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ESTABLISHED AND EMERGING PREBIOTICS FOR GUT MICROBIOTA

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Abstract – The concept of prebiotics was introduced more than two decades ago, but these bioactive molecules still represent an attractive area of research. This is due to their close connection with the intestinal microbiota and, consequently, of the entire human organism. Prebiotics are used as a food source by gut microbes, releasing various metabolites, of which short-chain fatty acids are key molecules in ensuring the normal functioning of the colon. Within the framework of this article, an overview of published scientific studies in the last year (from March 2023 to March 2024), on the impact on the intestinal microbiota residents of two groups of prebiotics (established and emerging), is given. The prebiotic effect of established prebiotics has been confirmed based on available in vitro and in vivo studies, while emerging prebiotics' effect yet needs to be elucidated by in vivo studies. The available information shows novelties in the field of health benefits and modifications of established prebiotics, as well as the potential of many polyphenols and polysaccharides from different natural sources to exhibit prebiotic activity. Presented data give insight into the effect of prebiotics on beneficial and pathogenic microbes, and potential effective solutions for preserving health and suppressing diseases. A detailed analysis of the latest scientific publications in this field is of great importance for the food, confectionery, pharmaceutical and other industries that use prebiotics as an integral part of their products, to improve the quality of existing ones or to develop new ones.

Keywords: Gut microbiota, Prebiotics, Probiotics, Gastrointestinal tract (GIT), Agro-food.

INTRODUCTION

The term "microbiota" is used to denote the community of present microorganisms and is often equated with the term "microbiome" although they are significantly different[1]. Microbiome is a broader term that basically denotes microorganisms, their genes, and environmental conditions[2]. Microorganisms are permanent residents of different regions of the human body (digestive system, oral cavity, skin, lungs, and vaginal flora), among which the digestive tract is considered not only the most colonized area with about 100 trillion microbes but also essential for maintaining human health[1]. Depending on the segment of the human digestive system (stomach, small or large intestine) due to different conditions that are more closely defined by factors like pH, transition time, presence of oxygen, acids, bile salts, etc., the composition of the microbiota also varies[3]. The highest concentration of microbes is found in the large intestine, where anaerobic species dominate due to the lack of oxygen. In contrast, the small intestine, with its higher oxygen availability, is primarily inhabited by facultative aerobes[3,4]. Available studies in this field demonstrate that the composition of the intestinal microbiota consists of bacteria (phylum *Firmicutes*, *Bacteroidetes*, *Proteobacteria*, *Actinobacteria*, *Verrucomicrobia* and *Fusobacteria*), fungi (phylum *Ascomycota* (genus *Candida*, *Saccharomyces*, *Cladosporium*) and *Basidiomycota* (genus *Malassezia*), viruses (phages) and archaea[1]. It was also reported that the bacterial phylum *Firmicutes*, which includes the

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genus *Lactobacillus*, *Clostridium*, *Enterococcus*, *Ruminicoccus,* etc., and *Bacteroidetes* represent 90% of the intestinal population[1,4].

The composition of the normal and healthy gut microbiota has not yet been defined, but it is certainly characterized by a significantly higher proportion of beneficial commensal bacteria compared to pathogenic ones[5]. This dynamic and complex ecosystem is essential for host health due to the numerous roles that microorganisms play, including food digestion, immune regulation, protection against pathogens, and production of vitamins and other metabolites[6,7]. However, in this community, a change in the composition of beneficial microbes and their inability to successfully control pathogens can easily occur, which is referred to as dysbiosis, with negative consequences for human health[8]. This state of imbalance in bacterial species can arise from factors such as diet, hygiene practices, antibiotic use, stress, and other influences[9,10]. Disturbance in composition is closely related not only to intestinal symptoms, such as bloating, abdominal pain, and diarrhea, but also to inflammatory bowel diseases, cardiovascular diseases, obesity, diabetes, arthritis, asthma, etc[9,11,12]. Recent studies in this field indicate that altered gut microbiota is closely correlated with psychological diseases, especially anxiety and depression. It is still questionable whether the change in intestinal microbiota is the cause or consequence of various disorders[9], but it is more certain that their development is connected with the intestinal microbiota, as well as to metabolic products and the immune response of the host[11].

Until now, various strategies have been applied to prevent or treat diseases associated with microbiota dysbiosis, and these include the use of probiotics, prebiotics, or the transplantation of fecal microbiota[13]. The use of pro- and prebiotics can be a potential therapeutic treatment in order to regulate the disbalance and enable the normal functioning of the gut ecosystem. Based on the revised definitions by the International Scientific Association for Probiotics and Prebiotics (ISSAP), prebiotics are “a substrate that is selectively utilized by host microorganisms conferring a health benefit”[14,15]. Prebiotics, as non-digestible components, reach the large intestine in an unchanged form, where the present microorganisms metabolize them through the enzymes they produce[1]. As a metabolic product, short-chain fatty acids (SCFAs) (such as acetate, propionate, and butyrate), alcohols, and gases are formed. Different pathways of bacterial anaerobic fermentation result in different final metabolites, of which SCFA are the most important because they participate in maintaining intestinal homeostasis and show different biological protective effects on the host (anti-inflammatory, anti-cancer, anti-obesity, immune-regulatory, etc.)[16-18].

