

Role of Plant-Derived Prebiotic in Modulation of Human Gut Microflora: A Review

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ABSTRACT

At the time of the coevolution of humans and microorganisms, the human digestive tract was colonized by thousands of species of bacteria. Mostly, intestine-borne microbes amount to the overall number of cells in the body tissue. The latest metagenomics study of the human intestinal microbiota confirmed the existence of some 3.3 million genes relative to only 23,000 genes found in tissue cells in the human body. There is increasing evidence for multiple beneficial functions of the gut microbiota in human health and illness. The best-described plant prebiotics is fructans and inulin. The best-known prebiotic carbohydrates comprise many plants, roots and tubers, and fruit crops, whereas prebiotic-richer grain crops contain maize, chickpea, lentil, lupin, and wheat. Some prebiotic enriched crop germplasm were documented in maize, chickpea, lentil, wheat, and yacon. Intestinal microbiota perturbation may contribute to persistent diseases such as autoimmune diseases, bowel cancers, stomach ulcers, colon disorders, and malnutrition. This can be impossible to recover the intestinal microbiome, but the usage of probiotics has contributed to a positive effect in a significant number of very well-designed (clinical) trials. Microbiomics has prompted a significant growth of interest in probiotics and prebiotics as potential mediators for the administration and regulation of gut microbiota in medicine, industry, and the general public. Developing prebiotic-rich healthy plants can mitigate the prevalent malnutrition challenge and facilitate worldwide global health. Bioinformatics and genomics tools may help to create mechanistic associations between gut microflora, a person's health status, and the outcomes of plant prebiotic drug treatments.

Keywords: Microbiota, Intestinal microbes, Microbiomics, Plant-derived carbohydrates, Probiotics

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Abbreviations

GI	Gastrointestinal tract	XOS	Xylo- oligosaccharide
SCAF	Short chain fatty acid	NDO	Non digestible oligosaccharide
IL	Interleukins	DFC	Dietary fibre concentrates
FOS	Fructo-oligosaccharide	GPH	Glactoside Pentose hexuronide
GOS	Gluco-oligosaccharide		

1. Introduction

It is even nearer to human cells, according to an estimation of ~ 10¹⁴ microorganisms that inhabit the human body. Such bacteria are represented mainly by the human gastrointestinal (GI) tract, mutually

recognized as gut microbiota. Previously, the gut or intestinal microbiota was identified as commensals, but at present, they are regarded as symbionts beneficial to people. Various obligate anaerobes such as Bacteroides

and Firmicutes are abundant phyla, representing 80-90% of overall gut microflora. Few other known phyla comprise, *Tenericutes*, *Proteobacteria*, and *Actinobacteria* (1). A declaration "all disease begins in the gut" was quoted by Hippocrates around 2000 years ago, and researchers are now beginning to understand his theory. Dysbiosis, described as disturbance of microbiota composition, is strongly linked to intestinal disease and obesity, insulin resistance, hypertension, and type 2 diabetes. Imbalance in the gut microbial culture influences the host's physiological status by dissimilar pathways, for instance, metabolism and immunomodulation. Unbalance in the intestinal microbial population influences the host's physiological conditions by different pathways, such as metabolism and immunomodulation. The diversity of intestinal microbiome species is influenced by both host (gender and hereditary) and several environmental factors (Standard of living, cleanliness and food) (2). Effective efficiency of stomach microflora plays a significant role in homeostasis by controlling metabolic pathways and basic modulators of GI physiological condition such as metabolizing nutrients and vitamin output. By means of broad-spectrum metabolites and their distinct action, healthy microbiota plays an essential role in humans. Current examinations have shown that they play a substantial role in the host's physiology, regulating immuno-modulation. SCFAs - Short-chain fatty acids such as butyrate and propionate cause an inflammatory regulatory differentiation of naive T cells. In addition, T cells contain interleukins (IL) (3).

The human intestinal microbiome creates a diverse GI tract environment and offers numerous human health benefits. This micro-ecosystem results from a synergetic relationship between the host and the intestinal microbiota, which is responsible for protecting contrast to opportunistic infections, metabolizing complex compounds supplying vital nutrients such as vitamins, low molecular weight SCFA molecules (4). Along with all the various intestinal microbes, those concerned are called probiotics to show possible health benefits to their host by regulating the microbial bowel constitution. Therefore, the live microorganisms positively affect the host when incorporated into a tolerable dosage. More specific species of the genera *Lactobacillus* and *Bifidobacterium* were found to have beneficial bacterial probiotic strains (5). Many specific inhabitant bacterial strains such as *Bifidobacteria*, *Lactobacillus rhamnosus*, *Lactobacillus reuteri*, some strains of *Enterococcus*, for instance, *Enterococcus faecium SF68*, *Escherichia coli strain Nissle 1917*, few strains of *Bacillus* such as *B. licheniformis* have various properties of probiotic and have a marked positive impact on the physiology of the host.

