
Probiotics and Prebiotics: A Brief Overview

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Probiotics and prebiotics are 2 food ingredients that confer physiologic effects through the gastrointestinal tract. *Probiotics* have been defined as viable microorganisms that (when ingested) have a beneficial effect in the prevention and treatment of specific pathologic conditions. These microorganisms are believed to exert biological effects through a phenomenon known as colonization resistance, whereby the indigenous anaerobic flora limits the concentration of potentially pathogenic (mostly aerobic) flora in the digestive tract. Other modes of action, such as supplying enzymes or influencing enzyme activity in the gastrointestinal tract, may also account for some of the other physiologic effects that have been attributed to probiotics. Conversely, prebiotics are nondigestible food ingredients that beneficially affect host health by selectively stimulating the growth and/or activity of 1 or a limited number of bacteria in the colon. The prebiotic, fructooligosaccharide (FOS), is found naturally in many foods, such as wheat, onions, bananas, honey, garlic, or leeks. They can also be isolated from chicory root or synthesized enzymatically from sucrose. Fermentation of FOS in the colon results in a large number of physiologic effects including 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. Other effects that have been observed in animal models include an increase in cecal weight and an increase in fecal nitrogen excretion. 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.

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THE NOTION that food could serve as medicine was first conceived thousands of years ago by the Greek philosopher and father of medicine, Hippocrates, who once wrote, "Let food be thy medicine, and let medicine be thy food."¹ However, during recent times, the concept of food having medicinal value has been reborn as *functional foods*, a term that refers to "any food or food ingredient that may provide a health benefit beyond the traditional nutrients it contains."¹ This article provides a brief overview of probiotics and prebiotics, 2 increasingly popular ingredients that can be found in functional foods and dietary supplements. The review first de-

scribes these ingredients and then explains how they are believed to work within the human body. Lastly, this article highlights some potential applications for these ingredients in patients with renal disease. For a more comprehensive treatment of these topics, the reader may consult several other articles.²⁻⁶

Probiotics

Definition and Strains

Probiotics may be defined as "viable microorganisms that (when ingested) have a beneficial effect in the prevention and treatment of specific pathologic conditions."⁷ The most popular strains are represented by the following genera: *Lactobacillus*, *Streptococcus*, and *Bifidobacterium* (Table 1), but other organisms including enterococci and yeasts have also been used as probiotics. Some of these strains were chosen based on selection criteria⁸ that are believed to be important for efficacy such as origin of strain, in vitro adherence to intestinal cells,⁹⁻¹¹ and survival during passage through the gastrointestinal tract.¹²⁻¹⁶ However,

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Table 1. Microorganisms That Are Commonly Regarded as Human Probiotics

Species
<i>Bifidobacterium bifidum</i>
<i>Bifidobacterium breve</i>
<i>Bifidobacterium infantis</i>
<i>Bifidobacterium longum</i>
<i>Enterococcus faecalis</i>
<i>Enterococcus faecium</i>
<i>Lactobacillus acidophilus</i>
<i>Lactobacillus casei</i> Shirota
<i>Lactobacillus delbrueckii</i> subspecies <i>bulgaricus</i>
<i>Lactobacillus</i> GG
<i>Lactobacillus johnsonii</i>
<i>Lactobacillus reuteri</i>
<i>Lactobacillus rhamnosus</i>
<i>Lactobacillus plantarum</i>
<i>Lactobacillus salivarius</i>
<i>Saccharomyces boulardii</i> (yeast)
<i>Streptococcus thermophilus</i>

whether these properties are absolutely required for clinical efficacy has not yet been clearly established in the literature.

Enterococci such as *Enterococcus faecalis* and *Enterococcus faecium* are common inhabitants of the human gastrointestinal tract. Both species have been used as probiotics, but their safety has been questioned¹⁷ because they have become an increasingly important cause of nosocomial infections.¹⁸ The use of enterococci as probiotics is discussed in greater detail later in this review.

