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Prebiotics in human health: The next frontier in nutrition and therapeutics

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Abstract
Prebiotics are digestible or non-digestible food elements that promote health by encouraging the growth and function of beneficial bacteria in the gut. They improve immune function, enhance mineral absorption, and support digestive health by generating short-chain fatty acids (SCFAs). Prominent prebiotic fibres include inulin, fructo-oligosaccharides (FOS), galacto-oligosaccharides (GOS), and resistant starch, which support the proliferation of beneficial bacteria such as *Lactobacillus* and *Bifidobacterium*. Research indicates that prebiotics contribute to metabolic health by reducing glycemic response, cholesterol levels, and body weight. They are also involved in preventing and managing conditions like colorectal cancer, irritable bowel syndrome (IBS), obesity, type 2 diabetes, and neurological diseases associated with gut dysbiosis. The International Scientific Association for Probiotics and Prebiotics (ISAPP) has broadened the definition of prebiotics to encompass their health benefits beyond just gut health. New research is investigating alternative prebiotic sources, such as agro-industrial by-products and plant oligosaccharides, as more affordable options. The combination of prebiotics and probiotics further bolsters gut health and immune responses. Innovations in enzymatic modification and microencapsulation have enhanced the stability and efficacy of prebiotic products. With rising consumer interest in functional foods, the nutraceutical sector is refining prebiotic formulations for health advantages. Upcoming research aims to develop personalized nutrition approaches, target specific microbiota adjustments, and create regulatory frameworks to optimize the therapeutic benefits of prebiotics in preventing diseases and promoting overall health.

Keywords: Short-chain fatty acids (SCFAs), Inulin, Fructo-oligosaccharides (FOS), prebiotics, gut microbiota, metabolic health and disease, functional foods

1. Introduction

Prebiotics are insoluble substances that our bodies cannot digest that help good gut bacteria like *Lactobacillus* and *Bifidobacterium* grow. When these bacteria break down prebiotics, they make short-chain fatty acids (SCFAs). These SCFAs boost our metabolism immune system, and gut health. Common prebiotics include fructo Oligosaccharides (FOS) Galacto-Oligosaccharides (GOS), and Trans-Galacto-Oligosaccharides (TOS).

Research on prebiotics in India sheds light on traditional dietary sources, levels of awareness, and the health advantages they offer. While many people are familiar with probiotics like curd and fermented foods, knowledge and consumption of prebiotics are still quite limited. Studies indicate that ancient Indian diets naturally included prebiotics from fibre-rich foods such as millets and legumes, which contributed to gut health and helped protect against enteric pathogens. Scientific investigations in India have examined prebiotic sources like oligosaccharides, highlighting their positive effects on gut microbiota balance, immune function, and lipid metabolism regulation. Additionally, Prebiotics have shown a scope in the treatment of inflammatory disorders, diabetes, and obesity, highlighting their significance in preventive healthcare and functional nutrition. Although there is still a lack of public awareness, which has led to the need of educational programs to create awareness. The growing interest in prebiotic-based functional foods offers a chance for market growth and additional clinical research. With increasing scientific support and government initiatives, prebiotics could become essential for gut health and disease prevention, positioning them as a vital part of India’s changing nutritional landscape.

Beyond prebiotics, microbiome-modulating interventions such as Synbiotics, postbiotics, microbial consortia, and live biotherapeutic products are gaining attention. Advances in personalized nutrition and precision medicine aim to tailor probiotic and prebiotic use to individual microbiome profiles.

2. Types of Prebiotics

Prebiotics are classified into different types, with carbohydrates (oligosaccharides) being the most prominent. However, non-carbohydrate prebiotics also exist. Below is a summary of the main types of prebiotics along with examples and their effects on gut microbiota.

2.1 Fructans

Fructans include inulin and fructooligosaccharides (FOS), composed of fructose chains linked by β (2,1) bonds. Inulin has a higher degree of polymerization (DP ~60), while FOS has a DP of less than 10. Fructans selectively promote the growth of beneficial lactic acid bacteria (LAB), particularly *Bifidobacteria* and *Lactobacilli*. However, the chain length of fructans influences their fermentability by different gut bacteria.