METHODS

Systematic searches were conducted in April and May 2024 in the Scopus, Google Scholar, and PubMed databases. In this paper, we review the most recent studies on the effects of various prebiotics on gut microbes, offering insights into the current advancements in this field. Titles and abstracts were independently reviewed by two authors (AV and KB). The authors (MV and APV) were consulted to resolve inconsistencies in screening decisions. Studies were required to be published in a peer-reviewed journals from March 2023 until March 2024, and written in languages spoken by authors performing filtering and extraction (English, Serbian).

ESTABLISHED AND EMERGING PREBIOTICS

Recent advancements in food science and the evolving definition of prebiotics are expanding the variety of prebiotic substrates for gut microbiota. Prebiotics can generally be classified based on their chemical structure into carbohydrates (dietary fibers) and non-carbohydrates (Figure 1). Dietary fibers, including oligosaccharides, are a structurally diverse class of polysaccharides that vary in molar mass, branching patterns, and monosaccharide composition[19]. Different microbial species in the human gut exhibit distinct abilities to utilize dietary fibers based on their nature and structure and the specific enzymes expressed by these species. Considering that scientific and regulatory definitions of prebiotics differ

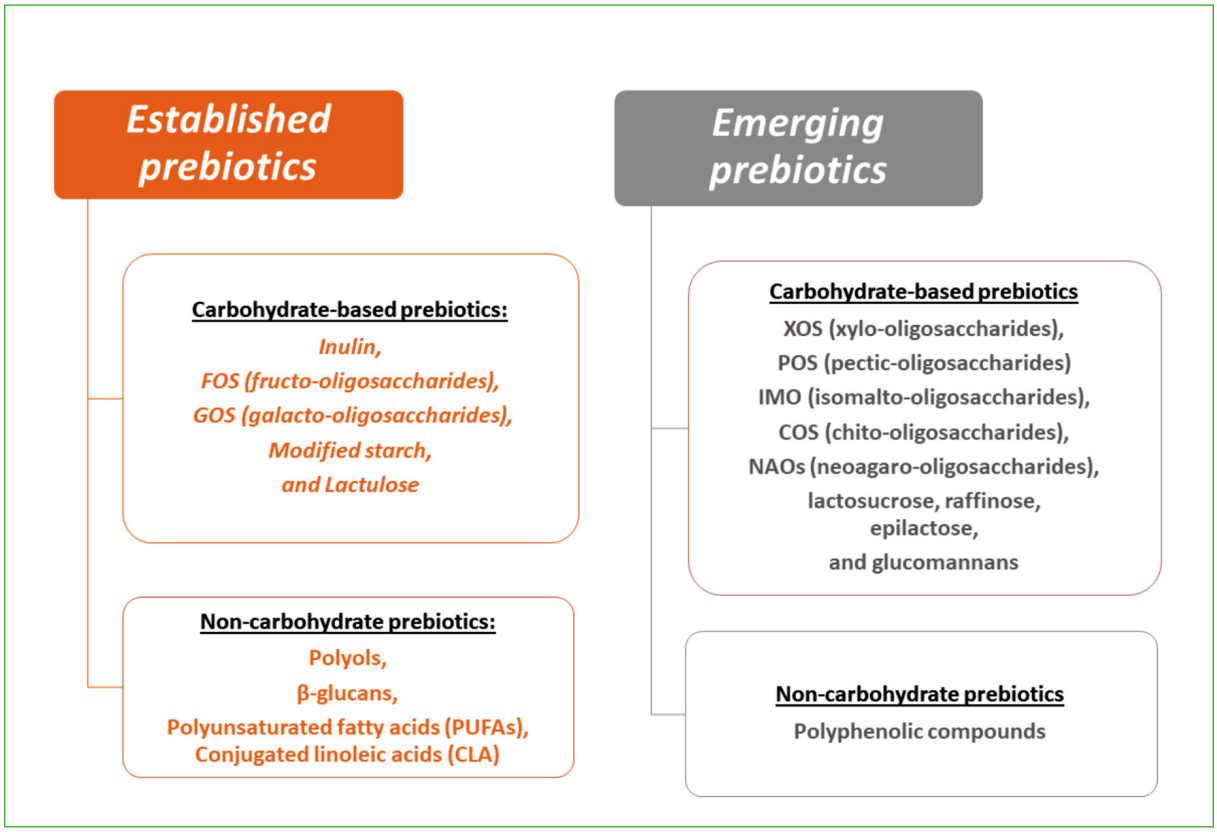

Figure 1. Established and emerging prebiotic ingredients for gut microbiota.

and that all dietary carbohydrates are not prebiotics, there is a consensus on the health benefits of dietary fibers linked to their fermentation by gut microbiota. Consequentially, the dietary fibers that are considered prebiotics are defined as specific compounds that promote the growth of beneficial gut microbiota, thereby providing health benefits to the host through their metabolism[20].

