

Prebiotics for Adults

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Recent research in gastroenterology has been exploring the interesting connection between the gut and the body's immune system. It is believed that the gastrointestinal tract (GI tract) is home to nearly 300 to 500 different species of bacteria and the large intestine has a dense population achieving concentrations of up to 10^{11} or 10^{12} cells per gram of luminal contents.¹ It has been demonstrated that about 55 percent of fecal mass consists of bacteria.² The gastrointestinal tract contains lymphoid tissue that functions similarly as other mucosa-associated lymphoid tissue (MALT) found in various sites of the body, such as the thyroid, lungs, salivary glands, and GI tract. GALT (gut-associated lymphoid tissue) is the specific name for the largest concentration of immunocompetent cells in the human body.³ It is this interaction between host and bacteria at the mucosal interface that seems to play an important role in development of a competent systemic immune system.⁴

Although the gut is sterile at birth, it is rapidly colonized.⁵ This mixture of metabolically active microbes that colonize the GI tract are referred to as the “commensal microbiota”—which literally means “small life” and “beneficial resident microbe.” The type and number of microbes increase down the length of the GI tract and are influenced by genetics, environment, disease, and diet.⁶⁻⁸

It is believed that the commensal microbiota are involved in several physiological functions⁴:

- Production of essential mucosal nutrients, such as short-chain fatty acids;
- Control of epithelial cell proliferation and differentiation allowing for expansion of the mucosal epithelium and an associated increase in digestion and absorption;
- Protection against incoming microbes. Also termed colonization resistance, where the commensal bacteria provide competition that inhibits pathogenic bacteria in attempts to infect the host;
- Provides an important stimulus for the maturation and function of the mucosal immune system;
- Exerts powerful anti-inflammatory activity within the intestinal mucosa.

The influence of diet on the commensal microbiota has been the topic of recent research especially highlighting the unique role of prebiotics. Gibson in 1995 introduced the concept of prebiotics and defined them as nondigestible food ingredients that benefit the host by selectively stimulating the growth of beneficial bacteria in the gut microbiota.⁹

As early as 1999, a European Commission funded project on non-digestible oligosaccharides (NDO) reported a consensus of their review of studies involving these non-digestible oligosaccharides. The consensus¹⁰ reached was that there is:

(1) strong evidence for a prebiotic effect of non-digestible oligosaccharides in human subjects, which they defined as a food-induced increase in numbers and/or activity predominantly of bifidobacteria and lactic acid bacteria in the human large intestine;

(2) strong evidence for the impact on bowel habits;

(3) promising evidence that consumption of inulin-type fructans may result in increased calcium absorption in humans;

(4) preliminary indications that inulin-type fructans interact with lipid metabolism;

(5) preliminary evidence in animals of a preventative effect against colon cancer. They agreed that more human nutrition studies were needed on non-digestible oligosaccharides to substantiate their findings.

In order to better understand, oligosaccharides are carbohydrates consisting of a small number, (two to ten) of monosaccharides.¹¹ Oligosaccharides are found naturally in many foods, such as human milk, soybeans, unrefined wheat, barley, oats, onions, bananas, honey, garlic, Jerusalem artichokes, and leeks.¹² Many types of nondigestible oligosaccharides are produced commercially from various sources of food materials.

Table 1. Sources of Non digestible Oligosaccharides Produced Commercially

Oligosaccharide	Source/origin
Short-chain fructooligosaccharides	Sucrose
Fructan-based oligosaccharides	Inulin (chicory roots)
Xylooligosaccharides	Xylan (corn, sugar cane, cottonseed, bamboo shoots)
Soybean oligosaccharides	Soybeans
Galactooligosaccharides	Lactose
Lactulose	Lactose

Adapted from Garleb¹¹

Fructooligosaccharides are one type of oligosaccharide, and can also be isolated from chicory root (inulin) or synthesized enzymatically from sucrose.¹³ Short-chain fructooligosaccharides are a sucrose molecule linked to a sequence of 1 to 3 fructose molecules via a (2-1)- β glycosidic bond to the fructose unit of sucrose.¹¹ They are enzymatically synthesized (β -fructosyltransferase) from sucrose and have been isolated from such foods as onion, wheat, barley, bananas, tomatoes, garlic, and artichokes.^{14,15}