Saccharomyces boulardii is a nonpathogenic yeast that is sometimes used to treat *Clostridium difficile* diarrhea.¹⁹ This organism, which was originally isolated from lychee fruit in southeast Asia, was used to treat diarrhea as early as the 1950s. Like other probiotic organisms, *S. boulardii* does not colonize the colon permanently; therefore, repeated dosings are needed to maintain detectable levels. Based on in vitro, animal, and human clinical studies, *S. boulardii* is thought to eradicate invasive pathogens by using multiple mechanisms including microbial interactions, antisecretory effects, inhibition of toxin binding to receptors, immunologic effects, and trophic effects on the intestinal mucosa.²⁰

History

The group of microorganisms most frequently regarded as probiotics, the lactic acid bacteria, has a long history of consumption by humans. These bacteria, which originally served to prevent spoilage of food by undesirable organisms, were con-

sumed in the form of fermented milk as early as 4000 BC. The consumption of fermented milk was first documented in the Old Testament, and ancient carvings indicated that humans purposely inoculated milk with cultures to produce sour milk as long ago as 2250 BC.²¹

During the modern era, consumption of fermented milk came into fashion during the early 1900s because of the efforts of Russian scientist Elie Metchnikoff. Metchnikoff first developed the notion that fermented milk products might have medicinal value. His hypothesis was based on the observation that Bulgarian peasants, who had extraordinary longevity, also happened to consume sour milk.

The consumption of fermented milk products fell out of fashion shortly thereafter, but growing concerns over antibiotic resistance and food safety have brought probiotics back into the spotlight of both animal and human health. Scientists from the US Department of Agriculture, in collaboration with Milk Specialties Bioscience (Dundee, IL), developed PREEMPT, a novel probiotic product for use in chickens. PREEMPT consists of 29 different microorganisms isolated from the intestines of adult birds and was the first commercial defined competitive exclusion culture against *Salmonella* colonization in poultry.²² This product, which is sprayed on newly hatched chicks, was approved by the US Food and Drug Administration and introduced in 1998.

Safety

Overall, traditional dairy strains of probiotic bacteria, particularly those belonging to the *Lactobacillus* and *Bifidobacterium* genera, are considered to be of low pathogenic potential when given to healthy humans.^{23,24} Even after many years of use, probiotics have been linked to only 1 clinical infection.²⁵ In this case, a purulent viscous fluid specimen was aspirated from a hepatic abscess in a 74-year-old woman with a history of hypertension, non-insulin-dependent diabetes mellitus, mild abdominal discomfort, and mild fever. The aspirate contained virtually a pure culture of gram-positive coccobacilli. Results from enzymatic testing and molecular analysis (polymerase chain reaction assay and pulsed-field gel electrophoresis) of the culture aspirate were indistinguishable from those of *Lactobacillus* strain GG. An interview with the patient revealed that she had been ingesting approximately 0.5 L *Lac-*

tobacillus GG dairy drinks daily for 4 months before the onset of symptoms in an attempt to relieve abdominal discomfort.

In fact, aside from the involvement of some lactobacilli species in dental caries, microorganisms belonging to the *Lactobacillus* and *Bifidobacterium* genera, whether considered probiotics or not, have been largely regarded as nonpathogenic.^{17,26,27} Members of both genera inhabit the human large intestine at concentrations exceeding 10^9 colony-forming units per gram dry feces.²⁸ However, these organisms occur infrequently in human infections, particularly when compared with members of the genus *Bacteroides*, which also inhabit the human digestive tract. For instance, Moore et al²⁹ isolated anaerobes from 81 consecutive clinical specimens that were submitted to their laboratory for culture. From these specimens, they cultured a total of 144 isolates, of which 33.3% were identified as members of the *Bacteroides* genus. In contrast, only 2.1% of the isolates were identified as members of the *Bifidobacterium* genus. Lactobacilli were not listed among the isolates, but some of the unidentified gram-positive nonsporing rods, which made up 2.1% of the total isolates, may have belonged to this genus. In a subsequent study, Saxelin et al³⁰ collected blood culture isolates over a 4-year period in Finland from cases of bacteremia. Of the 3,317 isolates that were detected, only 8 were identified as lactobacilli.

