

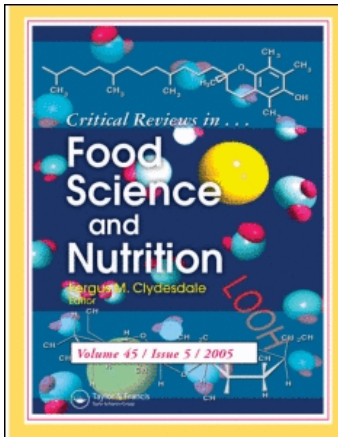
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# Gastrointestinal Effects of Low-Digestible Carbohydrates

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*Low-digestible carbohydrates (LDCs) are carbohydrates that are incompletely or not absorbed in the small intestine but are at least partly fermented by bacteria in the large intestine. Fiber, resistant starch, and sugar alcohols are types of LDCs. Given potential health benefits (including a reduced caloric content, reduced or no effect on blood glucose levels, non-cariogenic effect) the prevalence of LDCs in processed foods is increasing. Many of the benefits of LDCs are related to the inability of human digestive enzymes to break down completely the carbohydrates into absorbable saccharides and the subsequent fermentation of unabsorbed carbohydrates in the colon. As a result, LDCs may affect laxation and cause gastrointestinal effects, including abdominal discomfort, flatus, and diarrhea, especially at higher or excessive intakes. Such responses, though transient, affect the perception of the well-being of consumers and their acceptance of food products containing LDCs. Current recommendations for fiber intake do not consider total LDC consumption nor recommend an upper limit for LDC intake based on potential gastrointestinal effects. Therefore, a review of published studies reporting gastrointestinal effects of LDCs was conducted. We included only studies published in refereed journals in English. Additionally, we excluded studies of subjects with incomplete or abnormal functioning gastrointestinal tracts or where antibiotics, stimulant laxatives, or other drugs affecting motility were included. Only in studies with a control period, either placebo treatment or no LDC treatment, were included. Studies must have included an acceptable measure of gastrointestinal effect. Sixty-eight studies and six review articles were evaluated. This review describes definitions, classifications, and mechanisms of LDCs, evaluates published human feeding studies of fifteen LDCs for associations between gastrointestinal effects and levels of LDC intake, and presents recommendations for LDC consumption and further research.*

**Keywords** laxation, nonstarch polysaccharides, resistant starch, sugar alcohols, polyols, dietary fiber

## BACKGROUND

Low-digestible carbohydrates (LDCs) are carbohydrates that are incompletely or not absorbed in the small intestine but are at least partly fermented by bacteria in the large intestine (Marteau and Flourié, 2001). Dietary fiber is commonly associated with this mechanism, but LDCs also include resistant starches and sugar alcohols, also known as polyols.

Researchers have identified potential health benefits of consuming LDCs. Low-digestible carbohydrates affect satiety, gastric emptying, glucose absorption, fat metabolism, nitrogen excretion, fermentation, short-chain fatty acid (SCFA) production, microflora, and fecal bulk (Sheppach et al., 2001). In addition, clinical research has suggested that the consumption of some of these carbohydrates may decrease the factors associated with metabolic syndrome (obesity, diabetes, hyperlipidemia, and

hypertension) and may prevent or treat other chronic diseases (Sheppach et al., 2001). These carbohydrates provide less energy per gram than fully-digestible sugars (sucrose or high-fructose corn syrup), so food manufacturers use some LDCs (especially sugar alcohols) as sugar replacers. This may help consumers reduce their energy intake in order to lose or maintain weight over time. Also, these carbohydrates may modulate blood glucose levels, so foods with naturally-occurring or added LDCs may be appropriate choices for patients with diabetes (Gee et al., 1991; Livesey, 2003). In addition, patients with hepatic encephalopathy, bacterial translocation, colitis, colonic carcinogenesis, constipation, symptoms of diverticulosis, or irritable bowel syndrome may benefit from consuming LDCs (Sheppach et al., 2001). Due to these potential health benefits, the prevalence of LDCs in processed foods is increasing.

Many of the benefits of LDCs are related to the inability of human digestive enzymes to break down completely the carbohydrates into absorbable saccharides (Sheppach et al., 2001) and the subsequent fermentation of unabsorbed carbohydrates in the colon. As a result, these carbohydrates may affect laxation

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and contribute to gastrointestinal effects, including abdominal discomfort, flatus, and diarrhea (Livesey, 2001), especially at higher or excessive intakes. Such symptoms, though transient, affect the perception of the well-being of consumers and their acceptance of food products containing LDCs. Therefore, it is prudent to identify the upper intake levels so as to minimize the risk of undesirable gastrointestinal effects while maximizing the potential health benefits of LDC consumption.

Some recommendations have been made for general carbohydrate consumption by the Institute of Medicine (IOM): The Acceptable Macronutrient Distribution Range (AMDR) for carbohydrates is 45–65% of energy intake, and the Adequate Intake (AI) for total fiber is 38 grams for men and 25 grams for women (IOM, 2005). However, these recommendations are based on reducing the risk of coronary heart disease and other diseases, and do not consider total LDC consumption (fiber, resistant starches, and sugar alcohols) nor recommend an upper limit for LDC intake based on potential gastrointestinal effects. Therefore, it is necessary to review human feeding studies for associations between consumption of LDCs and gastrointestinal effects in order to make recommendations for acceptable levels of LDC consumption and further research in this area.

### CLASSIFICATIONS AND DEFINITIONS OF LDCS

Carbohydrates may be classified according to chemical, nutritional, or physiological criteria (Cummings et al., 1997; Englyst and Englyst, 2005). Chemical classifications consider units, linkages, degrees of polymerization (DP), and functional groups of carbohydrates. Nutritional classifications consider the behavior of carbohydrates in the gastrointestinal tract, whether they are absorbable, digestible, or fermentable. Physiological classifications consider the effects on blood glucose and other parameters. Chemical structure mediates the digestion, absorption, and fermentation of LDCs, and the nutritional perspective is predictive of potential gastrointestinal effects associated with LDC intake.

Absorbable carbohydrates (monosaccharides) are absorbed in the small intestine without any digestion in the mouth or small intestine. Although intestinal cells absorb a small percentage of monosaccharides passively, most monosaccharides require a carrier for absorption. In general, carbohydrates with at least two units must be enzymatically digested into monosaccharides before they can be absorbed in the small intestine and enter circulation.

Digestible carbohydrates include disaccharides such as lactose and sucrose as well as polysaccharides such as starch. Salivary alpha-amylase hydrolyzes the alpha-1,4 linkages in starch, yielding the disaccharide maltose, the trisaccharide maltotriose, and dextrans with 5–9 glucose molecules. Pancreatic alpha-amylase continues to digest starch into maltose in the small intestine. Disaccharidases in the brush border of the small intestine (maltase, sucrase, and lactase) complete carbohydrate digestion by hydrolyzing maltose, sucrose, lactose,

into the absorbable monosaccharides glucose, fructose, and galactose.

Fermentable carbohydrates are those that are not digested and absorbed in the small intestine but are metabolized by colonic bacteria. Carbohydrate fermentation may yield short-chain fatty acids (SCFAs) (acetate, propionate, and butyrate) and gases (carbon dioxide, hydrogen, and methane) (Cummings et al., 2001). These products of carbohydrate fermentation are absorbed in the large intestine (providing energy), used by the bacteria for energy, released as flatus, or expelled as biomass in the feces. The category of fermentable carbohydrates includes carbohydrates that cannot be digested because they have linkages for which humans do not have digestive enzymes. (In addition, carbohydrates such as sucrose and lactose though typically digested and absorbed in the small intestine, may be maldigested or malabsorbed; if this occurs, they are fermented in the large intestine.)

Nonfermentable or poorly-fermentable carbohydrates (such as components of plant cell walls) pass through the gastrointestinal tract largely unchanged and are excreted in the feces. These carbohydrates are neither digested in the small intestine nor fermented to a significant degree in the large intestine.

As defined by nutritional parameters, LDCs are carbohydrates that are incompletely or not absorbed in the small intestine and are fermented in the large intestine (Marteau and Flourié, 2001). There are two broad categories of LDCs: fiber and sugar alcohols (Table 1).

Fiber is a significant subset of LDCs. The various definitions and classifications of fiber are based on different chemical assays. Traditionally, definitions have relied on alcohol precipitation tests (IOM, 2001), but Roberfroid (2002) classifies both oligosaccharides and inulin, which do not precipitate in alcohol, as dietary fiber. A Panel on the Definition of Dietary Fiber, convened by the IOM, proposed a definition of dietary fiber that includes nondigestible animal carbohydrates, carbohydrates not recovered by alcohol precipitation but are resistant to human enzymes (such as inulin and oligofructose), nondigestible mono- and disaccharides, lignin, and resistant starch (IOM, 2001). The IOM (2001) definition distinguishes between dietary and added fiber:

1. *Dietary Fiber* consists of nondigestible carbohydrates and lignin that are intrinsic and intact in plants.
2. *Added Fiber* consists of isolated, nondigestible carbohydrates that have beneficial physiological effects in humans.

*Total Fiber* is the sum of *Dietary Fiber* and *Added Fiber*.

The Dietary Reference Intake (DRI) (IOM, 2005) report delineates and defines several types of fiber, most of which occur naturally in foods (dietary fiber) but may also be isolated or manufactured and added to foods (functional fiber); cellulose, chitin, chitosan, beta-glucans, gums, hemicellulose, polydextrose, inulin, fructooligosaccharides (FOS), lignin, pectin, psyllium, resistant dextrans, and resistant starch (RS). All dietary

**Table 1** Classifications and descriptions of low-digestible carbohydrates.

Classifications	Types	Characteristics	Sources
<b>Fiber</b>			
Nonstarch polysaccharides (Fermentable)	Guar gum and PHGG	Linear mannose chain (beta-1,4), galactose units	Guar seeds
	Inulin and fructo- oligosaccharide	Linear or branched fructose chain (alpha-1,2), glucose units; DP 10 (3.5 for FOS)	Wheat, onions, leeks, asparagus, artichokes, bananas, chicory root
Resistant starch (Fermentable)	Polydextrose	Branched glucose polymer; DP 12-15	Synthetic
	RS1	Plant cell walls make bonds physically inaccessible to enzymes	Coarsely ground cereals, legumes, grains, seeds
	RS2	Crystalline structure non-digestible unless gelatinized	Green bananas, raw potatoes, high-amylose starch
	RS3 RS4	Retrograded starch, hydrogen bonds Chemically modified: starch esters/ethers, cross-bonded starches	Cooked and cooled potatoes Synthetic
<b>Sugar alcohols</b>			
Hydrogenated monosaccharides (Absorbable; fermentable*)	Erythritol	4 carbons; synthesized from starch	Synthetic; natural
	Xylitol	5 carbons; synthesized from xylan	Synthetic
	Sorbitol	Hydrogenated glucose	Natural; synthetic
Hydrogenated disaccharides (Digestible; fermentable)	Mannitol	Hydrogenated glucose; isomer of sorbitol	Natural; synthetic
	Isomalt	Hydrogenated sucrose: glucose + sorbitol (alpha-1,6) or mannitol (alpha-1,1)	Synthetic
	Lactitol	Hydrogenated lactose: galactose + glucitol (beta-1,4)	Synthetic
Hydrogenated polysaccharide	Maltitol	Hydrogenated maltose: glucose + sorbitol (alpha-1,4)	Synthetic
	Polyglycitol syrup	Mixture of maltitol, sorbitol, and hydrogenated oligosaccharides	Synthetic

\*Erythritol is not fermentable (Arrigoni et al., 2005; Hiele et al., 1993)

DP = degree of polymerization; PHGG = partially hydrolyzed guar gum; RS = resistant starch.

fibers are potential functional fibers, depending on the evidence of physiological benefits linked to ingestion of these isolated fibers. Fibers may be further categorized separately into categories by starch content: nonstarch polysaccharides (NSP) or starch polysaccharides (RS). This review considers the gastrointestinal effects associated with the NSPs guar gum, inulin and FOS, and polydextrose and RS. These fibers are not digested by human enzymes but are at least partially fermented in the large intestine. There are functional fibers that are not fermented at all, and these fibers would not be considered LDCs.

Sugar alcohols are neither sugars nor alcohols but are hydrogenated saccharides having a hydroxyl group in the place of the ketone or aldehyde group that normally characterizes a sugar. They are also referred to as polyols, nutritive sweeteners, and sugar replacers. This category of LDCs includes the monosaccharides erythritol, xylitol, sorbitol, and mannitol; the disaccharides lactitol, isomalt, and maltitol and the polysaccharide polyglycitol syrup, which is a mixture of saccharides having various chain lengths and higher molecular weights than the mono- and disaccharide sugar alcohols. As a group, sugar alcohols have a wide range of molecular weights and other characteristics that affect their level of digestion, absorption, fermentation, and therefore, potential to cause gastrointestinal effects. Physiologically, they have a low-glycemic effect (Livesey, 2001). Sugar alcohols are partially digested and are excluded from the

definition of fiber because their mechanism of laxation is based on "rapidly changing luminal fluid balance," which the IOM definition does not recognize as a laxation mechanism of functional fiber (IOM, 2005). Di- and polysaccharide sugar alcohols are digestible by human enzymes, but their breakdown may occur more slowly, so these carbohydrates may be incompletely digested and absorbed in the small intestine. Monosaccharide sugar alcohols (erythritol, xylitol, sorbitol, and mannitol) may be incompletely absorbed due to a slower rate of absorption. Sugar alcohols are fermented if they reach the large intestine (Arrigoni, et al., 2005; Hiele et al., 1993).

Although most LDCs occur naturally in foods (Table 1), food manufacturers extract or synthesize LDCs and add them to processed foods in order to increase the fiber content or reduce the caloric content of the food in addition to providing potential health benefits. Low-digestible carbohydrates have numerous food and beverage applications, including dry cereals, baked goods, juices and thickened beverages, gum, chocolate, hard and soft candy, ice cream, dietetic foods, and pharmaceuticals. Guar gum, inulin and FOS, polydextrose, and RS are used by food manufacturers to increase the fiber content of foods. Guar gum can be used to thicken beverages. Inulin and FOS are prebiotics that stimulate the growth of beneficial bacteria in the gastrointestinal tract. Inulin can be used as a fat replacer, while FOS is sweeter and can be used as a sugar replacer. Polydextrose

is not sweet, so it is used to add bulk to foods when intense sweeteners are used. Generally, sugar alcohols are used as sugar replacers.

### **BOWEL FUNCTION AND ADVERSE GASTROINTESTINAL EFFECTS**

The consumption of LDCs has been associated with a number of gastrointestinal effects: acid reflux and heartburn, belching/burping, borborygmi (flatulence in the bowels) and gas emission, colic (spasmodic abdominal pain), laxation (softer and increased frequency of bowel movements), reduced appetite, meteorism (abdominal distention), nausea, rumbling in the gut, stomachache, watery feces, and diarrhea (Livesey, 2001).

Analysis of the frequency, consistency, and weight of bowel movements are used to evaluate bowel function. "Normal" function varies widely between individuals. Constipation and diarrhea are two extremes of abnormal bowel function. Constipation is defined as three or fewer spontaneous bowel movements per week (Lederle et al., 1990). As waste remains in the large intestine, water is absorbed and defecation becomes more difficult. Abdominal discomfort and nausea may be associated with constipation.

Clinical diarrhea is commonly defined as an elevated stool output (>200–250 g/day); watery, difficult to control bowel movements; and more than three bowel movements per day (McRorie et al., 2000). Some researchers used the term "laxation" to refer to a slight increase in the frequency of bowel movements and a softer consistency of feces (Livesey, 2001). A laxative effect is associated with increased stool weight and water content, decreased gastrointestinal transit time, loose stools, bloating and distention, borborygmi (flatulence in the bowels), abdominal discomfort, and flatus (Flood et al., 2004).

Many factors may contribute to changes in bowel function and adverse gastrointestinal effects (Fig. 1). Both LDC and host factors affect gut motility, transit time, enzyme activity, and the composition of intestinal microflora, and these, in turn, affect digestion, absorption, and fermentation, which may increase or decrease laxation.

