Health Effects and Sources of Prebiotic Dietary Fiber

Justin L Carlson,1 Jennifer M Erickson,1 Beate B Lloyd,2 and Joanne L Slavin1

1Department of Food Science and Nutrition, University of Minnesota, St. Paul, MN and 2Global Scientific & Regulatory Affairs, The Coca-Cola Company, Atlanta, GA

Abstract

Prebiotic dietary fibers act as carbon sources for primary and secondary fermentation pathways in the colon, and support digestive health in many ways. Fructooligosaccharides, inulin, and galactooligosaccharides are universally agreed-upon prebiotics. The objective of this paper is to summarize the 8 most prominent health benefits of prebiotic dietary fibers that are due to their fermentability by colonic microbiota, as well as summarize the 8 categories of prebiotic dietary fibers that support these health benefits. Although not all categories exhibit similar effects in human studies, all of these categories promote digestive health due to their fermentability. Scientific and regulatory definitions of prebiotics differ greatly, although health benefits of these compounds are uniformly agreed upon to be due to their fermentability by gut microbiota. Scientific evidence suggests that 8 categories of compounds all exhibit health benefits related to their metabolism by colonic taxa. Curr Dev Nutr 2018;2:nzy005.

Introduction

The health effects of dietary fiber have been extensively reviewed and accepted worldwide (Table 1). By contrast, prebiotics were first defined in 1995 and their definition has continued to evolve over time (Table 2). The health effects of prebiotic dietary fibers have not been as well defined (8, 9) and the objective of this review is to define prebiotic dietary fiber and summarize the fibers for which clinical trials support their designation as prebiotic dietary fibers.

Prebiotic dietary fibers are specific, microbiota-shaping compounds that function as a carbon source for growth of beneficial taxa, thus delivering a specific or selective change that confers the host health related to its metabolism.

Research on prebiotic dietary fiber has found that although changes in specific gastrointestinal (GI) taxa are often correlated with health, this effect alone is not considered a direct health benefit under most conditions (10). These health benefits rely on more than taxonomic changes, display health effects that are physiologically beneficial to the host or consumer, and are related to the metabolism of the prebiotic dietary fibers.

There have been many approaches to how prebiotics are defined and marketed. With an increased consumption of prebiotics and increased demand for foods with these ingredients, it’s imperative to understand where, how, and to what extent the phrase “prebiotic” can be used. Across the globe there are still regulatory hurdles in place for the use and advertisement of the phrase “prebiotic”, leading to discrepancies and confusion amongst consumers.

The goal of our review is to connect the research on fermentable dietary fibers with the research in prebiotics. Since dietary fiber has more regulatory acceptance around the world, we believe a review that defines prebiotic dietary fiber and presents the fibers that have been shown to be prebiotics will assist in bridging the gap between dietary fiber and prebiotics.

Prebiotic Fiber Definitions

Scientific definitions of prebiotic

The first published definition of the word “prebiotic”, in 1995, was, “nondigestible 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, thus improving host health” (1); 8 y later this changed to include “a selectively fermented ingredient that allows specific changes, both in the composition and/or activity in the gastrointestinal microbiota that confers benefits” (3). In 2010 the International Scientific Association for Prebiotics and Probiotics (ISAPP) widened that definition to include focus on the functionality of prebiotics: “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” (6). Recent definitions have suggested a more comprehensive approach: “a nondigestible compound that, through its metabolism by microorganisms in the gut, modulates composition and/or activity of the gut microbiota, thus conferring a beneficial physiologic effect on the host” (7). As scientific definitions evolve, the term “prebiotic” is being updated to reflect scientific changes that deepen our understanding and perception of the importance of the gut microbiota in their entirety (Table 2).

