

Recent findings in production and health benefits of prebiotics: a review of literatures

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Abstract

Prebiotics are known as fermented ingredients with specific health benefits. The two main fermentative substrates of dietary origin are non-digestible carbohydrates and proteins, which escape digestion in the small intestine. Beside traditional protocols for production of prebiotics, there are some commercial advanced methods for the mass production of prebiotics with acceptable health effects. On the other hand, different types of nondigestible oligosaccharides (NDO) are used in the food and drug industries as functional foods and nutraceuticals due to their prebiotic effects and also immunomodulation results (ex. SCFA modulate chemokine expression in the intestinal epithelial cells). Prebiotics with novel and various health benefits suggest a bright future for improving the public health.

Keywords: Health Benefits, Microbiota, Prebiotics, Production.

1. Introduction

Prebiotics were firstly defined as non-digestible food ingredients that beneficially affect the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon, and thus improve the host health (1). Then, Gibson *et al.* defined prebiotics as ‘a selectively fermented ingredient that allows specific changes, both in the composition and/or activity in the gastrointestinal microflora that confers benefits upon host well-being and health (2). The final definition was ‘A dietary prebiotic is a selectively fermented ingredient that results in specific changes in the composition and/or activity of the gastrointestinal microbiota, thus conferring benefit(s) upon host health (3). The prebiotic conception accentuates the specific stimulation of microbiota

to decrease the metabolic activity of potentially harmful bacterial. This section focusses essentially on primary metabolic pathways. Most of the colon’s micro-flora are strictly anaerobic bacteria, and their energy originate from fermentation. The two main dietary origin of fermentative substrates are non-digestible carbohydrates (dietary fibers, resistant starch, and non-digestible oligosaccharides of plant origin) and proteins that escape digestion in the small intestine (4-6). The other important group of substances for bacterial growth are proteins, peptides and amino acids. Currently, two chemical groups including inulin-type fructans and the galacto-oligosaccharides have gained the majority of the scientific research attentions for prebiotic effects (7). In this review article, we aim to present recent advances in the field of production and utilization of prebiotics as well as their nutritional and pharmaceutical properties.

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2. Current advances in the production of prebiotics

Traditional dietary sources of prebiotics include wheat, soybeans, bananas, barley, onion, garlic, asparagus, Jerusalem artichoke tuber, rye, and chicory root. Some of synthetic prebiotics are fructo-oligosaccharides, lactulose, galactooligosaccharides, xylo-oligosaccharides, isomaltose-oligosaccharide, malto-oligosaccharide, and isomaltulose (8). Prebiotics can be produced by transgalactosylation of carbohydrates from numerous raw materials such as starch, sucrose, lactose, and xylan via chemical and enzymatic methods (9). By transgalactosylation activity during the hydrolysis of lactose with β -galactosidase, galacto-oligosaccharides could be produced (10). Several sources of β -galactosidase for the transgalactosylation reaction include *Aspergillus oryzae* (11), *Sirobasidium magnum* (12), *Penicillium simplicissimum* (13), *Bacillus circulans* (14), *Bifidobacterium infantis* (15), *Bullera singularis* (16), *Escherichia coli*, *Kluyveromyces marxianus* (17), and *Kluyveromyces lactis* (15).

Lactulose is a non-digestible prebiotic by mammalian enzymes, which is not hydrolyzed or absorbed in the small intestine. As a disaccharide, it is composed of galactosyl β (1,4) fructose derived from the primary and secondary isomerization of lactose (18). *Bacillus subtilis* was found to be an effective producer of prebiotic disaccharide lactosucrose (19). Lactosucrose has been also produced from sucrose and lactose by the action of an enzyme, β -fructofuranosidase, from *Arthrobacter* sp. K-1 (20). In other studies, lactosucrose has been produced successfully by *Sterigmatomyces elviae* (21), *Zymomonas mobilis* (22), and *Bacillus circulans* (23). Lactulose has been also successfully synthesized by a dual-enzymatic method in organic-aqueous two-phase media using lactose and fructose as the raw materials (24, 25). The dual-enzymatic system consisted of immobilized lactase and immobilized glucose isomerase (26). Immobilized lactase is prepared by cross-linking of the free lactase into Fe_3O_4 -chitosan magnetic microspheres (26, 27). The continuous enzymatic process has been developed for the production of lactulose through transgalactosylation using free and immobilized β -glycosidase

from *P. furiosus* (28).

Fructo-oligosaccharides (FOS) can be produced by the degradation of polyfructose or inulin (29-31). Commercially, FOS is usually produced by the transfructosylation of saccharose by β -fructosidase (32). *Aspergillus japonicus*, *A. niger* (33), and *Xanthophyllomyce dendrorhous* (34) have been used for the production of FOS in several studies.

Isomaltulose has been produced from sucrose using free *Erwinia* sp. D12 (35), *Serratia plymuthica* (36), *Protaminobacter rubrum* (8), *Serratia plymuthica* (8), and *Enterobacter* sp. (37). Here, there is an opportunity to apply microalgae for the production of prebiotics such as carotenoids and fatty acids (38, 39).

Beta-glucans are found in algae, mushrooms, and marine plants, and are mainly made and extracted from barley and oat (40). Inulin, as a polymer of fructan monomers, is one of the main natural plant-derived polysaccharide with a various nutritional and pharmaceutical benefits. (41). Oligofructose can be achieved by chemical degradation of beta-glucans with endoglycosidase enzymes, while transfructosylation of sucrose leads to production of FOSs (41, 42).