#### ***Low-Digestible Carbohydrate Factors***

Medium characteristics and the chemical structure of the LDCs affect how the gastrointestinal tract responds to the consumption of particular LDCs. The most important medium characteristic is the form of the food, whether it is a solid or liquid. The form of foods containing LDCs affects oro-cecal transit time (the time from the beginning of consumption of the food until it reaches the large intestine). Liquids travel through the gastrointestinal tract and are absorbed relatively quickly, so LDCs are generally better-tolerated in solid foods rather than in liquids (Jenkins et al., 1980). Acceptability increases when low-digestible carbohydrates are consumed as part of a meal

(Livesey, 2001). The presence of other foods and nutrients such as fat and protein slow transit and decrease the potential for gastrointestinal effects. Factors that increase gastrointestinal transit time generally increase gastrointestinal acceptability of LDCs because they increase the time available for LDC digestion and absorption.

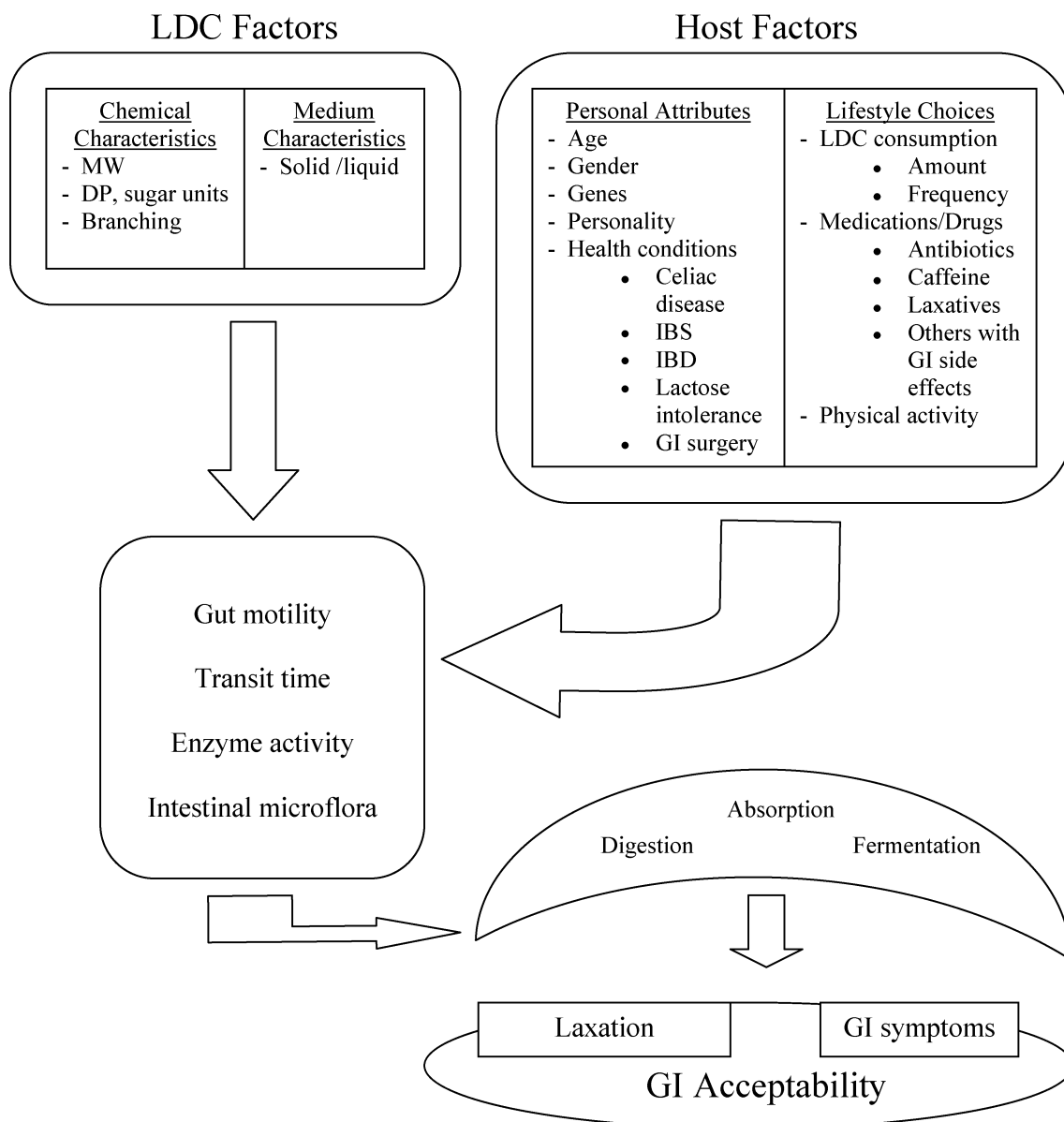
Chemical characteristics include sugar units and functional groups, linkages, branching, degree of polymerization (DP), and molecular weight. For example, the difference between glucose and sorbitol is an additional hydroxyl group on the latter; as a result, sorbitol is absorbed more slowly and incompletely. Sucrose is fully digestible, but isomalt is only partially digested because its alpha-1,6 linkages are more resistant to human digestive enzymes than the alpha-1,2 linkages in sucrose. Incompletely digested and absorbed carbohydrates increase the osmotic load in the intestines. This increase in the number of molecules causes more water to diffuse into the intestines in order to equalize the concentration of the intestinal contents. Low-digestible carbohydrates with relatively small DPs and, therefore, low molecular weights (monosaccharide sugar alcohols, for example) have a greater potential to affect laxation compared to those with higher molecular weights (such as resistant starch) because they have a greater osmotic force and more water reaches the large intestine.

Carbohydrates that reach the large intestine are fermented to different degrees, depending on the degree of polymerization, solubility, and structure of the carbohydrates (Nyman, 2002). Fermentation of the carbohydrates in the large intestine produces gases, which may cause bloating, distention, borborygmi, and flatulence. If the carbohydrates are not fermented in the large intestine, either because the bacteria do not metabolize the carbohydrates or because intake exceeds the fermentation capacity of the bacteria, the water remains bound to the carbohydrates that are eliminated in the feces, which increases fecal bulk (Stephen, 1991) but also may produce a watery stool or diarrhea (Livesey, 2001). In general, individuals would first notice symptoms related to carbohydrate fermentation such as borborygmi and excessive flatus, followed by abdominal discomfort such as bloating and cramps; when the colonic microflora's capacity to ferment the carbohydrates has been exceeded, diarrhea develops (Marteau and Flourie, 2001).

#### ***Host Factors***

Host factors include personal attributes and lifestyle choices. These factors vary largely between individuals and are significant mediators in gastrointestinal function. Some personal attributes are static (gender, genetics, personality), while others change over time (age, weight, health conditions). Lifestyle choices include the usual consumption pattern of LDCs by consumers, medication and drug use, and the level of physical activity.

The oro-cecal transit time varies significantly between individuals (Würsch et al., 1989). Decreased motility and the rate of transit time may lead to constipation as feces harden due



**Figure 1** Factors that affect gastrointestinal acceptability of low-digestible carbohydrates. MW = molecular weight; IBS = irritable bowel syndrome; IBD = irritable bowel disease.

to increased water absorption in the gastrointestinal tract; increased motility and rate of transit time may lead to diarrhea as the time for digestion and absorption may be inadequate and the excretion of water and undigested food increase. The composition of colonic microflora also varies between individuals. Although large intakes of LDCs may cause diarrhea, some people may adapt to moderately high intakes of LDCs over time, likely because the fermentation capacity of the colonic bacteria increases.

Health conditions affect gastrointestinal function and may be associated with gastrointestinal effects, regardless of LDC consumption. Deficiencies of intestinal enzymes cause nutrient maldigestion and gastrointestinal effects. For example, individuals may be deficient in enzymes that normally hydrolyze

disaccharides, as in those who are lactose intolerant. They experience gastrointestinal side effects when consuming milk and other dairy products because they have low activity levels of the enzyme lactase in the brush border of the small intestine. This deficiency is more prevalent in certain populations and often develops as people get older (Gudmand-Høyer and Skovbjerg, 1996), though Di Stefano et al. (2001) have shown that while the prevalence of lactose malabsorption increases with age, the symptoms of lactose intolerance may decrease.

Celiac disease also affects disaccharidase activity and carbohydrate digestion and absorption. Individuals with this disease are unable to digest gluten, a protein in wheat. Atrophy of enterocytes occurs with gluten consumption, and this reduces the digestion of disaccharides by decreasing the activity and amount

of the brush border enzymes (Gudmand-Høyer and Skovbjerg, 1996). A gluten-free diet has been shown to increase the activity levels of these enzymes (Murray et al., 2000).

Individuals with inflammatory bowel disease (IBD: Crohn's disease and ulcerative colitis) may experience exudative diarrhea when nutrient absorption is diminished, which adds to the increased osmotic load from the presence of mucus, blood, and protein from the inflamed gastrointestinal tract (Sartin, 2005). Irritable bowel syndrome (IBS) affects about 20% of adults in the United States and Europe (Sheppach et al., 2001); symptoms of IBS range from diarrhea to constipation as well as bloating, straining, urgency, feeling of incomplete evacuation, and passage of mucus (Zuckerman, 2006). Consumption of LDCs such as partially hydrolyzed guar gum (PHGG) may improve symptoms of patients with IBS (Giannini et al., 2006).

The total amount of LDCs in the diet affects tolerance. Many foods are natural laxatives because they contain indigestible carbohydrates (whole grains, fruits, and vegetables). Therefore, consuming combinations of natural laxatives with or without foods containing added LDCs may increase the occurrence and/or intensity of gastrointestinal effects. Other foods and medications influence the composition and health of colonic microflora. Prebiotics (inulin and FOS) stimulate the growth of bifidobacteria and lactobacilli, which ferment most low-digestible carbohydrates (Cummings and Macfarlane, 2002). Probiotics (live microbial cultures) in foods such as yogurt increase the numbers of intestinal bacteria. In addition, antibiotic treatments may alter colonic bacteria, reducing fermentation of LDCs and causing diarrhea.

### ASSESSMENT OF GASTROINTESTINAL EFFECTS

Gastrointestinal effects may be measured objectively with methods that quantify gastrointestinal function and subjectively with methods that survey subjects of their bowel movements and gastrointestinal symptoms. In addition, an assessment of other physiological parameters provides information on carbohydrate digestion, absorption, or fermentation and may indirectly assist in evaluating the potential gastrointestinal effects of LDC consumption.

Objective methods can measure diarrhea and stool consistency, defecation frequency, flatulence, and abdominal distention. Some studies require subjects to collect their feces during part or all days of the study. Of the fifty studies selected for this review, about one-third collected feces. Fecal collections allow investigators to measure frequency and consistency of bowel movements. Analysis of stool composition and weight (wet, dry, water, isolated nutrients) can identify subjects with diarrhea according to the clinical definition, based on weight, consistency, and frequency of bowel movements as discussed above and in McRorie et al. (2000). In addition, the presence of carbohydrate in the feces indicates carbohydrate malabsorption in the intestine, though this fecal analysis does not ac-

count for the amount of carbohydrate that is fermented in the large intestine. Though rarely used, the measurement of anal gas production may provide an indication of the degree of flatulence and other related symptoms in subjects; the measurement of abdominal girth provides information on abdominal distention.

Most studies reporting gastrointestinal responses to LDC consumption rely on subjective questionnaires. Some investigators provide subjects with a detailed list of potential gastrointestinal effects that may include descriptions of symptoms. Other investigators provide less direction for reporting symptoms by requiring subjects to complete diaries including the occurrence of gastrointestinal effects. Typically, subjects report the occurrence and severity or intensity of gastrointestinal effects and sometimes the duration of these effects. The symptoms and ranking systems vary widely from study to study. For example, subjects may be asked to rate symptoms as none, mild, moderate, or severe; or, subjects may be asked to compare their symptoms to how they normally feel (i.e., normal, slightly more than usual, etc.). In addition, subjects often report the frequency and consistency of bowel movements.

Questionnaires and other similar methods of gathering information on gastrointestinal symptoms are subjective because perceptions of discomfort vary between individuals. The inherent subjectivity of these methods must be taken into account when using results from these assessments to make recommendations for LDC intake to individuals and groups. However, such measurements of gastrointestinal effects provide useful information on the acceptability of LDCs based on factors that affect the quality of life of consumers because they are subjective.

Carbohydrates that are resistant to digestion and absorption in the small intestine may cause gastrointestinal effects, so measuring carbohydrate malabsorption may provide information about potential symptoms that might be associated with particular LDCs. Perfusion and ileostomy studies measure carbohydrate malabsorption directly by analyzing the contents of the ileum or ileostomy bags, respectively, after patients consume a test meal with a polyethylene glycol marker (Cummings and Englyst, 1991; Stocchi and Levitt, 1991). Perfusion studies are highly invasive because they require the insertion of a tube into the GI tract, which could affect gastrointestinal function, and ileostomy studies provide data on patients with incomplete GI tracts, so the application of the results to the general population is questionable.

Hydrogen breath studies measure malabsorption indirectly by measuring hydrogen expiration, which is a product of colonic fermentation (Rumessen, 1992). Individual variables and as well as protocol conditions affect the colonic fermentation capacity and hydrogen breath expiration of subjects; in addition, investigators must include methods to account for carbohydrates that are not fermented but are excreted in the feces (Rumessen, 1992). In addition, correlations between measurements of breath hydrogen levels and the occurrence or severity of gastrointestinal effects reported in study questionnaires or diaries are inconsistent (Jain et al., 1985; Jain et al., 1987). Therefore, studies

that quantify malabsorption based only on data from hydrogen breath measurements should be considered with caution and are only minimally useful for assessment of the gastrointestinal acceptability of LDCs. Generally, subjects are fasted before they consume the test product, which may be dissolved in liquid, so conditions are not necessarily representative of normal use and may even increase symptoms.

Some studies, particularly those focusing on endpoints related to a disease like diabetes, include oral tolerance tests. After an overnight fast, subjects ingest a bolus of carbohydrate; blood glucose and insulin levels are measured for several hours (Gee et al., 1991). Oral tolerance tests that measure the rise in serum glucose levels should be interpreted with caution with regard to carbohydrate malabsorption and potential gastrointestinal effects because they are measurements of carbohydrate absorption and do not provide information about the amount of carbohydrate that is malabsorbed and enters the large intestine (Strocchi and Levitt, 1991).

Although perfusion, ileostomy, hydrogen breath, and oral tolerance test studies can provide information on the digestion, absorption, or fermentation of LDCs, they should not be used as a substitute for direct methods, both objective fecal collections and subjective gastrointestinal questionnaires, for determining gastrointestinal acceptability of LDCs.

## Methods

The inherently subjective nature of assessing gastrointestinal effects and the wide variety of study design protocol for studies reporting gastrointestinal effects of LDC consumption makes reviewing the results of human feeding studies challenging. Therefore, it is necessary to develop criteria for selecting studies to and identify study characteristics and results to compare and compile for a comprehensive review. Low-digestible carbohydrates that had the potential to cause gastrointestinal effects when consumed in excess were identified based on clinical evidence in the scientific literature; these include: the NSPs guar gum, inulin, fructo-oligosaccharide, and polydextrose; RS; and the sugar alcohols erythritol, xylitol, sorbitol, mannitol, lactitol, isomalt, maltitol, and polyglycitol. Standard scientific databases for search were used, including PubMed, Medline, Agricola, and Web of Science.