2.2 Galactooligosaccharides (GOS)

GOS are derived from lactose and exist in different forms, including trans-galactooligosaccharides (TOS). These prebiotics enhance the growth of Bifidobacteria, contributing to a healthier gut microbiota. GOS also stimulate Bacteroides and Firmicutes, although to a lesser extent (Whelan, 2013). Lactulose, a synthetic disaccharide of galactose and fructose, also functions as a prebiotic by fermenting into short-chain fatty acids (SCFAs) and lowering fecal pH.

2.3 Starch-and Glucose-Derived Oligosaccharides

Resistant starch (RS) resists digestion in the upper gut and promotes the production of butyrate, a beneficial SCFA. It fosters the growth of gut bacteria such as *Ruminococcus bromii*, *Eubacterium rectale*, and *Bacteroides thetaiotaomicron*. Another glucose-derived oligosaccharide is polydextrose, a branched glucan with glycosidic linkages that stimulates Bifidobacteria growth.

2.4 Pectin Oligosaccharides (POS): Derived from pectin, POS are composed of homogalacturonan and rhamnogalacturonan I. Their structures vary depending on their source, with sugar side chains linked to ferulic acid, xylose, arabinose, and galactose. POS have shown potential prebiotic effects, but their exact impact on gut microbiota requires further research.

2.5 Xylooligosaccharides (XOS)

XOS are derived from xylan, a hemicellulose found in plant cell walls. They contain β(1,4)-linked xylose units and have been shown to selectively stimulate *Bifidobacteria* and *Lactobacilli*.

2.6 Arabinooligosaccharides (AOS)

AOS are obtained from arabinans and arabinoxylans, commonly found in cereal grains. They support the growth of SCFA-producing bacteria, contributing to improved gut health

2.7 Isomaltooligosaccharides (IMO)

IMOs are glucose-based oligosaccharides linked by α(1,6) bonds. They are partially digestible and promote the growth of *Lactobacilli* and *Bifidobacteria* while reducing harmful bacteria in the gut.

2.8 Beta-Glucans

Beta-glucans are soluble fibers found in oats, barley, and mushrooms. They enhance immune function and act as prebiotics by stimulating Bifidobacteria and SCFA production.

2.9 Human Milk Oligosaccharides (HMOs)

HMOs are a unique group of oligosaccharides found in human breast milk. They selectively promote the growth of *Bifidobacteria*, particularly *B. infantis*, and protect against pathogens.

Table 1: Types of Prebiotics, Natural Sources, and Food Sources

Type of Prebiotic	Natural Sources	Food Sources
Fructooligosaccharides (FOS)	Fruits, vegetables, grains	Bananas, onions, garlic, leeks, asparagus, wheat, barley
Galactooligosaccharides (GOS)	Dairy products, legumes	Cow's milk, yogurt, lentils, chickpeas, soybeans
Inulin	Root vegetables, grains	Chicory root, Jerusalem artichoke, onions, garlic, leeks, bananas
Resistant Starch (RS)	Whole grains, legumes, starchy vegetables	Green bananas, potatoes (cooled after cooking), rice, lentils, beans
Xylooligosaccharides (XOS)	Cereal grains, fruits, vegetables	Wheat bran, corn husks, bamboo shoots, mushrooms
Pectin Oligosaccharides (POS)	Fruits, citrus peels, apples	Apples, citrus fruits (oranges, lemons), pears
Isomaltooligosaccharides (IMO)	Fermented foods, starch hydrolysates	Miso, soy sauce, honey, sake, beer, corn syrup
Beta-Glucans	Cereal grains, fungi	Oats, barley, mushrooms, yeast
Human Milk Oligosaccharides (HMOs)	Human breast milk	Found only in human milk, but synthetic versions are used in infant formula

3. Role of Prebiotics on several diseases

3.1 Prebiotics and Gastrointestinal Disorders

3.1.1 Irritable bowel syndrome (IBS) and Crohn's Disease

IBS is a chronic gastrointestinal disorder characterized by abdominal pain and altered bowel habits without an organic cause, while Crohn's disease is an inflammatory bowel disease affecting any part of the gastrointestinal tract. Studies have shown that both conditions are associated with a reduced population of *Bifidobacteria* and *Faecalibacterium prausnitzii*, as well as an altered Bacteroides-to-Firmicutes ratio (Gibson *et al*., 2017) [22].

