

## SYNBIOTICS: A COMPREHENSIVE REVIEW ON THEIR COMPOSITION, MECHANISMS, AND THERAPEUTIC POTENTIAL IN DISEASE MANAGEMENT

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### ABSTRACT

Synbiotics combine probiotics consist of live beneficial microorganisms and prebiotics, non- digestible substrates that selectively enhance probiotic survival and activity. So when probiotics and prebiotics are put together as synbiotics, they attempt to ensure that your gut has a good proportion of living microorganisms more than when using probiotics and prebiotics together. However, synbiotics may act in different ways depending on how they act when mixed together. In some ways, they act as complements where each component does the exact same thing. Other times they act as synergists where the prebiotic is utilized by probiotics; as a result, you become even healthier. This is because, as stated above, the prebiotic is used specifically by probiotics to ensure that good things happen. A “synbiotic,” assists in improving the health status of your gut by using probiotics and prebiotics together. This article gives an entire description of synbiotic compounds and explains the

appropriate strains and substances that should be used as well as the major processes that occur when using synbiotics. There are several processes through which synbiotics work effectively. The increasing demand for syn- biotics can be identified from a few recent researches that reveal the potentiality of synbiotics in the management and treatment of various ailments such as insulin resistance, obesity, irritable bowel syndrome, and colon cancer. When the use of synbiotics or both probiotics and prebiotics are taken individually, a few benefits stand out in synbiotics such as their viability, activity, and efficacy rate.

**KEYWORDS:** Synbiotics, Probiotics, Prebiotics, Gut health, Therapeutic Applications.

## 1 INTRODUCTION

The human gastrointestinal tract harbors a dense and metabolically active microbial community that plays a crucial role in host nutrition, immune system development, intestinal barrier integrity, and protection against pathogenic microorganisms. Increasing evidence indicates that disturbances in gut microbial composition and function, commonly referred to as dysbiosis, are strongly associated with chronic disorders such as obesity, metabolic syndrome, type 2 diabetes, inflammatory bowel diseases, and colorectal cancer.<sup>[1,2]</sup> Consequently, modulation of the gut microbiota has emerged as an important therapeutic and preventive strategy in modern nutrition and medicine.

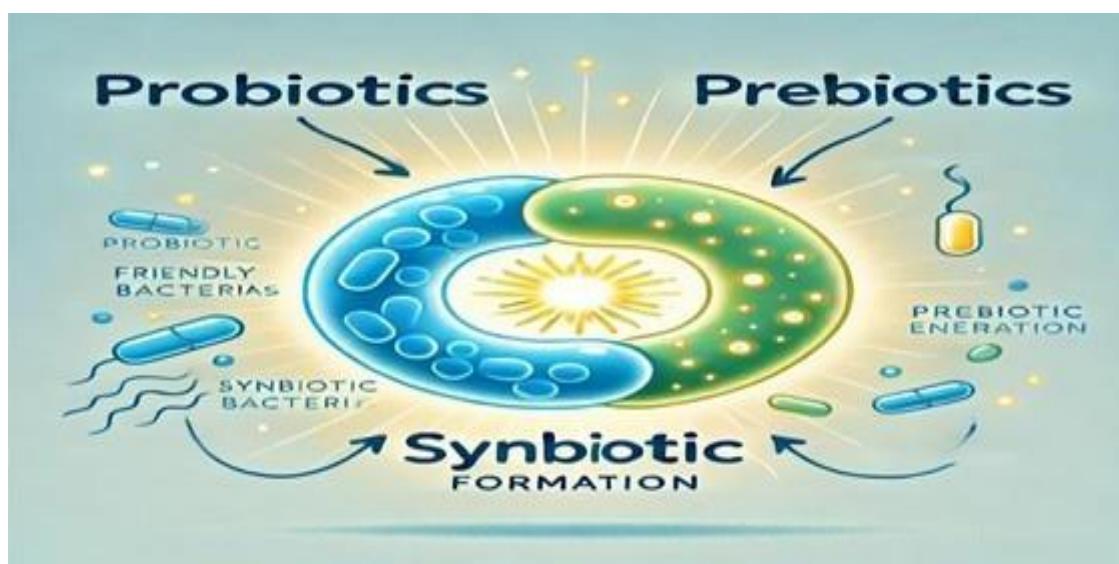
Among the dietary interventions aimed at improving gut microbial balance, probiotics and prebiotics have been extensively investigated. Probiotics are defined as live microorganisms that confer health benefits to the host when administered in adequate amounts, whereas prebiotics are selectively fermented substrates that stimulate the growth and metabolic activity of beneficial intestinal bacteria.<sup>[1]</sup> Although both probiotics and prebiotics have demonstrated beneficial effects on gastrointestinal health, immune modulation, and metabolic regulation, their individual application often yields variable outcomes. Probiotic efficacy may be compromised by reduced viability during processing, storage, and gastrointestinal transit, while the effects of prebiotics depend largely on host-specific microbiota composition and fermentability characteristics.<sup>[2]</sup>

To address these limitations, synbiotics were developed as formulations combining probiotics with compatible prebiotics to enhance microbial survival, colonization, and functional activity within the host. The underlying rationale of synbiotic use is to provide a selective substrate that supports the growth and metabolic performance of administered probiotic strains, thereby improving their persistence and biological effectiveness in the gastrointestinal environment.<sup>[1]</sup> Compared to single-component interventions, synbiotics have shown improved consistency in modulating gut microbiota and host metabolic responses.