The bacterial species of most recent research interest include the *Lactobacillus* and *Bifidobacterium* genera. As early as 1986 Hidaka et al reported that these strains of beneficial bacteria were able to selectively utilize short-chain fructooligosaccharides (scFOS), and that short-chain fructooligosaccharides improved the intestinal flora when feeding 1 g of short-chain fructooligosaccharides per day, which led to increased bifidobacteria in the stool.¹⁶ Certain indigestible oligosaccharides were found by Campbell et al. to benefit gastrointestinal tract health via fermentation and proliferation of desirable bacterial species. In this study, dietary incorporation of fermentable, indigestible oligosaccharides of short-chain fructooligosaccharides, were proposed to be beneficial in improving gastrointestinal health by lowering pH and increasing bifidobacteria.¹⁷ In another large study of 200 healthy volunteers, it was found that there was a significant correlation between the ingested dose of short-chain fructooligosaccharides and fecal bifidobacteria counts and that short-chain fructooligosaccharides were well tolerated from 2.5 to 10 g/day.¹⁸

Because fructooligosaccharides are a non-digestible carbohydrate, meaning it passes through and exits the small intestine intact, it allows fermentation of fructooligosaccharides in the colon. This local fermentation is critical to the nutritional needs of the colonocytes, and these cells derive the majority of their nourishment from fermentable fibers. This results in a large number of physiologic effects, which includes increasing the numbers of bifidobacteria in the colon, increasing calcium absorption, increasing fecal weight, shortening of gastrointestinal transit time, and possibly lowering blood lipid levels.¹⁹ Other effects that have been observed in animal models include an increase in cecal weight and an increase in fecal nitrogen excretion.²⁰ The increase in bifidobacteria has been assumed to benefit human health by producing compounds to inhibit potential pathogens, by reducing blood ammonia levels, and by producing vitamins and digestive enzymes.²¹

While prebiotics are carbohydrates and typically “feed” the beneficial bacteria in the GI tract, namely bifidobacteria and lactobacillus, the bulk of the evidence has been focused on these two strains of bacterium. Defined probiotic bacteria are not necessarily excluded from those that may have the ability to use prebiotic fibers as a substrate as well. Prebiotic substances have undergone extensive in vitro and in vivo testing across several species, including humans, which confirms prebiotics fermentation characteristics. And these fermentation characteristics include nutraceutical effects that extend beyond those of regular nutrition, such as optimizing colonic function and metabolism.²²

Recent observations in animal models demonstrate that prebiotics and probiotics may exert beneficial effects on gut health by enhancing gut-associated lymphoid tissue (GALT) responses either directly or indirectly through the production of short-chain fatty acids and enhancing growth

of lactic bacteria such as bifidobacteria and lactobacilli. Butyrate is one such short-chain fatty acid that results from fermentation and is a known preferred energy substrate for the colonocyte.²³

In a recent study by Bouhnik et al of human subjects, they studied the most common prebiotic ingredients currently in use. They found that short-chain fructooligosaccharides, soybean oligosaccharides, galactooligosaccharides, and type III resistant starch measurably raised fecal counts of *Bifidobacterium* species at reasonable dose ranges of 2.5 to 10 g/day within 7 days of administration. They also found that short-chain fructooligosaccharides were the only tested non-digestible carbohydrate that had a linear dose-response between bifidobacteria counts with a dose from 2.5 to 10 g/day.²⁴

Douglas²² and Sanders caution health care professionals from declaring whole foods and substances as “prebiotic” simply based on fermentability alone. They suggest that the word “prebiotic” must always refer to specific, defined substances that exhibit a particular, scientifically observed effect as stated by the definition of “prebiotic,” which is specialized ingredients targeted to influencing specific bacteria, their fermentation end products, and possible health effects on the host.⁹