The effects of prebiotics on IBS and Crohn's disease have mainly been evaluated through randomized controlled trials (RCTs) and dietary intervention studies. These studies administered defined doses of fructo-oligosaccharides (FOS) or galactooligosaccharides (GOS) for periods ranging from 3 to 12 weeks and assessed both microbial and clinical outcomes (Gibson *et al*., 2017; Walter *et al*., 2021) [22, 2].

Gut microbiota alterations were analyzed using 16S rRNA gene sequencing, quantitative PCR (qPCR), and fluorescence in situ hybridization (FISH) to quantify changes in Bifidobacterium, Lactobacillus, and *Faecalibacterium prausnitzii* populations. Clinical improvement was measured using standardized indices such as the IBS Symptom Severity Score (IBS-SSS) and Crohn's Disease Activity Index (CDAI), alongside inflammatory markers including C-reactive protein

(CRP) and fecal calprotectin (Roberfroid *et al*., 2010; Gibson *et al*., 2017) [25, 22].

Clinical trials on prebiotics for IBS have yielded mixed results. More recent trials suggest potential benefits, with improvements observed after 5 g/day of FOS for six weeks or 3.5 g/day of galactooligosaccharides (GOS) for 12 weeks (Walter, Martínez, & Ríos-Covián, 2021) [2].

For Crohn's disease, supplementation with 15 g/day of FOS for three weeks increased *Bifidobacteria* levels and showed symptom improvement.

3.1.2 Colorectal Cancer (CRC)

CRC is the third most common cancer globally, progressing through genetic mutations and adenomatous polyps to invasive malignancy. Prebiotics contribute to CRC prevention by producing fermentation byproducts like butyrate, which induces apoptosis in cancer cells (Gibson *et al*., 2017) [22].

Clinical studies indicate that synbiotic therapy (a combination of *Lactobacillus rhamnosus*, *Bifidobacterium lactis*, and inulin) may reduce CRC risk by slowing cell proliferation, promoting epithelial barrier integrity, and inducing necrosis in malignant cells (Johnson, Voreades, & Sadler, 2024) [6].

The protective role of prebiotics against colorectal cancer has been demonstrated using *in vitro* models, animal carcinogenesis models, and human synbiotic intervention trials. *In vitro studies* evaluated the effect of short-chain fatty acids (SCFAs), particularly butyrate, on cancer cell apoptosis and proliferation. These effects were measured using caspase activity assays, cell cycle analysis, and apoptosis markers (Gibson *et al*., 2017) [22].

Animal studies employed chemically induced colorectal cancer models to assess tumor incidence, epithelial integrity, and aberrant crypt foci formation following prebiotic supplementation. Human trials measured biomarkers such as cell proliferation index (Ki-67), DNA damage, and intestinal barrier function, while SCFA production was quantified using gas chromatography (GC) or high-performance liquid chromatography (HPLC), (Roberfroid *et al*., 2010; Johnson *et al*., 2024) [25, 6].

3.1.3 Necrotizing Enterocolitis (NEC)

NEC is a severe gastrointestinal condition in premature infants, leading to bowel necrosis and high mortality rates. Prebiotics such as FOS and GOS can promote *Bifidobacteria* growth and reduce pathogenic bacteria in preterm infants, potentially preventing NEC. Additionally, short-chain fatty acids (SCFAs) produced by prebiotics enhance gastric emptying and bowel motility, improving feeding tolerance (Gibson *et al*., 2017) [22]. However, a meta-analysis of four randomized controlled trials found that while prebiotics increased *Bifidobacteria* concentrations, they did not significantly reduce NEC risk or its progression, highlighting the need for further research (Swanson *et al*., 2022) [7].

Studies on necrotizing enterocolitis primarily involved randomized controlled trials in preterm infants, comparing prebiotic-supplemented formula with standard feeding practices. Stool microbiota composition was assessed using culture-based enumeration, qPCR, and molecular sequencing techniques to quantify beneficial and pathogenic bacterial populations (Gibson *et al*., 2017) [22].