Although probiotic organisms have a long track record of safe consumption, a number of circumstances warrant caution when choosing a particular strain. First, the species of probiotic should be considered. With the exception of some lactobacilli, organisms belonging to the *Lactobacillus* or *Bifidobacterium* genera are very rarely pathogenic,³¹ despite their ubiquitous presence in various body sites. Nevertheless, an extensive search of the literature suggests that certain species, such as *Lactobacillus rhamnosus* or *Lactobacillus casei* subspecies *rhamnosus*,³²⁻³⁷ *Lactobacillus plantarum*,^{33,36-38} and *Bifidobacterium dentium*³⁹⁻⁴¹ (formerly known as *Actinomyces eriksonni* or *Bifidobacterium eriksonni*), may have greater pathogenic potential than others.⁴²

Organisms other than lactobacilli and bifidobacteria have also been used as probiotics, and these other organisms should be examined closely for potential pathogenicity because closely related strains may be known patho-

gens. As an example, enterococci have been implicated as the primary pathogen in a variety of infections including enterococcal meningitis, endocarditis, bacteremia, and urinary tract infections.¹⁷ Hence, the use of enterococci, namely *E faecium* and *E faecalis*, as probiotics have fallen into disfavor because they have been found to be the third leading cause of nosocomial infections in the United States⁴³ and because they have acquired resistance to a large number of antimicrobial agents including vancomycin.¹⁸ Perhaps the most worrisome development regarding this genus was the acquisition of vancomycin resistance and the possibility that the resistance genes could be transferred to other gram-positive pathogens such as *Staphylococcus aureus*.¹⁸ Fortunately, the probiotic *E faecium* strain SF68 is sensitive to vancomycin, ampicillin, amoxicillin, chloramphenicol, and vibramycin; however, it is resistant to a large number of antimicrobials including erythromycin, gentamycin, neomycin, streptomycin, clindamycin, cloxacillin, cephalosporin, colicin, nitrofurantoin, nalidixic acid, and trimethoprim-sulfamethoxazole.⁴⁴

Qualitative data collected from case studies suggest that lactic acid bacteria can act as opportunistic pathogens by producing infections almost exclusively in debilitated patients.⁴⁵ Thus, the relative risk to the patient should be assessed before the administration of probiotics. Patients who are immunocompromised because of extreme age (infant or elderly), use of therapeutics (eg, immunosuppressive agents), or presence of underlying disease may be at greater risk for infection by lactic acid bacteria.⁴⁵

Additionally, patients who undergo dental procedures, have periodontal disease, or have underlying structural heart disease seem to be at increased risk for endocarditis.⁴⁵ Nonetheless, the risk of potential infection because of probiotic therapy should be weighed relative to the risk of side effects because of the administration of traditional medications, many of which are known to produce adverse effects.

The probiotic, *Lactobacillus acidophilus* strain NCFM, has been fed to a number of hemodialysis patients with end-stage kidney disease without adverse effects.^{46,47} However, other members of the *Lactobacillus* genus including unspecified strains of *L acidophilus*⁴⁸ and *L rhamnosus*^{33,49,50}

have been isolated from the peritoneal fluid of patients with peritonitis who were undergoing continuous ambulatory peritoneal dialysis. Each of the isolates was detected only after the patients had been treated with multiple antibiotics including vancomycin, and all of the isolates displayed resistance to this particular antibiotic. No attempts were made to identify the source of the lactobacilli, but the investigators^{33,48,50} assumed that the organisms originated in another body site such as the gastrointestinal tract.

Mechanisms of Action

The mechanisms by which probiotics exert biological effects are still poorly understood, but the nonspecific terms colonization resistance or competitive exclusion are often used to explain their mode of action. Colonization resistance or competitive exclusion describes a phenomenon whereby “the indigenous anaerobic flora limits the concentration of potentially pathogenic (mostly aerobic) flora in the digestive tract.”⁵¹ The concept of competitive exclusion was first developed during the early 1970s when it was discovered that the administration of mixed adult intestinal microorganisms conferred adult-type resistance against salmonella infection to newly hatched chicks.⁵² Even more striking evidence of the protective effect of the normal intestinal microbiota comes from studies of *Clostridium difficile* pseudomembranous enterocolitis in both animal models⁵³ and in patients who experience multiple recurrences of diarrhea or colitis after discontinuation of successful antibiotic therapy.⁵⁴⁻⁵⁸