In recent years, the concept of synbiotics has evolved beyond simple co-administration. According to updated scientific consensus, synbiotics are now classified into complementary and synergistic formulations. Complementary synbiotics consist of probiotics and prebiotics that independently provide health benefits, whereas synergistic synbiotics are specifically designed

so that the prebiotic component is selectively utilized by the co-administered probiotic microorganism, resulting in enhanced functional outcomes.<sup>[2]</sup> This classification highlights the importance of strain–substrate specificity in determining synbiotic efficacy. Mechanistically, synbiotics exert their health-promoting effects through multiple interconnected pathways, including modulation of gut microbial composition, increased production of short-chain fatty acids, enhancement of intestinal barrier function, and regulation of immune and inflammatory signaling pathways. These mechanisms contribute to improved metabolic homeostasis, reduced systemic inflammation, and strengthened host defense responses.<sup>[1,3]</sup>

Clinical and experimental studies increasingly support the therapeutic potential of synbiotics in the management of insulin resistance, obesity, irritable bowel syndrome, non-alcoholic fatty liver disease, and colorectal cancer.<sup>[4,5,3]</sup> Despite these promising findings, challenges related to strain selection, formulation stability, limited fermentation capacity of certain prebiotics, and lack of globally harmonized regulatory frameworks continue to hinder their widespread clinical application.<sup>[2]</sup>

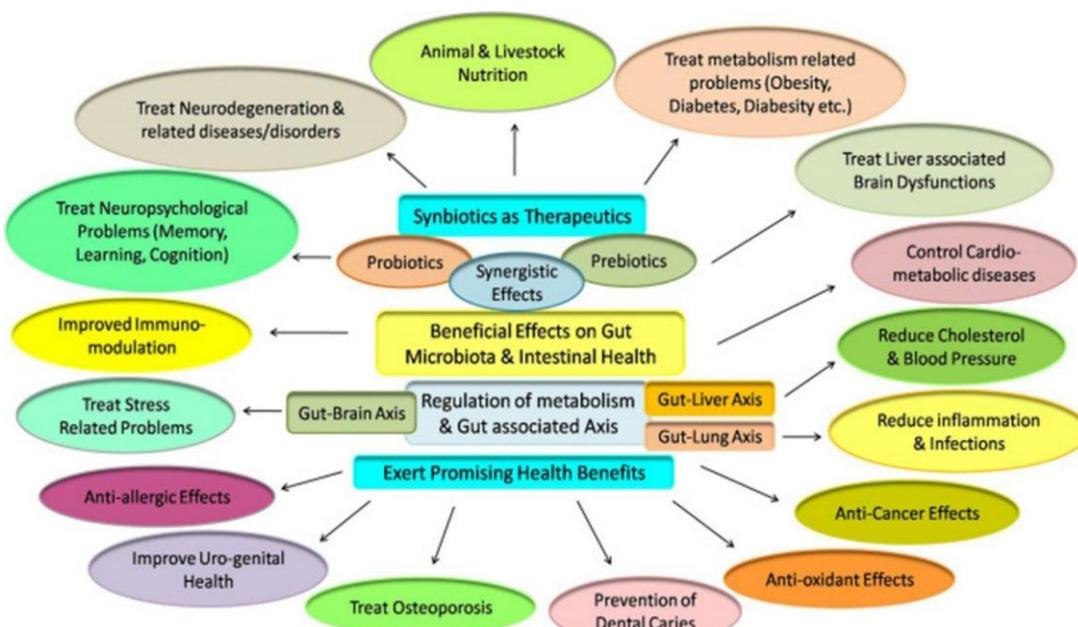


**Figure 1: Conceptual overview of synbiotics and their components.**

Therefore, a comprehensive evaluation of synbiotics is essential to better understand their classification, mechanisms of action, and therapeutic relevance. This review aims to critically analyze current evidence on synbiotics, focusing on their health benefits across major disease conditions, formulation challenges, and emerging technological advancements, while also highlighting future research directions for optimized clinical and nutritional applications.

## 2 General mechanisms

Synbiotics are intentionally designed combinations of probiotics and prebiotics that act in a complementary or synergistic manner to beneficially modulate the composition and metabolic activity of the gut microbiota, ultimately aiming to improve host health.<sup>[1,6]</sup> A synergistic effect refers to a situation where two or more factors act together in such a way that their combined effect is greater than the sum of their individual effects. This means that the interaction between them amplifies the overall biological response rather than just adding separate contributions. In synbiotics, this implies that the probiotic and prebiotic, when administered together, produce enhanced modulation of the gut microbiota and host physiology beyond what each could achieve alone at the same dose. In this concept, the prebiotic component serves as a selectively utilizable substrate that supports the growth and activity of beneficial microorganisms, including the co administered probiotic strain and/or resident commensals, while the probiotic component provides direct microbial functions such as barrier reinforcement, competitive exclusion of pathogens and immunomodulation.<sup>[7,8,9]</sup>



**Figure 2: Probiotic, Prebiotic and Synbiotic Mechanism across the gastrointestinal tract.**<sup>[12]</sup>

A substrate is recognized as a prebiotic only if it resists digestion and absorption in the upper gastrointestinal tract (GIT), is selectively fermented by beneficial bacteria in the colon, and induces specific luminal or systemic effects that are associated with improved health outcomes.<sup>[7,10]</sup>

Within the upper GIT, prebiotics can modulate gastric and small intestinal physiology through several mechanisms (Holscher, 2017; Davani Davari et al., 2019). Experimental and clinical data suggest that certain nondigestible carbohydrates reduce gastric acid secretion, alter orocecal transit time and exhibit a low glycemic index, thereby attenuating post prandial glucose excursions and insulin responses (Roberfroid, 2010; Holscher, 2017). In parallel, prebiotics have been associated with hyperplasia and functional enhancement of the small intestinal epithelium and with stimulation of enteroendocrine cells, leading to increased secretion of peptides such as glucagon like peptide 1 (GLP 1) and peptide YY (PYY), which participate in appetite regulation, glucose homeostasis and gut motility.<sup>[9,11]</sup>