Clinical outcomes included NEC incidence, feeding tolerance, intestinal permeability, and time to full enteral feeding, while meta-analyses pooled data from multiple trials to evaluate overall disease risk reduction (Swanson *et al*., 2022) [7].

3.2 Prebiotics and Immune Function

Prebiotics can enhance immune function by stimulating beneficial gut microbiota. Studies suggest that they reduce harmful bacteria populations while promoting *Lactobacilli* and *Bifidobacteria* growth (Chen *et al*., 2022) [1]. For instance, mannose can prevent *Salmonella* colonization by binding to its type 1 fimbriae, inhibiting epithelial adhesion (Gibson *et al*., 2017) [22]. Furthermore, prebiotics modulate immune responses by inducing cytokine expression, which plays a key role in immunity regulation (Walter, Martínez, & Ríos-Covián, 2021) [2].

The immunomodulatory effects of prebiotics were examined using controlled dietary intervention studies in both humans and animal models. Immune responses were evaluated by measuring cytokine profiles (IL-6, IL-10, TNF-α, IFN-γ) using enzyme-linked immunosorbent assay (ELISA) and flow cytometry (Yao *et al*., 2022) [11].

Additional assessments included serum immunoglobulin levels (IgA and IgG) and pathogen adhesion assays to evaluate the ability of specific prebiotics, such as mannose, to inhibit bacterial colonization of intestinal epithelial cells (Gibson *et al*., 2017; Walter *et al*., 2021) [22, 2].

3.3 Prebiotics and Weight Management

Several human studies have explored the relationship between gut microbiota composition and obesity, with mixed findings. Some research indicates that obesity is linked to an increased proportion of Firmicutes bacteria and a reduced abundance of Bacteroidetes. However, other studies have not confirmed this association or have suggested that different bacterial groups may play a role.

The relationship between prebiotics, gut microbiota, and body weight has been explored through longitudinal human intervention studies, twin cohort analyses, and diet-induced obesity animal models. Anthropometric measurements included body mass index (BMI), waist circumference, and body composition analysis using DEXA scans.

Gut microbiota composition was analyzed using 16S rRNA sequencing, while metabolic outcomes were assessed through fasting glucose, lipid profiles, and insulin resistance indices (HOMA-IR). Some studies also measured satiety-related hormones such as GLP-1 and PYY to establish mechanisms linking prebiotic intake with appetite regulation (Slavin, 2013; Chen *et al*., 2022) [24, 1].

Additionally, research on monozygotic and dizygotic twin pairs, along with their mothers, revealed that obesity was associated with reduced bacterial diversity and significant shifts in gut microbiota composition, including an increase in Actinobacteria and a decline in Bacteroidetes.

Weight loss interventions have also been linked to changes in gut microbiota. Adolescents who lost weight exhibited a reduction in *Clostridium histolyticum* and *E. rectale-C. coccoides* (both from the Firmicutes phylum), while levels of Bacteroides-Prevotella increased. Similarly, overweight adolescents who lost more than 4 kg had higher counts of *Bacteroides fragilis* and *Lactobacillus*, along with lower counts of the *C. coccoides* group.

The gut microbiota of overweight pregnant women also exhibited significant differences from that of normal-weight pregnant women, with lower *Bifidobacterium* and Bacteroides counts but higher levels of *Staphylococcus*, *Enterobacteriaceae* and *E. coli*. Moreover, excessive weight gain during pregnancy was linked to increased E. coli levels and reduced *Akkermansia muciniphila* counts, which may contribute to metabolic imbalances.

3.5 Prebiotics and Cardiovascular Disease (CVD)
The impacts of prebiotics on lipid metabolism remain vague, with some studies reporting positive outcomes while others report harmful effects. Some prebiotics like L-rhamnose and lactulose have been proven to lower triglyceride (TAG) levels without changing cholesterol amounts (Walter, Martinez, & Rios-Covian, 2021) [2], while others have been shown to increase blood cholesterol (10%) and B-apolipoprotein (19%) levels after lactulose intake (Swanson *et al*., 2022) [7]. Bimuno u GOS (B-GOS) supplementation for 12 weeks was shown to lower cholesterol, TAG, and the total to HDL cholesterol ratio in overweight patients with metabolic syndrome risk factors (Chen *et al*., 2022) [1], but in elderly patients, no significant effects were seen (Johnson, Voreades, & Sadler, 2024) [6]. Meta-analysis shows that beta-glucan lowers LDL and total cholesterol (Dini *et al*. 2023) [3], while Fructooligosaccharides (FOS) lower Triacyl glycerides levels by 7.5% (Swanson *et al*., 2022) [7].