Studies were selected for review based on three levels of criteria, as summarized in Table 2. This process considered issues of publication, study design, subject characteristics, and measurement techniques. First, only studies available to the general public and published in the English language in journals were evaluated for inclusion in the review; studies described only in abstracts or unpublished internal reports and in a language other than English were excluded. Then, from this preliminary pool of studies, studies passed the secondary level of evaluation for inclusion in the review if they used subjects who had a complete gastrointestinal tract, were free of gastrointestinal disease, and had not used antibiotics, laxatives, or other drugs affecting gas-

**Table 2** Criteria for study selection.

Level of evaluation	Inclusion Criteria	Exclusion Criteria
Primary	Published as complete paper in a journal English language	Published as abstract only  Unpublished internal report Language other than English
Secondary	Subjects have complete gastrointestinal tract; free of gastrointestinal disease; no recent use of antibiotics, laxatives, etc. Control (placebo or no LDC treatment)	Subjects have incomplete gastrointestinal tract; have gastrointestinal disease; recent or current use of antibiotics, laxatives, etc. No control or results compared only to another LDC
Tertiary	Report of methods for assessing gastrointestinal effects	No report of methods for assessing gastrointestinal effects

trointestinal motility. It was assumed studies met these criteria unless the authors reported otherwise. In addition, only studies with a control period (placebo or period without the treatment) were selected during this evaluation. Although studies comparing the effects reported during an LDC treatment with those from a control period with a placebo treatment (sucrose) are ideal, those studies designed with periods of "no LDC consumption" were also included. This requirement is necessary to ensure that the results account for the usual gastrointestinal function of subjects and the prevalence of adverse gastrointestinal symptoms among the general population. In a recent survey, 40.5% of American adults reported having at least one of the following symptoms in the last month: abdominal pain/discomfort, bloating/distention, or diarrhea/loose stools (Sandler et al., 2000). In addition, the secondary level of evaluation excluded studies introducing additional confounding factors such as incomplete gastrointestinal tracts or health conditions like celiac's disease, IBD, or IBS.

Finally, studies passed the tertiary level of selection only if authors reported their means (either fecal collections and/or subjective questionnaires, diaries, or interviews) for obtaining data for laxation and other gastrointestinal effects; studies were excluded if they commented on gastrointestinal effects in their results or discussion section without first discussing them in the methods section.

After selecting studies to be included in the review, study characteristics and results were selected for a qualitative analysis. The following study characteristics were considered: number of subjects, inclusion/exclusion criteria, and subject characteristics (gender, weight or body mass index), duration of treatment, control, and washout periods, study design (randomized, cross-over or parallel, blinded), LDC treatment dosage, protocol/conditions of consumption (fasting, meals or snacks, dietary limitations, medium for LDC, and whether the LDC treatment daily intake was acute or divided into two or more portions per day), and how laxation and/or gastrointestinal effects were measured (fecal collection and/or subjective methods). The

following results were noted: significant differences between the treatment LDC and control period for laxation and gastrointestinal effects, estimated laxation threshold intakes or no-effect intakes if they were calculated based on regression equations, and actual LDC intake (including any LDCs reported in the background diet).

## Results

Fifty studies were selected based on the selection criteria. Overall, the studies had a wide range of designs and protocols and also measured and reported data in a variety of ways. Study designs varied anywhere from the ideal randomized crossover trial with a placebo control period to parallel trials comparing the LDC treatment group to a group receiving no treatment. Intakes ranged from less than 5 g to more than 100 g per day in divided or single portions. Some treatments combined two different LDCs, and some studies compared two or more different LDCs. Many treatment periods lasted for one meal, whereas

others continued to three months. The treatment LDC was incorporated into various foods and beverages as well as tablets and gum. Subjects consumed the LDCs with or in place of meals or snacks and sometimes after an overnight fast. Some studies called for gradual increases in the amount or continued for several days or weeks in order to adapt subjects, but other studies used unadapted subjects. In addition, some studies reported high amounts of background fiber in the diets of subjects, while others reported low levels, required subjects to consume a low-fiber diet, or did not report background fiber or LDC intake. Many study protocols called for dietary limitations, including those that limited the fiber or sugar alcohol content of the background diet. These limitations for the studies in Tables 5–9 are listed in Table 3. Such different dietary limitations make it difficult to make comparisons between studies and to draw meaningful conclusions from the literature.

The number of subjects per study was highly variable; most studies had between ten and thirty subjects, but some had less than ten and others had more than 100. Some studies included both male and female subjects, and others included only one

**Table 3** Dietary limitations for studies summarized in Tables 5–9.

Reference	Study protocol
Beaugeriet et al., 1990	Meals prepared and eaten at center
Bouhnik et al., 1999	No foods with FOS or fermented dairy products with viable bifidobacteria
Culbert et al., 1986	Avoid foods with xylitol, oxalate; meals at center and based on basal metabolic rate requirements
Fritz et al., 1985	No fiber supplement, no extra sugar substitutes
Gee et al., 2005	Low-residue lunch 4 hours after treatment
Gostner et al., 2005	Controlled isoenergetic diet
Gråsten et al., 2003	No more than 1 additional cereal product/day; no foods that affect intestinal function
Heijnen et al., 1996; 1998	Minimize resistant starch intake
Hylla et al., 1998	Limit fruits and vegetable intake
Koizumi et al., 1983a	Avoid foods that might cause symptoms on the day before study
Koutsou et al., 1996	No more than 300 ml juice or milk
Koutsou et al., 1999	No more than 300 ml juice or milk; no sugar-free/energy-reduced foods; no foods with prebiotics
Langlands et al., 2004	Low-fiber diet the night before
Lee et al., 1994	No more than 100 mL milk, 300 mL fresh fruit juice; no high-fiber foods and no products containing sugar alcohols
Lee et al., 2002 (adults)	
Lee and Storey, 1999	
Lee et al., 2002 (children)	Limit fresh milk and fruit juice to 200 ml for 12 h before and after consumption
McRorie et al., 2002	Ad libitum food intake in metabolic ward; no more than 30% energy intake from fat
Muir et al., 1995	Eat foods low in fermentable fiber and resistant starch
Oku and Okazaki, 1996	Avoid food/beverage with sugar substitutes; no fermented foods on day of study
Pasman et al., 2006	No foods with pre-/probiotics; other food restrictions
Phillips et al., 1995	Constant nonstarch polysaccharide intake: 1 glass fruit juice, 1 fruit, 200 g vegetables, low-fiber cereals
Rouskoné-Formestreaux et al., 2003	No other foods with sugar alcohols or foods that promote abdominal discomfort
Sinaud et al., 2002	Low-fiber diet provided
Spengler et al., 1987	No additional mono- or disaccharides
Storey et al., 1998	No more than 300 ml juice or milk
Storey et al., 2002	Limit fresh milk and fruit juice to 200 ml for 12 h before and after consumption
Ten Bruggencate et al., 2006	No foods with high calcium content (including dairy); no foods with large amounts of fermentable nondigestible carbohydrate or pro-/prebiotics
Tuohy et al., 2001	No foods with pre- or probiotics/live yogurts
van den Heuvel et al., 2004	Exclusion of fiber-rich foods and foods with pre-/probiotics
van Dokkum et al., 1999	Controlled basal diet to maintain body weight; metabolic ward during last week
van Münster et al., 1994a	No beans/peas
Venema et al., 2005	No foods with probiotics and limited foods with prebiotics and fiber supplements
Vermorel et al., 2004	Low-fiber diet for lunch and dinner
Williams et al., 2004	Low-residue dinner (Ensure <sup>®</sup> ) the night before

gender. Most of the studies recruited only adults. The mean body mass index (BMI) for subjects was most often within the normal range, but some studies reported an overweight mean BMI.

Assessment of gastrointestinal effects of LDC consumption was the primary endpoint in about two-thirds of the studies, whereas the other third of the studies assessed these effects as secondary endpoints. Less than one-third of the studies included fecal collections, but more than three-quarters of the studies obtained data about gastrointestinal effects from subjects with questionnaires, diaries, or interviews. Subjects graded gastrointestinal effects with various scales. Investigators often asked subjects to grade or rank their symptoms on a scale of 0 to 3, but such systems are inconsistent between laboratories. For example, some systems ask subjects to compare their gastrointestinal effects to their normal experience on a scale from 0 for usual to 3 for considerably more than usual; others ask for an absolute grading from 0 for none to 3 for severe.

When describing the statistical analysis they employed, some authors specifically stated the tests they used to determine significant differences between treatments, whereas others did not make such a distinction or only specified statistical tests for other endpoints. In some papers the presentation of results included p-values or other statistical analysis indicating whether differences were significant, but others only presented raw data from questionnaires or gave results as percentages without any indication of significance levels.

Only studies that met all of the selection criteria are summarized in Tables 5–9. The tables provide the most important details of the study methods and results: the number of subjects in the study, the design, the duration of the LDC treatment period, the LDC treatment amount, whether the control was sucrose or another sugar or a period without the treatment LDC, conditions of the LDC consumption, methods for assessment of laxation and other gastrointestinal effects, and the results (gastrointestinal responses). The studies are arranged by LDC and authors. Table 4 lists all of the abbreviations used in Tables 5–9. The results of additional studies as well as conclusions of previously published review articles are included in the discussion of the fifty selected studies that follows.

## ***NON-STARCH POLYSACCHARIDES***

### ***Guar Gum***

According to a 1993 panel from the Life Sciences Research Organization of the Federation of American Societies for Experimental Biology, daily intakes of up to 20 g guar gum per day are safe (Greenberg and Sellman, 1998). However, there are few guar gum published feeding studies with data for gastrointestinal effects, and the intakes in these studies are less than 20 g/day. Only two studies of guar gum met the criteria presented in Table 2 (Tuohy et al., 2001; Williams et al. 2004) and were selected for inclusion in the NSP summary tables (Tables 5 and 6); the

latter study administered a treatment of partially hydrolyzed guar gum (PHGG) combined with FOS and is discussed below.

In a study designed to assess the glycemic effect of guar gum, Williams et al. (2004) demonstrated the acceptability of 5.5 g guar gum incorporated into a crispy bar (containing an additional 1.76 g fiber) compared to a control bar (containing 1.48 g fiber); following a 12 h fast, only one of the 48 subjects complained of diarrhea, and that was associated with the control treatment rather than the guar treatment. Guar gum consumption may contribute to other gastrointestinal effects such as abdominal pain, bloating, flatulence, but in terms of the frequency and intensity of gastrointestinal effects, any differences between the guar gum and control treatments were insignificant in this study; however, the authors reported great variations between individuals.

Greater amounts of guar gum have been administered as laxatives for constipated subjects. In one such study, 12 g PHGG was associated with flatulence, but increases in severe flatulence were not significant compared to baseline data (Patrick et al., 1998). Some authors have reported adaptation to consumption of 7–9 g/day guar gum or PHGG as evidenced by decreases in flatulence after one or two weeks of consumption (Okubo et al., 1994; Takahashi et al., 1994).

Consumption of up to 15 g guar gum throughout the day have been reported as acceptable with only “minimally increased flatus production” when it was incorporated into a solid food like crisp bread (1 g per slice), but the hydrated guar gum (5 g mixed into soup, milk, or juice three times per day) was associated with loose stools and excessive flatulence that was termed “problematic” (Jenkins et al., 1980). The main primary hypothesis of this study by Jenkins et al. (1980) was to assess the efficacy of guar gum as a treatment for hypercholesterolemia, and the authors did not report the methods they used for measuring gastrointestinal effects or laxation and did not compare these effects for 15 g guar gum with those of a control period.

Further studies with higher amounts are needed in order to determine a laxative threshold and amounts at which flatulence and other effects become unacceptable; studies should investigate the effects of single and daily divided intake of guar gum and PHGG in unadapted and adapted individuals. It may be useful to examine the differences between the effects of guar gum and PHGG. Additional consideration should be given to the level of LDCs in the background diet during the study and in the subjects’ usual diets.

### ***Inulin and Fructo-Oligosaccharide (FOS)***

Several investigators and reviewers have reported on the gastrointestinal acceptability of inulin and FOS. Table 5 includes eight studies with inulin or FOS. Four of these studies examined gastrointestinal effects as primary endpoints (Dahl et al., 2005; Gråsten et al., 2003; Koutsou et al., 1999; van Dokkum et al., 1999). Intakes of inulin or FOS ranged from 2.5–34 g/day.

**Table 4** Abbreviations used in Tables 5–9.

Abbreviation	Explanation
ab	abdominal
am	morning
bLDC	low-digestible carbohydrates in the background diet
bloat	bloating
bm	bowel movements
bor	borborygmi (flatulence in the bowels)
Br	breakfast
bw	body weight
CD	gamma cyclo-dextrin
combo	combination treatment
Con	control
d	day
db	double-blinded
DC'd	discontinued
df	dietary fiber
div	dose of LDC treatment divided into 2 or more portions/day
DL	dietary limitations; see Table 3 for more information
Dose	dose of treatment LDC(s)
D-tag	D-tagatose
ED50	estimated dose at which 50% of the subjects would be expected to experience diarrhea and/or another GI effect
eryth	erythritol
F	fasted
FC	fecal collection
flat	flatulence
FOS	fructo-oligosaccharide
freq	frequency
GG	guar gum
GI	gastrointestinal
glc	glucose
h	hour(s)
HPF	high-performance
HRS	high resistant starch treatment
inc	increased
lact	lactitol
lax	laxative
LRS	low resistant starch treatment
Lu	lunch
malt	maltitol
max no-eff dose	maximum dose at which subjects would not be expected to experience diarrhea and/or other GI effects
med	medium
mod	moderate
N	total number of subjects in the study
NDO	non-digestible oligosaccharides
NS	no significant difference between the treatment and control to another treatment
P	parallel
PG	polyglycitol
PHGG	partially hydrolyzed guar gum
pm	afternoon
Q	questionnaire
R	randomized
RTE	ready-to-eat
RS	resistant starch
sb	single-blinded
sev	severe
sig	significant or significantly
Sn	snack
sorb	sorbitol
subj	subject(s)

**Table 4** Abbreviations used in Tables 5–9.

Abbreviation	Explanation
suc	sucrose
TD	threshold dose
TG	triglyceride
tx	treatment
Tx dur	duration of the treatment period
VAS	visual analog scale
vom	vomiting
wk	week
WO	washout period between treatment and control periods
wt	weight
X	crossover
xyl	xylitol
yo	years old

Most of the studies with lower intakes ( $\leq 20$  g/day) of inulin or FOS reported few effects on bowel movements compared to the control, though some investigators reported significant increases in fecal weight (Dahl et al., 2005; Ten Bruggencate et al., 2006). Venema et al. (2005) (Table 6) found increases in softer stools, though not significant, with 7.5 g FOS. Koutsou et al. (1999) investigated the effects of a cyclic oligosaccharide that is at least partially digested in the small intestine. (Gamma-cyclodextrin is produced from liquefied starch and has eight glucose molecules; it is digested by salivary and pancreatic enzymes, yielding maltose, maltotriose, and glucose (Koutsou, et al., 1999). In this acute feeding study, 24 subjects consumed 8 g of gamma-cyclodextrin mixed in yogurt for a morning snack; the authors reported only mild symptoms within 3–4 h after consumption of the oligosaccharide, no significant differences in gastrointestinal symptoms compared to the placebo maltodextrin, and no diarrhea, indicating this amount of the cyclic oligosaccharide was well-tolerated.