In the lower GIT, prebiotics act primarily as fermentable substrates for saccharolytic microbiota, particularly bifidobacteria and lactic acid bacteria, promoting a shift away from proteolytic fermentation toward a more saccharolytic profile (Holscher, 2017; Davani Davari et al., 2019). This fermentation yields short chain fatty acids (SCFAs), mainly acetate, propionate and butyrate, which lower luminal pH, inhibit the growth of certain pathogens, provide an energy source for colonocytes and exert anti inflammatory, antiproliferative and pro apoptotic effects relevant to cancer prevention.<sup>[13,14,15]</sup> Prebiotic intake is also associated with increased stool bulk, improved stool consistency and reduced intestinal transit time, reflecting osmotic effects, increased bacterial mass and stimulation of colonic motility.<sup>[9]</sup> Through these combined actions, prebiotics contribute to maintenance of epithelial integrity, mucus production and a more resilient colonic ecosystem.<sup>[9,13]</sup>

Probiotic strains used in synbiotic formulations must satisfy strict safety and functional criteria before being considered suitable for human or animal consumption<sup>[16,17]</sup> These criteria include precise taxonomic identification at the strain level; absence of known virulence factors; lack of transferable antibiotic resistance determinants; and demonstration of non-pathogenicity and non-toxicity in appropriate *in vitro* and *in vivo* models.<sup>[16,17]</sup> Functionally, candidate strains should show resistance to gastric acidity and bile salts, the capacity to survive gastrointestinal transit and at least transient colonization or persistence in the intestinal lumen or mucus layer.<sup>[18,17]</sup> Adhesion to epithelial cells or mucus is considered important for close interaction with the host epithelium, competitive exclusion of pathogens and effective immunomodulation, while industrially relevant features such as genetic stability, technological robustness during processing and storage, and maintenance of high viable counts in the final product are essential for commercial application.<sup>[18,19]</sup>

Within symbiotic products, the presence of a suitable prebiotic can enhance the survival and functional activity of the probiotic during passage through the upper GIT and in the colon.<sup>[1,6]</sup> The prebiotic substrate may protect probiotic cells through microenvironmental effects (for example, buffering and water holding) and then selectively fuel their growth in the large intestine, leading to higher viable counts, prolonged persistence and more pronounced modulation of the endogenous microbiota.<sup>[1,2]</sup> These interactions translate into several microbiological and physiological effects, including increased abundance of lactate- and SCFA-producing bacteria, inhibition of pathogen colonization by competition for adhesion sites and nutrients, production of organic acids and bacteriocins, and reinforcement of the mucosal barrier via stimulation of mucin secretion and tight junction expression.<sup>[20,21,6]</sup> Synbiotic interventions have been associated in experimental models and some clinical studies with reduced intestinal permeability, decreased endotoxemia and attenuation of low-grade inflammation linked to metabolic and gastrointestinal disorders.<sup>[1,6]</sup>

A key mechanistic axis for synbiotics is immune modulation at the level of the gut-associated lymphoid tissue (GALT).<sup>[21,15]</sup> Probiotics and their structural components are recognized by pattern-recognition receptors, including Toll-like receptors (TLRs) and NOD-like receptors, expressed on epithelial and immune cells in the lamina propria.<sup>[21,20]</sup> Engagement of these receptors enhances antimicrobial peptide production, phagocytic activity, and cytokine regulation.<sup>[15,6]</sup> Synbiotics have been shown to increase secretory IgA responses and downregulate pro-inflammatory signalling pathways such as NF- $\kappa$ B and MAPK.<sup>[21,15]</sup>

Beyond local gut effects, symbiotic-induced changes in microbial metabolites, particularly SCFAs, exert systemic metabolic and immunological actions.<sup>[13,15]</sup> SCFAs interact with G-protein-coupled receptors, influencing GLP-1 and PYY secretion, insulin sensitivity, and inflammatory tone.<sup>[11,22]</sup> Experimental evidence indicates that synbiotics may exert oncosuppressive effects via barrier reinforcement, reduction of genotoxic metabolites, histone deacetylase inhibition, and modulation of apoptosis and proliferation.<sup>[14, 23, 6]</sup>

