; combine both	Potential therapeutic, enhance the hypercholesterolemic activity [70–73]
Cancer	probiotics and synbiotics	probiotics: <i>L.acidophilus</i> , <i>B.longum</i> and <i>Comprehensive preventing pro-carcinogen transformation and inducing cell death</i>	Preventing the onset of cancer, treatment of existing [34,74–76]
Urinary tract infection	probiotics and synbiotics	<i>Lactobacillus GG</i> , <i>L.rhamnosus</i>	Stimulate the growth of different indigenous gut bacteria, immunomodulation, adjuvant therapy [35,77–79]

The information provided encompasses a wide range of health conditions and their potential improvement through the use of probiotics. For the ease of understanding, below are the key takeaways for each condition:

**Diarrhea:** Triggers: Rotaviruses, use of antibiotics, and bacterial infections (specifically, *E. coli* in cases of traveler’s diarrhea). Management: Swift oral rehydration and probiotics (such as *Lactobacillus* and *Saccharomyces boulardii*) are recommended to restore healthy bacteria and alleviate symptoms. (31,55,56,57,58,59)

**Irritable Bowel Syndrome (IBS):** Features: Repeated discomfort in the abdominal area, pain, bloating, and unpredictable bowel patterns. Probiotics: *Lactobacillus plantarum*, *L. rhamnosus GG*, *B. infantis*, and *E. coli Nissle 1917* have shown potential in reducing symptoms. Prebiotics: Soluble fibers with low viscosity, like partially hydrolyzed guar gum. (32,60-63)

**Inflammatory Bowel Disorder (IBD)** is a condition that encompasses several types, including Ulcerative Colitis (UC), Crohn’s Disease (CD), and pouchitis. To manage this disorder, probiotics such as *S. boulardii*, *Lactobacillus casei*, and *Bifidobacterium bifidum* have been found to be helpful for UC, while providing general benefits for CD. For pouchitis, a combination of probiotics is recommended. (33,64-68)

**Lactose Intolerance** is a common issue that can cause uncomfortable symptoms like abdominal pain, bloating, diarrhea, and flatulence, all stemming from a deficiency of  $\beta$ -galactosidase. To address this, treatment options such as lactase tablets, *Lactobacillus bulgaricus*, and *Streptococcus thermophilus* have been effective, as well as milk enriched with probiotics [69].

**Cardiovascular Health and Lipid Metabolism:** Exploring the Benefits of Probiotics, Prebiotics, and Synbiotics: Probiotic strains such as *L. bulgaricus*, *L. reuteri*, and *B. coagulans*, along with *L. acidophilus L1 in milk* and *B. longum BL1* in yogurt, have shown promising results in promoting cardiovascular health. Additionally, prebiotic inulin has been found to enhance hypocholesterolemic activity. The combination of probiotics and prebiotics, known as synbiotics, may have a regulating effect on lipid profiles [70–73].

In the realm of **cancer** control, *L. acidophilus* and *L. bulgaricus* have been found to potentially reduce the proliferation of colon tumors. These probiotics are thought to work by modulating the immune system, regulating apoptosis, and cell differentiation. Furthermore, using synbiotics as a comprehensive approach could induce cell death [34,74–76]

Probiotics, specifically *Lactobacillus* species like *L. reuteri*, have shown promise in preventing and treating **Urinary Tract Infections (UTIs)**. Through competitive exclusion, production of antimicrobial substances, immune modulation, and promoting a healthy microbial environment, these probiotics are being studied as potential solutions for UTIs [35,77–79].

## Exploring the Role of Probiotics, Prebiotics, Synbiotics, and postbiotics (ppsp) as Antibiotic Alternatives

In the early 20th century, treating infections relied heavily on traditional remedies and the use of plant-based mixtures with supposed antimicrobial properties. However, a turning point in history came in 1874 when cultures of *Penicillium glaucum* were found to be free from bacterial contamination. This discovery piqued the curiosity of Sir Alexander Fleming and he went on to uncover the power of penicillin in 1928. The widespread use of this drug proved to be immensely beneficial during times of war. Other significant discoveries, such as Ehrlich's introduction of salvarsan, the first synthetic antibacterial organoarsenic compound, and the introduction of new antibiotic substances for medical use between 1935 and 1968, marked a new era in the fight against infections. However, the overuse of antibiotics has sparked a dangerous phenomenon known as antibiotic resistance (AMR), (as shown in Figure 5) which poses a serious threat to human, animal, and environmental health by reducing the effectiveness of clinical treatments [81].