### Consumption of prebiotics worldwide

The consumption of prebiotics is difficult to measure since they are found in very diverse food groups, in wide ranges of supplements, and there isn’t an analytic test or universally agreed-upon method. Inulin is a prebiotic that occurs naturally in leeks, asparagus, onions, wheat, garlic, chicory, oats, soybeans, and Jerusalem artichokes. Estimated consumption in US and European diets is several grams a day for natural and/or activity in the gut microbiota. Estimated consumption in US and European diets is several grams a day for naturally occurring prebiotics [inulin and fructooligosaccharides (FOSs)] (11, 12). Without universal definitions of prebiotics and inclusive lists of ingredients included, epidemiologic tracking of prebiotic consumption patterns will be difficult to obtain. Although hard to measure with epidemiologic analysis, the increase in the functional food market, specifically in regards to foods that contain prebiotics, has been tremendous over the last 2 decades. Globally, the prebiotic market is expected to continue to grow, exceeding $7.5 billion by 2023 (13).

### Why do we care about our microbiome?

The gut microbiome coevolves within the host—bacteria eat what consumers eat. Short-term, diet rapidly alters the composition of the gut microbiota, often dependent on the diet duration and its macronutrient composition (14). Differences in gut bacteria exist between individuals in various countries; however, the similarity of fecal microbiomes among family members extends across countries and cultures (15). External factors also have a significant influence on the composition and/or activity of the gut microbiota, including antibiotics, stress, climate, infection, disease, cancer, exogenous organisms, and many other factors (16–18).

All regulatory and scientific definitions emphasize the importance of prebiotics demonstrating “health benefits”. Acting as a primary carbon source for fermentation is still the most critical component for prebiotics. Future research will have to address casual, mechanistic pathways of suggested health benefits for a wide spectrum of dietary compounds with beneficial and therapeutic effects, not limited to only changes in GI taxa.

Literature, marketing, and regulation have produced more health-conscious consumers that want to consume a diet that supports their gut and digestive health. The purpose of this paper is to summarize the 8 most prominent health benefits of prebiotic dietary fibers that are due to their fermentability by colonic microbiota, as well as summarize the 8 categories of prebiotic dietary fibers that support these health benefits.

### Regulatory definitions of prebiotics and fiber worldwide

Regulatory agencies around the world are changing their definitions of dietary fiber to adapt to physiologic function rather than only chemical composition. Nearly all scientific and regulatory definitions include prebiotics as dietary fiber, although there are many emerging prebiotics that don’t fall under any dietary fiber definition. Regulatory definitions have suggested a more comprehensive approach: “a nondigestible compound that, through its metabolization by microorganisms in the gut, modulates the composition and/or activity of the gut microbiota, thus conferring a beneficial physiologic effect on the host.”

### TABLE 2

#### The evolution of the changes in the scientific definitions of “prebiotic”†

| Year | Definition | Reference                  |
|------|------------|----------------------------|
| 1995 | A nondigestible food ingredient 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. | Gibbons and Roberfroid (1) |
| 2003 | Nondigestible substances that provide a beneficial physiologic effect on the host by selectively stimulating the favorable growth or activity of a limited number of indigenous bacteria. | Reid et al. (2) Inaugural ISAPP Meeting |
| 2004 | A selectively fermented ingredient that allows specific changes, both in the composition and/or activity in the gastrointestinal microbiota that confers benefits upon host well-being and health. | Roberfroid (4) IDF/FAO Meeting |
| 2007 | A selectively fermented ingredient that allows specific changes, both in the composition and/or activity in the gastrointestinal microbiota, that confer benefits upon host well-being and health. | FAO Technical Meeting (5) (2007) |
| 2008 | A nonviable food component that confers a health benefit on the host associated with the modulation of the microbiota. | Gibbons et al. (6) ISAPP 6th Annual Meeting |
| 2010 | A selectively fermented ingredient that results in specific changes in the composition and/or activity of the gastrointestinal microbiota, thus conferring benefits upon host health. | Bindels et al. (7) |
| 2015 | A nondigestible compound that, through its metabolization by microorganisms in the gut, modulates the composition and/or activity of the gut microbiota, thus conferring a beneficial physiologic effect on the host. |                         |

†IDF, International Dairy Federation; ISAPP, International Scientific Association for Prebiotics and Probiotics.
The phrase “prebiotic” has been defined very differently around the world (Table 3). Globally there is a wide variation in claimed health benefits of prebiotics, and many gaps within and between global regulatory agencies.