Some of the specific mechanisms by which the intestinal microbiota exclude undesirable organisms are thought to include the following:^{59,60} (1) production of inhibitory substances, (2) blocking of adhesion sites, (3) competition for nutrients, (4) degradation of toxin receptor, and (6) stimulation of immunity. Although probiotic bacteria are thought to mediate their effects by using some of the same mechanisms as the native intestinal flora, probiotics may also work through other modes of action such as supplying enzymes or influencing enzyme activity in the gastrointestinal tract.⁵⁹ In fact, some studies have even suggested that probiotics, killed cells, or certain cell fractions exert antimutagenic⁶¹ or adjuvant effects,⁶² influence cytokine expression,⁶³ or influence the development of allergies.⁶⁴

Potential Applications for Improving Human Health

Given the wide variety of mechanisms by which probiotics are thought to work, scientists have proposed a variety of clinical applications for these organisms (Table 2). Much of the past research examined the application of probiotics to rotavirus diarrhea or lactose intolerance, but a number of intriguing results have also been published regarding probiotic use in antibiotic-associated diarrhea,⁶⁵ *Candida* vaginitis,⁶⁶ *Clostridium difficile*,⁶⁷⁻⁶⁹ cryptosporidiosis,⁷⁰ *Helicobacter pylori* gastroenteritis,⁷¹ hepatic encephalopathy,⁷² inflammatory bowel disease,⁷³ necrotizing enterocolitis,^{74,75} small bowel bacterial overgrowth in uremia,^{46,47,76} suppression of chemically induced large bowel tumors,⁷⁷ and urinary tract infections.^{78,79}

A unique application for probiotics in renal patients is the reduction of toxic metabolites, which are generated as a result of small bowel bacterial overgrowth during uremia.⁷⁶ These metabolites are thought to be responsible for some of the general symptoms of chronic renal failure, such as neurologic abnormalities, and they may also interfere with the absorption of nutrients from the gut.⁸⁰ In a pilot clinical study,⁴⁷ 19 patients with chronic renal failure ingested capsules containing 1 of 2 human strains of *L acidophilus*, strain NCFM or strain BG2F04. Each capsule contained at least 10⁹ colony-forming units, and 1 capsule was taken twice daily for an average of 76 ± 26 days. Results showed that oral ingestion of *L acidophilus* reduced the serum levels

Table 2. Potential Applications for Probiotics and Sample References

Clinical Application	Reference
Antibiotic-associated diarrhea	65
<i>Candida</i> vaginitis	66
<i>Clostridium difficile</i>	67-69
Cryptosporidiosis	70
<i>Helicobacter pylori</i> gastroenteritis	71
Hepatic encephalopathy	72
Inflammatory bowel disease	73
Lactose intolerance	120
Necrotizing enterocolitis	74,75
Rotavirus diarrhea	121-123
Small bowel bacterial overgrowth in uremia	46,47,76
Suppression of chemically induced large bowel tumors	78
Urinary tract infections	79,80

of the marker compound, dimethylamine, from $257 \pm 45 \mu\text{g/dL}$ to $150 \pm 49 \mu\text{g/dL}$ ($P = .001$), and blood nitrosodimethylamine levels decreased from $236 \pm 69 \text{ ng/kg}$ to $118 \pm 38 \text{ ng/kg}$ ($P = .0053$). These results were subsequently reconfirmed in a placebo-controlled, double-blind, parallel study in patients undergoing hemodialysis.⁴⁶

Commercial Products

Many culture-containing dairy products such as yogurts and culture-added milks contain live microorganisms, but these products require refrigeration and have relatively short shelf lives that are measured in terms of weeks instead of months. On the other hand, freeze-dried microorganisms can remain viable indefinitely under ideal storage conditions. Therefore, because it has been assumed that viability is required for biologic activity, probiotic product forms have been largely limited to capsules, tablets, and powders. Even so, some commercial products, including those in tablet and capsule forms, display a marked discrepancy between the claimed and actual count of viable bacteria and/or a discrepancy between the species shown on the label and the actual species present in the product.⁸¹