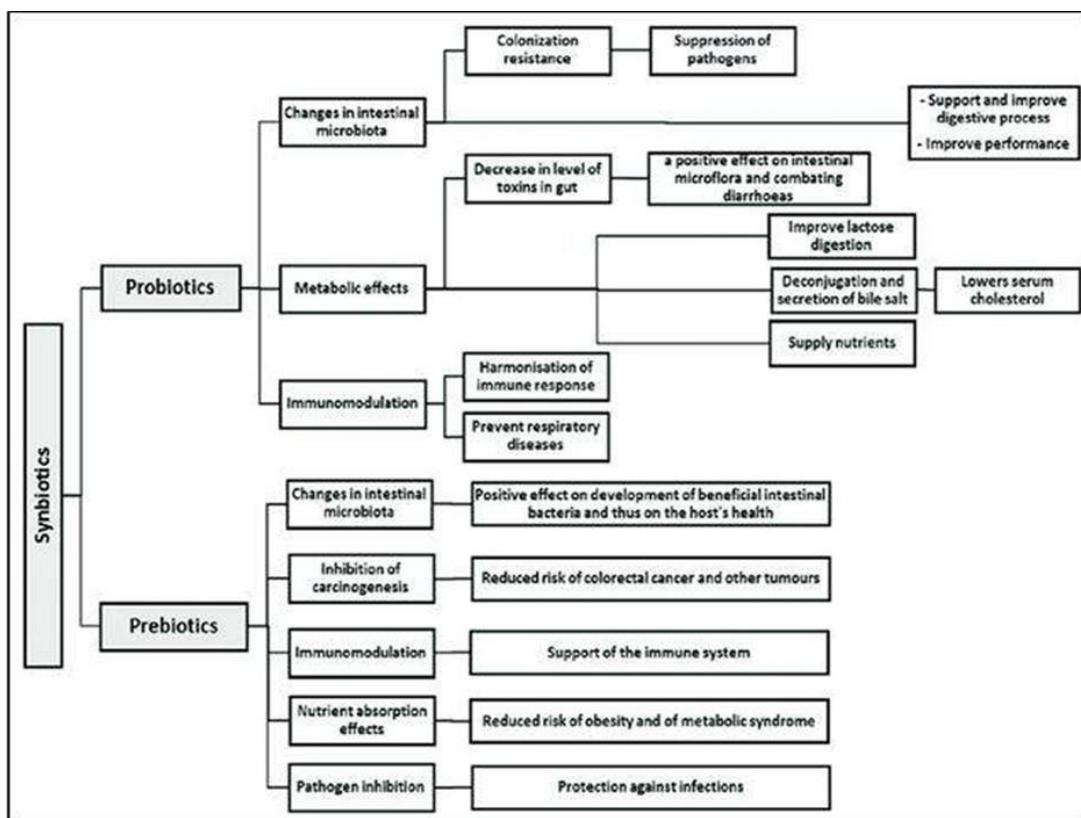
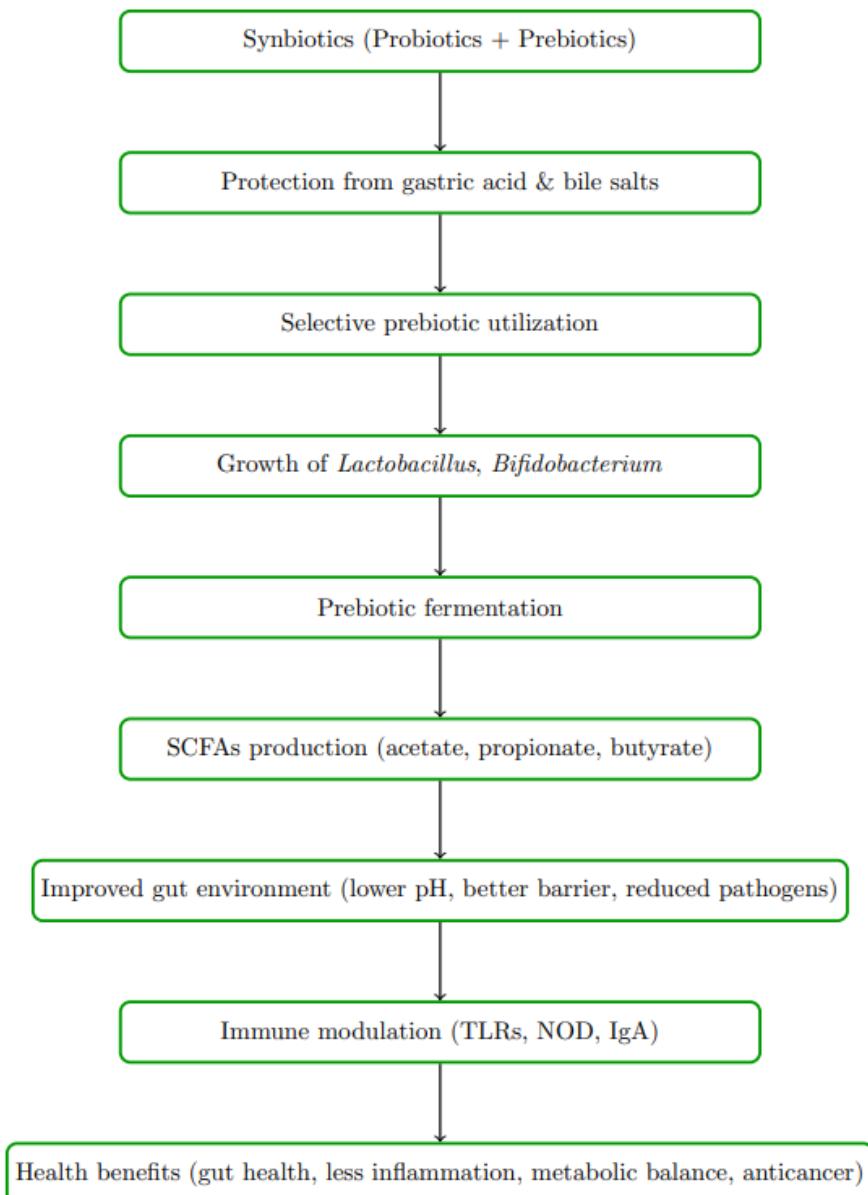


Figure 3: Mechanism of action of synbiotics and its effects<sup>[24]</sup>

### Working Mechanisms of Synbiotics

- Enhancing Probiotic Survival – Helps probiotics survive and implant in the gastrointestinal tract.
- Modulating Selective Prebiotic Utilization – Prebiotics selectively fuel the growth of co-administered probiotics.
- SCFA Production – Generates short-chain fatty acids (SCFAs) and other beneficial metabolites.
- Gut Microbiota – Different probiotic strains metabolize prebiotics in unique ways, influencing microbiota composition.