Most of the studies with intakes of 15 g or less of inulin or shorter chain oligosaccharides showed that subjects generally tolerated these intakes with only mild and transient side effects, if any (Bouhnik et al., 1999; Brighenti et al., 1999; Dahl et al., 2005; Gråsten et al., 2003; Koutsou, et al., 1999; van Dokkum et al., 1999). Flatulence was the most common effect reported with inulin and FOS consumption. Bouhnik et al. (1999) found a significant increase in the occurrence and severity of flatulence compared to a sugar placebo at 20 g; reports of flatulence and bloating were very mild for other amounts in this controlled parallel design study. Ten Bruggencate et al. (2006) also reported a significant increase in flatulence and bloating complaints and higher scores for abdominal pain and cramps with 20 g FOS compared to the placebo. Kruse et al. (1999) gave subjects 22–34 g inulin per day, depending on energy needs, and noted general signs of abdominal discomfort in subjects, with flatulence and bloating being the most common symptoms; however, subjects appeared to adapt as the flatulence decreased within 2–4 weeks, though two subjects withdrew from the study due to intestinal discomfort. Based on these studies, amounts greater than 15 g are associated with more symptoms related to fermentation in the colon, such as flatulence and bloating. In general, the

**Table 5** Nonstarch polysaccharides: Guar gum, inulin, or fructo-oligosaccharide.

Study	N	Design	Tx dur	Dose	Con	Conditions	Assessment	GI responses
Bouhnik et al., 1999	40	R, P	7 d	2.5, 5, 10 or 20 g FOS	Sugar	Powder mixture at end of meal; div; DL	Chart (bm, symptoms, intensity); FC	For 20 g FOS vs 0–10 g FOS: Reports of excessive flat sig greater. For 20 g FOS vs 0–5 g FOS: excessive flat was sig more intense
Brighenti et al., 1999	12	X, sb, WO	4 wk	9 g inulin	Placebo	RTE rice cereal; Br; 20 g bLDC	Q (bm, symptoms)	NS bm; inc flat occasionally reported for inulin but no ab pain
Dahl et al., 2005*	15	R, X, db	3 wk	15 g inulin	Starch	Juice; div	Chart (bm); interviews (symptoms)	For inulin vs starch: sig inc in bm freq (weighted); sig dec in enema administration; no GI discomfort reported
Gråsten et al., 2003*	14	R, P	19–22 d	15 g inulin or wheat pentosan	Run-in period	Bread; div; DL	Q (bm, symptoms, intensity); FC	Results for both tx and control compared to 2–3 wk run-in period; bm: NS for either group; significant inc in overall occurrence of GI symptoms for both groups; sig inc in flat for wheat pentosan group
Koutsou et al., 1999*	24	R, X, db, WO	1 dose	8 g CD	Malto-dextrin	Yogurt; am Sn; DL	Side effect record (bm, symptoms, intensity)	No diarrhea with tx; similar bm consistencies between placebo and CD tx; NS for other symptoms; all symptoms mild
Kruse et al., 1999	11	X	64 d	22–34 g inulin	No inulin tx	Yogurt; Br	Q (symptoms, intensity); FC	NS bm; flat and bloat most common symptoms for inulin, but usually mild or mod; flat improved w/in 2–4 wks of tx but still sig more compared to control periods
Ten Bruggen-cate et al., 2006	34	R, X, db	2 wk	20 g FOS	Suc	Lemonade; div; DL; 30 g bLDC	Diary (symptoms, intensity), FC	For FOS vs suc: bm wt sig more; reports of flat, bloat sig more; intensity scores for ab pain and cramps sig higher
van Dokkum et al., 1999*	12	R, X, db	3 wk	15 g inulin, FOS, or GOS	No added NDO	Orange juice; div DL; 24 g bLDC	Q (symptoms); FC	For inulin and GOS vs FOS: wet fecal wt sig more (after log transformation). Generally no inc in GI symptoms; flat most common report, including during control period
Williams et al., 2004	48	R, X, db	1 dose	5.5 g GG w/ 1.76 g df	Crispy bar w/ 1.48 g df	Crispy bar; Br; F	GI Q (freq, intensity)	NS

\*Assessing laxative and/or other GI effects was the primary focus of this study.

**Table 6** Nonstarch polysaccharides: Combination treatments of fructo-oligosaccharide and inulin, PHGG, or D-tagatose.

Study	N	Design	Tx dur	Dose	Con	Conditions	Assessment	GI responses
Langlands et al., 2004	29	P	2 wk	15 g FOS + inulin	No FOS + inulin tx	div; DL; 30 g bLDC	Diary (symptoms)	10 subj reported laxative effect (mild or mod); flat reported by all subj for inulin + FOS (10 mild or mod; 7 sev); most reports of bloat mild or mod
Tuohy et al., 2001	31	R, X	21 d	11 g FOS + PHGG	Sugar	Biscuits; div; DL	Diary (bm, symptoms, intensity); FC	bm consistency varied but more often softer than placebo; reports of sev bloat inc by 18.38%, sev flat inc by 8.96%; other symptoms mostly mild or mod
Venema et al., 2005	30	R, X, db	14 d	7.5 g FOS; 7.5 g D-tag; 15 g combo	Suc	Jam; DL	Q (bm, symptoms); FC	For FOS, D-tag, and combo tx vs suc: bm freq sig greater in wk 2. For FOS vs suc, more thin or very thin bm but most bm normal; NS symptoms

results of these studies suggest that inulin and FOS are well-tolerated at levels of 15 g/day; as the amount increases, increased gastrointestinal symptoms, such as flatulence or bloating, are more likely.

Although the degree of polymerization and molecular weight of LDC may affect gastrointestinal tolerance, van Dokkum et al. (1999) compared the effects of 15 g inulin, FOS, and GOS and did not find significant differences for reported symptoms; however, significantly more hydrogen was expired with FOS compared to the control, and there was a significant increase in wet fecal weight with inulin and GOS compared to FOS. The differences in these parameters may indicate a potential for differences in degrees of side effects at higher dosages of inulin, FOS, and GOS, thus warranting further research.

Based on the above studies, individuals may notice an increase in mild flatulence but little if any effect on bowel movements when consuming 15 g inulin or FOS per day, so this level of intake should be acceptable to most people. Daily intakes above 20 g, however, are more problematic (Kruse et al., 1999). However, many of the published studies did not report the amount of dietary fiber in the normal diets of subjects or their diets during the studies; this may explain increased or decreased tolerance in some individuals. In another study, two subjects reported looser and more frequent stools on days they consumed sweet potatoes with the 4 g of FOS, indicating the potential interaction between the added FOS and their diet (Buddington et al., 1996).

In another study, Clausen et al. (1998) compared the laxative effects of FOS to those of lactulose. Intakes of the LDCs were increased from 20–160 g per day until bowel movements reached more than 1000 g per day, which is four times the weight of criteria for clinical diarrhea (McRorie et al., 2000). The authors found that subjects could tolerate twice as much FOS as lactulose before the fermentation capacity of the microflora was

exceeded: About 40 g FOS resulted in an average fecal volume of 238  $\pm$  38 g per day; 40 g of lactulose increased the fecal volume to 400  $\pm$  64 g per day, which is significantly higher than the fecal weight with FOS (Clausen et al., 1998).

Previously published review articles presented similar conclusions about the gastrointestinal acceptability of inulin and FOS. Carabin and Flamm (1999) conducted a review of studies on the gastrointestinal tolerance of inulin and oligofructose and FOS and noted that gastrointestinal tolerance is the limiting factor in the consumption of these compounds. They surveyed the results of 17 studies from 1987–1999. Based on the results of these studies, Carabin and Flamm (1999) concluded that a 20–30 g intake of inulin or oligofructose can cause gastrointestinal symptoms (some studies showed symptoms such as increased flatulence at 15 g/day); however, intakes of up to 20 g may be well-tolerated. In another review of fructans, Roberfroid and Delzenne (1998) evaluated studies of inulin supplements in liquid food products and found a relationship between intake and symptoms. They noted 10 g inulin did not cause symptoms, but 20 g and 30 g were associated with mild symptoms and major discomfort, respectively; however, 20–30 g could be well-tolerated if these intakes were divided throughout the day (Roberfroid and Delzenne, 1998).

Three studies administered a single supplement of FOS in combination with another LDC: inulin (Langlands et al., 2004), PHGG (Tuohy et al., 2001), and D-tagatose (Venema et al., 2005) (Table 6). Such studies can help investigators to determine whether there is an additive or interactive effect when more than one type of LDC is incorporated into a food or meal.

The mixture of 7.5 g FOS with 7.5 g inulin for a total of 15 g (divided into three daily intakes), was associated with one “severe laxative effect,” though this was not defined and the dietary fiber intake by the subject was not reported (Langlands et al., 2004), and the other subjects reported only mild or moderate

laxative effects, flatulence, and bloating. It would have been useful for the authors to include treatments of 15 g inulin and 15 g FOS.

Tuohy et al. (2001) evaluated the prebiotic effects of a supplement containing 3.4 g PHGG combined with 6.6 g FOS incorporated into biscuits compared to a sugar placebo. The reports in the diaries showed no significant differences between the treatment and placebo as there was great variation between subjects in both stool frequency and consistency, though the PHGG-FOS treatment was associated with an increase in soft stools. However, there were more reports of moderate and severe gastrointestinal symptoms like flatulence and bloating with the PHGG-FOS treatment (3.4 g PHGG + 6.6 g FOS) compared to the placebo (Tuohy et al., 2001). It would have been useful to give treatments with only PHGG and only FOS as well as the PHGG-FOS combination and to report the presence of other LDCs in the background diet.

Venema et al. (2005) investigated the effects of 7.5 g FOS and a mixture of 7.5 g FOS and 7.6 g D-tagatose as well as different levels of D-tagatose and sucrose. The authors noted 9 of the 19 "adverse events" (term not defined) were related to the combination of FOS and D-tagatose (about 15 g fiber-sugar mixture) and 6 occurred during the FOS supplementation; thin or very thin stools were also increased with these supplements. (D-tagatose is a monosaccharide that differs from fructose only in the position of the hydrogen and hydroxyl groups around the fourth carbon of the molecule; it is synthesized from lactose (Donner et al., 1999)).

More of these LDC combination studies are needed as different types of low- or non-digestible carbohydrates are added to the food supply.

### **Polydextrose**

Flood et al. (2004) summarized published and unpublished studies addressing the gastrointestinal effects associated with consumption of polydextrose. Nine of these studies, with intakes that ranged from 15–150 g polydextrose per day in single treatments and prolonged treatments of up to two months, focused on gastrointestinal tolerance based primarily on the development of diarrhea (Flood et al., 2004). Based on this review, the following conclusions may be drawn:

- Adults should tolerate polydextrose at levels of at least 50 g per day, even in fasting conditions and dissolved in water.
- Higher intakes of polydextrose are associated with an increase in gastrointestinal symptoms (75 g) and diarrhea (88 g).
- Children may tolerate up to 1 g polydextrose per kg body weight, though this amount may cause diarrhea in children ages 2–3 years. (Flood et al., 2004)

Flood et al. (2004) discussed six additional studies that focused on other physiological endpoints, noting that intakes of 30 g were associated with softer stools and increases in fecal

weight. One study reported more than 50% of subjects experiencing soft stools or diarrhea with only 15 g polydextrose, but Flood et al. (2004) commented this study did not define gastrointestinal tolerance parameters.

### **RESISTANT STARCH**

Ten feeding studies reporting gastrointestinal effects of resistant starch (RS) are summarized in Table 7. In four of these studies, the gastrointestinal effects of RS consumption were primary endpoints (Pasman et al., 2006; Phillips et al., 1995; Tomlin and Read, 1990; van den Heuvel et al., 2004). The other studies focused on measurements for other various primary endpoints: risk factors for colon cancer (Heijnen et al., 1998; Hylla et al., 1998), serum cholesterol (Heijnen et al., 1996), breath hydrogen excretion (Muir et al., 1995; van Munster et al., 1994a), serum acetate (Muir et al., 1995), and energy value and mineral absorption (Vermorel et al., 2004). The duration for chronic consumption of an RS treatment ranged from one to five weeks; the acute study (Muir et al., 1995) required subjects to consume 59 g and then report gastrointestinal effects for 28 h. Together, these studies of RS provide data about the laxative effects of RS, common gastrointestinal symptoms associated with RS, differences between RS2 and RS3, and tolerancethresholds.

Data from questionnaires or interviews and, in some studies, fecal collections, indicate RS may have a mild laxative effect. Phillips et al. (1995) reported significant increases in the ease of defecation with a high-RS diet (38.6 g RS) compared to a low-RS diet (5.3 g RS). A significant increase in mean stool frequency compared to a glucose placebo was reported with 30 g/day RS2 (Heijnen et al., 1998) and with 30 g RS2 and RS3 (Heijnen et al., 1996); the latter study by Heijnen et al. (1996) also reported a softer consistency with the two types of RS compared to glucose, whereas their 1998 study did not see a significant difference in stool consistency. Van den Heuvel et al. (2004) reported inconsistent results for stool consistency with increasing intakes of RS from 10 to 80 g/day RS, and Pasman et al. (2006) reported no difference in frequency and consistency, and wet stool weight between a glucose placebo, 30 g/day RS and 45 g/day RS. The daily intake of 10.33 g RS given by Tomlin and Read (1990) also did not affect these fecal parameters.

As with other fibers, RS increases fecal weight. Phillips et al. (1995) found significant increases in fecal wet and dry weights with 38.6 g RS compared to 5.3 g RS. Other studies showed a significant increase in stool weight with RS (Heijnen et al., 1998; Hylla et al., 1998; van Munster et al., 1994b; Vermorel et al., 2004). The aforementioned studies provided at least 28 g/day RS, but the lower intake of 10.33 g/day RS provided by Tomlin and Read (1990) did not affect fecal bulk compared to the placebo treatment having less than 1 g/day RS. In addition, Pasman et al. (2006) did not report differences in wet weight between the placebo, 30 g RS, and 45 g RS.

In other studies designed to compare RS treatments to NSP rather than a sugar placebo or baseline period, investigators have

**Table 7** Resistant starch.

Study	N	Desig	n Tx dur	Dos	e	Con	Conditions	Assessment	GI responses
Heijnen et al., 1996	60	R, X, sb	3 wk	30 g RS2 or 30 g RS3	Glc		Yogurt, milk, fruit mixture; div; DL; 20–23 g bLDC	Q (bm, symptoms, intensity)	For RS3 vs RS2 and glc: bm freq sig higher. For control vs RS2 and RS3: bm sig harder. For RS vs glc: flat score sig higher. For RS3 vs glc and RS2: bloat and belching sig more. For RS vs glc: sig more bellyache. Mean scores for all symptoms were mild.
Heijnen et al., 1998	24	R, X, db	1 wk	30 g RS2 or 30 g RS3	Glc		Yogurt, milk, fruit mixture; div; DL; 34 g bLDC	Q (bm, symptoms, intensity)	For RS2 vs glc: bm freq sig higher; NS bm consistency and wt. GI effects: subj reporting flat: 82% RS2, 91% RS3, 55% glc; subj reporting bloat: 28% RS2, 41% RS3, 9% glc
Hylla et al., 1998	12	X, WO	4 wk	55.2 g RS (HRS)	Corn-starch (LRS): 7.7 g RS		Starchy foods; DL; 11.2 g bLDC in HRS and 9.8 g bLDC in LRS control	Q (bm, symptoms, intensity), FC	For HRS vs LRS: bm wet and dry wt sig inc; NS bm water content; NS intensity scores for flat, ab distention and ab cramps (all mild)
Muir et al., 1995	8	R, X, WO	28 h	59 g RS (HRS)	5.2 g RS (LRS)		div; DL; 31 g bLDC in HRS, 29 g bLDC in LRS	Q (bm, symptoms, intensity)	For HRS vs LRS: NS bm scores; mean symptom scores for flat, ab distention, ab cramp sig greater but all mild to mod
Pasman et al., 2006*	43	R, P, db	5 wk (1st wk dose 50%)	30 or 45 g RS	Malto-dextrin		Yogurt or beverages; div; DL	Q (bm, symptoms, intensity), FC	For 45 g RS vs maltodextrin: NS bm; rumbling inc sig but this was lower after wk 4 compared to week 3
Phillips et al., 1995*	11	R, X	3 wk	LRS: 2–8 g, HRS: 26–50 g	Baseline (2 wk)		Cereal, cold drinks, cold desserts, cookies; DL; 20 g bLDC	Q (bm, symptoms, intensity), FC	For HRS vs baseline, ease of defecation sig greater, fecal wet and dry wt sig greater; sig correlation between RS intake and fecal wet wt; flat sig more for HRS vs baseline; all subj reported flat for HRS
Tomlin and Read et al., 1990*	8	R, X, WO	7 d	10.33 g RS3 (HRS)	Rice cereal w/ 0.86 g RS3		Cornflakes; 18 g bLDC	Diary (bm, flatus); FC	For HRS vs rice control: NS bm consistency, output, freq, ease of defecation; more but NS flat reports; less flat than usual for subjects for both HRS and control
van den Heuvel et al., 2004*	20	R, X (P for dose: A or B), WO	3 wk	A: 0, 10, 30, or 60 g RS3; B: 0, 15, 45, or 80 g RS3	Placebo		Juice, yogurt; div; DL; 2.9 g bLDC	Q (bm, symptoms, intensity)	Inconsistent effect on bm consistency and freq w/ higher doses; no inc in diarrhea for RS vs placebo. For 30, 60, 80 g RS vs placebo: sig more reports flat. For 60, 80 g RS vs placebo: sig more flat freq. For 80 g RS vs placebo: severity of flat and freq of bloat sig greater. Belching inc w/ dose
van Munster et al., 1994a	19	X, WO	7 d	28 g RS2	Malto-dextrin		div; DL; 29 g bLDC in RS, 31 g bLDC in control	Q (bm, symptoms, intensity)	NS bm; NS symptoms
Vermorel et al., 2004*	10	X, WO	20 d	20–100 g RS3	Dext		Water; div; intake gradually inc; DL	Diary (bm, symptoms)	For RS vs dext: wet and dry bm wt inc sig; NS bm freq. 2 reports of diarrhea; excessive gas emission reported especially above 50 g; other reported symptoms slight and diminished after 20 d when intake reached plateau

\*Assessing laxative and/or other GI effects was the primary focus of this study.

demonstrated that resistant starch has less of an effect on fecal parameters than NSPs. A bran-NSP supplement containing 18.4 g NSP significantly increased the wet weight and dry mass compared to the rapidly digested and slowly digested starch (RDS-SDS) control and the RS treatments having 17.4–30.0 g RS and also significantly increased water weight compared to the control (Cummings et al., 1996). Jenkins et al. (1998) fed 24 subjects a low-fiber (control), high fiber (30 g wheat bran), and two types of resistant starch (30 g fiber from RS2 and RS3) in muffin supplements for 4 weeks with a two-week washout period between each treatment; fecal bulk increased significantly for all supplements compared to the low-fiber diet, but the weight of stools on the high-fiber supplement was significantly greater than during both of the RS periods. These results for fecal bulking are in agreement with the findings of Topping and Clifton (2001) who reviewed studies of RS and wheat bran and concluded resistant starch has a mild laxative effect as it increases fecal bulk (1–1.7 g additional stool/g RS consumed) but not to the extent of NSP such as wheat bran (4.9 g/g consumed).