1.2. The Theory of Prebiotics, Probiotics, and Synbiotic Prebiotics

Gibson and Roberfod first introduced in 1995 the groundbreaking concept of prebiotics as non-digestible constituents of foods that selectively cause growth or development in gastrointestinal microbiota and recover the overall health condition of the organism. In 2015 FAO and UN established a number of times prebiotic definitions. The necessity of selective fermentation of dietary products provided another definition (6). According to these researchers, prebiotics are non-digestible compounds that have beneficial physiological effects on the host by metabolic activity via microorganisms living in the colon modulating the gut microbiota's structure or function (7). In fact, inducing *Bifidobacterium* and *Lactobacillus* to inhibit the development of infectious organisms such as *E.coli* was among the first prebiotics tested in humans and often used commercially. *Escherichia coli* and members of the genus *Clostridia* Phytomedicine, such genera are often known as probiotics, but probiotics and prebiotics are goods. These prebiotic products can also be used as a substitute to probiotics. Relevant simulation of *Bifidobacterium* and *Lactobacillus* by inducing the development of various endogenous gut inhabitants was found to have diverse functions. Outside of fermentable probiotics providing a nutraceutical impact, it needs to provide additional values outside those of everyday nutrition. Mostly, prebiotics are fermentable fibers where the species selectively ferment as beneficial for the host. Types of most widely used reported prebiotics are fructooligosaccharide (FOS) and glucooligosaccharide (GOS). Prebiotics have therefore identified diet constituents that disturb the behavior of precise microbes, and the end product generated after fermentation has beneficial effects on their host. Prebiotics tolerate digestion or adsorption by their host by different current gut microbiota strains until fermentation (8).

1.2.1 Prebiotics: Although prebiotics, including dominant strains and resident microbiota, are non-viable products, probiotics are living microorganisms. The phrase probiotic derives for life from the Greek word. The most commonly accepted explanation for Fuller's formulation of the probiotic definition is that 'live microbial feed additives which have a beneficial effect on the host animal by improving the balance of colonic microflora.' Later, WHO and FAO suggested alternative ideas similar to probiotics as 'living microorganisms.' The definition is updated regarding food by focusing on the idea that microorganisms have a positive effect when included in a sufficient amount as part of a meal. Maintaining good well-being, improving the immune system, lowering serum cholesterol, and counteracting multiple cancer triggers are the most widely recognized beneficial probiotic-related findings (9). Probiotics are well established as clean, environment-friendly microbes, which have several benefits, showing different

mechanisms such as intestinal pH reduction, mucosal barrier function SCFA growth, nutritional and dietary competition, and immuno-modulation. In contrast, probiotics are also used as a medicinal treatment for urological and oral illness and to alleviate stress and anxiety by heart-brain regulation (9). Commonly recorded probiotic roles include:

1. Cancer Plant-derived prebiotics and protection of their safety benefits.
2. Removal of antibiotic or rotavirus-associated diarrhea.
3. Avoidance of atopic and hypersensitive responses in newborn infants.

4. Infectious disease prevention in the gastrointestinal tract (10). Gibson has given another synbiotic concept besides the prebiotics; synbiotic goods contain the properties of both prebiotics and probiotics. The word synbiotic originates from the Greek word "synergism," which means that the selectivity of prebiotic components promotes the growth or functioning of probiotic microorganisms existing in GI tract colon in the combination drug. Combining prebiotics and probiotics in a sole drug has given it a noticeable action relative to its activity alone (10). The synbiotic formulations provide the host with numerous advantages such as:

1. The prevention of dysbiosis and thereby aid in sustaining gut microbiota.
2. The prevention of pathogens translocation decreases the occurrence of nosocomial diseases.
3. Transmission and regulation of various immune responses.
4. The reduction of hepatic damages (11).

1.3. What is Plant derived Prebiotics?

The completely non-digestible oligosaccharides (NDOs) are known to be prebiotics formed since these non-digestible oligosaccharides possess anomeric C-atom, and the glycosidic bond inhibits mammalian hydrolytic enzymes in such a structure. NDOs are low-calorie food additives and also improve the possible fermentation substrates for mineral absorption. Prebiotics were therefore defined as non-digestible oligosaccharides and polysaccharides that promote the development of important bacteria like *Bifidobacteria* and *Lactobacilli* in the host gut colon and bring to bear an antagonistic relationship to *Salmonella* spp., *E. coli*, and *Clostridial* species, reducing the spread of both. Inulin and its derivatives, including Fructo-oligosaccharides and Gluco-oligosaccharides, are the most popular prebiotics. Prebiotic ingestion increases human immune response, metabolism in the colon, and microbiome equilibrium and prevents risks correlated with digestion. Besides that, prebiotics often speeds up the absorption of

different micronutrients such as magnesium, calcium, and zinc and substantially minimize or avoid the risks of bowel-associated tumors, cholesterol, and extremely high triacylglycerol rates (12).