**Figure 4: Mechanism of action of synbiotics and their effects on gut health and host immunity.**

#### Synbiotics Benefits for Human Health

- Increases *Lactobacillus* and *Bifidobacterium* genus count and maintains intestinal microbiota balance.
- Improves hepatic function in cirrhosis patients.
- Enhances immunomodulative abilities.
- Prevents bacterial translocation and reduces nosocomial infections post-surgical procedures.
- Inhibits hepatic detoxication and steatosis of the organ.
- Increases intestinal IgA levels and reduces blood cholesterol levels and lowers blood

pressure.

- Improves absorption of calcium, magnesium, and phosphorus.
- Reduces the incidence of eczema in infants aged < 2 years.
- Verifies anti-carcinogenic properties of synbiotics.
- Reduces the risk of colorectal carcinoma and lowers DNA damage and colonocyte proliferation ratio.
- Synbiotics are used in the treatment of hepatic conditions.

### 3 Disease conditions

#### 3.1 Insulin Resistance

Insulin resistance is a major problem in metabolic syndrome where the body's cells (such as muscle and adipose tissue) do not respond effectively to insulin, the hormone responsible for regulating blood glucose levels. This results in elevated blood sugar concentrations, compensatory hyperinsulinemia, and an increased risk of type 2 diabetes and cardiovascular complications. Central adiposity and chronic low-grade inflammation driven by gut microbial dysbiosis further exacerbate insulin resistance through the release of inflammatory mediators into systemic circulation.

Synbiotics help counteract these processes by modulating gut microbial composition toward beneficial taxa. Prebiotics selectively nourish commensal bacteria, while probiotics introduce metabolically active strains directly into the gut. Together, these components enhance the production of short-chain fatty acids (SCFAs), particularly butyrate, which suppress inflammation, improve insulin sensitivity, and regulate hepatic glucose metabolism. Synbiotics also reduce metabolic endotoxemia by limiting translocation of lipopolysaccharides (LPS) into circulation. In a randomized, double-blind, placebo-controlled clinical trial, synbiotic supplementation significantly improved insulin resistance and inflammatory markers in patients with metabolic syndrome, highlighting the therapeutic potential of synbiotics in restoring metabolic homeostasis.<sup>[4]</sup>

#### 3.2 Obesity

Obesity develops when long-term caloric intake exceeds energy expenditure, leading to excessive adipose tissue accumulation, particularly in the abdominal region. Gut microbiota plays a crucial role in obesity by influencing energy harvest, appetite regulation, lipid metabolism, and adipose tissue inflammation. Certain microbial profiles enhance caloric extraction from the diet and promote low-grade systemic inflammation.

Synbiotics mitigate these effects by promoting the growth of beneficial bacteria such as *Bifidobacterium* and *Akkermansia*, which are associated with improved metabolic profiles. Prebiotics act as fermentable substrates for these microbes, while probiotics ensure their immediate availability in the gastrointestinal tract. The resulting increase in SCFA production stimulates satiety hormones including glucagon-like peptide 1 (GLP-1) and peptide YY (PYY), alters bile acid metabolism to reduce lipid absorption, and promotes browning of white adipose tissue. Additionally, synbiotics help normalize the Firmicutes-to-Bacteroidetes ratio, reducing dietary energy extraction.

A 12-week double-blind randomized controlled trial demonstrated significant reductions in body weight and fat mass among overweight adults receiving synbiotic supplementation, underscoring its potential role in obesity management.<sup>[25]</sup>

### 3.3 Irritable Bowel Syndrome (IBS)

Irritable bowel syndrome (IBS) is a functional gastrointestinal disorder characterized by abdominal pain, bloating, altered bowel habits, and visceral hypersensitivity in the absence of identifiable structural abnormalities. Its pathophysiology involves dysregulated gut motility, increased intestinal permeability, low-grade mucosal inflammation, stress-related gut–brain axis disturbances, and microbial imbalance.

Synbiotics alleviate IBS symptoms by restoring gut microbial equilibrium, strengthening epithelial barrier integrity, and increasing SCFA production, which exerts anti-inflammatory and neuromodulatory effects. They suppress gas-producing and pathogenic bacteria, enhance mucin secretion, downregulate pro-inflammatory cytokines such as TNF- $\alpha$ , and normalize gut–brain signaling pathways involved in bowel function.

A double-blind placebo-controlled clinical trial reported dose-dependent improvements in abdominal pain, bloating, and fatigue following synbiotic administration in IBS patients, demonstrating the efficacy of synbiotics in symptom management.<sup>[26]</sup>

### 3.4 Cancer (Colon Cancer)

Colorectal cancer develops through a multistep process involving genetic mutations, chronic inflammation, dietary carcinogens, oxidative stress, and microbial dysbiosis. Pathogenic gut

bacteria can produce genotoxic metabolites and pro-carcinogenic enzymes, contributing to tumor initiation and progression.

Synbiotics exert protective effects by enhancing gut barrier integrity, modulating immune surveillance, suppressing inflammation, and increasing SCFA production—particularly butyrate—which induces apoptosis, inhibits cell proliferation, and regulates epigenetic pathways through histone deacetylase inhibition. Synbiotics also reduce bacterial enzymes involved in carcinogen activation and support detoxification of dietary mutagens.