### Health Impacts of Prebiotic Dietary Fibers

#### Effect on hind gut bacteria composition

Because of the many health-promoting properties of these genera of bacteria, they are commonly used markers of microbiota health and common targets for dietary stimulation. Lactobacilli and Bifidobacteria have been shown to downregulate mucosal inflammation in the GI tract (21). Lactobacilli play a role in helping digest lactose for lactose-intolerant individuals, alleviate constipation, improve irritable bowel syndrome (IBS) symptoms, and potentially help prevent traveler’s diarrhea (22). Bifidobacteria reside naturally in the GI tract of healthy human adults and have a strong affinity to ferment select oligosaccharides, making them a common marker for prebiotic capacity. Similar to the Lactobacillus, these bacteria are saccharolytic, an often-used marker for beneficial bacteria (23). Bifidobacteria also do not produce any known carcinogenic substances in vivo. Bifidobacteria concentrations have been negatively associated with obesity and weight gain (24–27). Specific species might play a critical role in this association, as not all species of Bifidobacteria may have identical influence (28). Decreases in Bifidobacteria, along with decreases in bacterial diversity, have been associated with higher inflammation and IBS (29, 30). The mechanisms behind disease states and Lactobacilli and Bifidobacteria are unclear, but sufficient studies show that these bacteria are highly associated with health.

#### Metabolite production

Primary and secondary metabolites that are formed due to the direct or indirect fermentation of selective compounds have been correlated with many health benefits in humans. SCFAs (< 6 C) are produced by the gut microbiota due to the fermentation of carbohydrates, amino acids, and other nutrients that are unabsorbed in the proximal small intestine. Acetate, propionate, and butyrate represent 90–95% of all SCFAs produced in the colon. Acetate resembles over half of the SCFAs detected in human feces (31) and is a preferred source of metabolizable energy for muscles (32). Propionate and butyrate are negatively associated with some GI disorders that are due to inflammatory response pathways, including ulcerative colitis (33). Although SCFA production has many positive outcomes, there is a wide range in response between individuals for the same dietary fiber, even in controlled systems (34). The beneficial effects of SCFAs have been extensively reviewed elsewhere (35).

The fermentation of inulin-type fructans has been shown to increase urinary hippurate concentrations in clinical studies (36). Hippurate is a microbial mammalian co-metabolite, and has been found in decreased concentrations in obese individuals compared to lean individuals, and also in diabetics compared to nondiabetics (37–39). Increased urinary hippurate concentrations are considered a beneficial effect of inulin consumption due to its fermentation (36).

#### Effect on mineral absorption

Decreasing risk of osteoporosis and bone fractures is a critical issue worldwide, with >28 million people in the US having osteoporosis or low bone mass, and 1 in 8 EU citizens > 50 y of age fracturing their spine each year (40). Increasing the bioavailability and absorption of calcium with the intake of prebiotics is a critical target for healthy bone structure in adolescent and elderly populations (41). The distal intestine is one of the primary sites of calcium absorption, and absorption is stimulated by the chemical changes and increases in acid fermentation of the prebiotic dietary fibers by various bacteria.

Clinical studies measuring mineral absorption in varying populations have reported mixed results. Inulin, oligofructose, galactooligosaccharides (GOSs), and short-chain FOSs have been shown in 4 studies not to have a significant impact on calcium absorption when...
participants consumed 1–17 g/d (42–45). Six clinical studies with the same treatments, plus a lactulose treatment, and similar dosages (8–40 g/d) all showed significant increases in calcium absorption (46–51). Results in studies may depend on the age and physiology of participants, as subjects during puberty and after menopause may have a higher affinity and demand for calcium uptake, and could be dependent on the variation and development of the participants’ microbiota. Extensive reviews of animal and human studies and their impact on bone structure have been conducted (52).

