Prebiotic Capacity of Inulin-Type Fructans¹–³

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Abstract

The human gut microbiota plays a significant role in human health through its ability to digest food ingredients and manufacture metabolites. This can be positive or negative for host welfare. Moreover, the microflora plays an active role in host defense whereby colonization resistance affords protection against pathogens. Prebiotics are nondigestible food ingredients that target beneficial components of the gut microflora (mainly colonic), particularly the bifidobacteria. In vitro and in vivo evidence has accumulated to confirm the prebiotic effects of inulin-derived fructans. J. Nutr. 137: 2503S–2506S, 2007.

Introduction

The bacterial microbiota in the human gastrointestinal tract is thought to compromise the majority of total cells in the body, mainly because of high densities in the colon. Through the activities of the resident microflora, the gut plays a major role in host nutrition and welfare. In fact, because of the highly profuse and diverse colonic microflora, this organ is among the most active in the body. Having said that, within the gut, there exists much variability in bacterial numbers and populations among the stomach, small intestine, and colon. The total bacterial count in gastric contents is usually below 10³/g, with numbers in the small intestine ranging from ~10⁷/mL of contents in the jejunum to ~10⁹/10⁳ at the terminal ileum. A low pH in the stomach, with rapid transit times and bile/pancreatic secretions into the small bowel, maintains populations at such low levels.

The colon is by far the most heavily populated area of the gastrointestinal tract, with numbers typically in the region of 10⁹/g of contents. The environment is favorable for bacterial growth with a slow transit time, ready availability of nutrients, and favorable pH. From culture-based data, it is thought that at least 500 different microbial species exist, although on a quantitative basis ~10–20 genera probably predominate. Examples include Bacteroides, Lactobacillus, Clostridium, Fusobacterium, Escherichia, and Veillonella (1).

The colonic microbiota ferments substances that cannot be digested by the host in the upper gut. These include resistant starch, nondigestible carbohydrates, oligosaccharides, other carbohydrates and proteins/amine acids. The 2 main types of fermentation that are carried out in the gut are saccharolytic and proteolytic. Saccharolytic fermentation is more favorable to the host than proteolysis because of the types of metabolic endproducts formed. The main products of carbohydrate metabolism are the short-chain fatty acids acetate, propionate, and butyrate. Acetate is metabolized in systemic areas such as muscle and used to generate ATP, whereas propionate and butyrate are important sources of energy for the colonicocytes and has antitumor properties. The endproducts of proteolytic fermentation, on the other hand, include toxic metabolites (such as certain phenolic compounds, amines, and ammonia), some of which are carcinogens (2).

Evidence from a variety of sources supports the view that some components of the human gut flora play a role in gut-mediated disorders. Conversely, there is convincing evidence that beneficial bacteria can reduce the risk of disease through pathogen inhibition and the production of benign and beneficial metabolites. As a result, the resident gut flora can be divided into benign, beneficial, and potentially harmful groups, although certain genera contain species belonging to 2 groups; e.g., bacteroides may be saccharolytic (beneficial) or proteolytic (potentially harmful). Bacterial metabolism can result in a number of advantageous effects, including the production of vitamins, modulation of the immune system, enhanced digestion and absorption, inhibition of harmful species, and removal of carcinogens and other toxins (3,4). Negative effects include the production of toxins and carcinogens, constipation or diarrhea, liver damage, predisposition toward gut disorder, and intestinal putrefaction. More specifically, the resident microflora is known to contain pathogensthat, if allowed to overgrow, can disrupt normal gut function and predispose toward disorder (5,6).

Gut microflora modulation

The concept of modulating activities directed toward improving gut microbial function has a long history, largely driven by the
probiotic concept (7–11). Bifidobacteria and lactobacilli are the most common ingredients used as live microbial feed additions because they are thought to exert powerful antipathogenic capabilities and are mainly responsible for “colonization resistance” in the gut. The probiotic approach advocates the targeting of selected indigenous bacteria through nonviable food ingredients (12).