A systematic review and meta-analysis of randomized controlled trials demonstrated that synbiotic supplementation significantly reduced postoperative infections, gastrointestinal complications, hospital stay duration, and antibiotic usage in colorectal cancer patients undergoing surgery, highlighting their clinical relevance in cancer care.<sup>[27]</sup>

### 3.5 Microbe Species, Associated Disease Condition, and Effect on Disease Condition

| Microbe Species  | Associated Disease Condition                   | Effect on Disease Condition  |
|--|--|--|
| Lactobacillus spp. ( <i>L. rhamnosus</i> GG, <i>L. acidophilus</i> , <i>L. casei</i> , <i>L. plantarum</i> , <i>L. reuteri</i> ) | Insulin resistance, obesity, IBS, colon cancer | Increases SCFAs, reduces gut inflammation (IL-6/TNF- $\alpha$ ↓), improves insulin sensitivity and barrier function; <sup>[28]</sup> eases IBS pain and bloating. <sup>[26]</sup>                  |
| Bifidobacterium spp. ( <i>B. bifidum</i> , <i>B. breve</i> , <i>B. longum</i> , <i>B. infantis</i> , <i>B. lactis</i> BB-12)     | Insulin resistance, obesity, IBS, colon cancer | Boosts endogenous bifidobacteria, lowers metabolic syndrome markers, enhances gut barrier and mucin production; <sup>[29]</sup> supports SCFA production for anti-obesity effects. <sup>[30]</sup> |
| <i>Escherichia coli</i> Nissle 1917  | IBS (limited colon cancer support)             | Antibacterial activity via bacteriocins, strengthens immune responses (IgA ↑), reduces relapse in gut disorders; <sup>[31]</sup> alleviates IBS inflammation <sup>[32]</sup>                       |
| Lactobacillus spp. + Inulin  | IBS, gut health, obesity                       | Improves probiotic survival under acidic and bile conditions, balances Firmicutes/Bacteroidetes ratio, and relieves bloating <sup>[29]</sup>   |

|  | Associated Disease Condition           | Effect on Disease Condition  |
|--|--|--|
| Bifidobacterium spp. + FOS                   | Metabolic syndrome, IBS, obesity       | Enhances bifidobacterial growth, increases acetate and butyrate production, improves insulin sensitivity, and eases constipation <sup>[10]</sup>   |
| Bifidobacterium + Lactobacillus + FOS/Inulin | Gut health, obesity, IBS, colon cancer | Synergistic microbiota modulation (bifidogenic effect), reduces postoperative infections, improves metabolic outcomes; <sup>[27]</sup> enhances SCFA production and gut barrier Integrity. <sup>[30]</sup> |

#### 4 Examples of clinical trials regarding the effect the Synbiotic

| Alleviation of lactose intolerance                                |  |   |          |  |  |
|---|--|---|----------|--|--|
| [206]   | 20 females and males                           | <i>Lactobacillus</i> , <i>Bifidobacterium</i> , FOS   | 5 weeks  | Consumption of the probiotic mixture improved the gastrointestinal performance associated with lactose load in subjects with LL. Symptoms were additionally reduced by the addition of prebiotics. The supplementation was safe and well tolerated, with no significant adverse effect observed. |  |
| Different types of cancer and side effects associated with cancer |  |   |          |  |  |
| [192]   | 43 polypectomized and 37 colon cancer patients | <i>L. rhamnosus</i> GG, <i>B. lactis</i> Bb12, inulin | 12 weeks | Increased <i>L. rhamnosus</i> and <i>B. lactis</i> in faeces, reduction in <i>C. perfringens</i> , prevents increased secretion of IL-2 in polypectomized patients, increased production of interferon- $\gamma$ in cancer patients.   |  |

**Figure 5: Clinical trial evidence demonstrating synbiotic efficacy across metabolic syndrome, obesity, IBS, and colorectal cancer management.<sup>[1]</sup>**

| References                         | Subjects                                  | Composition of Synbiotic   | Time of Administration | Main Outcome  |
|------------------------------------|---|--|------------------------|---|
| <b>Obesity</b>                     |   |  |                        |   |
| [193]                              | 153 obese men and women                   | <i>L. rhamnosus</i> CGMCC1.3724, inulin  | 36 weeks               | Weight loss and reduction in leptin. Increase in Lachnospiraceae.                                       |
| [194]                              | 70 children and adolescents with high BMI | <i>L. casei</i> , <i>L. rhamnosus</i> , <i>S. thermophilus</i> , <i>B. breve</i> , <i>L. acidophilus</i> , <i>B. longum</i> , <i>L. bulgaricus</i> , FOS | 8 weeks                | Decrease in BMI z-score and waist circumference.  |
| [195]                              | 77 obese children                         | <i>L. acidophilus</i> , <i>L. rhamnosus</i> , <i>B. bifidum</i> , <i>B. longum</i> , <i>E. faecium</i> , FOS   | 4 weeks                | Changes in anthropometric measurements. Decrease in TC, LDL-C, and total oxidative stress serum levels. |
| <b>Insulin resistance syndrome</b> |   |  |                        |   |
| [196]                              | 38 subjects with IRS                      | <i>L. casei</i> , <i>L. rhamnosus</i> , <i>S. thermophilus</i> , <i>B. breve</i> , <i>L. acidophilus</i> , <i>B. longum</i> , <i>L. bulgaricus</i> , FOS | 28 weeks               | The levels of fasting blood sugar and insulin resistance improved significantly.                        |