Effect on protein fermentation
Protein fermentation, from either undigested or endogenous protein sources, occurs in the absence of fermentable carbohydrates, which can potentially lead to formation and accumulation of potentially harmful metabolites such as sulfides, amines, ammonia, and various phenols (53). In the absence of fermentable carbohydrates, SCFA concentration decreases and the pH of the environment increases, which results in a favorable environment (distal colon) for efficient protein fermentation, leading to the production of branched-chain fatty acids and various phenols and indoles, which are unique to bacterial metabolism. Increases in saccharolytic fermentation, rather than proteolytic fermentation, have many potential health benefits.

Clinical studies in which subjects consumed lactulose have consistently shown decreases in major proteolytic markers. Ballongue et al. (54) found lactulose (2 × 10 g/d) feeding led to a decrease in fecal phenol, p-cresol, fecal indole, and skatol. De Preter et al. (55) found decreases in urinary ammonia, whereas fecal ammonia was unaffected after subjects were fed either 15 g/d or 2 × 10 g/d. The same treatments have also been shown to decrease urinary p-cresol (56). Four-week inulin treatments (3 × 5 g/d) resulted in decreases in both urinary and fecal ammonia (57). Similar studies (n = 11) have shown resistant starch (RS) mixture (39 g/d) to decrease fecal ammonia (58) whereas urinary ammonia was unaffected, whereas other studies found that RS2 didn’t affect fecal ammonia (n = 23; 32 g/d) but RS3 significantly decreased fecal ammonia concentrations (59). Arabinooligosaccharides (n = 10; 2 × 5 g/d) have been shown to decrease urinary p-cresol (60).

Change in pathogenic bacterial populations
The gut mucosa and microbiota are key components that act against pathogenic invasion within the GI tract, inhibiting pathogens such as E. coli, Salmonella spp, Campylobacter, and other pathogenic bacteria (61). Five potential mechanisms include: acidic metabolic end products (acids) that lower the colonic pH below pathogenic bacterial thresholds, competitive effects due to limitations in numbers of colonization sites, antagonism through inhibitory peptides (produced by lactic acid bacteria), competition for limited nutrients, and enhancement of the immune system (62).

Effect on allergy risk
Microbial diversity in the gut plays an influential role in the development of many inflammatory diseases and conditions, including allergic diseases, which can be influenced by disturbed gut colonization or by generally reduced microbial diversity (63). Decreased levels of Bifidobacteria and Lactobacilli have been associated with the development of allergy diseases in the first 5 y of life (64, 65). Many mechanisms have been identified showing the importance of dietary oligosaccharides and their immune-modulating effects (66). FOS/GOS (8 g/L hypoallergenic formula) supplementation has shown allergy-protective effects, specifically against the development of eczema and rhinoconjunctivitis. The Cochrane report study also showed a significant reduction in eczema in 1218 infants analyzed in the early stages of life when supplemented with GOS/FOS (9:1 ratio; 8 g/L added to

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**TABLE 4** Regulatory prebiotic definitions worldwide

| Regulatory body          | Prebiotic regulatory status or definition                                                                                                                                 |
|--------------------------|-----------------------------------------------------------------------------------------------------------------|
| FDA2                     | “Complementary and alternative medicine products” are subject to FDA regulation. Prebiotics are included in the “biologically-based” group of foods, under the Center for Complementary and Integrative Health (a subset of NIH), using the 1995 definition. Manufacturers can also self-affirm GRAS status for products labeled as prebiotics (19). |
| EFSA2                    | FAO definition, “a nonviable food component that confers a health benefit on the host associated with modulation of the microbiota” (5, 20)                                                                                     |
| Health Canada            | The phrase “prebiotic” is only allowed for products that satisfy the requirement for an approved health claim. The phrase “prebiotic” on labels is regulated as an implied health claim (Canada Food Inspection Agency).                                  |
| Japan (FOSHU)            | “Prebiotic” not used, but rather “foods to modify gastrointestinal conditions.”3                                                                                           |
| Costa Rica (RTCA)       | A prebiotic substance must: be preferred by ≥1 species of beneficial bacteria in the large intestine or colon, be resistant to gastric acids, be fermentable by intestinal microflora, be resistant to endogenous enzymatic hydrolysis, stimulate selectively the growth and/or activity of those bacteria that are associated with health and wellness.4 |
| Colombia                 | A prebiotic substance must: be a preferred substance by ≥1 species of beneficial bacteria in the large intestine or colon, be resistant to gastric acids, be fermentable by the intestinal microflora, be resistant to endogenous enzymatic hydrolysis, have the ability to produce changes in the lumen of the large intestine or in the host organism showing health benefits, selectively stimulate the growth and/or activity of those bacteria that are associated with health and wellness.4 |