1.4. Sources of prebiotics

Many products and other molecules are known as prebiotics, which are dependent on fermentability. Some of them are fermentable and available in numerous food products comprising specific forms of fibers. While fermentable fibers have a crucial beneficial impact on their host, they are not prebiotics of this nature. Prebiotics are unique components targeted at activating colon-specific microbes, providing a large variety of end products that are helpful to the host. Prebiotics can also be fermentable nutritional fibers, but not all fermentable fibers are prebiotics (13). Two terminologies like nutritional fibers are broken down by most living intestinal microorganisms, while prebiotics are fermented by the clearly specified community, or strain of microorganisms are substantially different. Plant-based prebiotic origins contain inulin, FOS, and GOS. Many polysaccharides, composed of plant cell wall components such as pectin and xylan, are present in the daily diet (14). Furthermore, chicory root-related inulin (FOS), isomalto-oligosaccharides (IMOs), xylo-oligosaccharides (XOSs), soybean oligosaccharides (SBOs), sorbitol, lactulose, and raffinose have broad prebiotic uses and several health benefits to humans (15). Total grain resilient starch is often known as possible prebiotic starches because they cannot be assimilated by host gastrointestinal enzymes and are not ingested by the intestine, thereby promoting the development of valuable gut microflora. Fermentability of SCFAs of dietary fibers such as β -glucans and fenugreek gum often exert a variety of positive health consequences (16).

1.4.1 Prebiotics from Other Food Sources

Analysis of the situation undertaken by the European Commission or the European Food Safety Authority specifies that every product or product ingredient that does not have any prior record of healthy usage is called "New Products." A variety of prebiotics are recognized to be identified as new foods. The Yacon (*Smallanthus sonchifolius*) is used as a common food in South America. Yacon's defense concerns are in question in the European Union. It offers myriads of health benefits and has a strong background of healthy usage and prebiotic effects. This is non-toxic metabolites and antinutrients safe from prebiotics which are derived from different plants, and its safety benefits (17). Prebiotics in carbohydrate shape are found in various food crops such as tomatoes, roots like tuber crops such as garlic, onion, okra, artichoke, and shallot, including gourd family of tomatoes such as protection of bottle or wax

ground. There is a big source of inulin among fruits like chicory and Yacon. On top of this, Dahliya, which is a tuber flower, has fructose-based prebiotic results. Several of the mushroom's varieties, such as *Agaricus bisporus* have been documented to have possible prebiotic advantages. *Pleurotus* species (pleuran) fruiting body extract containing β -glucan has been used in various food supplements, which imparts immuno-suppression and probiotic gut growth for human health. *Pleurotus ostreatus*, and *Pleurotus eryngii* are useful organisms. The development and function of intestinal lactic acid bacteria (LAB) were induced by a steroid sapogenin compound named diosgenin derived from yam plants (18).

Later, more experiments were performed by this community in the murine model to show the influence of diosgenin has immunomodulatory effects through ingestion of intestinal control T cells (13). Farm legumes are a significant source of dietary fibers, such as chickpea farm consisting of α -Gluco-oligosaccharides, which is used as a prebiotic in functional foods and lupin kernel-related fibers inhibit gut microbial diversity, primarily enhancing *Bifidobacterium* species and lowering the number of *clostridial* communities such as *Clostridial spiroforme*, *Clostridial ramosus*, and preventing colon infection. Spices are very well recognized for their healing qualities and have many beneficial properties such as anti-mutagenic, anti-inflammatory, and antimicrobial. Spices of diverse sources, such as plant leaves, nuts, bark, and berries, have different phytoconstituents and often show prebiotic properties, thereby affecting the comparable proliferation of *Lactobacilli* and *Bifidobacteria* in the intestinal microbiota and reducing the amount of diseases/infections producing organisms including both Gram-positive and Gram-negative (19). Cinnamaldehyde, a bioactive extract of cinnamon, exhibits a more effective antibacterial function against specific enteric bacteria with low MIC compared to their basic crude extract without any mouse model modulation on gut probiotics. Studies were performed indicating that enrichment with Rosemary extract inhibits the proliferation of the species of *Pediococcus* and *Leuconostoc* and affects the development of the genus Bacteroids (20).