A number of probiotic products are available in the United States. As an example, Lactinex (Becton-Dickinson; Franklin Lakes, NJ), a powdered or tableted product consisting of a mixture of *L acidophilus* and *Lactobacillus bulgaricus*, has been on the market since the early 1960s. However, clinical studies suggest that this preparation was ineffective for preventing or altering the course of enterotoxigenic *Escherichia coli* diarrhea in adults^{82,83} and for reducing the incidence or duration of traveler's diarrhea.⁸⁴ In addition, a number of new probiotic-containing products such as Culturelle (*L GG* capsules; CAG Functional Foods, Omaha, NE) and Probiotica (*Lactobacillus reuteri* tablets; McNeil Consumer Healthcare, Ft Washington, PA) have been launched during recent years. Some of these organisms have undergone extensive clinical testing.

Prebiotics

Definition

The term *prebiotic*, first coined by Gibson and Roberfroid,⁵ refers to "a nondigestible food in-

redient that beneficially affects the host by selectively stimulating the growth and/or activity of one or a limited number of bacteria in the colon, and thus improves host health." At the present time, a large number of ingredients are known to escape hydrolysis in the small intestine, but only 4 ingredients also meet the criteria set forth for prebiotics in stimulating the growth of certain bacteria: transgalactosylated disaccharides, xylooligosaccharides, soybean oligosaccharides and fructooligosaccharides (FOSs). This review focuses solely on FOS because it was the first prebiotic oligosaccharide made available in the United States and because much more is known about it than other prebiotics.

Structure of FOSs

FOSs are short- and medium-length chains of β -D-fructans in which fructosyl units are bound by β 2-1 glycosidic linkages (Fig 1). Some molecules also contain glucose as the first moiety. These compounds occur naturally in many foods⁸⁵ including wheat, onions, bananas, honey, garlic, and leeks, but more purified forms may be purchased commercially. Long-chain fructan polymers, referred to as inulin (Raftiline [DRAFTI Active Food Ingredients, Tienen, Belgium] or Frutafit [Imperial-Suiker Unie, Sugar Land, TX]), are isolated from chicory root. These fructans can be partially hydrolyzed by enzymes to make a type of FOS known as oligofructose (Raftilose [DRAFTI Active Food Ingredients]). FOSs can also be synthesized from sucrose by using enzymes from *Aspergillus niger* to make Neosugar (Actilight [Beghin-Meiji Industries, Paris, France], Meiologo [Meiji Seika Kaisha, Tokyo, Japan], NutraFlora [GTC Nutrition, Westminster, CO]).

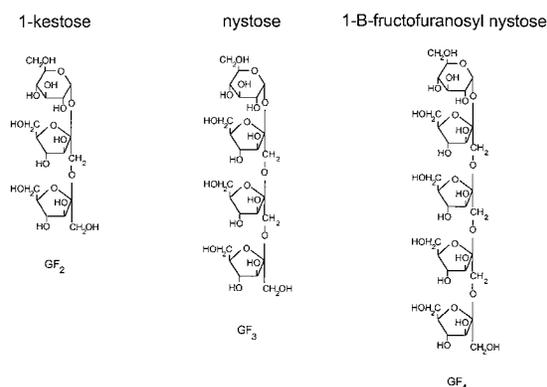


Figure 1. Chemical structure of Neosugar FOSs.

Safety of FOSs

The US Food and Drug Administration has not yet approved FOS as generally recognized as safe (GRAS), but existing evidence suggests that the government will eventually grant this ingredient GRAS status.⁸⁶ As mentioned previously, FOSs occur naturally in a wide variety of foods. In fact, Americans consume approximately 2.5 g of inulin and oligofructose daily (range of 1 to 4 g), mostly from wheat and onions.⁸⁷ In addition, several US companies have already self-affirmed either oligofructose or Neosugar FOS as GRAS by having an expert panel review documentation regarding the safety of this ingredient. On a worldwide basis, NutraFlora FOS has been incorporated into at least 500 food products. In Japan, FOSs have been approved by the Minister of Health and Welfare as foods for specified health use (FOSHU) and have been included in at least 13 products that function as table sugar.