Prebiotic enrichment is frequently used now in enteral nutrition products as a means to provide short-chain fatty acids to colonocytes by way of fermentation, and to normalize and maintain bowel function and colon integrity, as well as to build colonization resistance in hospitalized patients.²⁵ Patients found to benefit from prebiotic enrichment are those with antibiotic associated diarrhea, irritable bowel conditions, colitis, and those needing bowel maintenance while receiving medical nutrition therapy.²⁶ Of particular interest is the effect prebiotics may have on increasing nitrogen

excretion via the colon and lowering blood nitrogen level in renal patients.²⁷ Cockram and colleagues have demonstrated the safety and established tolerance levels for prebiotics in medical nutrition products with hemodialysis patients.²⁸ Generally, enteral nutritional products containing prebiotics deliver 10 - 15 g/day, which is thought to be effective to elicit, the above benefits.²⁹

Garleb et al¹¹ suggest that fructooligosaccharides are an ideal source of fermentable fiber for medical foods. Because short-chain fructooligosaccharides do not contribute to the viscosity of medical nutrition products, and cannot undergo Maillard nonenzymatic browning reaction, they therefore lend themselves as a viable additive. Garleb's rationale for adding short-chain fructooligosaccharides as an ingredient in medical foods include normalization of bowel function, maintenance of large bowel integrity, restoration of colonization resistance, alteration in route of nitrogen excretion, and improvement in calcium absorption. The normalization of bowel function refers to the treatment or prevention of constipation or diarrhea in patients receiving a medical food. Fructooligosaccharides, through anaerobic fermentation by colon bacteria and production of short chain fatty acids, may be useful in preventing large bowel atrophy or treating distal ulcerative colitis. Fructooligosaccharides, by selectively supporting the growth of specific bacterial species such as bifidobacteria, producing an environment in the colon whereby it increases short-chain fatty acid concentration and decreased pH that is not conducive to the growth of certain pathogenic organisms, may help restore colonization resistance.¹¹

Anaerobic fermentation of fructooligosaccharides, leading to bacterial cell growth and reduction in colonic pH, may shift nitrogen excretion from the urinary to fecal route.³⁰ Improvements in calcium absorption may occur through mechanisms involving short chain fatty acid absorption and a

reduction in large bowel pH.³¹ Recent studies on inulin and short-chain fructooligosaccharide combinations in both animal and human studies have shown to increase the bioavailability and absorption of minerals such as calcium and magnesium in adolescents and post-menopausal women.³²⁻³⁵

There is also special interest, as well as ongoing investigations, in the arena of using prebiotics and probiotics together (called synbiotics) in treating disorders of the GI tract such as Crohn's disease, ulcerative colitis, and pouchitis. Sartor³⁶ reports that clinical and experimental studies suggest that the relative balance of aggressive and protective bacterial species is altered in these disorders. Antibiotics can selectively decrease tissue invasion and eliminate aggressive bacterial species or globally decrease luminal and mucosal bacterial concentrations, depending on their spectrum of activity. Alternatively, administration of beneficial bacterial species (probiotics), poorly absorbed dietary oligosaccharides (prebiotics), or combined probiotics and prebiotics (synbiotics) can restore a predominance of beneficial *Lactobacillus* and *Bifidobacterium* species. These physiologic approaches offer considerable promise for treating inflammatory bowel diseases (IBD), but must be supported by rigorous controlled therapeutic trials. Sartor suggests that synbiotics will likely become an integral component of treating Inflammatory Bowel Diseases in combination with traditional anti-inflammatory and immunosuppressive agents.³⁶ Douglas²² further suggests that scientific verification of benefits for combinations of probiotics and prebiotics are necessary and critical to the success of the synbiotic concept.

Conclusions

Consumption of non-digestible carbohydrates known as prebiotics in adult diets have been proven to be valuable for altering the growth and activity of specific health-promoting bacterial species in the colon, enhancing immune function, improving colonic integrity, increasing absorption of bone-health minerals, and improving digestion and elimination. Douglas and Sanders²² support enrichment of oral intake with prebiotic supplements and prebiotic enriched foods to increase fiber consumption. They believe this enrichment of the diet gives the consumer a clear, convenient, and foolproof way to obtain a particular type and consistent dose level of prebiotics. Continued research in humans is needed to document the physiological benefits of oligosaccharides and perhaps lead to discovery of new functions and consequences affecting the entire body.

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