The most recognized and studied carbohydrate-based prebiotics related to human gut microbiota are inulin, fructo-oligosaccharides (FOS), galacto-oligosaccharides (GOS), modified starch, and lactulose (Figure 1). However, new carbohydrate-based prebiotics are emerging, including xylo-oligosaccharides (XOS), isomalto-oligosaccharides (IMO), chito-oligosaccharides (COS), lactosucrose, raffinose, neoagaro-oligosaccharides (NAOs), epilactose, and glucomannans.

It should be noted that in addition to prebiotic dietary fibers and oligosaccharides, non-carbohydrate substrates such as polyunsaturated fatty acids (PUFAs), conjugated linoleic acids (CLA), and polyphenols have also shown potential as prebiotic candidates (Figure 1). This section will present and discuss the latest advances in these established and emerging prebiotics for gut microbiota.

Prebiotic Oligosaccharides

The growing consumption of healthy foods is followed by the rising demand for the production of prebiotic compounds. The review paper by Belmonte-Izquierdo et al[21] covers the production of recognized prebiotics FOS by fructosyltransferase and also illuminates the future perspectives for the production of FOS through microbial fructosyltransferase enzymes. Already established prebiotics FOS and inulin have been used in *in vitro* fermentation test, and it has been proven that different health benefits of FOS and inulin are dependent from the gut microbiota

composition, such as baseline *Bacteroides*/*Bifidobacterum* ratio, which directly influences the prebiotics' consumption and effect on the microbial diversity. Additionally, baseline Ba/Bi ratios also influenced the prebiotic induced SCFAs production[22].

Also, rising demands and various applications of established prebiotic GOS highlight the need for the development of novel purification processes for the removal of monosaccharides and/or lactose, leading to the production of high-purity GOS. Cao et al[23] developed a purification process of a commercially available GOS which besides GOS contains lactose and monosaccharides. In order to prepare high-purity GOS with low residual lactose and monosaccharide content, purification by hydrolysis of lactose using *β*-galactosidase and sequential simulated moving bed chromatography for the removal of monosaccharides yielded high-purity GOS with retained functionality and structural integrity. High-purity GOS showed equal bifidogenicity and comparable effects on the gut microbiota composition by *in vitro* fecal batch fermentation as reference GOS low in monosaccharides, indicating that the integrity of all GOS components, especially bifidogenic DP2 fractions was retained.

The production of novel type of oligosaccharides will expand the diversity of prebiotic options available to target a wider range of gut microbiome needs.

In the review paper of Dutra Pierezan et al[24] recent advantages in emerging oligosaccharide prebiotics and potential prebiotic foods are presented. Hereby, focus will be on evaluation of novel oligosaccharides prebiotic development concepts which are directly related to human health and gastrointestinal microbiota composition.

In order to upgrade carbohydrate-based prebiotic compounds, such as FOS, there have been indications that different modification techniques can be applied with the goal of improving the functionality of already established prebiotics and, hence, yielding novel compounds with better potency. Tan et al[25] reported the chemical and enzymatic synthesis of propyonil-FOS, while Yang et al[26] reported the synthesis of butyril-FOS using a commercial FOS. In both cases, chemically synthesized ester had a higher esterification degree in comparison with the FOS ester synthesized through an enzymatic process and exhibited a lower prebiotic effect, thus indicating that the high esterification degree negatively influenced the prebiotic activity of the compound, mainly due to the inability of the gut microbiota to ferment such complex substrate. Both propyonil-FOS as well as butyril-FOS obtained through enzymatic synthesis could be regarded as a potential prebiotics due to their beneficial health effect through gut microbiota modulation and propionic acid/butyric acid delivery to the colon[25,26]. Considering previously described findings, it could be noted that esterification of FOS can serve as a potential method in developing the mechanism for the constant release of different organic acids into the colon and also prolong the time for the FOS degradation in the gut and extend the transport of SCFAs to the distal colon region[25].

Additionally, microbial production of novel compound with prebiotic potential was reported by Wu et al[27]. Novel extracellular acidic oligosaccharide succinoglucan COGs-3 from *Rhizobium radiobacter* ATCC 13333 showed resistance to degradation and the ability to modify gut microbiota composition by promoting the proliferation of beneficial bacteria (*Bifidobacterium*, *Faecalibacterium*, *Lactococcus*) while expressing the potential to decrease the abundance of the pathogenic ones. Its structure, mainly succinate groups and *β*-(1,4) glycosidic bonds, contributed to the increase of the gut microbiota production of propionic and butyric acid.

In recent years, research has focused on the prebiotic activity of xylo-oligosaccharides (XOS). These compounds are composed of xylose residues linked by *β*-(1,4)-glucoside bonds and can be naturally found in fruits, honey, and vegetables, but in very low quantities. The prebiotic activity of XOSs directly depends on the source of origin, purity, and degree of polymerization. They are commonly produced *via* the enzymatic hydrolysis of commercial xylan or xylan derived from lignocellulosic biomass[28]. To reduce production costs, low-cost lignocellulosic materials, such as wheat and rice straw, sugarcane bagasse, corncob, miscanthus, birch-, and beechwood are often used[24]. In the study of Zhao et al[28], it has been demonstrated that bamboo shoot shells, bio-waste produced during bamboo processing, could be used for production of XOS solution by hydrothermal pre-treatment. Since probiotics exhibit a preference for metabolizing lower-degree oligosaccharides, such as xylobiose (X2) and xylotriose (X3), the obtained XOS solution from bamboo shoot shells was additionally treated using the endo-xylanase in order to enrich it with X2 and X3. The

results demonstrated that enriched XOS solution with X3 and X2 stimulates the growth of *Firmicutes* and inhibits the growth of *Proteobacteria* far better than the standard solution of XOS, confirming once more that bio-waste could be a valuable source for prebiotic synthesis.