In the studies summarized in Table 7, reports of diarrhea were rare and only with high intakes of RS. Two of eight subjects reported diarrhea with RS consumption of 59 g/day in addition to 30 g NSP (Muir et al., 1995), and two of ten subjects reported diarrhea with increasing intakes of 20–100 g/day (Vermorel et al., 2004).

All investigators collected subjective gastrointestinal data from subjects with questionnaires or diaries. Increases in gastrointestinal symptoms were associated with high RS consumption (an average of least 30 g/day) in many of the studies. Muir et al. (1995) reported a significant increase in symptom scores with about 60 g RS compared to a glucose placebo, while Phillips et al. (1995) also reported a significant increase in symptom scores with about 40 g/day RS compared to 5 g/day RS. Hylla et al. (1998) observed an increase in the symptom score with 55 g/day RS compared to 8 g/day RS, but this increase was not significant. With lower intakes of RS, other studies did not show significant increases in symptoms when subjects consumed about 10 g/day RS (Tomlin and Read, 1990) and 28 g/day RS (van Munster et al., 1994a; van Munster et al., 1994b).

Some studies reported significant increases in specific symptoms. As they gradually increased the intake of RS, van den Heuvel et al. (2004) noted flatulence became significantly more serious with daily intakes  $\geq 60$  g RS. Vermorel et al. (2004) reported increases in flatulence with intakes above 50 g/day RS, though the significance was not noted. Van Munster et al. (1994b) concluded that flatulence was the most common symptom associated with 28 g/day RS. Pasman et al. (2006) reported significant increases in stomach rumbling with 45 g/day RS compared to the placebo, and Heijnen et al. (1996) reported significantly more bloating with 30 g/day RS compared to the glucose placebo.

While some study designs included adaptation periods during which intakes were gradually increased, only two studies were designed to increase amounts to high levels to determine a threshold intake for intolerance (van den Heuvel et al., 2004;

Vermorel et al., 2004). These studies found that about 45 g/day RS3 were well-tolerated (van den Heuvel et al., 2004) but at levels between 50–60 g/day RS causes a significant increase in symptoms or severity of symptoms. Van den Heuvel et al. (2004) observed a decrease in the severity of symptoms with prolonged intake of 60 g RS, but this adaptation did not occur at levels as high as 80 g/day. Muir et al. (1995) and Phillips et al. (1995) also observed 60 g and 50 g, respectively, were associated with significantly greater reports of gastrointestinal symptoms compared to lower amounts of 3–8 g/day; however, it should be noted that both of these studies included about 30 g (Muir, et al., 1995) and 20 g (Phillips et al., 1995) additional fiber in the background diet, so the total fiber levels were 90 g in Muir et al. (1995) and 70 g in Phillips et al. (1995).

Many of these studies with RS include breath hydrogen measurements (Heijnen et al., 1998; Hylla et al., 1998; Muir et al., 1995; Pasman et al., 2006; Tomlin and Read 1990; van den Heuvel et al., 2004; van Munster et al., 1994a; van Munster et al., 1994b). Although such methods provide some data on colonic fermentation, hydrogen levels have not been shown to correlate with gastrointestinal effects (Hylla et al., 1998) and so are of limited value when predicting gastrointestinal acceptability of RS.

Most gastrointestinal studies of RS use RS2 or RS3 or a combination of the two types of RS, and others do not specify the type of RS in their methods section. Some investigation has been done into possible differences in gastrointestinal effects between these two types of RS. Heijnen et al. (1996, 1998) compared the effects between RS2 and RS3. With intakes of 30 g/day RS, bloating, belching, and bellyache were significantly greater for RS3 than RS2 (Heijnen et al., 1996); however, for most of the symptoms and stool parameters reported in these two studies, there were no significant differences between the two types of starch, although one type but not another may have been significantly different from the glucose placebo. Cummings et al. (1996) also compared the effects of RS<sub>2</sub> and RS<sub>3</sub>, but the only difference between the RS treatments was that the biscuit supplement containing the banana-RS<sub>2</sub> was associated with a significant increase in the mean transit time compared to the RDS-SDS control; however, it should be noted that the potato-RS<sub>2</sub> supplement contained 30 g RS<sub>2</sub>, and the other RS supplements contained only 17.4–19.0 g RS. Based on Heijnen et al. (1996, 1998) and Cummings et al. (1996), RS<sub>2</sub> and RS<sub>3</sub> have similar effects on the gastrointestinal tract at intakes of 30 g or less, but studies that compare these two types of RS at higher intake levels may be warranted.

Variances in study protocols and inconsistencies in results also suggest avenues for future research. Differences in the results of the above studies could be attributed to the LDC content of the background diets. For example, subjects in the study conducted by Pasman et al. (2006) consumed equal and greater amounts of RS compared to the two studies by Heijnen et al. (1996, 1998). Subjects in the studies by Heijnen et al. (1996, 1998) consumed an additional 20–23 g and 34 g dietary fiber, respectively, in their background diet for a total of 50 g and 65 g

LDCs, but Pasma et al. (2006) restricted fiber in the background diet of subjects and did not report the actual LDC content of the diets of subjects during the study. Therefore, it is possible that the additional dietary fiber mediated the significant results achieved by Heijnen et al. (1996, 1998). To investigate the gastrointestinal effects of RS, it is necessary to compare the effects of the consumption of various levels of RS without additional LDCs and to compare the effects of the consumption of various levels of RS with constant levels of additional LDCs.

As has been noted, dietary and host factors also mediate gastrointestinal effects, so an examination of other details of study designs and protocols provides further explanations for inconsistencies in results. Sample sizes ranged from eight to sixty subjects, and three-fifths of the studies had sample sizes of less than twenty. Treatment periods ranged from 28 h to five weeks. Most of the studies used a crossover design, but only seven of the ten studies were randomized, and only three studies were blinded (two double- and one single-blinded). The RS was provided in a variety of foods and beverages within most of the studies, which makes it difficult to trace differences in results to the form (solid or liquid) of the supplement. Higher intakes were generally divided throughout the day. The studies in Table 7 obtained information about gastrointestinal effects with symptom questionnaires or diaries and some also obtained stool samples. Other studies discussed here but excluded from Table 7 (Cummings et al., 1996) did not specify the methods used for collecting data for gastrointestinal effects.

## SUGAR ALCOHOLS

Twenty-four studies of sugar alcohols were selected and summarized in Table 8. Some of the studies compare the effects of one sugar alcohol to a placebo, whereas others compare the effects of multiple sugar alcohols to a placebo and to each other. Very few of these studies reported the LDC content of the background diet, but many of them included dietary limitations meant to reduce the fiber and/or sugar alcohol content of the diets of subjects shortly before and during the studies.

### Erythritol

Bornet et al. (1996) reviewed clinical studies of erythritol and concluded that single or repeated intakes of up to 1 g/kg body weight could be acceptable. Since that time, four groups of investigators have conducted and published studies having a primary focus of determining the gastrointestinal acceptability of erythritol (Bornet et al., 1996; Oku and Okazaki, 1996; Storey et al., 2007; Tetzloff et al., 1996). In the three acute studies (Bornet et al., 1996; Oku and Okazaki, 1996; Storey et al., 2007), intakes of erythritol ranged from about 25 to 75 g per day; in the study that gradually increased the intake over

a one-week period, the highest daily amount (divided) was 1 g/kg body weight or about 79 g (Tetzloff et al., 1996). The laxative and other gastrointestinal effects were measured with questionnaires and interviews.

A single acute intake of about 20–55 g erythritol (Bornet et al., 1996; Storey et al., 2007) or up to 1 g/kg body weight (mean intake of 79.0 g after a gradual increase in intake) (Tetzloff et al., 1996) were not associated with significant differences in the frequency or consistency of bowel movements compared to a sucrose placebo. Tetzloff et al. (1996) reported there were more reports of “softer than usual” bowel movements with erythritol compared to sucrose, but the increase was not significant; the authors also reported no change in the frequency between the erythritol and placebo treatments.

Oku and Okazaki (1996) designed their study to determine laxation threshold intakes for erythritol, so for up to three days, subjects received increasing intakes until they reported diarrhea; as part of the questionnaire on diarrhea, subjects were given pictures to assist them in classifying their stool shape. On a per kg body weight basis, females were shown to have a higher toleration threshold (0.80 g/kg body weight or about 41 g) than males (0.66 g/kg body weight or about 43 g). In comparison, subjects taking the sucrose placebo did not experience diarrhea even at intakes greater than 1.2 g/kg body weight. The differences between the laxation results published by Oku and Okazaki (1996) and those by Bornet et al. (1996), Storey et al. (2007), and Tetzloff et al. (1996) could be attributed to differences in body weights, study design, and conditions of erythritol consumption.

Increases in other gastrointestinal effects such as nausea and borborygmi were reported with intakes of about 50 g/day. Storey et al. (2007) reported significant increases in nausea, borborygmi, and the calculated mean symptom score with a single acute intake of 50 g erythritol compared to 45 g sucrose dissolved in a beverage, though they did not observe any significant differences with lower intakes of erythritol compared to 45 g sucrose. Oku and Okazaki (1996) reported that borborygmi was a common complaint with erythritol in their study, which provided up to 75 g erythritol in jelly; however, they did not comment on the significance of these results. Bornet et al. (1996) noted more total complaints of gastrointestinal effects with erythritol than sucrose, but these differences were not statistically significant in a parallel study with six subjects in each treatment. For flatulence and nausea, there were more reports with the higher intake of erythritol (0.8 g/kg body weight or about 55.2 g) compared to the lower intake (0.4 g/kg body weight or about 26.8 g), but the opposite relationship was reported for bloating (Bornet et al., 1996).

However, higher intakes of erythritol were tolerated at least as well as a sucrose placebo when they were preceded by a two-day adaptation period that gradually increased the intake and divided into five portions consumed throughout the day in yogurt, cookies, drinks, and chocolate: Tetzloff et al. (1996) noted reports of flatulence, bloated feelings, and sensations of fullness from half of the 12 subjects consuming about 79.0 g/day

**Table 8** Sugar alcohols.

Study	N	Design	Tx dur	Dose	Con	Conditions	Assessment	GI responses
Abraham et al., 1981*	31	R, X and P, db	1 dose	20, 30, 40, 60 g PG	Suc	Water; am Sn; tx for each group was a dose of PG and control	Interview (bm, symptoms, intensity)	For 20, 30, 40 g PG vs suc: NS bm and similar symptoms. For 60 g PG (n = 10): 40% reported inc watery stools and flat, 60% reported inc ab discomfort, 80% reported inc symptoms (1 or more). (For suc, 20% for ab discomfort and having at least 1 symptom)
	10	R, X and P, db, WO	2 d	30, 60, 120 g PG	Suc	Beverages; div	Same as above	For 30–120 g PG vs suc: NS bm wt. Flat most common symptom and inc w/ dose (20% for 30 g, 30% for 60 g, 50% for 120g) but none for suc; 20–30% had ab distention, flat, bor, ab discomfort, colic to a “troublesome and socially inconvenient extent”
	10	R, X, db	21 d	30 g PG	Suc	Same as 2-d study above	Same as above	Most found 30 g PG acceptable but 50% subj reported mod or sev flat (1 subj reported excess flat w/ suc)
	12	R, X, db	28 d	15 g PG and 15 g sorb	Suc	Same as 2- and 21-d studies above	Same as above	For PG: No loose bm reported and no consistent adverse symptoms
Beaugerie et al., 1990*	6	R, X, WO	11 d	30 g sorb, 57 g malt, 69 g PG	Suc	Consumed at end of meals; div; dose gradually increased during days 1-4; DL	Record symptoms of ab pain or diarrhea; FC	No diarrhea or ab pain reported with any treatment
Bornet et al., 1996	24	R	1 dose	0.4 or 0.8 g/kg bw eryth (about 27–54 g eryth)	Suc; no tx	Chocolate (am Sn)	Q (bm, symptoms)	NS bm and symptoms
Culbert et al., 1986	12	R, X	5 wk	30, 45, 60, 100 g xyl	Glc	Mix w/ drink or food; div; DL	Interview (symptoms)	Reports of diarrhea and other symptoms (gas, bloat) increased with dose of xyl (most had diarrhea w/ 100 g). For 100 g xyl div into 3 doses vs div into 2 doses: sig higher mean symptom score
Fritz et al., 1985	11	R, X, WO	1 wk	10, 30 or 35, 40, or 50 g isomalt	No tx	OJ (Br), yogurt (Lu); div; dose inc each wk; DL; 12 g bLDC	Note symptoms each day; FC	Thin bm occasionally during first days of a given dose but no diarrhea; change NS in wet bm wt or freq; subj variability of symptoms; inc ab noise, fullness, flat, meteorism with inc isomalt dose
Gee et al., 1991	6	R, X, db	1 dose	45.1 g isomalt	Suc; fruct	Choc bar; F	Asked to describe side effects	No sig discomfort reported; mild flat (n = 2)
Gee et al., 2005	10	X, sb	1 dose	10 g lact	Suc	Flavored drink; Br; F; DL	Q (symptoms with VAS)	No gastrointestinal effects reported for 10 g lactitol
	12	X, sb	1 dose	15, 20 g lact	Suc	Same as above	Same as above	For 20 g lact: some subj reported inc nausea associated with mild stomach pain 5 h after; NS VAS comparisons
Gostner et al., 2005*	19	X, db, WO	4 wk	5-30 g isomalt	Suc	Various foods; div; wk 1: dose inc 5-30 g; DL; 12-16 g bLDC	Daily record (bm, symptoms, intensity—none to sev); interview	For isomalt vs suc: freq bm inc sig but NS wet, dry, water wt; symptoms usually mild or mod but distention score was sig higher for isomalt (1.8) vs suc (0.7)