Lipid metabolism can also be affected by prebiotics through Short-Chain Fatty Acids (SCFAs). Acetate, a fermentation by-product, may enhance lipogenesis for it can be converted to acetyl CoA, a precursor of fatty acid, which may result to higher cholesterol and Triacyl glycerides levels (Gibson *et al*., 2017) [22]. Infusion of rectal acetate has been associated with increased blood cholesterol and triglycerides (Johnson, Voreades, & Sadler, 2024) [6].

Cardiovascular effects of prebiotics were investigated using placebo-controlled dietary supplementation trials and meta-analyses. Serum lipid parameters including total cholesterol, LDL, HDL, and triglycerides were measured using standard enzymatic assays (Dini *et al*., 2023; Swanson *et al*., 2022) [3, 7]. Fecal SCFA concentrations were quantified using chromatographic techniques, and correlations were drawn between acetate production and lipid metabolism. Meta-analytical approaches were employed to evaluate dose-dependent lipid-lowering effects of beta-glucans and fructooligosaccharides (Gibson *et al*., 2017; Johnson *et al*., 2024) [22, 6].

3.6 Prebiotics and Bone Health
Clinical trials have explored the effects of prebiotic dietary fibers on mineral absorption, particularly calcium, with mixed results. Some studies indicate that lactulose, transgalactooligosaccharides (TOS), and inulin-oligofructose combinations (5-20 g/day) significantly enhance calcium absorption, whereas no such effect has been observed for galactooligosaccharides (GOS) or fructooligosaccharides (FOS), (Gibson *et al*., 2017) [22].

The influence of prebiotics on bone health has been assessed using calcium absorption studies and bone mineral density (BMD) measurements. Calcium absorption was quantified using stable isotope labeling techniques, while BMD was evaluated using dual-energy X-ray absorptiometry (DEXA) (Roberfroid *et al*., 2010; Gibson *et al*., 2017) [25, 22].

Additional parameters included fecal pH, SCFA concentrations, and mineral balance studies to correlate enhanced fermentation with improved calcium solubility and uptake (Slavin, 2013; Carlson *et al*., 2018) [24, 27].

Table 2: Prebiotics and Their Role in Health Condition

Health Condition	Types of Prebiotics	Role of Prebiotics
Irritable Bowel Syndrome (IBS)	FOS (5 g/day), GOS (3.5 g/day)	Increase beneficial gut bacteria like Bifidobacteria; potential improvement in symptoms.
Crohn's Disease	FOS (15 g/day)	Increase Bifidobacteria; symptom improvement.
Colorectal Cancer (CRC)	Inulin (synbiotic), Lactobacillus rhamnosus, Bifidobacterium lactis	Produce butyrate to induce apoptosis in cancer cells; slow cell proliferation; strengthen epithelial barrier.
Necrotizing Enterocolitis (NEC)	FOS, GOS	Promote Bifidobacteria growth; reduce pathogenic bacteria; enhance gastric emptying and motility, though evidence on reducing NEC risk remains inconclusive.
Immune Function	Mannose	Prevent harmful bacteria colonization; enhance beneficial bacteria like Lactobacilli and Bifidobacteria; modulate immune response by inducing cytokine expression.
Weight Management	Not specified	Modulate gut microbiota composition linked to obesity and weight loss (e.g., increase Bacteroidetes and decrease Firmicutes).
Cardiovascular Disease (CVD)	L-rhamnose, lactulose, B-GOS	Lower triglycerides and cholesterol; influence lipid metabolism via short-chain fatty acids.
Bone Health	Lactulose, TOS, inulin-oligofructose combinations	Enhance calcium absorption, though effects vary between specific prebiotics like GOS or FOS.