**Figure 6: Clinical trial evidence demonstrating the effects of synbiotics on obesity and insulin resistance.<sup>[1]</sup>**

| Irritable bowel syndrome (IBS), gastrointestinal disorders, elimination of Helicobacter, inflammatory bowel disease (IBD), diarrhoeas |  |   |         |   |
|---|--|---|---------|---|
| [201]   | 76 patients with IBS   | <i>L. acidophilus</i> La-5®, <i>B. animalis</i> ssp. <i>lactis</i> BB-12®, dietary fibres (Beneo) | 4 weeks | On average, an 18% improvement in total IBS-QoL score was reported and significant improvements in bloating severity, satisfaction with bowel movements, and the severity of IBS symptoms' interference with patients' everyday life were observed. However, there were no statistically significant differences between the symbiotic group and the placebo group. |
| [202]   | 69 children aged 6–16 years who had biopsy proven <i>H. pylori</i> infection | <i>B. lactis</i> B94, inulin  | 14 days | From a total of 69 <i>H. pylori</i> -infected children (female:male = 36/33; mean ± SD = 11.2 ± 3.0 years), eradication was achieved in 20 out of 34 participants in the standard therapy group and 27/35 participants in the symbiotic group. There were no significant differences in eradication rates between the standard therapy and the symbiotic groups.    |
| [203]   | 40 patients with UC  | <i>B. longum</i> , psyllium   | 4 weeks | Patients with UC on symbiotic therapy experienced greater quality-of-life changes than patients on probiotic or prebiotic treatment.  |

**Figure 7: Clinical trial evidence demonstrating the effects of synbiotics in irritable bowel syndrome (IBS)<sup>[1]</sup>**

## Abbreviations

BMI—body mass index; CFU—colony-forming-unit; CRP—C-reactive protein; FOS—fructo-oligosaccharides; IBS-QoL—quality of life with IBS; HDL-C—high-density lipoprotein cholesterol; HOMA-IR—homeostasis model assessment of insulin resistance; IHTG—intrahepatic triacylglycerol; IRS—insulin resistance syndrome; LDL-C—low-density lipoprotein cholesterol; LI—lactose intolerance; NAFLD—non-alcoholic fatty liver disease; NF- $\kappa$ B—nuclear factor  $\kappa$ B; T2D—type 2 diabetes; TAG—triacylglycerols; TC—total cholesterol; TGL—total glutathione levels; TNF- $\alpha$ —tumour necrosis factor  $\alpha$ ; UC—ulcerative colitis.

FOS—fructooligosaccharides; GOS—galactooligosaccharides; TOS—ransgalactooligosaccharides; XOS—xylooligosaccharides.

## 5 Host Variability in Synbiotic Efficacy

When we talk about synbiotics—these powerful combinations of probiotics and prebiotics designed to supercharge our gut health—one of the biggest hurdles researchers face is that they don't work the same way for everyone. While synbiotics show tremendous promise in reshaping the gut microbiome and tackling various health issues, their real-world effectiveness often varies dramatically from person to person.<sup>[33]</sup> This phenomenon, commonly referred to as host variability, reflects the unique interplay of each individual's biology, genetics, existing gut microbes, diet, and lifestyle, all of which determine how well synbiotics take hold, generate beneficial compounds, and deliver meaningful health improvements. Understanding this variability helps explain why clinical trials sometimes produce mixed or inconsistent results, even when using identical formulations and dosages.<sup>[1]</sup>

## Drivers of Individual Differences

At the heart of host variability lies the baseline gut microbiota—that personal ecosystem of

trillions of microbes already living in your intestines—which acts as the gatekeeper for new probiotic arrivals. Some people have microbial communities primed to welcome and nourish incoming synbiotics, leading to smooth engraftment and efficient prebiotic breakdown, while others face resistance that limits these benefits.<sup>[33]</sup> Layer on top of that genetic factors, like inherited traits affecting digestion or immune responses, along with age, gender, and immune health, which influence everything from stomach acid levels and gut transit speed to bile tolerance and signaling through key immune pathways like Toll-like receptors (TLRs) and NOD proteins. Everyday realities amplify this further: medications such as antibiotics or antacids can wipe out or alter gut flora, while dietary habits (high-fiber vs. processed foods) and lifestyle choices (stress, exercise, sleep) reshape the microbial landscape and fermentation potential, creating truly personalized responses.

### **Biological Mechanisms at Play**

Synbiotics work their magic through a few core processes: probiotics selectively munch on prebiotics to thrive, they churn out short-chain fatty acids (SCFAs) like acetate, propionate, and butyrate, and they help rebalance the overall gut community for better health. But host traits throw curveballs into this equation. For one person, their unique mix of carbohydrate-digesting microbes might produce a flood of protective SCFAs that strengthen the gut lining and dial down inflammation; for another, the same synbiotic might yield minimal SCFAs, offering little systemic relief. The resident microbiota's colonization resistance—essentially the gut's defense squad—often blocks probiotics from sticking around long-term, and individual epithelial and immune reactions dictate how much of those precious metabolites actually make it into the bloodstream to combat issues like metabolic disorders or IBS.<sup>[1]</sup>

### **Evidence from Clinical Studies**

Time and again, human trials paint a clear picture of this patchwork response. In studies on synbiotics for metabolic conditions or irritable bowel syndrome, you'll see "responders"—folks whose guts transform positively, with boosted beneficial bacteria, tamed inflammation markers, and tangible improvements in symptoms—right alongside "non-responders" who barely register a change despite the same intervention.<sup>[34]</sup> Research targeting obesity, insulin resistance, and gut disorders consistently shows that your starting microbial profile is a strong predictor of success, making a compelling case for screening patients before treatment. Cutting-edge multi-omics tools (analyzing DNA, RNA, proteins, and metabolites) now reveal just how wildly gut trajectories diverge post-synbiotic, with some individuals blooming into

healthier profiles while others stay stubbornly static.<sup>[33]</sup>

### **Broader Challenges and Implications**

This inherent variability poses real headaches for synbiotic developers, regulators, and clinicians. Standardized trials often report average benefits that hide dramatic subgroup differences, muddying efficacy claims and slowing product approvals. It compounds classic hurdles like ensuring strain-prebiotic compatibility or gastrointestinal survival, especially since certain hosts simply aren't wired for success with off-the-shelf formulas. Ultimately, ignoring host variability risks underwhelming real-world performance, eroding trust in these otherwise revolutionary gut therapies.