(Continued on next page)

**Table 8** Sugar alcohols. *Continued*

Study	N	Design	Tx dur	Dose	Con	Conditions	Assessment	GI responses
Koizumi et al., 1983a*	42	X, b	1 dose	20–26 g, 40–51 g, and 80–102 g sorb or malt (based on bw)	Suc	Water; DL	Report time, onset of symptoms and diarrhea, bm details	Sorb: ED50: 0.4 g/kg bw for males and 1.0 g/kg bw for females; max no-eff dose 0.15 g/kg bw for males and 0.3 g/kg bw for females. Malt: ED50: 0.8 g/kg bw for males and females; max no-eff dose 0.3 g/kg bw for males and females. Incidence of diarrhea higher for sorb than malt but onset the same (about 6 h or less). Gurgling most common (sorb 76%; malt 69%); flat (sorb 48%, malt 54%); ab pain (sorb 26%, malt 31%)
Koutsou et al., 1996*	59	R, X, db, WO	1 d	30, 40 g isomalt, lact, malt	Suc	Liquid; F; DL	Q (bm, symptoms, intensity)	For 30–40 g lact vs suc: bm freq and symptom incidence and severity inc sig. For 30–40 g isomalt vs suc: symptoms incidence and sev of bor and flat sig greater. For 40 g isomalt vs suc: bm freq and incidence and sev of loose bm inc sig. For 30–40 g malt vs suc: NS bm but mild flat inc sig. For 40 g malt vs suc: mild bor and colic inc sig. Lact not tolerated as well as isomalt or malt; isomalt not tolerated as well as malt
Lee et al., 1994*	10	R, X, db, WO	1 dose	31.5 g sorb or isomalt	Suc	Chocolate bar; F; DL	Q (bm, symptoms, intensity)	For sorb vs isomalt and suc: reports of diarrhea sig higher; NS symptoms but more reports for sorb and isomalt and higher freq of mod or sev symptoms for sorb
Lee and Storey, 1999*	50	R, X, db, WO	1 dose	20 g lact	Suc	Chocolate bars; Sn; DL	Q (bm, symptoms, intensity)	For lact vs suc: freq watery bm sig higher; mild laxative effect; sig more bloat, bor, flat, colic, and flat graded 2–3 out of 3 (considerably more than usual)
Lee et al., 2002*	50	R, X, db, WO	2 d	25, 40 g isomalt and PG	Suc	Candy; Sn; DL	Q (bm, symptoms, intensity)	For 25 g isomalt vs suc: NS bm freq but sig more bloat, bor, flat, colic. For 25 g isomalt vs PG: sig more colic. For 40 g isomalt vs suc: sig inc freq bm and bor, flat, colic inc sig. For isomalt and PG vs suc: sig more reports of watery bm. For 25 g PG vs suc: NS bm freq but sig more bor. For 40 g PG vs suc: sig more reports of watery bm, bloat, bor, flat, and mod-sev bor and flat. For 25 g PG vs suc and for 40 g PG vs 25 g PG: mean symptom score sig higher
McRorie et al., 2002*	66	P, db	5 d	40 g sorb (also: 20 or 40 g olestra)	Suc TG	All had control; DL	Diary (bm, symptoms), FC	For sorb vs suc: bm water content sig greater; number of days with reports of ab cramp sig more; severity of nausea and urgency sig greater (NS for olestra vs TG). 3 subj w/drew during sorb (pain, diarrhea, vom)

*(Continued on next page)*

**Table 8** Sugar alcohols. *Continued*

Study	N	Design	Tx dur	Dose	Con	Conditions	Assessment	GI responses
Oku and Okazaki et al., 1996	38		1 dose per d, up to 3 d	25, 50, 75 or 25, 37.5, 62.5 g eryth; 12.5, 25 g sorb	Suc	Jelly 2 h after meal; inc dose each day until diarrhea; DL	Q (bm, symptoms)	Laxative threshold for eryth: 0.8 g/kg bw for females and 0.66 g/kg bw for males; laxative threshold for sorb: 0.24 g/kg bw for females and 0.17 g/kg bw for males; nausea more common and flat less common with eryth than sorb; bor freq with both eryth and sorb; however, statistical sig for symptoms not reported
Patil et al., 1987*	21	R, X, db, WO	10 d	20 up to 110 g sorb or 40 up to 130 g lact	Glc	Water (w/in 30 min after meal); div; dose inc until lax TD reached (un-acceptable level of side effects)	Scored symptoms based on usual and effect on activities	For sorb vs lact: NS laxation TC (mean sorb lax TD 71 g; mean lact lax TD 74 g); more than half subj reported diarrhea for sorb and lact (only 1 for control). 7 subj on sorb and 4 on lact DC'd b/c sev symptoms. For sorb and lact vs glc: symptom score sig higher. For sorb vs lact: NS symptom score; flat had highest score followed by bor, bloat, ab pain
Peters and Lock, 1958*	101	X, sb	7 d	25 g sorb	Glc	Liquid after meals; div	Q (number of bm, wind, discomfort, pain)	For sorb vs glc: NS laxation (though 2 of 5 subj reporting "marked laxation" and discomfort with sorb DC'd; 15 subj DC'd for other reasons); flat tendency with sorb
Rouskone-Formestaux et al., 2003*	12	X, db, WO	10 wk (1 d/wk)	10 up to 100 g malt	Suc	Chocolate bar; div; inc dose gradually until grade 3 symptom or diarrhea; DL	Diary (symptoms, intensity)	TD (grade 3 symptoms or diarrhea): 92 g for malt and 106 g for suc. For malt vs suc: sig inc diarrhea but NS symptoms. Most common symptoms for malt were excess flat and ab pain
	12	X, db, WO	Up to 9 d	25% TD dose from above up to 30 g + TD malt	Suc	Same as above	Same as above	TD (grade 3 symptoms or diarrhea): 93 g for malt and 113 g for suc (sig); NS symptoms. Most common symptoms for malt were excess flat and ab pain
Sinaud et al., 2002*	15	P	25 d	20–100 g PG or PG-HPF	Dext	Water; div; doses gradually inc	Diary (bm, symptoms, intensity), FC	Low intensity diarrhea for each treatment, including control. Symptoms for PG and PG-HPF included gas, gurgling, flat, ab pain (low-intensity)
	9	X	32 d	20–100 g PG or PG-HPF	Dext	Same as above but with DL	Same as above	For PG and PG-HPF vs suc: NS bm freq; sig inc wet and dry bm wt but no reports of diarrhea. Symptoms for PG and PG-HPF: most subj reported gas emission HPF (med intensity); some subj reported gurgling (med intensity), flat, ab pain
Spengler et al., 1987*	60	P, db	12 wk	12–48 g isomalt	Suc	Various foods; div; inc dose over 12 wk; DL	Checklist (symptoms, bm)	NS bm freq, diarrhea or constipation; flat occurrence sig higher for isomalt vs suc; flat inc with inc dose isomalt; subj variability (inc, dec) for flat with 24 g over 6 wks; slight preference for suc

**Table 8** Sugar alcohols. *Continued*

Study	N	Design	Tx dur	Dose	Con	Conditions	Assessment	GI responses
Storey et al., 1998*	20	R, X, db, WO	1 dose	30, 40 g malt	Suc	Choc w/ water; F and non-F; Br; DL	Record of bm, symptoms, intensity; interview	For 30 and 40 g malt vs suc: NS bm freq but sig more bor and flat (ranked as mild). For 30 vs 40 g malt: mean symptom score showed sig correlation between dose of malt and number of symptoms
Tetzloff et al., 1996	12	R, X, db	1 wk	1 g/kg bw eryth (about 79 g eryth)	Suc	Yogurt, cookies, soft drinks; div	Interview (bm, symptoms)	NS bm freq and consistency and symptoms
Zumbé and Brinkworth, 1992*	80	X, WO	7 d	10.75 g sorb	No tx	Chocolate bar	Diary (bm, symptoms, intensity)	For sorb vs no sorb: freq of bm and diarrhea inc sig; flat and wind inc sig (but symptoms mostly slight)
	80	X, WO	7 d	19.35 g isomalt	No tx	Same as above	Same as above	For isomalt vs no isomalt: flat, cramps, wind inc sig (but symptoms mostly slight)
	97	X, db, WO	7 d	45 g isomalt	Suc	Same as above	Same as above	For isomalt vs suc: Diarrhea, bm freq inc sig; flat, wind inc sig (but symptoms mostly slight)
Zunft et al., 1983*	4	X	10 d	35 g malt	No malt	Sweetener given with meals	Report flat, gripes, N; FC	NS change from control period in bm freq or amt; "did not show any negative effect"

\*Assessing laxative and/or other GI effects was the primary focus of this study.

erythritol, but the total number of reports were less than those for the sucrose placebo.

Other reviews of clinical studies with erythritol have concluded single or repeated intakes as high as 1 g/kg body weight (Bernt et al., 1996) or even 132 g/day, (Livesey 2001) could be well-tolerated. Such high intakes may be perfectly acceptable if intake is increased gradually over days and the daily intake is consumed as divided portions throughout the day.

Future research on the gastrointestinal effects of erythritol should continue to study the effects of moderate and high single and daily intakes of erythritol. When the dosage is selected and reported based on body weight, the mean body weights of subjects should reflect the average population. Investigators should include an analysis of the usual and background intake of dietary fiber by subjects, for the studies presented here did not include this information. In addition to comparisons with other sugar alcohols and LDCs, studies should look at the effects of combining erythritol with other LDCs.

### Xylitol

Few studies have been published concerning the gastrointestinal effects of xylitol consumption compared to a placebo or control diet as well as report methods for assessing effects. Two studies assessing gastrointestinal effects in adults as primary endpoints are summarized in Table 8; the intakes for the chronic study (Culbert et al., 1986) ranged from 30–100 g/day xylitol, and the intakes for the acute study (Storey et al., 2007) ranged from 20 to 50 g/day.

Thirty grams xylitol divided and with meals was well-tolerated by most subjects; there were reports of mild abdominal distention and cramps, and two of twelve subjects reported diarrhea at this intake (Culbert et al., 1986). However, when 35 g xylitol were consumed dissolved in liquid in another study, there was a significant increase in the frequency of watery bowel movements compared to the sucrose control, and when the intake was increased to 50 g xylitol, there was a significantly greater number of subjects reporting nausea, bloating, borborygmi, colic, and watery bowel movements as well as an increase in the frequency of bowel movements (Storey et al., 2007). In the study by Culbert et al. (1986), intakes of 60 g/day and greater were associated with increasing occurrences of diarrhea and other symptoms, and when the daily intake reached 100 g, all subjects experienced gastrointestinal effects, which included diarrhea and intense cramping. Some subjects appeared to adapt over time as their reports of diarrhea and other symptoms as well as their severity decreased when the daily intake remained constant but the individual amount increased from 33.3 g to 50 g (Culbert et al., 1986). Most people may tolerate 30 g/day and adapt to higher intakes if the daily intake is divided and in the solid rather than the liquid form.

### Sorbitol

Researchers have conducted numerous studies specifically to assess the gastrointestinal effects of sorbitol. Nine studies focused on the gastrointestinal effects of sorbitol are summarized in Table 8. Study designs and protocols vary widely with intakes ranging from about 10 to 100 g per day. Most of the studies provided a digestible sugar placebo to serve as the control.

**Table 9** Sugar alcohols and children.

Study	N	Design	Tx dur	Dose	Con	Conditions	Assessment	GI responses
Lee et al., 2002*	48 (6–9 yo)	R, X, db, WO	2 d	25 g isomalt or 25 g PG	Suc	Fruit-flavored candy, Sn at school; DL	Interview (bm, symptoms, intensity)	For isomalt vs suc: sig inc in freq of bm and freq of watery bm; sig inc in total number of reports of bloat, bor; sig inc in number of children reporting bloat, bor, colic. For PG vs suc: NS bm; sig inc number of children reporting bor; NS mean symptom score. For isomalt vs PG: sig inc in total number of watery bm; sig inc in bloat and colic
Paige et al., 1992*	21 (8–12 yo)	R, X, db, WO	1 dose	15, 25, or 35 g isomalt	Suc	Chocolate made w/o milk or milk products	Observation and interview (bm, symptoms)	For isomalt vs suc: NS diarrhea incidence; NS symptoms after 24 h (after 4 hours, some reports of ab cramps with each dose of isomalt but none with suc)
	20 (13–18 yo)	R, X, db, WO	1 dose	15, 25, or 35 g isomalt	Suc	Same as above	Same as above	No reports of diarrhea or loose stools. For isomalt vs suc: NS symptoms 24 h NS symptoms (only one report of ab cramps with 25 g isomalt)
Storey et al., 2002*	67	R, X,db, WO	2 d	25 g isomalt	Suc	Candy; DL	Interview (bm, symptoms, intensity)	For isomalt vs suc: sig inc in number of watery bm but NS bm freq; sig more stomachaches, rumbling noises and symptoms rated as 2–3 (out of 3)
Uhari et al., 1988	306	R, P, db	2 mos	8.4 g or 10 g g xyl	Suc w/ 0.5 g xyl	Syrup, gum, or lozenge after meal; div	Daily symptom reports completed by parents	More discomfort reported with xylitol in syrup and lozenge than in gum; 21 subj dropped out due to ab discomfort: 5 w/ suc in syrup, 8 w/ xyl in syrup, 0 w/ suc in gum, 1 w/ xyl in gum, 7 w/ xyl in lozenge
Uhari et al., 1996	857	R, P, db	3 mos	8.4 g g xyl	Suc	Gum; div	Symptoms noted by parents	For xyl vs suc: incidence of diarrhea and vomiting NS. No other GI effects reported

\*Assessing laxative and/or other GI effects was the primary focus of this study

Sorbitol has been shown to have laxative effects and has been approved by the U.S Food and Drug Administration for use as a laxative (Lederle et al., 1990). Sorbitol intake has been associated with an increased prevalence of diarrhea (Badiga et al., 1990); most of the studies of sorbitol focus on the development of diarrhea in subjects. Intakes of 2.5–10 g, even dissolved in liquid, were not generally associated with diarrhea in two studies comparing the laxative effects of sorbitol with those of lactulose (Hyams, 1983; Vernia et al., 1995). Abraham et al. (1981) reported only two of fifteen subjects developed diarrhea with 15 g/day sorbitol. In some studies, intakes of 20–30 g had little if any laxative effect in the majority of subjects. For example, 20 g dissolved in liquid was associated with mild diarrhea in three of 92 subjects (Vernia et al., 1995), and none of the six

subjects reported diarrhea with the 30 g/day sorbitol provided by Beaugerie et al. (1990). Peters and Locke (1958) reported marked diarrhea in five subjects (two withdrew from the study), but the other 96 subjects did not experience such a laxative effect.

However, similar intakes were associated with significant increases in diarrhea in other studies. Lee et al. (1994) also reported significant increases in diarrhea with 31.5 g sorbitol in a chocolate bar after an overnight fast compared to sucrose. An even higher intake of 40 g sorbitol in candy was associated with a significant increase in the mean stool weight and water content (McRorie et al., 2000); while those subjects in the placebo group did not have any liquid stools during their treatment, a total of 140 liquid stools were reported by the subjects consuming

sorbitol over the six-day treatment period. About half of the subjects in a small study by Hyams (1983) developed diarrhea with 20 g sorbitol.

Several researchers planned studies to determine threshold intakes associated with laxative effects or diarrhea. Koizumi et al. (1983a) estimated the sorbitol diarrhea ED50 as 0.4 g/kg body weight for men and 1.0 g/kg body weight for women and the maximum no-effect intake as 0.15 g/kg body weight for men and 0.3 g/kg body weight for women. Oku and Okazaki (1996) gave daily intakes of 25 g of sorbitol in jelly to a group of 28 adults and also noted different tolerance levels between men and women; they used laxation data to develop a regression equation to calculate the laxative threshold for men as 0.17 g/kg body weight and 0.24 g/kg body weight for women. These values for the laxative threshold for sorbitol in jelly calculated by Oku and Okazaki (1996) are lower than the no-effect intake reported by Koizumi et al. (1983a) for sorbitol dissolved in liquid; it should be noted that 10% of the men and 59% of the women had constipation in the study by Koizumi et al. (1983a). Based on the mean body weights of the subjects in these studies (approximately 65 kg for men and 50 kg for women in both studies) (Koizumi et al., 1983a; Oku and Okazaki, 1996), intakes of 10–15 g would be expected to be generally well-tolerated by most people, though a laxative effect could be experienced, and greater single and daily intakes may be similarly tolerated; these data are supported by the results of the previously discussed studies.