Date seeds are widely used in animal feedings, such as goats, sheep, and cows, and even in the fish industries and poultry farms. They are thought to provide possible health advantages for humans as prebiotics because of the availability of a significant amount of dietary fiber. In a research performed on the influence on proliferation of the isolated LAB *Lactobacillus paracasei* of two items from date palm (*Phoenix dactylifera* L.), the fine powder of date seed and the aqueous solution extract of date seed powder was examined along with the ssp. *paracasei* as

probiotics (21). The dietary fiber concentrate (DFC) i.e. *P. dactylifera* L. Seed oil, has been established as a carbon source for anaerobic fermentation. The DFC offered the ability to be used as a novel prebiotic supply by growing the inhabitants of *L. paracasei* ssp. *paracaseis* F19 as probiotics along with reducing the pH levels. Overall, the optimal features of prebiotics or screening requirements are:

1. They should always be non-digested by host gut bacteria and enter the bowel in an unaffected type.
2. They would never be ingested in the gastrointestinal tract.
3. They should be a lesser amount or very little fermented by residual bacteria in the oral cavity.
4. They should be extensively fermented or ingested by different classes of helpful gut bacteria.
5. Not metabolized by pathogenic bacteria in the intestine at all or may be badly metabolized (22).

1.5. Mode of Action of Prebiotics

After administration, the primary aim of prebiotics is to induce development and operation, or an enhanced quantity of advantageous bacteria living in the Gastrointestinal tract. The stimulated gut microbiome, in effect, provides the host with the potential health benefits by multiple pathways such as contradistinction (by generating antimicrobial constituents) and nutrient or epithelial surface interaction. Several of the beneficial results of the probiotics prebiotic-directed roles are described as follows:

- The development of inhibitory compounds by *Bifidobacterium* and *Lactobacilli* that act as a deterrent to GI pathogens and decrease the pH of the intestine as a result of the fermentation of prebiotic substrates.
- *Bifidobacteria* maintain strong tolerance to developed SCFAs and also to pH following acidification of gut lumen (23).
- Prebiotic delivery often improves the absorption of complex nutrients such as Magnesium and Calcium.
- *Lactobacilli* and *Bifidobacteria* develop many anti-mutagenic properties and enable the host immune system to destroy the cancerous enzymes generated by gastrointestinal microbiota and thus preserve intestinal and bacterial equilibrium porosity.
- Prebiotics used as an energy and carbon source and manipulate the behavior and morphology of Gastrointestinal microflora, for instance, studies performed with Gluco-oligosaccharides prebiotics by using genotyping study, indicate that Gluco-

oligosaccharide in *Lactobacilli acidophilus* NCFM induces gut lac operon which results in the development of two cytoplasmic β -galactosidases i.e., Lac A and Lac LM and galactoside pentose-hexaboride (GPH) permease i.e., Lac S. Such gene clusters also play a substantial role in the acquired mix of intestinally developed advantages such as bile salt-resistance and acquisition of nutrients.

The literature explains a few of the positive effects of prebiotics on the regulation of the immune system as defined in the succeeding:

- Prebiotics have the ability to control the release of lipogenic hepatic enzymes mediated by the development of butyric acid, propionic acid, and SCFAs by helpful bowel microbiota.
- Significantly improved synthesis of SCFAs as a by-product of fermentation results in its histone regulation by acetylation that modifies the chromatin and enables the proteins that bind DNA to remain intact with various expressed genes that enable transcription and activity of cellulase.
- Attenuate the protective mechanism, which protects against biotic agents (bacterial viruses/pathogens) and harmful chemicals such as glycoprotein mucin covering epithelial cells (24).
- Fructo-oligosaccharides and numerous other prebiotics have also been shown to cause the release of both responses i.e., innate and acquired immune, and thus raise leukocytes / β -lymphocytes in peripheral blood and lymphoid gut-associated tissues (GALTs).
- The phagocytosis process activation and decreased secretion of IgA by GALTs in intra-inflammatory macrophages stimulate host immune response and antibacterial development

1.6. The Gut Microbiota and Their Functions

A premature infant has a clean, germ-free bowel that is inhabited by the mother's microbes and from the infant's body or atmosphere. The adult person has 10 times more microorganisms in and on the whole body than the overall human cells. The human microbiota is dynamic and very different. The distribution and quantity vary from the distal colon and rectum to the nose and mouth. The intestinal microbiota's structure and function shift as the infant is weaned on solid foods. The makeup of intestinal microbiota is also largely responsible for dietary adjustments in adulthood. The creation of gene-sequence-based proteomic methods of 16S ribosomal RNA (rRNA) has contributed to significant advances in the description of the entire intestine microbial community. This method was used to explain that 90 percent of the microorganisms, being

the part of two phyla, specifically the *Bacteroidetes* and *Firmicutes* (25).

The gastrointestinal microbiome plays a significant part in health treatment. They are listed below.