4. Future Prospects of Prebiotic Research
The field of prebiotic research is evolving rapidly, with new findings suggesting their expanding applications beyond traditional gut health benefits. Recent studies highlight the potential of prebiotics in metabolic health, immune modulation, and even cosmeceuticals. Here are some key future directions in prebiotic research.

4.1 Expansion into Cosmeceuticals
Beyond gut health, prebiotics are now being considered in skincare and cosmetic applications. Bockmühl *et al*. (2007) reported that prebiotic-based skincare formulations effectively reduced acne-causing bacteria, suggesting a potential role in dermatology.

4.2 Natural Alternatives to Antibiotics in Animal Feed
To help animals grow healthy, researchers are looking for natural alternatives due to concerns about antibiotic resistance. Certain prebiotics like xylooligosaccharide (XOS) and mannan oligosaccharides (MOS), are being tested as a safer option in fish farming and livestock. These prebiotics promote the growth of good bacteria in the gut of the animals. They also help in boosting the immune system of the fish, poultry and cattle.

4.3 Novel Sources of Prebiotics
New plant-based and marine-derived prebiotics are being investigated. Recent findings suggest that algal polysaccharides, seaweed-derived oligosaccharides, and fruit-derived prebiotics (such as those from dragon fruit and blueberry) can effectively stimulate beneficial gut bacteria.

4.4 Prebiotic-Infused Functional Foods
The food industry is incorporating prebiotics into various functional foods and beverages. For example:

Bakery products fortified with resistant starch and inulin improve satiety and blood sugar control (Health.com, 2023).

Fermented dairy products with galactooligosaccharides (GOS) and fructooligosaccharides (FOS) enhance probiotic activity (González *et al*., 2019) [15]. Plant-based beverages enriched with prebiotics provide additional health benefits (Charalampopoulos & Rastall, 2012) [16].

4.5 Genetic engineering for enhanced prebiotic production
The potential use of genetic engineering to improve prebiotic biosynthesis by modifying plants and bacteria to produce bioactive prebiotic compounds which have better bioactivity is promising. Probiotic strains that can produce certain prebiotic metabolites can be used for specific gut health issues. For instance, there is exopolysaccharide producing *Bifidobacterium* and oligosaccharide-producing *Lactobacillus* strains which are supported to augment the proliferation of intestinal probiotics. Likewise, with the help of gene editing technologies like CRISPR/Cas9, the production of fructooligosaccharides and galactooligosaccharides is being improved by plant biotechnologists. Such breakthroughs could develop better targeted prebiotic interventions for gut health and metabolic conditions.

5. Indian Prebiotic Products

Table 3: Common Indian Ayurvedic and Natural Digestive Aids.

Name of Product	Ingredients	Health Benefits
Dabur Pudin Hara	Pudina Satva (Mint Extract)	Provides quick relief from indigestion, gas, and acidity.
Zandu Pancharishta	Ayurvedic herbs and spices	Improves digestion, appetite, and provides relief from digestive disorders.
Himalaya Gasex	Ginger, Triphala, and other herbs	Relieves gaseous distension, indigestion, and abdominal discomfort.
Organic India Psyllium Husk	Psyllium husk (Isabgol)	Promotes healthy elimination, supports digestive health, and aids in cholesterol maintenance.
Baidyanath Isabgol	Psyllium husk	Acts as a natural fiber supplement, aids digestion, and provides relief from constipation.

6. Conclusion
In summary, prebiotics selectively feed friendly gut bacteria, which promotes gut health, metabolic processes, and protection against diseases. New sources of prebiotics, and new technologies like microencapsulation and enzymatic alterations, are improving their stability, effectiveness, and availability. Moreover, the heightened focus on synbiotics underscores the potential for integrated advantages for the modulation of gut microbiota. Further development in and use of formulated prebiotics will greatly enhance health and wellness in response to the rising popularity of functional foods.

Despite their numerous benefits, further research is necessary to explore the long-term effects of prebiotics, their safety, and personalized applications in nutrition and medicine. With advancements in micro biome science, genetic engineering, and functional food technology, prebiotics are poised to become a key component in preventive healthcare and disease management. Future studies should focus on optimizing prebiotic formulations for targeted health outcomes, ensuring regulatory compliance, and expanding their applications beyond gut health into cosmeceuticals and alternative therapeutic strategies.

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