Ellis and Krantz (1941) reported a laxative threshold for sorbitol syrup at 20–30 g and crystalline sorbitol at 50 g, but they did not indicate information of how they calculated these threshold levels but defined the “threshold dose” as the dose “considered the minimum amount of each substance which produced very soft or watery stools.” The intakes they reported caused such laxation in the majority of their subjects (Ellis and Krantz, 1941). In addition, Patil et al. (1987) reported a mean laxative threshold dose for sorbitol of 71 g/day.

With the exception of the study conducted by Beaugerie et al. (1990), intakes as low as 10 g sorbitol were associated with gastrointestinal effects such as flatulence and abdominal pain (Hyams 1983; Vernia et al., 1995). Abraham et al. (1981) reported excessive flatulence with 15 g/day sorbitol. In another study, Koizumi et al. (1983b) identified gurgling, flatulence, and abdominal pain as the most common of these other gastrointestinal effects with a mean intake of 18.6 g for women and 24.7 g for men; other studies by these authors also noted these three symptoms were common with sorbitol intake (Koizumi et al., 1983a; Koizumi et al., 1983b), though it should be noted that in one study (Koizumi et al., 1983b) several of the women were taking laxatives. Peter and Locke (1958) commented on a “definite tendency to flatus due to sorbitol” after providing subjects with 25 g sorbitol dissolved in liquid. Although the symptoms were generally described as mild or moderate by subjects, Lee et al. (1994) noted the total number of reports of symptoms were more for 31.5 g sorbitol compared to the sucrose placebo. The severity of the reported effects increased with increasing intakes of sorbitol (Hyams, 1983).

Some studies compared the gastrointestinal effects reported by subjects after consuming a sorbitol treatment to those experienced after a placebo (sucrose) treatment. Koizumi et al. (1983b) noted that symptoms were more common with sorbitol consumption compared to the placebo. McRorie et al. (2002) found significantly more abdominal cramps and significantly greater severity of nausea with 40 g sorbitol compared to the placebo. Patil et al. (1987) found statistically significant increases in gastrointestinal effects for sorbitol versus the placebo with regard to a calculated symptom score and noted the highest score was for flatus followed for borborygmi, bloating, and abdominal pain. Seven subjects withdrew from the study due to the effects associated with sorbitol consumption (Patil et al., 1987).

Some of the studies included hydrogen breath tests. Significant increases in hydrogen expiration have been reported with increasing intakes (Hyams, 1983) or compared to other sugar alcohols such as isomalt (Lee et al., 1994). Often, the results of these studies do not show a correlation between the maximum rise in breath hydrogen and symptom severity (Hyams, 1983). Badiga et al. (1990) noted all subjects who experienced abdominal symptoms within four hours of consuming sorbitol had an increase in breath hydrogen expiration of at least 20 ppm compared to the baseline test before consuming the sorbitol; however, they could not identify a correlation between the hydrogen breath samples and the severity of the abdominal symptoms of subjects.

Jain et al. (1985), however, identified a relationship between the quantity of breath hydrogen levels and the severity of gastrointestinal symptoms: the mean maximum hydrogen excretion was higher in those experiencing more severe symptoms. Jain et al. (1985) also noted in 80% of the subjects who experienced gastrointestinal symptoms, the breath hydrogen levels rose within 30 minutes (usually before) of the onset of the symptoms. Jain et al. (1987), however, reported that peak as well as average per hour hydrogen breath levels were related to transit time, but neither were related to the severity of the abdominal symptoms.

Overall, single intakes of about 10–15 g sorbitol may have laxative effects and are associated with other gastrointestinal symptoms; however, 20–30 g/day may be well-tolerated. When evaluating and comparing results of the sorbitol feeling studies, it is necessary to consider the study design and protocol details and note differences between studies such as subject characteristics, dosing (single or daily intakes), and dietary factors as well as how authors calculate and report threshold intakes.

### *Mannitol*

Few studies concerning the gastrointestinal tolerance of mannitol have been published. Ellis and Krantz (1941) reported a laxation threshold of 10–20 g for mannitol; however, in addition to describing their endpoint as “very soft or watery stools,” they discussed neither their study design nor their methods for

calculating the threshold dose. In a discussion of the properties, food applications, and effects of mannitol, 20 g/d of mannitol was reported as an intake that would not cause laxation in most adults (Le and Mulderrig, 2001).

Nasrallah and Iber (1969) gave subjects 40–100 g mannitol on an empty stomach. The authors noted an increase in mannitol in diarrheal stools versus normal stools and that mannitol ingestion in amounts greater than 40 g generally caused diarrhea; however, they did not comment directly on the number of subjects who suffered from diarrhea or other gastrointestinal effects (Nasrallah and Iber, 1969).

### **Lactitol**

Although some clinical studies of lactitol have focused on its cathartic effects in patients with cirrhosis and related conditions (Heredia et al., 1987; Metzger et al., 1988; Morgan et al., 1987; Morgan et al., 1989; Riggio et al., 1989; Riggio et al., 1990); this discussion of lactitol focuses on laxative and other gastrointestinal effects as reported by four studies among healthy subjects. The primary endpoints of three of these studies (Koutsou et al., 1996; Lee and Storey, 1999; Patil et al., 1987) were gastrointestinal effects; one study (Gee and Johnson, 2005) focused on peptide YY circulation levels but also reported on gastrointestinal effects. Lactitol amounts ranged from 10 to 40 g in the three acute studies and up to 130 g in the threshold dose study (Patil et al., 1987).

Twenty g lactitol in chocolate was associated with a significant increase in the frequency of watery bowel movements compared to the placebo treatment (Lee and Storey, 1999). Intakes of 30 g and 40 g lactitol dissolved in liquid were also associated with significant increases in loose stools and the frequency of bowel movements (Koutsou et al., 1996). During the course of the laxative threshold study conducted by Patil et al. (1987), fifteen subjects developed diarrhea with lactitol (one with the sucrose placebo), but the authors did not identify the intakes that were associated with the diarrhea.

Gastrointestinal effects reported by subjects consuming lactitol included flatulence, abdominal pain, borborygmi, bloating, colic, and nausea. Although 10 g of lactitol did not contribute to such gastrointestinal effects, increases in nausea and mild stomach pain were noted, though these were not identified as significant (Gee and Johnson, 2005). Lee and Storey (1999) however, found significant increases in bloating, borborygmi, flatulence, and colic compared to the placebo. In addition, intakes of 30–40 g lactitol were associated with significant increases in borborygmi, colic, and flatulence (Koutsou et al., 1996), but in another study there were no complaints of diarrhea or abdominal pain with 25 g lactitol (Natah et al., 1997).

Patil et al. (1987) estimated a laxative threshold daily intake, which they defined as the intake that produces unacceptable levels of side effects or the maximum intake of the study, for lactitol of 74 g/day; the authors calculated symptom scores for each treatment and noted a significantly higher symptom score

for lactitol compared to the placebo; flatus had the highest score, and other effects included borborygmi, bloating, and abdominal pain. They suggested 40 g/day lactitol would be an acceptable daily intake. Others have suggested that under normal conditions, individuals may be able to consume 50 g lactitol per day with only transient intestinal gas (van Es et al., 1986).

The various types of studies on the gastrointestinal effects of lactitol provide information on the effects of lactitol at intakes ranging from 10 g to 130 g/day. While 10 g does not appear to induce gastrointestinal effects in healthy subjects, intakes of 20 g affect bowel movements and may be associated with other gastrointestinal symptoms. As the intake increases, symptoms are likely to increase; however, intakes of 30–40 and even 50 g could still be considered acceptable, especially if they are divided throughout the day.

### **Isomalt**

Published data on the gastrointestinal effects of isomalt are available from several investigators. Eight studies of the gastrointestinal effects of isomalt are summarized in Table 8; five are primary studies (Gostner et al., 2005; Koutsou et al., 1996; Lee et al., 2002; Spengler, 1987; Zumbé and Brinkworth, 1992), and three are secondary studies (Fritz et al., 1985; Gee et al., 1991; Lee et al., 1994). The study protocols are varied with isomalt treatment durations ranging from one meal to 12 weeks, single servings ranging from 25–45 g isomalt, and daily intakes ranging from 5–50 g.

Three studies required subjects to fast overnight (Gee et al., 1991; Koutsou et al., 1996; Lee et al., 1994); two of these studies and an additional study compared isomalt not only to sucrose but also to one or more other sugar alcohols: lactitol and maltitol (Koutsou et al., 1996), sorbitol (Lee et al., 1994), and a polyglycol syrup (Lee et al., 2002). Only Fritz et al. (1985) collected stool samples; the other investigators as well as Fritz et al. (1985) relied on information obtained from questionnaires and diaries to assess gastrointestinal effects associated with isomalt consumption.

Four studies administered isomalt in a divided daily amount of 5 to 50 g/day for 1 to 12 weeks. Fritz et al. (1985) reported occasional thin stools, though no diarrhea, in subjects consuming gradually increasing amounts of 20–50 g isomalt per day for 3 weeks in orange juice and yogurt with breakfast and lunch but no significant differences in the wet weight and frequency of bowel movements during these weeks compared to the week before and after isomalt consumption. In a parallel study, Spengler et al. (1987) also reported divided daily amounts of 12–48 g isomalt consumed for 12 weeks did not have a significant effect on the number or frequency of bowel movements and the development of diarrhea compared to equal amounts of sucrose in various foods; the authors noted great variances between individuals on the isomalt treatment. Gostner et al. (2005) and Zumbé and Brinkworth (1992) however, identified significant effects on bowel movement frequency with 5–30 g/day for 4 weeks and 45 g/day for 1 week, respectively,

compared to sucrose. Although Gostner et al. (2005) reported differences in wet and dry stool weights between isomalt and sucrose treatments were not significant, Zumbé and Brinkworth (1992) reported significant increases in diarrhea with the higher amount of 45 g isomalt per day compared to sucrose.

In adults, Lee et al. (2002) reported that 40 g isomalt was associated with a significant increase in the mean frequency of bowel movements and watery bowel movements compared to sucrose.

Five studies provided isomalt after an overnight fast and/or dissolved in a liquid. Koutsou et al. (1996) reported significantly more severe loose bowel movements and greater frequency of bowel movements under fasted conditions with one 40 g isomalt intake consumed in a beverage compared to sucrose. Lee et al. (1994) identified a significant increase in diarrhea with 31.5 g sorbitol in chocolate compared to isomalt but not such a difference between isomalt and sucrose under fasted conditions. Gee et al. (1991) provided 45.1 g isomalt in chocolate under fasted conditions but did not report any information about an effect on subjects' bowel movements. Two other studies (Fritz et al. 1985; Spengler, 1987) provided isomalt in divided amounts throughout the day in beverages and other foods with meals, but these authors did not discuss any effects that were specifically related to isomalt consumption in a beverage.

Other gastrointestinal effects associated with isomalt consumption include flatulence, borborygmi, bloating, stomach distention, and colic. When 25 g isomalt was given, isomalt was associated with significantly more bloating, borborygmi, flatulence, and colic (Lee et al., 2002) compared to sucrose. Lee et al. (2002) reported significant increases in all reports of borborygmi and flatulence and reports of these effects and colic rated as 2–3 out of 3 with 40 g isomalt compared to 40 g sucrose. Isomalt (31.5 g) was not associated with a significant difference in gastrointestinal effects such as flatulence, colic, stomach ache, and bloating or belching compared to sucrose (Lee et al., 1994), and even 45 g isomalt was well tolerated with only mild flatulence reported by two of six subjects according to Gee et al. (1991).

Divided amounts of isomalt were generally associated with mild effects even if they were significantly increased compared to sucrose; effects increased as intake increased. Amounts of 5–30 g isomalt per day were associated with mild to moderate distention, though the symptom score for isomalt was significantly greater than the score for sucrose, and although 30 g isomalt was well-tolerated (Gostner et al., 2005). Up to 45 g/day isomalt was associated with a significant increase in flatulence and wind compared to sucrose although these effects were reported as mostly slight (Zumbé and Brinkworth, 1992). Fritz et al. (1985) noted a variety of effects, including abdominal noises, fullness, flatulence, and meteorism, which varied by individual and increased as the intake of isomalt increased from 20 to 50 g/day, although they did not report if these effects were significant. Spengler et al. (1987) reported a significant increase in flatulence with 12–48 g isomalt per day compared to sucrose and commented that the frequency of flatulence increased as the

intake increased; however, as the intake was maintained at 24 g in weeks 3–9, three subjects had a decrease in the frequency of flatulence, while four subjects had an increase in the frequency of flatulence.

Under fasted conditions, 40 g isomalt consumed in a beverage was associated with an increase in the incidence of symptoms compared to sucrose as well as significantly greater severity for borborygmi and flatulence for 30 g and 40 g isomalt compared to sucrose (Koutsou et al., 1996).

Threshold amounts for diarrhea or other gastrointestinal effects have not been estimated for isomalt, but based on the published studies, a single intake of up to 30 g isomalt should be tolerated by most adults, and adapted individuals may be able to tolerate daily intakes of 50 g per day. When incorporated into foods, 30–50 g isomalt was associated with significant increases in bowel movement frequency, watery stools, and diarrhea and/or other effects such as flatulence in some studies, though other studies suggested these intakes did not significantly affect laxation.

Conflicting results may be related to differences in study designs and protocols, for some studies gradually adapted subjects to higher amounts over days or weeks and/or divided the daily amount into two or more portions, which could reduce the likelihood of identifying significant differences compared to sucrose. In addition, the sample size of the population varied from 6 to 97, and since investigators have reported great variability between individuals, results of studies with small sample sizes should be considered carefully. Based on the results of other studies, 40 g isomalt has a significant laxative effect when consumed in a beverage after an overnight fast (Koutsou et al., 1996), but 31.5–45.1 g isomalt in chocolate is well-tolerated, even after an overnight fast (Gee et al., 1991; Lee et al. 1994).

### *Maltitol*

Six primary studies of the gastrointestinal effects associated with maltitol consumption are summarized in Table 8 (Beaugerie et al., 1990; Koizumi et al., 1983a; Koutsou et al., 1996; Ruskoné-Fourmestreaux et al., 2003; Storey et al., 1998; Zunft et al., 1983). These studies provide data about threshold amounts of maltitol as well as the gastrointestinal effects of consuming a single dose of 30–40 g maltitol and divided daily amounts of 35 g and 57 g maltitol for more than one week.

Single amounts of 30–50 g and total daily divided intakes of 35 g and 57 g maltitol in chocolate had little effect on bowel movements, but similar intakes of maltitol dissolved in liquid were associated with diarrhea. Koutsou et al. (1996) and Storey et al. (1998) provided fasted subjects with 30–40 g maltitol in chocolate, and both reported no significant increase in the frequency of bowel movements compared to the sucrose chocolate treatment; Koutsou et al. (1996) also found no significant difference in the occurrence of loose feces between the treatments, and Storey et al. (1998) reported most of the bowel movements were normal with subjects having no more than one loose stool

per treatment. Storey et al. (1998) compared the effects of 30–40 g maltitol in fasted and non-fasted subjects and noted no significant differences in bowel movements of their twenty subjects between these conditions. Zunft et al. (1983) provided 35 g maltitol with meals and reported no differences in the frequency or amount of bowel movements of their four subjects between the 10-day maltitol period and the no-maltitol control period for the four subjects. Beaugerie et al. (1990) gradually increased the daily amount of maltitol administered with meals three times per day from about 15 g to 57 g given to six subjects for eleven days and reported no diarrhea or other gastrointestinal effects. In another study, Koizumi et al. (1983c) provided 26 subjects with a single 0.8 g/kg body weight (about 30–50 g) serving of maltitol or sucrose dissolved in 200 ml water and noted that subjects did not have diarrhea after consuming sucrose, but 75% of the subjects developed diarrhea after the maltitol treatment. In addition, Koizumi et al. (1983c) observed a higher incidence, though not significant, of diarrhea among the 10 men compared to the 16 women with the maltitol treatment; it should be noted that some of the women took laxatives in addition to the maltitol treatment.