1. EFSA, European Food Safety Authority; FOSHU, food for specified health uses; GRAS, generally recognized as safe; RTCA, Reglamento Tecnico Centroamericano.
2. Neither FDA or EFSA has their own definition of prebiotics.
3. Accepted foods/ingredients include: oligosaccharides, lactose, bifidobacteria, lactic acid bacteria, ingestible dextrin, polydextrol, guar gum, psyllium seed coat, etc.
4. The amount of food to be consumed to obtain the beneficial effect should be reasonable in the context of the daily diet.
cow milk–based formula) (67). Although evidence is limited for the potential mechanisms, human and animal studies have recently been conducted to further explore these allergy prevention pathways (68–71).

**Effects on gut barrier permeability**

Epithelial cells are the cellular barriers that line the mucosal surfaces in the body that provide protection against the environment. Intestinal goblet cells produce mucus, which form a hydrated gel that prevents large particles (most bacteria) from contacting the epithelial cell layer. The phrase “leaky gut” comes from the phenomena in which tight junctions that promote the barrier mechanisms of the GI epithelial lining (the paracellular space between epithelial cells) become compromised. This occurrence is typically associated with inflammation (72, 73). Claudins, zonula occludens-1, and occludin are proteins responsible for tight junctions, which can be modulated and suppressed by high-fat diets in mice (74, 75). SCFAs, produced by the fermentation of prebiotic dietary fiber, can also contribute to improved intestinal barrier function. Research has shown that the application of individual and combination SCFA mixtures increased transepithelial electrical barrier function. Research has shown that the application of individual and combination SCFA mixtures increased transepithelial electrical resistance, and decreased paracellular transport markers in rat caecal walls (76). Oligofructose has been shown to promote selective microbiota change (*Bifidobacterium* spp), leading to increases in endogenous glucagon-like peptide-2 (GLP-2) production, thus improving gut barrier functions and providing tighter junctions and less inflammation (77).

Improved GI barrier integrity can help reduce plasma LPS. LPSs are a bacterially derived endotoxin, are an inflammatory reagent that plays a role in the development of inflammatory metabolic disorders and conditions, and are primarily found in gram-negative bacteria (78). LPSs induce the activation of Toll-like receptor 4, which leads to inflammation due to the release of pro-inflammatory cytokines and chemokines (79). Oligofructose-enriched inulin (10 g/d) has been shown to significantly decrease plasma LPSs, compared to maltodextrin, for women with type 2 diabetes (80).

**Effects on immune system defense**

Many types of cells found in the GI tract of the host play a critical role in immune system response and signaling. T*REG* cells, effector T cells, natural killer cells, and B cells are all influenced by prebiotics and the metabolites that are formed by their fermentation (81, 82). Although the exact mechanisms influencing the immune system are unknown, it is likely a result of the metabolites, including SCFAs, occurring from the fermentation of prebiotics. Butyrate in particular has been shown to influence macrophages, T cells, and dendritic cells (81).

**Prebiotic Dietary Fiber Sources**

Various categories of prebiotic dietary fibers show different health benefits. FOSs, inulin, and GOSs have long been considered prebiotics. However, many other categories and compounds offer health benefits to consumers, although in varying ranges of efficacies. The following 8 categories of prebiotic dietary fiber have sufficient evidence that they promote digestive health for consumers.

**Beta-glucan**

Beta-glucans are soluble compounds located in the endosperm cell walls of cereal grains, composed of linear D-glucopyranosyl units with a mixture of β-(1,3) and β-(1,4) glycosidic linkages, and are also found in foods like mushrooms, algae, and other marine plants. Oat and barley are the 2 highest sources of beta-glucans today in the diet (83). Because of their variation in terms of branching and length, beta-glucans can have a wide range of impacts on host GI health (84).