In terms of safety, the ingestion of FOSs cause few adverse effects, and the adverse effects are minor in nature.⁸⁸ Because FOSs possess many of the same physiologic properties as dietary fiber, the consumption of FOSs can lead to symptoms just like those encountered after a sudden increase in dietary fiber intake with the severity of symptoms related to intake level.⁸⁸ Common symptoms include flatulence, cramping, and diarrhea, but effects are only temporary.

The safety and tolerance of FOSs were actually measured in stable hemodialysis patients.⁸⁹ Seventy-nine normally nourished, stable, anuric, adequately dialyzed, adult outpatients with end-stage renal disease were randomized to 1 of 3 treatment groups in a prospective, controlled, single-blind, parallel study. The treatment groups included a standard medical nutritional and 2 renal nutritionals with one of the renal nutritionals containing added β -carotene and FOSs. During the 3-week long study, gastrointestinal symptoms and bowel habits were recorded during a 1-week baseline period and during 2 weeks of treatment. Subjects who were randomized to the FOS-containing treatment ingested an average of 15.6 ± 0.9 to 18.5 ± 1.2 g FOSs daily, and those in the other 2 groups did not ingest any FOSs. Results from the study showed that the number of instances in which gastrointestinal symptoms required treatment was not different between the renal nutritional without FOSs and the renal

nutritional with FOSs. Similarly, there were no differences between the 3 treatment groups regarding the number of patients who experienced symptoms that required treatment, the number of patients who withdrew because of gastrointestinal symptoms, the number of patients who experienced symptoms for at least 3 days, and the number of patients who had diarrhea that required treatment. On the other hand, significantly fewer of the patients who consumed the FOS-containing product experienced constipation that required treatment than those who received the renal product without FOS. Thus, the study showed indirectly that ingestion of as much as 18.5 g of FOSs daily was well tolerated by adult hemodialysis patients.

Physiologic Effects of FOSs

Fructooligosaccharides resist degradation by human alimentary enzymes⁹⁰ and pass intact through the stomach and small intestine. Once these compounds reach the colon, anaerobic bacteria ferment them to obtain energy and carbon for their own growth (Fig 2). During the process, bacteria also generate short-chain fatty acids (SCFAs) gas, and heat. As a result of the fermentation, there is an increase in the concentration of bifidobacteria in the large intestine,^{88,91} an increase in calcium absorption,⁹² an increase in fecal weight,⁹³ a shortening of gastrointestinal transit time,⁹⁴ and a possible hypolipidemic effect.⁹⁵ Other effects observed in animal models include (1) an increase in cecal weight⁹⁶ because of the increased availability of energy in the form of SCFAs for the gut wall and (2) an increase in fecal nitrogen excretion⁹⁷ because of the additional capture of ammonia nitrogen as microbial mass and increased excretion of colonic bacteria in the feces. The increased numbers of bifidobacteria in

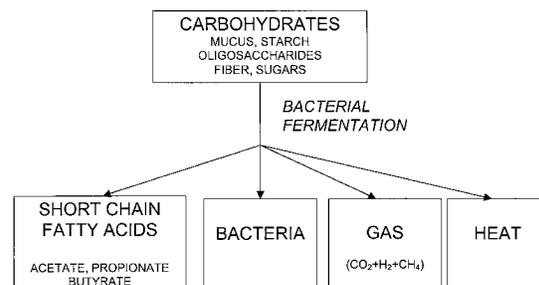


Figure 2. Fermentation of carbohydrates by colonic bacteria. Fermentation results in the production of SCFAs, bacteria cell growth, gas, and heat.

the colon have been assumed to positively benefit human health through a number of mechanisms⁶ including (1) the production of strong acids⁹⁸ and other inhibitory substances^{99,100} that inhibit the growth of potential pathogens, (2) the lowering blood ammonia levels by protonating ammonia in the colon,¹⁰¹ and (3) the production of vitamins¹⁰² and digestive enzymes.¹⁰³

Potential Application for Renal Patients

In populations that are frequently affected by diabetes, such as the end-stage renal disease population, FOSs could potentially serve as a sugar substitute. FOSs have 40% of the sweetness of sucrose, and they have no unpleasant aftertaste. Because FOSs are neither digested nor absorbed in the small intestine, their ingestion does not elevate blood glucose levels.¹⁰⁴ In addition, FOSs contain only 40% of the caloric content of hexoses (glucose or fructose) on a gram-for-gram basis (1.5 kcal/g for fructans *v* 3.9 kcal/g for hexoses¹⁰⁵).