1.6.1 Structure and Histological Feature: The microbiota present within maintaining the bowel structure and work. The matrix of intestinal mucus is a result of the production and removal of mucins. The mucin matrix presents a barrier to the taking up of antigens and pro-inflammatory compounds. Research shows that butyrate causes antimicrobial peptides mucin formation and some other influences. This enhances the Colon protective barrier (26). Furthermore, intestinal microbiota plays a part in cell and tissue growth. Butyrate is synthesized by these gastrointestinal microbiotas, controls cell development and differentiation, prevents cell growth alteration, and supports to revert of cells from a neoplastic to a non-neoplastic phenotype. The production of the intestinal villi microvasculature is based on the indigenous microbes.

1.6.2 Metabolic Functions: The intestinal microbiota is identified to contain a significant variety of vitamins such as vitamin B, synthesize proteins and conduct biotransformation of bile. The bile biotransformation via microbial enzymes is essential for glucose and cholesterol metabolism. Specifically, the microbial ecosystem supplies the biochemical mechanisms that are much required for fermenting non-digestible substrates such as fibers and endogenous mucus. The digestion or oxidation of non-digestible substrates contributes to developing these bacteria and forming fatty acids and gases in the short-chain (27). The key fatty acids formed in the short chains are acetate, butyrate, and propionate. Bacterial fermentation happens in the colon and cecum, in which short-chain fatty acid absorption takes place and promotes water and salts absorption. Such short-chain fatty acids provide a defensive impact on the epithelium of the intestines (27). The colonic bacteria consider butyrate to be the primary source of nutrition, and much of it is broken down entirely. Acetate is a key short-chain fatty acid formed in the colon, which serves as a substratum for cholesterol biosynthesis.

1.6.3 Protective Functions: Most other commensal species develop antimicrobial agents that also compete in the intestinal lining and binding locations for nutrition, thereby stopping pathogens from colonizing. It tends to diminish the development of peptidoglycans and lipopolysaccharides; both might cause toxicity in the host body. The immunological production is often controlled by the indigenous microflora character. Sterile specimens have fewer dendritic cells, and information suggests that

microbial systems play a part in B cell development. Butyrate has been shown to suppress NF- κ B in patients with Crohn's disease and thus induce immunosuppressive activity (28). Such principles demonstrate a complex connection between the microbiome and the immune system. The mucosal lining averts risks through toll-like channels, signaling the adaptive immune system. Such identify and bind to different bacteriological macromolecules, such as peptidoglycan, lipopolysaccharides, N-formylated peptides, and flagellin, the induction of toll-like receptors in the intestinal mucosa initiates nuclear factor- κ B channels, protein kinase regulated with mitogen, and caspase-dependent signaling cascades. This allows defensive cytokines, peptides, phagocytes, and chemokines to be produced and released. The effect can be a defensive reaction to intestinal bacteria, an allergic reaction to pathogenic species, or an apoptosis cause. Hence, gastrointestinal tract commensal bacteria perform important roles in immune system growth and homeostasis.

1.7. Modulation and Dysbiosis of the Gut Microbiota

Regular host physiology relies on the signals that the gut microbiota send. The abdominal lumen, composed of IgA, digestive enzymes, and gastric acid, forms the initial layer of protection and is deadly to harmful bacteria that are entering and being swallowed. The indigenous microbes kill intraluminal antigens and prevent the adhesion and colonization of pathogenic microbes. They are therefore essential for regulatory T cells induction. Some alteration in the bacterial environment may trigger a microbiota imbalance or dysregulation (dysbiosis) frequently correlated with different disease conditions varying from the more normal IBD and IBS to the additional uncommon activation of HIV infection and atopy generation (29).

That is why it is necessary to restore microbial homeostasis, which could have been disrupted by one or more factors. One approach to modifying the gut microbiota effectively is through utilizing prebiotics, probiotics, and synbiotics (a mixture of both probiotics and prebiotics that are provided mutually). Such compounds may benefit microbial encounters with the immune system and epithelium in the stomach. Good bacteria that have an established relationship with health contain genera, for instance, *Lactobacilli* or *Bifidobacteria*, that generate lactic acid. Both of these bacteria may be incorporated within the intestine and/or stimulated to replicate either by absorption of suitable probiotic strains by the organism or by providing suitable substrates for the growth of prebiotics, often known as soluble fibers. Probiotics and prebiotics are becoming increasingly popular, as demonstrated by steadily growing funding for science and an ever-expanding product option. Probiotics and

prebiotics are commercially available in several other forms, including orally or non-orally delivered foods, nutritional supplements, and clinical therapies.