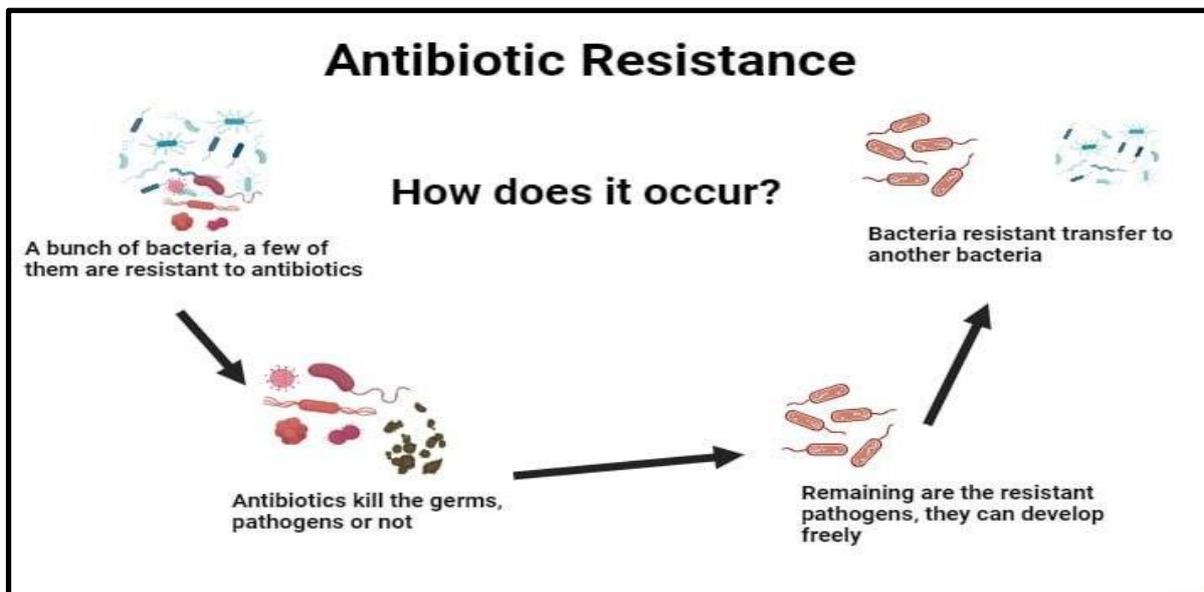


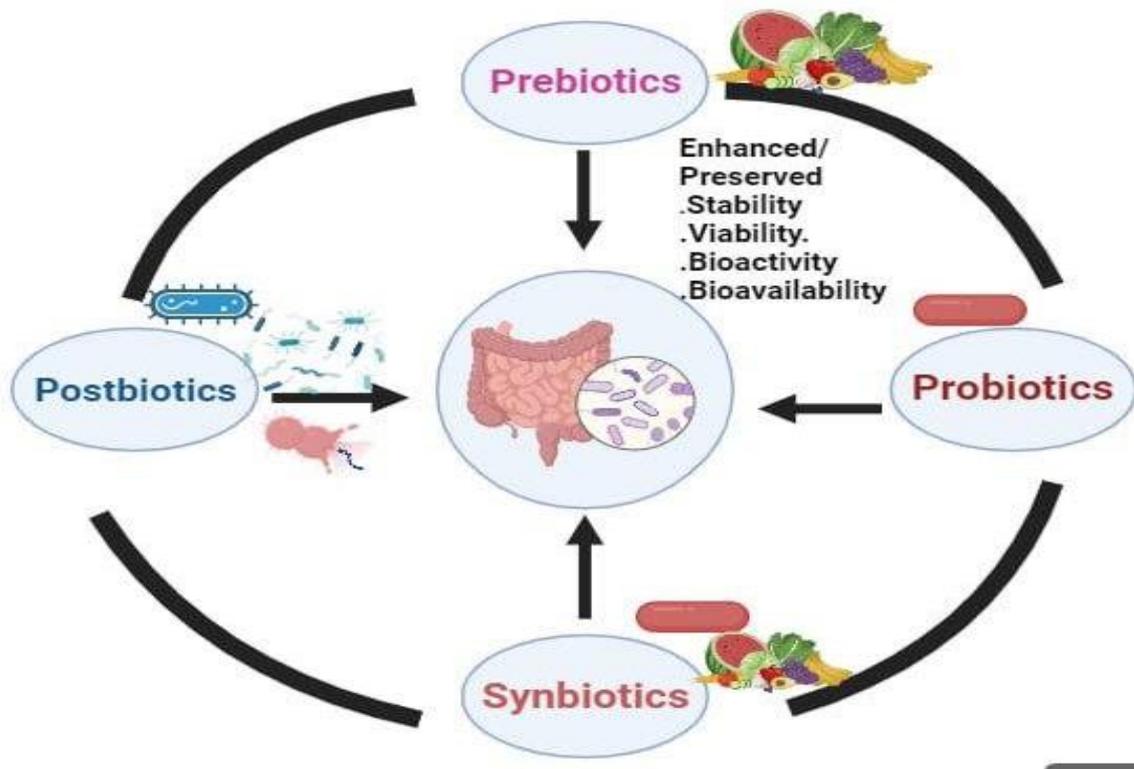
Figure 5. Antimicrobial resistance development.