**FOSs, oligofructose, and inulin**

Fructan compounds (β[2,1]-fructans) are found in a wide range of structures and foods. Inulin typically has a degree of polymerization (DP) of between 3 and 60 fructan monomers. Oligofructose is made from the chemical degradation of these products with endoglucosidase enzymes, yielding a product with a DP of 2–20. FOSs are typically produced from the transfructosylation of sucrose and contain 2 and 4 β(2,1)-linked fructosyl units. All of these compounds exert strong bifidogenic effects, although the length of polymerization influences these effects (85).

**GOSs**

GOSs are mixtures of oligosaccharides derived from the enzymatic glycosylation of primary lactose, primarily using β-galactosidases to catalyze various transgalactosylation reactions (86). Typical GOSs are composed of 2–10 molecules of galactose and 1 molecule of glucose, primarily synthesized from enzymatic activity (87). The purity, degree of polymerization, type, and dosage of GOSs influence the prebiotic capacity in many clinical studies (86).

**Isomaltooligosaccharides**

Isomaltooligosaccharides are glucose monomers linked by α(1,6)-glucosidic linkages made from the enzymatic treatment of cornstarch with α-amylase, pullulanase, and α-glucosidase (88), and its primary components are isomaltose, isomaltotriose, and panose. Depending on the final DP, effective doses range from 5–10 g/d for most individuals (89). Doses as high as 30 g/d have also been shown to be tolerated in adults, with only mild GI side effects being noted (90).

**Guar gum**

Guar gum, in its intact state, is a gel-forming galactomannan made from the endosperm of the plant *Cyamopsis tetragonolobus*, and is composed primarily of high molecular weight polysaccharides ([1,4]-linked β-D-mannopyranosyl units with [1,6]-linked α-D-galactopyranosyl side chain residues) (91). Guar is commonly used in dairy, bakery, cereal, and meat products.

**Lactulose**

Lactulose is a disaccharide composed of galactosyl β(1,4) fructose derived from the primary and secondary isomerization of lactose, not digestible by mammalian enzymes, nor hydrolyzed or absorbed in the small intestine. Although not found naturally in foods, limited clinical studies have consistently shown beneficial effects due to the fermentation of these compounds.
RSs and maltodextrin

RSs are a broad categorization of many classes of starches formed under a variety of conditions, but all escape digestion in the upper GI tract. Resistant maltodextrin is a low-viscosity, highly water-soluble dextrin that is produced by treating cornstarch with numerous acid, enzymatic, and heating processes, and used in a variety of applications. Some RSs are found naturally in foods, whereas others are purely synthetic (92).

Xylooligosaccharides and arabinoxylooligosaccharides

Xylooligosaccharides (XOSs) are composed of between 2 and 10 xylose monomers linked with $\beta$ 1,4 bonds with DP $\leq$ 20 (93, 94). XOSs are commonly found in dairy products, cereals, bars, sports drinks, and isotonic beverages (95). Doses of $\leq$ 12 g/d have been shown to be well-tolerated in human intervention studies. Japan is responsible for nearly half of the production and consumption of XOSs worldwide, and they have been approved as an ingredient for “Food for Specified Health Use” since 1991, and according to regulation, are expected to have a specific effect on health (96).

Conclusion

Prebiotic dietary fibers are broad categories of compounds, that all display health benefits to improve the digestive health of consumers. As with other dietary compounds, moderation and variety still constitute the most critical part of recommendation and usage. The 8 classes of prebiotic dietary fibers all display $\geq$ 1 of the 8 health benefits directly due to the fermentation of the compounds. The traditional prebiotics of FOSs, inulin, and GOSS still provide the most evidence of beneficial health effects due to their fermentation, but many other categories of compounds may be as effective as, or more effective than, the traditional prebiotics. When taken in appropriate dosages, all 8 of these categories of compounds support digestive health due to their fermentation.

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