1.7.1 Extra Intestinal Effects of Prebiotics

The health-benefiting components of prebiotics are not only limited to the intestine but also have safety benefits outside the gastrointestinal system. Such advantages to the extra-essential area may be direct by modifications in the indigenous microbiome, for instance, of the vaginal or oral tract, or indirectly affected by improvements in the intestinal microbiota in metabolism or structure. Potential prebiotics such as Gluco-oligosaccharides and Fructo-oligosaccharides can enhance the different helpful intestinal microbial communities, which play a significant role in controlling the occurrence of several respiratory diseases, optical dermatitis, and enhanced ingestion of minerals such as Magnesium and Calcium (30). Through modifying both adaptive and innate immune systems by including anti-inflammatory metabolites, prebiotics result in protective results beyond the intestinal tract. The same as prebiotics, galactose promotes an increased amount of *Bifidobacteria*, which subsequently leads to the development of anti-inflammatory cytokines and induces phagocytosis (31). It is also noted that nutrient accumulation outside of the digestive tract is facilitated by prebiotic fermentation and corresponding advancement in the development of SCFA. This mechanism is assisted in decreasing the luminal pH, for instance, using substrates for *Bifidobacterium longum* and developing acetate as a by-product of feeding, thereby defending against enteropathogenic illnesses. In addition, another bacterium *Faecalibacterium prausnitzii* (strong SCFA consumer in the lumen of the gut) absorbs this acetate (32) that has a critical need for such a fatty acid under in-vitro environments. Furthermore, health-encouraging properties are correlated both with helpful sources of lactic acids such as *Lactobacillus* and *Bifidobacterium* and with certain living products of SCFA.

2. Conclusion and Future Directions

Prebiotic use is certainly correlated with plenty of beneficial effects by their development enhancement and intestinal microflora operation. Within this study, we examined the generic concept of probiotic activation directed by prebiotics and prebiotics and its resulting advantageous results, incorporating both prebiotics and probiotics, i.e., synbiotics. Plants have a sufficient supply of nutritional prebiotics, including prebiotics that are not digestible. A study on the positive impact of prebiotics on well-being together with probiotics has rattled the sky-high over the past decades. The plant-based balanced nutritional ingredients were traditionally beyond researchers' understanding, but now it is known that they can use

their prebiotic influence to avoid or treat different illnesses or diseases such as tonsillitis, obesity, CVD, and cirrhosis (promoting a healthy gastrointestinal microbiome). Regarding structure and function, prebiotics is not exactly similar and therefore cause various forms of microorganisms in specific people, which can contribute to an aggravating disease situation. Furthermore, significantly better prebiotic and wildly different fiber interpretation and human involvement findings are needed to classify their health-related benefits. The diet constituents also affect intestinal microbial metabolome, altering the microbial composition, thus affecting individual disease status. There should be microbiota classification of the individual for both the diagnosis, inhibition, and treatment or medication of several diseases in the future. Further research may clarify the

process of action of mixing prebiotics and probiotics, which will have a valuable influence on the health of humans.

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Conflict of Interest

The authors declare no conflict of interest.