Consequently, the treatment of diseases is becoming increasingly challenging, leading to a notable rise in mortality rates during various outbreaks.

**IMPACT OF GUT MICROBIOTA DYSBIOSIS ON ANTIBIOTICS:** Research has demonstrated the profound impact of dysbiosis on the effectiveness and breakdown of numerous medications by the help of the MHI (Microbiome health index) which commonly examines bacterial levels after taking antibiotics and compares the levels of beneficial bacteria to those of potentially harmful bacteria. Example of MIH is used knowing the influence of gut microbiota on the metabolism of tacrolimus, resulting in the production of less powerful compounds and consequently varying drug exposure for those taking oral tacrolimus [94]. Another striking example is the significant reduction in the antihyperglycemic effects of metformin when co-administered with oral vancomycin, highlighting how the presence of commensal bacteria is crucial to its efficacy [95]. The microbe *Eggerthella lenta* has also been linked to the deactivation of digoxin, and the use of antibiotics to target vitamin K-producing microbiota may interfere with the performance of vitamin K antagonists, such as warfarin [96]. Moreover, promising findings have shown that supplementing specific commensal bacteria can enhance or restore the effectiveness of immune checkpoint inhibitors, which hinder tumor growth [97]. Despite these groundbreaking insights, further research is needed to fully understand gut microbiome's role in medication metabolism. Recent studies have suggested a potential link between P-glycoprotein expression and certain bacterial species belonging to the Clostridia and Bacilli classes [98]. These bacteria, found in the gut, could potentially interact with gut receptors and compounds derived from microbiota, as well as external substances such as

medications. These interactions could have an impact on important systems involved in drug metabolism, like cytochrome P450. As a result, imbalances in the gut microbiome, known as dysbiosis, may have the ability to disrupt the efficiency of drug metabolic pathways [99].

**COMBATING ANTIBIOTICS RESISTANCE BY THE HELP OF PPSP:** To combat antibiotic resistance, it is important to use antibiotics judiciously and only when necessary. This includes proper diagnosis of bacterial infections, appropriate selection of antibiotics based on susceptibility testing, and adherence to prescribed treatment regimens.



**Figure 6.** Probable way to combat antibiotics resistance by the help of PPSP.

Our novel understanding of the gut microbiota has long been proven to contribute to numerous health beneficial functions as well as disease by influencing gut maturation, host nutrition and pathogen resistance by facilitating horizontal transfer of antimicrobial resistance (AMR) genes to potential pathogenic bacteria [36]. Therefore, it is crucial to study the AMR potential of natural environments, such as indigenous microbiota, and not merely as mechanisms already emerged in pathogens [37].

### Discussion:

This review provides an overview of probiotics, prebiotics, and synbiotics in the context of their systemic effects on the host's health, metabolism, and immune system. Emphasizing the importance of the symbiotic relationship between prebiotics and probiotics, the review suggests that the utilization of prebiotics by probiotics should be a prerequisite for optimal symbiotic selection. Understanding the underlying mechanisms of probiosis and prebiosis is crucial for designing enhanced functional foods that can positively impact host health. The ability to modulate the microbiota composition through prebiotic dietary substances and probiotic microorganisms is seen as a promising approach in controlling and treating major diseases.

While there is a wealth of published reports on the use of probiotics in humans, information on prebiotics, postbiotics and synbiotics is limited. The review highlights the need for more comprehensive and well-designed large-scale clinical trials to substantiate health claims associated with these components. The potential to target specific organisms in the large intestine for defined health-promoting purposes is recognized as valuable. The diversity in bacterial carbohydrate

utilization patterns among different strains and species is acknowledged as a consideration for developing new synbiotics. The recent technological advances in deep sequencing and microbial analysis of the gastrointestinal tract offer opportunities to prevent diseases and maintain better health by understanding and manipulating the gut microbiota.

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