Lately, interest has shifted towards pectic-oligosaccharides (POS), which could be produced from pectin by enzymatic and/or chemical methods. For the enzymatic hydrolysis of pectin, different types of pectinases (esterases, hydrolases, and lyases) are combined, and as a result, breaking down of the pectin network occurs, thus the mixture of POS with different degrees of polymerization was produced[29]. Several studies confirmed that pectins and POSs, their enzymatic-hydrolysates from different sources (sunflower stalks pith, apple, orange, hawthorn and okra), could be considered a novel category of prebiotics due to the facts that they selectively enhance the growth of probiotic bacteria (*Bifidobacteria* and *Lactobacilli*), modify the ratio of the number of *Bacteroidetes* and *Firmicutes*, reduce the potential of *Proteobacteria*, especially the enteric pathogens present in this group of microorganisms, and inhibiting the growth of pathogenic bacteria (*Escherichia-Shigella*)[20,30]. For instance, the treatment of citrus juice with pectinases generates enzymatic hydrolysates that promote an abundance of beneficial bacterial taxa such as *Bacteroides*, *Collinsella*, *Parabacteroides*, and *Alistipes*[29]. In terms of POS productions on an industrial scale, they are generated from agro-food processing waste (fruit and vegetable peels (orange, onion), beet pulp, *Actinidia latifolia* and fresh artichokes)[20,31]. Published studies are focused on novel sources of pectic prebiotics, for example, the study of Almutairi et al[31], where Australian native fruit *Terminalia ferdinandiana* (Kakadu plum) as a new source of pectic prebiotic was examined. This study demonstrated that Kakadu plum and its POS extracts could serve as effective prebiotics for enhancing the growth, fermentation, and survival of the six lactic-acid probiotic bacteria as well as antimicrobial agents against foodborne pathogens *Staphylococcus aureus* ATCC 9144 and *Listeria monocytogenes* ATCC 19111.

In the study of Wang et al[32], the impact of galactomannan oligosaccharides (GMOS), derived from *Gleditsia microphylla,* on human intestinal bacteria was examined in order to assess their potential as a prebiotic. GMOS exhibited a significant inhibitory potential toward *Fusobacteria* phyla.

Prebiotic Polysaccharides

Recently published studies clearly elucidate that starch-based polysaccharides like arabinoxylan and dextran have a prebiotic potential. The search for new sources of natural starch has become an emerging trend due to increasing health awareness and the flourishing application of natural ingredients with biological activities in the food industry.

Researchers are exploring various plant-based sources to identify starches that can be used for their prebiotic properties. For instance, pulses, such as lentils, chickpeas, and various beans, are rich in protein, fiber (approximately 50 % of pulse weight is from resistant starch), and essential nutrients, making them attractive as healthful and eco-friendly food options. The resistant starch isolated from pulse (adzuki, black-eyed, field and garbanzo peas, great northern, large lima, lentil, light-red kidney, navy, and Nigerian honey beans) seeds modulate gut microbiota composition by promoting *Bacteriodetes*, *Faecalibacterium*, *Ruminococcus*, and *Blautia* growth, while decreasing proliferation of *Firmicutes*, meaning that this type of starch has prebiotic potential[33]. Additionally, it has been demonstrated that resistant starch from pulse seeds promotes acetate and butyrate production in upper GIT. Furthermore, kidney beans (*Phaseolus vulgaris*), a popular legume in the Chinese diet, were categorized into non-digestive foods due to the fact that they contain up to 45% of resistant starch. Incorporating kidney beans into the diet not only supports the proliferation of beneficial bacteria like *Bifidobacterium* but also helps in inhibiting harmful bacteria such as *Fusobacterium*[34]. This dual action underscores the importance of kidney beans in promoting gut health and reducing the risk of colorectal cancer[34].

The synthesis of a water soluble slow digestion dextrin from maltodextrin by combining α-glucosidase with cyclodextrin glucosyltransferase (CGTase) was investigated by Wei et al[35]. The obtained product had a higher dietary fiber content, higher molecular weight, and α-(1,6)

linkage in comparison with the one obtained in the reaction catalyzed solely by α-glucosidase, indicating the positive effect of CGTase in the dietary fiber content increase. The product showed its prebiotic effect on beneficial bacteria (*Bifidobacterium, Veillonella, Dialister,* and *Blautia*) through *in vitro* human fecal microbiota fermentation monitoring and also in pure cultures *of Bifidobacterium*. In all cases, it also contributed to the increase of SCFAs production. Furthermore, the fraction of grapefruit peel rich in soluble dietary fibre identified as dextran has been revealed to increase the relative abundances of *Lactobacillus, Bacteroides, Bifidobacterium* and *Faecalibacterium*, and decrease the relative abundances of *Clostridium* and *Clostridioides*[36]. Development processes and implementation of novel sources for the generation of starch-based prebiotics with improved dietary fiber content are undergoing and represent an important aspect in the field of food technology.