We have recently updated the probiotic concept and reviewed evidence for candidate forms (13). Any dietary component that reaches the colon intact is a potential prebiotic; however, 3 criteria are required for success, in that the ingredient should 1) resist host digestion, absorption, and adsorption processes; 2) be fermented by the microflora colonizing the gastrointestinal system; and 3) selectively stimulate the growth and/or the activity of 1 or a limited number of bacteria within the gastrointestinal system.

The latest probiotic definition is “a selectively fermented ingredient that allows specific changes, both in the composition and/or activity in the gastrointestinal microflora, that confer benefits on host well-being and health” (13). Prebiotics allow the selective growth of certain indigenous gut bacteria. Thus, the prebiotic approach involves administration of a nonviable food component and considers that many positive microorganisms such as bifidobacteria and lactobacilli are already resident in the human colon.

Types of prebiotics

Much of the interest in the development of prebiotics is aimed at nondigestible oligosaccharides. Oligosaccharides are sugars consisting of between 2 and 20 saccharide units, i.e., they are short-chain polysaccharides. Examples include inulin-type fructans, trans-galactooligosaccharides, isomaltooligosaccharides, xylo-oligosaccharides, sojooligosaccharides, glucooligosaccharides, and lactosucrose (14,15). In Europe, inulin-type fructans, galactooligosaccharides, and lactulose have been shown to be prebiotics, based on results from in vitro studies and human subjects, that provided evidence of their ability to change the gut flora composition after a short feeding period. The Japanese market has more candidate prebiotics. Inulin-type fructans are by far the most widespread and researched current prebiotics that fit the selection criteria mentioned above.

Inulin occurs naturally in several foods such as leek, asparagus, chicory, Jerusalem artichoke, garlic, artichoke, onion, wheat, banana, and oats as well as soybean. However, these foods contain only trace levels of prebiotics, so functional food developments have taken the approach of removing the active ingredients from such sources and adding them to more frequently consumed products to attain levels at which a prebiotic effect may occur (5–8 g/d). Examples include cereals, confectionery, biscuits, infant feeds, yogurts, table spreads, bread, sauces, and drinks (15).

The prebiotic activity of inulin-type fructans has been confirmed (Table 1). As a result, these prebiotics are the current market leaders. This is because these carbohydrates have a specific colonic fermentation directed toward bifidobacteria. Bifidobacteria are able to break down and utilize inulin-type fructans because of their possession of the β-fructofuranosidase enzyme, providing a competitive advantage in a mixed culture environment such as the human gut (16). Inulin-type fructans are oligo-/polymers of D-fructose joined by β(2→1) bonds with an α(1→2) linked D-glucose at the terminal end of the molecule. Molecules with DP between 3 and 10 are referred to as oligofructose, and those with a DP between 10 and 65 are known as inulin.

Bifidobacteria have long been regarded among the beneficial members of the human gut microflora, which explains their being the most common target for prebiotic intake. The bifidobacteria-dominated gut microbiota of breast-fed infants has been associated with improved health benefits (17,18). High numbers of bifidobacteria are also seen as positive for adult health. Bifidobacteria have been suggested to inhibit growth of pathogenic bacteria, modulate the immune system, produce digestive enzymes, repress the activities of rotaviruses, and restore microbial integrity of the gut microbiota following antibiotic therapy or antibiotic-associated diarrhea (19–21).

Published results from various human feeding studies have demonstrated the bifidogenic (prebiotic) nature of inulin and its partial hydrolysis product oligofructose. Gibson et al. (22) reported a significant increase in fecal bifidobacteria levels on ingestion of 15 g/d inulin or oligofructose in 8 healthy volunteers. Williams et al. (23) reported a significant increase in bifidobacteria levels and increase in lactobacilli in 6 volunteers at the lower dose of 4 g/d oligofructose. Similar results were reported by Buddington et al. (24) in 12 healthy volunteers at 4 g/d oligofructose. Kleessen et al. (25) reported a significant increase in bifidobacterial levels and a concomitant decrease in enterococci and entrobacterial numbers on the ingestion of inulin at doses ranging from 20 to 40 g/d in 35 elderly constipated patients. Den Hond et al. (26) exhibited a significant increase in stool frequency, and fecal bulk was observed with inulin administration at 15 g/d in 6 healthy humans with low stool frequency in a double-blind placebo-controlled crossover study. Kruse et al. (27) observed a significant increase in fecal bifidobacteria levels with ingestion of 34 g/d inulin in 8 healthy volunteers. Bouhnik et al. (28) investigated the tolerance and threshold dose of oligofructose that significantly increased fecal bifidobacteria counts in a 7-d study of 40 healthy human volunteers and reported that the optimal dose without significant side effects was 10 g/d. In a later study Tuohy et al. (29) exhibited the bifidogenic effect of 6.6 g/d oligofructose delivered as a processed food product (biscuit) in 30 healthy humans using fluorescence in situ hybridization to monitor changes in fecal microflora. These results therefore confirm the prebiotic effect using high-fidelity molecular-based procedures (29). Inulin-type fructans are therefore able to exhibit bifidogenic effects at various daily intakes in healthy humans.