Reference

- Xu X, Jia X, Mo L, Liu C, Zheng L, Yuan Q, et al. Intestinal microbiota: a potential target for the treatment of postmenopausal osteoporosis. *Bone Res.* 2017;5(1):1-18. [DOI:10.1038/boneres.2017.46] [PMID] [PMCID]
- Conlon MA, Bird AR. The impact of diet and lifestyle on gut microbiota and human health. *Nutrients.* 2014;7(1):17-44. [DOI:10.3390/nu7010017] [PMID] [PMCID]
- Sridharan GV, Choi K, Klemashevich C, Wu C, Prabakaran D, Pan LB, et al. Prediction and quantification of bioactive microbiota metabolites in the mouse gut. *Nat. Commun.* 2014;5(1):1-13. [DOI:10.1038/ncomms6492] [PMID]
- Mills RH, Vázquez-Baeza Y, Zhu Q, Jiang L, Gaffney J, Humphrey G, et al. Evaluating metagenomic prediction of the metaproteome in a 4.5-year study of a patient with Crohn's disease. *Msystems.* 2019;4(1):e00337-18. [PMCID] [DOI:10.1128/mSystems.00337-18] [PMID]
- Martín R, Miquel S, Ulmer J, Kechaou N, Langella P, Bermúdez-Humarán LG. Role of commensal and probiotic bacteria in human health: a focus on inflammatory bowel disease. *Microb Cell Factories.* 2013;12(1):1-11. [DOI:10.1186/1475-2859-12-71] [PMID] [PMCID]
- Bindels LB, Delzenne NM, Cani PD, Walter J. Towards a more comprehensive concept for prebiotics. *Nat Rev Gastroenterol Hepatol.* 2015;12(5):303-10. [DOI:10.1038/nrgastro.2015.47] [PMID]
- Gibson GR, et al. Expert consensus document: The International Scientific Association for Probiotics and Prebiotics (ISAPP) consensus statement on the definition and scope of prebiotics. *Nat Rev Gastroenterol Hepatol.* 2017;14(8):491-502. [DOI:10.1038/nrgastro.2017.75] [PMID]
- Floch MH, Walker WA, Madsen K, Sanders ME, Macfarlane GT, Flint HJ, et al. Recommendations for probiotic use-2011 update. *J Clin Gastroenterol.* 2011;45:S168-S71. [DOI:10.1097/MCG.0b013e318230928b] [PMID]
- Kechagia M, Basoulis D, Konstantopoulou S, Dimitriadi D, Gyftopoulou K, Skarmoutsou N, et al. Health benefits of probiotics: a review. *Int Sch Res Notices.* 2013;2013. [DOI:10.5402/2013/481651] [PMID] [PMCID]
- Vrese Md, Schrezenmeier. Probiotics, prebiotics, and synbiotics. *Food Biotechnol.* 2008;1-66. [DOI:10.1007/10_2008_097] [PMID]
- Pandey K, Naik S, Vakil B. Probiotics, prebiotics and synbiotics-a review. *J Food Sci Technol.* 2015;52(12):7577-87. [DOI:10.1007/s13197-015-1921-1] [PMID] [PMCID]
- Dwivedi S, Sahrawat K, Puppala N, Ortiz R. Plant prebiotics and human health: Biotechnology to breed prebiotic-rich nutritious food crops. *Electron J Biotechnol.* 2014;17(5):238-45. [DOI:10.1016/j.ejbt.2014.07.004]
- Holscher HD. Dietary fiber and prebiotics and the gastrointestinal microbiota. *Gut microbes.* 2017;8(2):172-84. [PMCID] [DOI:10.1080/19490976.2017.1290756] [PMID]
- Yoo H-D, Kim D, Paek S-H. Plant cell wall polysaccharides as potential resources for the development of novel prebiotics. *Biomol Ther.* 2012;20(4):371. [PMID] [PMCID] [DOI:10.4062/biomolther.2012.20.4.371]