Classically, GOSs contain 2-10 molecules of galactose and 1 molecule of glucose, and are mainly produced by glycosylation of lactose generally by β -galactosidases (43, 44). Isomaltooligosaccharides containing glucose monomers are made from the enzymatic digestion of corn starch with α -glucosidase, α -amylase, and pullulanase (45). Guar gum is frequently utilized in dairy, bakery, and is made from the endosperm of the plant *Cyamopsis tetragonolobus* (46).

3. Health benefits of prebiotics

Different types of nondigestible oligosaccharides (NDO) are used in food and pharmaceutical industries because of their prebiotic effects (47, 48). As mentioned before, prebiotics are nondigestible food ingredients that stimulate the growth and/or activity of one, or a limited number of microbial flora in the gut and bring health benefits to the host (49).

As prebiotics have very low toxicity and have reputable health benefits for the host, these

products present a great supplementary value from a hygienic point of view. In addition, exploitation of prebiotics as a part of functional foods by the food industry has important economic advantages, and is frequently presented as an example of knowledge-based economic growth (50, 51).

Structurally, prebiotics are carbohydrates that reach the lower gastrointestinal tract in substantial amounts. NDOs are not hydrolyzed by enzymes secreted into the upper gastrointestinal tract because of glycosidic bonds such as $\beta(2\rightarrow1)$ in FOS (52). Therefore, the molecule remains too large to be absorbed in the small intestine. However, these glycosidic bonds can often be hydrolyzed by enzymes produced by the bacteria present in the lower gastrointestinal tract, and the hydrolysis products are mostly fermented by the micro-flora population. Short-chain fatty acids are produced and the colonic pH decreases. It also causes rushing of the intestinal transit due to stimulation of the growth of colonic microbiota leading to increased gas production and water retention in feces (53-57). These properties as well as their selective promotion of beneficial bacteria, have led to the application of prebiotics in the treatment or prevention of conditions such as constipation, diarrhea, inflammatory bowel disease, necrotizing enterocolitis, septic shock, diabetes, and allergies to dietary proteins (58-60). The possible benefits of prebiotics are enhanced by the low toxicity credited to these compounds. However, it should be emphasized that in some cases prebiotics/probiotics may be harmful, such as in one study that patients with acute pancreatitis were treated with probiotics (61). In addition to the above, these NDO may wield different properties independent of their prebiotic activity. For instance, they prevent the adhesion of pathogenic bacteria to human epithelial cells. Galactooligosaccharides have the highest antiadhesion ability among all prebiotics (62). Prebiotics also modulate cytokine production by the intestinal epithelial cells, which is applicable in the control and prevention of infections and malignancies (63). Interestingly, prebiotics have been reported to be taken up by Caco-2 cells, and may modulate sub-epithelial cells (64). In addition, *in vitro* studies have shown that prebiotics regulate cytokine production in human cord blood mono-

nuclear cells (65, 66).

GI tract hosts various types of the cells with important roles in immune system responses, which are influenced by prebiotics (67, 68). There is no known exact mechanisms affecting on the immune system. However, the metabolites such as SCFAs, especially butyrates, are shown to influence macrophages, T cells, and dendritic cells (69).

Prebiotics are known as modulatory agents that regulate the bioavailability of nutrients, energy, and storage, the agents associated with the host obesity (70, 71). On the other hand, bifidobacteria population is inversely correlated with fat mass and glucose intolerance (72, 73). Other instances are inulin-type fructans, which affect gut metabolism and stimulate immune cell activity leading to declined weight gain and fat mass (74).

Several clinical purposes could be proposed by modulating effects of prebiotics on the immune system (67). Boosting the immune function for resistance against infections may serve as a complementary tool for prevention or treatment of infectious diseases. Indeed, preventing or treating consequences of undesired immune responses, such as allergic responses or chronic inflammatory diseases, are other health benefits of prebiotics (75-77). There is a wide variety of immune markers reflecting body resistance to infection, and prebiotics were discovered to play a more prominent role in certain types of infections or other health problems (77, 78). However, it is clear that prebiotics can modulate certain parts of the immune system.

Several studies in gnotobiotic animals have demonstrated that the microbiota is essential for an optimal structural and functional development of the immune system, whereas microbiota could be boosted and strengthened by prebiotics (79-82). The collaborative effects of microbiota beside the immune system in the intestinal tract (gut-associated lymphoid tissue) have gone forward to provide optimal defense against intestinal pathogens (83, 84). On the other hand, microbial products such as short chain fatty acids (SCFA) may interact with immune cells and enterocytes, and modify their activity (69, 85).

G-protein-coupled receptors (GPR) 41

and GPR 43 expressed on leukocytes especially polymorphonuclear cells as well as on enterocytes and enteroendocrine cells in the human colon (86, 87) are diagnosed as receptors for SCFA (87, 88). SCFA indeed, modulate chemokine expression in the intestinal epithelial cells (89).

4. Conclusion

In summary, there are traditional and industrial methods for production of different prebiotics with determined health benefits. Conceivable mechanisms for the health benefits of prebiotics

are suggested for example modulation of immune system. The unreachability of the immune system of the GI tract confounds the investigation in this area, and most human studies rely on the measurement of *ex vivo* systemic immune markers, demonstrating the overall resistance to infections and disorders. However, prebiotics with acceptable health outcomes are dealt with high output commercially and industrial methods of production.

Conflict of Interest

None declared.

5. References

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