Nonstarch polysaccharides (NSPs) are complex carbohydrates composed of various monosaccharides, including rhamnose, arabinose, galactose, mannose, glucose, and uronic acids. Their degradation in the human body relies on the assistance of gut microbes, particularly those from the *Firmicutes* and *Bacteroidetes* genera. Additionally, the hydrolyzed low-molecular-weight carbohydrates can serve as an energy source and substrate, promoting the proliferation of beneficial bacteria while restraining the growth of opportunistic pathogenic bacteria and increasing the production of SCFAs[37].

Arabinoxylan is a major type of non-starch polysaccharide present in cereals. It is a significant component of hemicelluloses and a major contributor to dietary fiber intake globally[19]. Moreover, it is well known that the molar mass and chemical structure of wheat arabinoxylan fiber has a direct effect on the growth and metabolism of two health-related microbial species, *Faecalibacterium prausnitzii* and *Lacticaseibacillus rhamnosus* LGG. Recently, research has shown that by modifying low-molecular-weight wheat arabinoxylan fibers with α-L-arabinofuranosidase B25, the stronger prebiotic effect on *L. rhamnosus* and *F. prausnitzii,* as well as stimulation SCFAs production, were detected. These findings suggest that modifying the chemical structure of wheat arabinoxylan enhances the growth of beneficial microbes linked to positive health outcomes. Scholars have studied the effects of wheat bran and wheat-derived arabinoxylan on gut bacteria, SCFA production, and IgA secretion[38]. In addition to wheat-derived arabinoxylan, rice bran arabinoxylan compound (RBAC) is a widely used dietary supplement whose effect on the gut microbiota has not been exploited. Schupfer et al[39] investigated the effect of RBAC on healthy adults' microbiota by examining the changes in the microbiota composition during the supplementation of RBAC. Research has demonstrated that its impact is strongly influenced by an individual's lifestyle, age, and diet. Although some individuals showed an increase in beneficial microbes, it is essential to identify the factors that contribute to the positive effects of RBAC supplementation on gut microbiota modulation. The gut microbiome modulatory potential of arabinoxylan isolated from Brewer's spent grain, a by-product of the brewing industry, which is rich in fiber, was also investigated[40]. The results showed that obtained arabinoxylan fractions have unique abilities to modulate gut microbiota, meaning that it is possible to create prebiotics that are tailored to the needs of specific populations or health conditions.

The synthesis of homopolysaccharide glucan through strain fermentation and glucan-oligosaccharides by glucansucrase obtained from *Leuconostoc mesenteroides* CICC6055 in the reaction system with sucrose and maltose was reported[41]. *In vitro* fecal fermentation showed that both glucan and oligo-glucans contributed to the rise in SCFAs content and abundance of microbial populations, such as *Bacteroides*, *Firmicutes*, *Verrucomicrobia* and *Proteobacteria*.

Several published *in vitro* studies have demonstrated that novel types of polysaccharides isolated from different natural sources have beneficial effects on human gut microbiota. Their biological activity and potential prebiotic effects are highly dependent on their structural characteristics, molecular weight, monosaccharide composition, and functional groups. Table 1 summarizes recently published studies focusing on novel polysaccharides as prebiotics.

Prebiotic Phenolic Compounds

Polyphenols are natural compounds in foods available daily in the human diet, namely fruits, vegetables, whole grains, and beverages[66]. Generally, polyphenols have good antioxidant effect and are recognized as prebiotics due to the fact that they stimulate the

TABLE 1. EMERGING NONSTRACH POLYSACCHARIDES WITH PREBIOTIC POTENTIAL.