### **Future Directions**

The path forward lies in personalization: harnessing AI-powered multi-omics to profile individuals, predict who'll respond best, and craft bespoke synbiotics tailored to their unique microbiome. Imagine large-scale trials that stratify participants by gut type, incorporate next-generation engineered probiotics, and deploy innovative delivery systems like nanoparticles to bypass harsh gastrointestinal conditions for more predictable outcomes. Regulators could step up by requiring microbiota baselines for health claims, paving the way for precision nutrition that truly works for everyone.

## **6 Future Scope**

People are starting to see the good that probiotics, prebiotics, and synbiotics can do for human health. This growing awareness highlights the need for extensive research on probiotics, prebiotics, and synbiotics to fully understand their potential. Although some progress has already been made, there are still several important aspects that remain unclear and require further investigation.

**1. Clinical Trials on Probiotics and Prebiotics** Most of the research conducted so far has focused on only a few types of bacterial strains. There is a strong need for well- planned clinical trials to evaluate whether probiotics and prebiotics are truly effective, safe, and beneficial for people with different health problems. Studying a wider range of probiotic and prebiotic strains will help in understanding how these interventions can support individuals with diverse health conditions.

**2. Next-Generation Probiotics and Synthetic Biology** Advances in genetic engineering and synthetic biology have made it possible to develop next-generation probiotics. These probiotics can be designed to perform specific functions such as fighting diseases, surviving longer in the human body, and releasing beneficial compounds when required. This represents a major advancement in the field of probiotics and synthetic biology.

**3. Combining Multiomics and Artificial Intelligence** Approaches such as systems biology, metagenomics, transcriptomics, and metabolomics are essential for understanding complex interactions between the host and microorganisms. Artificial intelligence and machine learning can further help in predicting how probiotics affect individual microbial communities. The integration of multiomics data with artificial intelligence can lead to the development of personalized probiotic treatments.

**4. Application of Nanotechnology in Probiotic Delivery** Nanotechnology offers innovative ways to improve probiotic delivery by enhancing their stability and survival. Techniques such as nano-encapsulation and nano-formulations help deliver probiotics more efficiently to specific sites in the body. Nanotechnology-based delivery systems can also improve the performance of probiotics and prebiotics in food and pharmaceutical applications.

**5. Probiotics in Emerging and Non-Traditional Therapeutic Areas** Probiotics are commonly associated with gut health, but their benefits extend beyond the gastrointestinal system. Probiotics and prebiotics show potential in managing metabolic disorders, mental health conditions (often referred to as psychobiotics), immune regulation, and infectious diseases. Further research is needed to explore their role in viral infections, including COVID-19.

**6. Standardization and Consumer Awareness** The probiotic-based product market is expanding rapidly, which necessitates clear regulatory guidelines and standardization. Both manufacturers and consumers must understand product quality, efficacy, and proper usage. Collaboration between regulatory authorities and industry stakeholders is essential to ensure product quality and build consumer trust.

**7. Multidisciplinary Research and Industry–Academia Collaboration** Bridging the gap between laboratory research and real-world applications requires collaboration among

microbiologists, biotechnologists, clinicians, and industry professionals. Future research should focus on translational studies that accelerate the commercialization of innovative probiotic-based health solutions.

## 7 Synbiotic product

| Product                    | Image   | Description   | Key Features                                |
|----------------------------|---|---|---|
| Ritual Synbiotic+          |    | A clinically-studied formula combining prebiotics, probiotics, and postbiotics. | Vegan, non-GMO, 11 billion CFUs per capsule |
| Seed DS-01 Daily Synbiotic |    | A premium synbiotic supplement designed for gut health support.                 | Comprehensive gut health support            |
| Vitl Daily Biotic          |   | Offers a blend of beneficial bacteria for digestion and overall well-being.     | Budget-friendly, diverse bacterial strains  |
| Symprove Daily             |  | A liquid synbiotic formulation designed for better gut health.                  | Liquid formulation for better absorption    |

| Product                    | Image   | Description   | Key Features                   |
|----------------------------|---|---|--------------------------------|
| Peak Performance Synbiotic |  | Provides comprehensive digestive, gut, and immune health support. | High-quality digestive support |

## CONCLUSION

Synbiotics offer superior efficacy over solo probiotics or prebiotics due to consistent viability and targeted gut modulation. By acting from different angles, such as increasing short-chain fatty acids, inhibiting pathogenic bacterial growth, strengthening gut barrier function, and down-regulating immune-inflammatory mediators, synbiotics clearly have many beneficial applications in treating different types of metabolic and gut disorders. There are many indications that synbiotics could also find specific applications in treating diseases such as insulin resistance, obesity, irritable bowel syndrome, and colon cancer, all of which have an association between gut microbiota imbalance and pathogenesis. The advantage of synbiotics over probiotic or prebiotic supplements in treating different diseases clearly lies in their

relatively consistent efficacy levels that are significantly higher than those of probiotics or prebiotic treatments alone. Some challenges in choosing strains, individualized gut response, product stability, and development of standardized synbiotic formulations still exist in their application and will have to be planned in an innovative manner in future clinical studies in order to unlock their full potentials in disease management via nutritional interventions.

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