15. Patel S, Goyal A. The current trends and future perspectives of prebiotics research: a review. *3 Biotech*. 2012;2(2):115-25. [\[DOI:10.1007/s13205-012-0044-x\]](https://doi.org/10.1007/s13205-012-0044-x) [\[PMCID\]](#)
16. Lin B, Gong J, Wang Q, Cui S, Yu H, Huang B. In-vitro assessment of the effects of dietary fibers on microbial fermentation and communities from large intestinal digesta of pigs. *Food Hydrocolloids*. 2011;25(2):180-8. [\[DOI:10.1016/j.foodhyd.2010.02.006\]](https://doi.org/10.1016/j.foodhyd.2010.02.006)
17. Campos D, Betalleluz-Pallardel I, Chirinos R, Aguilar-Galvez A, Noratto G, Pedreschi R. Prebiotic effects of yacon (*Smallanthus sonchifolius* Poepp. & Endl), a source of fructooligosaccharides and phenolic compounds with antioxidant activity. *Food Chem*. 2012;135(3):1592-9. [\[DOI:10.1016/j.foodchem.2012.05.088\]](https://doi.org/10.1016/j.foodchem.2012.05.088) [\[PMID\]](#)
18. Huang C-H, Cheng J-Y, Deng M-C, Chou C-H, Jan T-R. Prebiotic effect of diosgenin, an immunoactive steroidal sapogenin of the Chinese yam. *Food Che*. 2012;132(1):428-32. [\[DOI:10.1016/j.foodchem.2011.11.016\]](https://doi.org/10.1016/j.foodchem.2011.11.016) [\[PMID\]](#)
19. Lu QY, Summanen PH, Lee RP, Huang J, Henning SM, Heber D, et al. Prebiotic potential and chemical composition of seven culinary spice extracts. *J Food Sci*. 2017;82(8):1807-13. [\[DOI:10.1111/1750-3841.13792\]](https://doi.org/10.1111/1750-3841.13792) [\[PMID\]](#) [\[PMCID\]](#)
20. Romo-Vaquero M, Selma M-V, Larrosa M, Obiol M, García-Villalba R, González-Barrio R, et al. A rosemary extract rich in carnosic acid selectively modulates caecum microbiota and inhibits β -glucosidase activity, altering fiber and short chain fatty acids fecal excretion in lean and obese female rats. *PloS One*. 2014;9(4):e94687. [\[PMID\]](https://doi.org/10.1371/journal.pone.0094687) [\[DOI:10.1371/journal.pone.0094687\]](https://doi.org/10.1371/journal.pone.0094687) [\[PMCID\]](#)
21. Al-Thubiani AS, Khan MSA. The prebiotic properties of date palm (*Phoenix dactylifera* L.) seeds in stimulating probiotic *Lactobacillus*. *J Pure Appl Microbiol*. 2017;11(4):1675-86. [\[DOI:10.22207/JPAM.11.4.05\]](https://doi.org/10.22207/JPAM.11.4.05)
22. Markowiak P, Śliżewska K. Effects of probiotics, prebiotics, and synbiotics on human health. *Nutrients*. 2017;9(9):1021. [\[DOI:10.3390/nu9091021\]](https://doi.org/10.3390/nu9091021) [\[PMID\]](#) [\[PMCID\]](#)
23. Grajek W, Olejnik A, Sip A. Probiotics, prebiotics and antioxidants as functional foods. *Acta Biochim Pol*. 2005;52(3):665-71. [\[DOI:10.18388/abp.2005_3428\]](https://doi.org/10.18388/abp.2005_3428) [\[PMID\]](#)
24. Kumar M, Kumar A, Nagpal R, Mohania D, Behare P, Verma V, et al. Cancer-preventing attributes of probiotics: an update. *Int J Food Sci Nutr*. 2010;61(5):473-96. [\[DOI:10.3109/09637480903455971\]](https://doi.org/10.3109/09637480903455971) [\[PMID\]](#)
25. Mariat D, Firmesse O, Levenez F, Guimaraes VD, Sokol H, Doré J, et al. The Firmicutes/Bacteroidetes ratio of the human microbiota changes with age. *BMC Microbiol*. 2009;9(1):1-6. [\[DOI:10.1186/1471-2180-9-123\]](https://doi.org/10.1186/1471-2180-9-123) [\[PMID\]](#) [\[PMCID\]](#)
26. Kleessen B, Blaut M. Modulation of gut mucosal biofilms. *Br J Nutr*. 2005;93(S1):S35-S40. [\[DOI:10.1079/BJN20041346\]](https://doi.org/10.1079/BJN20041346) [\[PMID\]](#)
27. Wong JMW, De Souza R, Kendall CWC, Emam A, Jenkins DJA. Colonic health: fermentation and short chain fatty acids. *J Clin Gastroenterol*. 2006;40(3):235-43. [\[DOI:10.1097/00004836-200603000-00015\]](https://doi.org/10.1097/00004836-200603000-00015) [\[PMID\]](#)
28. Maslowski KM, Vieira AT, Ng A, Kranich J, Sierro F, Yu D, et al. regulation of inflammatory responses by gut microbiota and chemoattractant receptor GPR43. *Nature*. 2009;461(7268):1282-6. [\[DOI:10.1038/nature08530\]](https://doi.org/10.1038/nature08530) [\[PMID\]](#) [\[PMCID\]](#)
29. Hemarajata P, Versalovic J. Effects of probiotics on gut microbiota: mechanisms of intestinal immunomodulation and neuromodulation. *Therap Adv Gastroenterol*. 2013;6(1):39-51. [\[DOI:10.1177/1756283X12459294\]](https://doi.org/10.1177/1756283X12459294) [\[PMID\]](#) [\[PMCID\]](#)
30. Scholz-Ahrens KE, Adolphi B, Rochat F, Barclay DV, de Vrese M, Açıllı Y, et al. Effects of probiotics, prebiotics, and synbiotics on mineral metabolism in ovariectomized rats-impact of bacterial mass, intestinal absorptive area and reduction of bone turn-over. *Nfs Journal*. 2016;3:41-50. [\[DOI:10.1016/j.nfs.2016.03.001\]](https://doi.org/10.1016/j.nfs.2016.03.001)
31. Vulevic J, Drakoularakou A, Yaqoob P, Tzortzis G, Gibson GR. Modulation of the fecal microflora profile and immune function by a novel trans-galactooligosaccharide mixture (B-GOS) in healthy elderly volunteers. *Am J Clin Nutr*. 2008;88(5):1438-46. [\[PMID\]](https://doi.org/10.3945/ajcn.2008.26242) [\[DOI: 10.3945/ajcn.2008.26242\]](https://doi.org/10.3945/ajcn.2008.26242)
32. Sokol H, Pigneur B, Watterlot L, Lakhdari O, Bermúdez-Humarán LG, Gratadoux J-J, et al. Faecalibacterium prausnitzii is an anti-inflammatory commensal bacterium identified by gut microbiota analysis of Crohn disease patients. *Proc Natl Acad Sci*. 2008;105(43):16731-6. [\[DOI:10.1073/pnas.0804812105\]](https://doi.org/10.1073/pnas.0804812105) [\[PMID\]](#) [\[PMCID\]](#)