Chronic constipation is a common problem among the dialysis population,¹⁰⁶⁻¹⁰⁹ with an estimated 40%¹⁰⁸ to 71% of patients¹¹⁰ affected by this gastrointestinal disorder. The magnitude of the problem is not surprising given that this patient population carries many of the risk factors associated with constipation such as uremia, electrolyte imbalances, and restricted water intake.¹¹¹ In addition, the advanced age of these patients, inactivity, and comorbid conditions such as diabetes mellitus and cardiac disease adversely affect bowel function.¹¹¹ The administration of multiple medications including iron supplements, calcium- or aluminum-containing phosphate binders, and opioids and the dietary restrictions imposed on dialysis patients likely contribute to the problem.

FOSs could potentially serve to alleviate constipation in the dialysis population.¹¹²⁻¹¹⁶ The mechanism by which FOSs is thought to alleviate constipation is likely to be similar to that of lactulose and sugar alcohols.¹¹⁶ If the rate at which these undigested compounds enter the colon exceeds the colonic capacity to ferment them, excess molecules create an osmotic effect and draw water into the colon. In turn, the water drawn into the colon acts to soften stools. Moreover, because 30% of wet fecal weight is made up of bacteria,¹¹⁷ these compounds may also increase

stool weight by supplying energy and carbon for bacterial growth. However, unlike lactulose and sugar alcohols, the severity of side effects associated with ingestion of FOSs, such as abdominal cramping, should be significantly less because of its lower osmolarity on a weight-to-weight basis.¹¹⁶

Despite the presence of bacterial overgrowth in the small bowel of patients with chronic renal failure, FOSs would still likely reach the colon fully intact. Although the bacterial species present in small bowel bacterial overgrowth aspirates are similar if not identical to those found in the colon,¹¹⁸ the mean concentration of bacteria in small bowel bacterial overgrowth is only 10^8 organisms per milliliter (*v* 10^2 colony-forming units per milliliter in healthy humans¹¹⁹), whereas the concentration of bacteria in the colon often exceeds 10^{11} colony-forming units/mL. Thus, the concentration of bacteria in the colon would be at least 1,000 times greater than that in the small bowel. Consequently, fermentation should occur at a much slower rate in the small bowel than in the colon, even in small bowel bacterial overgrowth.

Products Containing FOSs

In Japan, where FOSs have been officially recognized as a food for Specified Health use by the government, FOSs have been incorporated into numerous products including candies, beverages, and even infant formula. In contrast, the use of FOSs in the United States has been primarily limited to dietary supplements in which it frequently appears in combination with probiotics because of the belief that a mixture of these 2 ingredients would benefit the host "by improving the survival and the implantation of live microbial dietary supplements in the gastrointestinal tract, by selectively stimulating the growth and/or by activating the metabolism of one or a limited number of health-promoting bacteria, and thus improving host welfare."⁵ Only during the last several years have FOSs started to appear in food products. For example, inulin, a long-chain fructan polymer, was recently added to a commercial yogurt (Stonyfield Farm, Manchester, NH), and NutraFlora FOS has been added to a number of liquid nutritional formulas including 1 intended for use in people with end-stage renal disease.

Conclusions

Probiotics and FOSs could potentially provide several benefits to renal patients. As an example, probiotics may reduce the levels of certain toxic compounds generated by the small bowel flora that are thought to contribute to some of the neurologic symptoms of uremia. On the other hand, FOSs, which also happen to have a very low glycemic index and lower energy content than glucose or fructose, could potentially function in the capacity of a dietary fiber supplement to help maintain regularity in this patient population or as a reduced calorie sweetener for diabetic patients.

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