An inulin dose of 5–8 g/d should be sufficient to elicit a positive effect on the gut microbiota. One possible side effect of prebiotic intake is intestinal discomfort from gas production. However, bifidobacteria and lactobacilli cannot produce gas as part of their metabolic process. Therefore, at a rational dose of up to 20 g/d, gas distension should not occur. If gas is being generated, then the carbohydrate is not acting as an authentic prebiotic. This is perhaps because dosage is too high and the prebiotic effect being compromised, i.e., bacteria other than the target organisms are becoming involved in the fermentation. A further explanation is that at high doses, the prebiotic causes osmotic diarrhea, and the more rapid transit of digesta through the small bowel thus reduces digestion/absorption of other dietary components. These other dietary components (e.g., unabsorbed nutrients, including other carbohydrates and proteins) are then available for fermentation by the bacteria in the distal bowel. This may explain the production of gas and distension, which would/should not occur if only the prebiotic were entering the distal bowel.

The prebiotic effect of inulin-type fructans has been extensively confirmed. The usual target microorganisms are bifidobacteria, with major increases in their numbers occurring on ingestion. Often, 0.5–1.0 log10 numerical increases are seen. This constitutes a major shift in the gut microbiota toward a “healthier” composition. Lactobacilli are other obvious target populations, but it is also likely that future research will unravel the capacity
for prebiotics to increase the densities and metabolic activities of populations of other beneficial bacteria such as the butyrate producing flora. The positive benefits of prebiotic intake are reviewed elsewhere in this journal.