Source	Chemical composition	Biological activity	Reference
The medical herb *Ficushirta* Vahl	Heteropolysaccharide: rhamnose (Rha, 51.2 mol %), galactose (Gal, 25.8 mol %), and arabinose (Ara, 14.9 mol %), with small amounts of xylose (Xyl, 4.2 mol %), fuctose (Fuc, 1.2 mol %), and galacturonic acid (GalA, 2.8 mol %)	• Enrich abundance of *Faecalibacterium*, *Bifidobacterium*, *Bacteroides*, *Phascolarctobacterium*, and *Blautia* • Suppress the abundance of opportunistic pathogenic genera *Dorea*, *Clostridium* XIVa, and *Desulfovibrio* • Increase the concentrations of SCFAs, including acetate, propionate, and butyrate • Antioxidant activity and a significant anti-inflammatory effect	Xiao et al[42]
The sea cucumber *Thelenotaananas*	Marine polysaccharide fucoidan: L-fucose, sulfate groups, and a small number other monosaccharides.	• Strong mucin adhesive function • Stimulate production of various SCFAs • Promote the relative abundance of *Bacteroidota* and *Firmicute*s • Reduce the proportion of *Proteobacteria*	Chen et al[43]
Genistein-stimulated Monascus purpureus	Exopolysaccharides: arabinose, xylose, rhamnose, mannose, glucose, and galactose with molarratios of approximately 1, 0.37, 0.14, 3.15, 4.15, and 5.04, respectively	• Immunomodulatory potential • Vary gut microbiota composition • Enchase proliferation of beneficial bacteria (*Lactobacillaceae*, *Prevotellaceae*, and S24-7)	Xie et al[44]
Lactobacillus delbrueckii (EPS-LB3) and *Lacticaseibacillus rhamnosus* (EPS-MLB3)	Two types of exopolysaccharides: Glu:Rib:Man:Xyl (1.0:16.4:6.6:6.5) and Rib:Man:Xyl:GA:Ara (7.1:1.6:4.8:1.0:9.0)	• Exhibit antioxidant, antidiabetic, antimicrobial, antibiofilm, and antiproliferative activities • Promote growth of selective bacteria like *Faecalibacterium prausnitzii* and *Ruminococcus bromii*	Tarique et al[45]
Fruiting bodies of the fungus *Hericiumerinaceus*	Polysaccharide: fucose, rhamnose + arabinose, glucosamine, galactose (19 mol%),glucose (73 mol%), mannose, glucuronic acid.	• Increase the relative abundance of the dominant butyric acid-producing genera • Regulate the microbial community, the gas production and SCFAs production	Zhuang et al[46]
Mushroom *Agaricus bisporus*	Mushroom polysaccharides: glucose, galactose, mannose, rhamnose	• Promote production of SCFAs and causes a decrease in pH value • Modulate the gut microbiota composition by increasing the abundance of beneficial bacteria • Immune regulation and anti-oxidation	Fu et al[47]

CONTINUED

TABLE 1 *(CONTINUED).* EMERGING NONSTRACH POLYSACCHARIDES WITH PREBIOTIC POTENTIAL.

Source	Chemical composition	Biological activity	Reference
Fruit Persimmon (Diospyros kaki L. cv. Mopan)	Carboxymethylated persimmon polysaccharide: total sugar content 76 %, glucose (97 %), galactose, mannose, ribose	• Promote the proliferation of *Lactobacillus* • Inhibit the proliferation of *Staphylococcus aureus* and *Escherichia coli* • Antioxidants, anti-inflammatory agents, antiwrinkle remedies, and anticoagulants	Chen et al[48]
Seafood mushroom *Hypsizygus marmoreus*	1. Water-soluble polysaccharide: β-(1–6)-glucan; 2. Fucomannogalactan:α-(1–6)-linked galactopyranose, and substituted by α-L-fucopyranose and β-D-mannopyranose 3. Polysaccharide: α-glucans, galactoglucans, and fucomannogalactans	• Promote the production of SCFAs, especially acetate and propionate, which in turn reduce the pH value in colon • Reduce the abundance of *Fusobacterium* and *Desulfovibrio* • Enchase the abundance of *Prevotella* and *Faecalibacterium*	Ye et al[49]
Medicinal and food homologous crop Adlay (*Coixlacrymajobi*)	Polysaccharide: amylopectin-like glucan containing (1,4)-linked alpha-D-glucose as a backbone. Polysaccharides are composed of monomeric units such as rhamnose, arabinose, xylose, galactose, galacturonic acid, and glucuronic acid.	• Regulate gut microbiota and barrier function to against *Clostridioides difficile* infection • Promote the expression of tight junction proteins and mucin in intestinal cells	Lee et al[50]
Hard shells of nut *Juglansregia* L.	Nut polysaccharide: glucose, ribose, galactose, mannose, arabinose and rhamnose in a ratio of 10.7:4.9:16.4:2.3:10.8:2.3	• Modulate the structure and composition of gut microbiota through promoting the growths of beneficial bacteria and correspondingly inhibiting the growths of harmful bacteria. • Promote the metabolic functions of gut microbiota including amino acid, carbohydrate, coenzyme and lipid transport and metabolism abilities	Li et al[51]
Herbal medicine Polygonatum odoratum	Polysaccharides: Fructose and glucose 99%, minor values of arabinose, galactose and xylose Fru:Ara:Glc:Gal:Xyl=87.72:0.30:11.56:0.19:0.23	• Promotion of the growth • Increase of antimicrobial activity of *L. johnsonii* towards *Klebsiella pneumonia* • Significant increase in the levels of acetic, isobutyric, isovaleric acids	Liu et al[52]

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TABLE 1 *(CONTINUED).* EMERGING NONSTRACH POLYSACCHARIDES WITH PREBIOTIC POTENTIAL.

Source	Chemical composition	Biological activity	Reference
Kiwi fruit (*Actinidiachinensis*) pomace	Total polysaccharides 77.69%±1.15% Total uronic acid 28.59%±1.93% Total phenolics 2.31±0.03 mg GAE/g Monosacharide composition molar ratio Fuc:Ara:Rha:Gal:Glu:Xyl:Man:GalA:GlcA= 0.05:0.023:0.09:0.73:1:0.08:0.07:0.49:0.04	• Increase of SCFAs levels (especially acetic, propionic and butyric) • Promotion of beneficial bacteria (*Bacteroides*, *Lactobacillus*, *Bifidobacterium*) and inhibiton of harmfull bacteria	Chan et al[53]
Medicinal and edible fungus *Tremellafuci formis*	Polysaccharides: Fructose:glucose: xylose:mannose: glucuronic acid molar ration 0.271:0.016:0.275:0.400:0.038	• Promotion of the growth of beneficial bacteria • Decrease of *Firmicutes* growth • Increase of SCFAs production	Song et al[54]
Polynatum cyrotonema	Hua polysaccharides:Fuctose:galactose:glucose:mannose: xylose:fructose molar ratio 4.15:4.57:71.21:4.47:13.21:2.39 Glucose and xylose most abundant components	• Increased production of SCFAs (acetic and propionic acid) • Regulation of intestinal microbiota composition and metabolism • Positive effect on the growth of *Bifidobacterium*, Megamonas species • Decrease of *Klebsiella*, *Fusobacter* and *Escherichia-Shigella*	Gao et al[55]
Chrorellazo fingiensis Green microalga	Polysaccharides: Mannose 62.92 mol%, Glucose 17.45 mol%, galactose 15.62 mol%, rhamnose 4.01 mol% Main chain and two branched repeating units	• SCFAs increase (acetic, propionic, butyric) • Gut microbiata composition regulation • Bacteroides, Bifidobacterium, Akkermansia increase • Effect on the lowering of Firmicutes/Bacteroides ratio	Wan et al[56]
Boletus mushrooms	Polysaccharides: glucose, galactose and mannose, followed by fucose, xylose and rhamnose	• Promote the production of SCFAs • Increase the relative abundance of beneficial bacterial genera such as Bacteroides and Faecalibacterium • Reduce the relative abundance of harmful bacterial genera such as Sutterella and Escherichia–Shigella	Chen et al[57]

CONTINUED

TABLE 1 *(CONTINUED).* EMERGING NONSTRACH POLYSACCHARIDES WITH PREBIOTIC POTENTIAL.

Source	Chemical composition	Biological activity	Reference
Huangshui a typical organic wastewater in Chinese Baijiu production	Three polysaccharides: two fractions contained manose, ribose, galacturonic acid, glucose, galactose, xylose, arabinose and fucose. In case of third fraction, ramnose, galacturonic acid and fucose were not detected	• Anti-inflammatory effects on LPS-treated Caco-2 cells • Increase the relative abundance of *Bacteroidota* and *Phascolarctobacterium*	Li et al[58]
Date fruit pomace	Polysaharides:mannose, galacturonic acid, galactose, glucose, and fructose (several fractions with specific proportion of these monosaccharides)	• Antiproliferative effects, inhibition against Caco-2 and MCF-7 • Antibacterial properties against both Gram-positive and Gram-negative foodborne bacteria • Increase growth of *Gemmiger formicilis*, *Blautia species*, Collinsellaaer ofaciens, and *Bifidobacter iumlongum* • Decrease of growth Escherichia and *Enterococcus saccharolyticus* • Abundant in Firmicutes, Actinobacteria, and *Proteobacteria phyla*	Bamigbade et al[59]
Ginger (*Zingiber officinale Roscoe*)	Heteropolysaccharide with helix structure: galactose, arabinose, rhamnose, glucose, mannose and glucuronic acid, among which galactose (29.32%) and arabinose (19.55%) accounted for the highest proportion	• Promote SCFAs production (acetic acid, propionic acid, n-valeric acid and a bit of i-butyric acid and n-butyric acid)	Lin et al[60]
Coix (*Coix lacrymajobi L. var. mayuen Stapf*) seeds	Homopolysacharide: glucose (96.88%)	• Increase of the relative abundance of beneficial bacteria, such as *Limosilicactobacillus, Bifidobacterium* and *Collinsella* • Increase production of SCFAs (acetic acid, propionic acid and n-butyric acid)	Ge et al[61]

CONTINUED

TABLE 1 *(CONTINUED).* EMERGING NONSTRACH POLYSACCHARIDES WITH PREBIOTIC POTENTIAL.

Source	Chemical composition	Biological activity	Reference
Traditional Chinese medicine *Dendrobium officinale* Orchidaceae family	Polysaccharides: β-glucan and inulin	• The abundance of unclassified *Enterobacteriaceae* • Promote the growth of *Parabacteroides*, *Bifidobacterium* and *Faecalibacterium* • Reduction of branched-chain fatty acids (BCFAs), sulfides, phenols, and indole	Sun et al[62]
Jackfruit peel waste	Heteropolysaccharide: glucose, mannose, galactose, arabinose, and rhamnose	• Promote the growth of beneficial flora *Weissella*, *Enterococcus*, *Bifidobacterium*, Lactococcus and *Prevotella* • Resease free oligosaccharides, • ProduceSCAFs, particularly acetic acid	Li et al[63]
Bergamot and Laoxianghuang	Bergamot and Laoxianghuang polysaccharides: mannorhamnan (comprising mannose and rhamnose) and polygalacturonic acid (comprising galacturonic acid and galactose),	• Bergamot polysaccharide decrease harmful *Fusobacterium* and promoted beneficial *Bifidobacterium* • Laoxianghuang polysaccharides stimulate growth of *Lactobacillus*	Wu et al[64]
Inulin-type fructan from roots of *Codonopsis pilosula* (Franch.) Nannf.	Linear structure of β-D-fructose linked via β-(1→2) fructosylglycosidic bonds terminated with α-D-glucose	• *Prevotella*, *Faecalibacterium* and *Bifidobacterium* stimulation • Inhibition of Fusobacterium • pH lowering effect	Li et al[65]