### Literature Cited


### Table 1 Examples of in vitro and in vivo studies on the prebiotic effect of fructans

<table>
<thead>
<tr>
<th>Test carbohydrate</th>
<th>Study type</th>
<th>Dose</th>
<th>Duration of feeding</th>
<th>Effect</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Various carbohydrates tested</td>
<td>Mixed culture, batch</td>
<td>Various</td>
<td>In vitro</td>
<td>Inulin and oligofructose were more bifidogenic than starch, polydextrose, fructose and pectin</td>
<td>Wang and Gibson (30)</td>
</tr>
<tr>
<td>Oligofructose, inulin and sucrose</td>
<td>Mixed culture, continuous</td>
<td>Various</td>
<td>In vitro</td>
<td>Oligofructose more rapidly fermented than inulin.</td>
<td>Gibson and Wang (31)</td>
</tr>
<tr>
<td>Oligofructose</td>
<td>Pure cultures</td>
<td>Various</td>
<td>In vitro</td>
<td>Oligofructose had a bifidogenic effect compared with their ability to fortify clostridia, bacteroides, enterococci or E. coli</td>
<td>Gibson and Wang (32)</td>
</tr>
<tr>
<td>Oligofructose</td>
<td>Pure cultures</td>
<td>Various</td>
<td>In vitro</td>
<td>Various species of bifidobacteria were able to metabolise oligofructose</td>
<td>Marx et al. (33)</td>
</tr>
<tr>
<td>Oligofructose, levan, branched fructans, maltodextrin</td>
<td>Mixed culture, batch</td>
<td>Various</td>
<td>In vitro</td>
<td>Branched chain fructans seen to be bifidogenic</td>
<td>Probert and Gibson (34)</td>
</tr>
<tr>
<td>Inulin</td>
<td>Pure culture</td>
<td>Various</td>
<td>In vitro</td>
<td>Butyrate producing Roseburia spp. able to degrade inulin</td>
<td>Dunca et al. (35)</td>
</tr>
<tr>
<td>Oligofructose</td>
<td>23 subjects</td>
<td>8 g/d</td>
<td>2 wk</td>
<td>10-fold increase in bifidobacteria and decreased stool pH</td>
<td>Mitsouka et al. (36)</td>
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<tr>
<td>Oligofructose</td>
<td>Double-blind placebo-controlled crossover IBS patients</td>
<td>6 g/d</td>
<td>4 wk</td>
<td>No therapeutic effect</td>
<td>Hunter et al. (37)</td>
</tr>
<tr>
<td>Inulin and oligofructose</td>
<td>8 healthy humans</td>
<td>15 g/d</td>
<td>45 d</td>
<td>Bifidobacteria becoming predominant in feces with both inulin and oligofructose</td>
<td>Gibson et al. (22)</td>
</tr>
<tr>
<td>Oligofructose</td>
<td>20 subjects</td>
<td>12.5 g/d</td>
<td>12 d</td>
<td>Significant increase in bifidobacteria and reduced levels of colorectal cancer markers</td>
<td>Bouchnik et al. (38)</td>
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<tr>
<td>Oligofructose</td>
<td>12 healthy adult humans</td>
<td>4 g/d</td>
<td>42 d</td>
<td>Significant increase in bifidobacteria, no change in total bacteria levels</td>
<td>Buddington et al. (24)</td>
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<tr>
<td>Inulin and lactose</td>
<td>35 elderly constipated humans</td>
<td>20 g/d and 40 g/d</td>
<td>19 d</td>
<td>Significant increase in bifidobacteria, decreases in enterococci and fusobacteria. Better laxative effect than lactose</td>
<td>Kleessen et al. (25)</td>
</tr>
<tr>
<td>Inulin</td>
<td>8 healthy humans, placebo controlled</td>
<td>34 g/d</td>
<td>64 d</td>
<td>Significant increase in bifidobacteria established</td>
<td>Kruse et al. (27)</td>
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<tr>
<td>Oligofructose</td>
<td>40 healthy humans</td>
<td>2.5–20 g/d</td>
<td>14 d</td>
<td>Significant increase in bifidobacteria levels without excessive gas production</td>
<td>Bouhnik et al. (28)</td>
</tr>
<tr>
<td>Inulin</td>
<td>6 healthy humans (low stool frequency) double-blind placebo-controlled crossover study</td>
<td>15 g/d</td>
<td></td>
<td>Significant increase in stool frequency and fecal bulk</td>
<td>Den Hond et al. (26)</td>
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<tr>
<td>Oligofructose</td>
<td>8 healthy humans, placebo controlled</td>
<td>8 g/d</td>
<td>5 wk</td>
<td>Significant increase in fecal bifidobacteria and decrease in fecal pH</td>
<td>Menne et al. (39)</td>
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<tr>
<td>Oligofructose</td>
<td>8 young healthy volunteers</td>
<td>5 g/d</td>
<td>3 wk</td>
<td>Increased fecal bifidobacteria</td>
<td>Rao (40)</td>
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<td>Oligofructose in biscuits</td>
<td>31 healthy humans, double-blind placebo-controlled</td>
<td>7 g/d</td>
<td>42 d</td>
<td>Significant increase in bifidobacteria established via fluorescent in situ hybridisation (FISH). No change in total bacterial levels</td>
<td>Tuohy et al. (29)</td>
</tr>
<tr>
<td>Oligofructose</td>
<td>19 elderly persons</td>
<td>8 g/d</td>
<td>3 wk</td>
<td>Increase in bifidobacteria (almost 3 log() values)</td>
<td>Guigoz et al. (41)</td>
</tr>
<tr>
<td>Inulin</td>
<td>14 adult volunteers</td>
<td>9 g/d</td>
<td>2 wk</td>
<td>Probes (FISH) confirmed an increase in bifidobacteria and Erec group.</td>
<td>Harmsen et al. (42)</td>
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</table>