growth of gut microbial species, such as *Lactobacillus, Bifidobacterium, Faecalibacterium, Akkermansia, and Roseburia*, and on the other hand, simultaneously lower the prevalence of pathogenic bacteria like *Clostridium perfringens*, *Escherichia coli*, and *Helicobacter pylori*. In recent years, several *in vitro* and *in vivo* studies have shown the prebiotic effect of dietary phenolic compounds on gut microbiota[67]. The phenolic compounds present in the form of glycosidic derivatives in various plants (peel of fruits, parsley, and celery, cereals) display unique digestion patterns within the GIT. The majority of these phenolic compounds remain bound to dietary fibers in plant cell walls and reach the colon intact, where they can be metabolized by the colonic microbiota (*Enterococcus avium* or *Clostridium orbiscinde*)[66]. In the *in vitro* study by Zhang et al[67], phenolic compounds extracted from oat bran using ultrasonic-assisted extraction proved to have prebiotic activity in addition to strong antioxidant activity. Results showed that they promote the proliferation of beneficial gut microbiota members (*Lactobacillus/Enterococcus* spp. and *Bifidobacterium* spp.) and inhibit the proliferation of other bacterial groups. Moreover, phenolic compounds rutin and kaempferol-3-O-rutinoside extracted from fruit Noni (*Morindacitrifolia* L.) affected the intestinal microbiome by reducing the *Firmicutes/Bacteroidetes* ratio and increasing bacteria with prebiotic properties like *Prevotella* and *Rumi nococcus*. These findings suggest that noni polyphenols have the ability to improve the structure of the intestinal microbiota and that these polyphenols have prebiotic potential[68].

The prebiotic activity of one more phenolic compound, the diester chlorogenoborate (5-DCB) complex, was investigated. The 5-DCB complex was synthesized using boron organic species isolated from plants and chlorogenic acids (esters of caffeic and quinic acids) isolated from coffee beans. Chlorogenic acids are already recognized as prebiotics while boron spices have become novel prebiotic candidates and target the colon as novel colonic food. Consequently, 5-DCB, as a B prebiotic compound claimed to be nutritionally essential for the symbiosis between the microbiota and the host[69]. Cai et al[70] also found that combining flavonoids and phenolic acids with starch can create polyphenol-starch complexes that have a prebiotic effect. These complexes help the growth of beneficial bacteria (like *L. rhamnosus* and *B. bifidum*), increase short-chain fatty acids (SCFAs), and reduce the harmful bacteria *E. coli*.

CONCLUSIONS AND FUTURE PERSPECTIVES

Recent years have yielded novelties in the field of prebiotics research, mainly polyphenols and polysaccharides for different natural sources like herbs, fruits, and by-products of the fruit processing industry (peels or pomaces rich in bioactive components). Additionally, research has focused on already established prebiotics, their health benefits, and the expansion of their potential use. Given the importance of microbiota for human health, novel strategies and concepts for the production of established and potential prebiotics as functional food ingredients are being developed. Waste by-products' value can be elevated by different methods, such as the synergistic prebiotic effect of different bioactive compounds[71,72], synbiotic formulations[73,74], or microbial fermentations[75]. These approaches have the potential to innovate the food industry, creating products that support consumer health while promoting environmental responsibility. Keeping in mind that dietary fibers and polyphenol compounds exhibit various beneficial health effects, it is of immense interest to explore how the combination of these bioactive ingredients will affect the human intestinal microbiota and health.

Furthermore, the potential prebiotic effect of food hydrocolloids, a diverse group of natural ingredients present in food, has drawn the attention of researchers since they are often indigestible polysaccharides, and most of them are resistant to GIT digestion, which makes them potential substrates for beneficialbacteria[76,77]. For example, flaxseed, also known as linseed (*Linum usitatissimum*), contains a significant concentration of mucilage, a type of hydrocolloid[76], highly applicable as a functional agent in the food industry which bioactivities, such as prebiotic effect in the alteration of gut microbiota composition make it a good candidate for further studies[78].

Future research could be driven towards the development of microbiota-targeted prebiotics for the specific population groups[22,40,79], the development of delivery systems for prebiotics[80-82], and the production of functional food rich in bioactive components such as prebiotics[83].

Conflict of Interest

All authors declare no potential conflicts of interest.

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Authors' Contributions

Katarina Banjanac: study conception and design, review and editing; Milica Veljkovic: wrote Introduction and review and editing. Anja Petrov Ivanković and Ana Vukoičić: collected and selected literature data, wrote first draft.

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