Two studies estimated threshold amounts for maltitol. Ruskoné-Fourmestraux et al. (2003) defined the threshold dose as the dose associated with diarrhea or severe indigestion and estimated this dose for occasional (once a week for ten weeks) and regular (daily for nine days) consumption. The authors asked their 12 subjects to consume chocolate bars sweetened with maltitol or sucrose six times throughout the day; they reported the threshold dose for occasional consumption as about 92 g, which was not significantly lower than the dose for sucrose (about 106 g). In addition, six of twelve subjects reached their threshold dose at levels as low as about 63 g maltitol, and one subject reached his threshold dose for sucrose at 60 g, which was significantly different. The threshold dose for regular maltitol consumption was similar to occasional consumption (about 93 g maltitol and about 113 g sucrose), but the difference between these amounts of maltitol and sucrose was identified as significant, and eight subjects developed diarrhea after about 69 g maltitol and two after 90 g sucrose. Comparing the results for occasional and regular use of maltitol, the authors concluded that the colonic bacteria did not adapt during the nine days of regular consumption. For both occasional and regular consumption, the incidence of diarrhea increased significantly with maltitol compared to sucrose (Ruskoné-Fourmestraux et al., 2003).

Koizumi et al. (1983a) estimated the maximum no-effect dose of maltitol dissolved in 100–200 ml liquid two hours after lunch as 0.3 g/kg body weight and the ED50 as 0.8 g/kg body weight. Using the mean body weights reported by the authors (64.4 kg for men and 49.9 kg for women), these amounts translate to a maximum no-effect dose of 19 g for men and 15 g for women and an ED50 dose of about 52 g for men and 40 g for women. In this study, all subjects who consumed 1.6 g maltitol per kg body weight (104 g for men and 80 g for women) reported diarrhea but only 25% who consumed 0.4 g/kg bodyweight (26 g for men and 20 g for women) reported diarrhea.

When 30–100 g maltitol was incorporated into chocolate and administered in divided portions throughout the day, investigators reported only insignificant increases, if any, in gastrointestinal complaints such as flatulence and abdominal pain for maltitol compared to sucrose treatments. Zunft et al. (1983) commented when subjects consumed 35 g maltitol per day with meals, they “did not show negative effect.” Subjects who consumed 57 g maltitol in six portions throughout the day also did not experience any gastrointestinal effects (Beaugerie et al., 1990). Even when Ruskoné-Fourmestraux et al. (2003) gave subjects up to 100 g maltitol or sucrose until they developed severe indigestion or diarrhea, the authors did not identify a significant difference in the occurrence of the most common effects, flatulence and abdominal pain, between maltitol and sucrose.

Significant differences in flatulence and other related effects were reported in studies administering maltitol as a single amount on one occasion. Koutsou et al. (1996) reported 30 g maltitol was associated with a significant increase in mild flatulence, and 40 g was associated with significant increases in mild borborygmi, colic, and flatulence compared to sucrose, and Storey et al. (1998) reported significantly more flatulence and borborygmi with 30–40 g maltitol. In two studies, Koizumi et al. (1983a, c) reported gurgling, flatus, and lower abdominal pain were the most common symptoms with up to 1.6 g/kg body weight and 0.8 g/kg body weight, respectively, maltitol dissolved in water; in the first study, Koizumi et al. (1983a) identified the incidence of these symptoms as 69%, 54%, and 31%, respectively.

Maltitol is better tolerated as an ingredient in chocolate or other foods rather than dissolved in water. As the level of a single dose increases, gastrointestinal effects like flatulence and borborygmi become more common, but these effects are generally mild so that even single intakes of 40 g maltitol may be generally well-tolerated in unadapted individuals. Higher daily intakes may be tolerated if the total amount is divided throughout the day and gradually increased over time, but intakes above 60 g or 70 g/day would contribute to diarrhea in most individuals.

Future studies should be designed to analyze occasional and regular consumption as the study designed by Ruskoné-Fourmestraux et al. (2003) and consider both single and divided daily intakes in foods and beverages as well take background fiber and other low-digestible carbohydrate intakes.

### *Polyglycitol*

Investigators have reported on the gastrointestinal effects of polyglycitol syrups that have been incorporated into candy and other food products as well as beverages in studies ranging in duration from one or two days to thirty-two days per treatment. Results published by four investigators administering single intakes ranging from 20–60 g or divided amounts ranging from 15–120 g polyglycitol syrups in crossover studies are summarized in Table 8.

Polyglycitol syrup formulations vary depending on the manufacturer. Table 10 provides the formulations of the polyglycitol

**Table 10** Formulations of polyglycitol syrups used by investigators.

Study	Formulation
Abraham et al. (1981)	58% Maltitol 15% Glucose-sorbitol polymer 3% Sorbitol
Beaugerie et al. (1990)	52.5% Maltitol 40.5% Hydrogenated oligosaccharides and polysaccharides 7% Sorbitol
Lee et al. (2002)	55% Maltitol 21% Hydrogenated oligosaccharides, and polysaccharides 19% Maltitriitols 5% Monsaccharides
Sinaud et al. (2002)	50% Maltitol 50% Hydrogenated polysaccharide syrup

syrups discussed in this review as provided by the authors of the studies summarized in Table 8. Most of the studies used polyglycitol syrups having similar maltitol content (50–58%) and sorbitol content (3–7%); the matitriitol and hydrogenated oligosaccharide and polysaccharide content was about 50% in one laboratory (Sinaud et al., 2002), 40% in two laboratories (Beaugerie et al., 1990; Lee et al., 2002), and about 10–15% in another laboratory (Abraham et al., 1981).

The consumption of 25 g polyglycitol syrup in candy as a snack for two days did not significantly affect the frequency of bowel movements in adults or the mean number of watery bowel movements in children compared to the sucrose treatments (Lee et al. 2002). Adults consuming 40 g polyglycitol syrup in candy, however, reported significantly more watery bowel movements (Lee et al., 2002). When 20–60 g polyglycitol syrup was taken in liquid between meals for a single day, there were no significant differences in the development of diarrhea between the treatment of 40 g polyglycitol syrup combined with 10 g sucrose compared to the treatment of 50 g sucrose; however, 40% of the subjects consumed 60 g polyglycitol syrup combined with 10 g sucrose developed diarrhea, whereas these subjects did not develop diarrhea after consuming 70 g sucrose, which was significant (Abraham et al., 1981). The difference in effect for those subjects consuming 40 g polyglycitol syrup in candy (Lee et al., 2002) compared to 40 g in liquid (Abraham et al., 1981) could be related to differences in study design, sample population, or polyglycitol syrup formulation.

The laxative effect of polyglycitol syrup was decreased when subjects consumed divided amounts. When 30–120 g polyglycitol syrup was provided in liquids with meals for two days, subjects did not have significant increases in stool weights, and subjects consuming divided intakes of 15 g polyglycitol syrup per day for four weeks did not have any loose stools (Abraham et al., 1981). Two other studies gradually adapted subjects to higher intakes of polyglycitol syrups. Beaugerie et al. (1990) reported subjects did not develop diarrhea with 69 g polyglycitol syrup divided into three portions, which were dissolved in 100 ml water. In a preliminary parallel study running for 25 days,

Sinaud et al. (2002) reported no differences between the number of occurrences of diarrhea among the five subjects in each of three treatment groups consuming about 98 g/day polyglycitol syrup, higher performance (HPF) polyglycitol syrup, and sucrose; in the main crossover study running for 32 days, the authors reported no significant difference in the frequency of bowel movements and no diarrhea for the three treatments, although they observed a significant increase in the wet and dry weights of the polyglycitol and HPF polyglycitol treatments and the water weight of the polyglycitol treatment compared to the sucrose treatment.

Other gastrointestinal effects reported with polyglycitol consumption included flatulence, abdominal distention and discomfort, borborygmi, gurgling, and bloating. Koizumi et al. (1983b) reported effects such as gurgling, the most common symptom, flatulence, and abdominal pain which was experienced by no more than 25% of the subjects consuming about 20 g polyglycitol syrup in foods, though this incidence was greater when the sweetener was incorporated into a tablet and beverages; the authors also noted that these symptoms were often accompanied by diarrhea. Twenty-five g polyglycitol syrup in candies for two days was associated significantly with more borborygmi and a significantly higher mean symptom score than the sucrose treatment; 40 g polyglycitol syrup was associated with significant increases in borborygmi, bloating, and flatulence, and borborygmi and flatulence rated as moderate to severe compared to sucrose as well as a significantly higher mean symptom score than 25 g polyglycitol (Lee et al., 2002). Forty percent of subjects consuming a single dose of 60 g polyglycitol syrup combined with 10 g sucrose in liquid reported increased flatulence, and 60% reported abdominal discomfort, but after consuming 70 g sucrose in liquid, none of the subjects reported increased flatulence and 20% reported abdominal discomfort; symptoms associated with single polyglycitol intakes of up to 40 g were similar to those of sucrose (Abraham et al., 1981).

Abraham et al. (1981) also conducted trials of divided daily intakes of polyglycitol syrup. A trial of 15 g polyglycitol was not associated with the occurrence of any consistent adverse symptoms, and although 50% of the ten subjects in another trial consuming 30 g polyglycitol moderate or severe flatulence, 90% rated the treatment as acceptable (Abraham et al., 1981). When Abraham et al. (1981) gave daily divided amounts of 30 g polyglycitol and sucrose and 30–120 g polyglycitol and 30–70 g sucrose in liquid in two other trials, increased flatulence was experienced by 20–50% of the subjects with 30 g polyglycitol, 30% with 60 g, and 50% with 120 g, while no such effect was reported with 15 g polyglycitol or any amount of sucrose. Regarding the administration of 30–120 g polyglycitol syrup per day, the authors commented 20–30% of subjects experienced abdominal distention, flatulence, borborygmi, abdominal discomfort, and colic to a “troublesome and socially inconvenient extent” (Abraham et al., 1981). Beaugerie et al. (1990) observed better tolerance as their subjects did not report any gastrointestinal effects when their daily divided intake of polyglycitol in 100 ml water gradually increased from about 17 g/day to 69 g per

day. Gas emission was the most common symptom reported after subjects consumed divided daily amounts of about 65 g or more polyglycitol and HPF polyglycitol syrup in the preliminary and main trials of amounts gradually increasing from 20–100 g polyglycitol syrup and HPF polyglycitol syrup provided by Sinaud et al. (2002); in the preliminary parallel trial, this effect was rated as low intensity, but in the main crossover trial, it was rated as medium intensity. Other effects for polyglycitol and HPF polyglycitol included gurgling, flatulence, and abdominal pain, though reports of such effects with sucrose were not mentioned.

Based on these studies, polyglycitol should be expected to cause few if any gastrointestinal side effects with amounts between 20–30 g and increased symptoms and possibly diarrhea at amounts of 40 g per day and above, though tolerance may be increased over time and with divided daily amounts even as high as 65 g/day, though another study reported polyglycitol syrups are generally tolerated up to 30–50 g/day after adaptation (Schweck and Ziesenitz, 1996), and Eberhardt (2001) commented greater intakes or the consumption of polyglycitol syrups on an empty stomach by unadapted individuals may have a laxative effect.

### *Comparisons of Sugar Alcohols*

Many of the aforementioned studies of sugar alcohols were designed to assess the relative gastrointestinal acceptability of a particular sugar alcohol to not only a sugar placebo but also to another sugar alcohol. Such studies are useful because the conditions of consumption are more consistent across treatments than they are for treatments given in different studies.

The effects of erythritol consumption have been compared directly to those of xylitol and sorbitol. When consumed in a liquid single intakes of 35 g and 50 g xylitol had significantly higher symptom scores than intakes of erythritol (Storey et al., 2007). In addition, Storey et al. (2007) reported a significant increase in the frequency of watery feces with both 35 and 50 g xylitol compared to the sucrose control treatment but not a significant increase in the intake of 50 g erythritol compared to sucrose; 50 g xylitol (compared to sucrose) was associated with a significant increase in the number of subjects reporting nausea, bloating, borborygmi, and colic, whereas 50 g erythritol (compared to sucrose) was only associated with a significant increase in the number of subjects reporting nausea and borborygmi. Erythritol was calculated to have a higher laxation threshold than sorbitol in both men and women; the laxation threshold dose for sorbitol was reported as 0.17 g/kg body weight for men and 0.24 g/kg body weight for women, and the dose for erythritol was reported as 0.66 g/kg body weight for males and 0.80 g/kg body weight for females (Oku and Okazaki, 1996). In the same study, the authors noted that reports of nausea were more common and those for flatulence were less common with erythritol compared to sorbitol.

In addition to the work with erythritol and sorbitol published by Oku and Okazaki (1996), other studies have compared the ef-

fects of sorbitol to those of lactitol, isomalt, maltitol, and polyglycitol; the results indicate that sorbitol is generally associated with more symptoms of intolerance compared to polyglycitol syrups, maltitol, and isomalt, but sorbitol is tolerated about as well as lactitol.

One study looked at the tolerance of sorbitol and lactitol (and a glucose placebo) and found a laxative threshold that was similar between lactitol (74 g) and sorbitol (71 g), and though the symptom scores for sorbitol and lactitol were significantly greater than for control, there was not a significant difference in the scores between the two sugar alcohols (Patil et al., 1987).

Beaugerie et al. (1990) reported no symptoms for 35 g sucrose, 30 g sorbitol, 57 g maltitol (which contained 27 g glucose and 30 g sorbitol), and 69 g polyglycitol (which contained 30 g sorbitol) in a study of six men, which suggests that intakes of 30 g or less of sorbitol are tolerated equally well as higher intakes of maltitol and polyglycitol.

Lee et al. (1994) compared the effects of 31.5 g of sucrose, sorbitol, and isomalt in a chocolate bar and found that diarrhea and the frequency of moderate or severe symptoms were significantly higher for sorbitol versus sucrose and isomalt. The ten adults received one dose of each product with a one-week washout period between each treatment (Lee et al., 1994).

Abraham et al. (1981) reported increased reports of flatulence and loose stools with 12 subjects on 15 g sorbitol but no such reports with maltitol (polyglycitol) syrup. Koizumi et al. (1983a) found similar symptoms in the increasing-dose study of sorbitol and maltitol (stomach gurgling, flatulence, and lower abdominal pain), but the maltitol maximum no-effect dose was estimated as 0.3 g/kg bw for both men and women and for sorbitol this dose was estimated at 0.15 g/kg bw for men and 0.3 g/kg bw for women; the maltitol ED<sub>50</sub> was estimated as 0.8 g/kg bw for men and women, which is twice the dose of sorbitol estimated for men and 20% less than the amount estimated for women. In a related study, Koizumi et al. (1983b) compared sorbitol and hydrogenated glucose syrup (HGS), which contained 88–92% maltitol in tablet form (0.4 and 0.8 g/kg bw) as well as in foods and beverages (20 g); there was a significant difference between sorbitol and the sucrose control in tablet form but not between HGS and the control in tablet form for diarrhea.

Although lactitol has been shown to be tolerated about as well as sorbitol in water (Patil et al., 1987), Koutsou et al. (1996) found that lactitol was not tolerated as well as isomalt or maltitol when used as an ingredient in chocolate (40 g or 30 g in addition to 10 g sucrose) and administered to fasted subjects, although 30 g lactitol and isomalt as well as 40 g of lactitol, isomalt, and maltitol all were associated with significant increases in borborygmi, flatulence, and colic, and the increase in loose feces was similar between isomalt and lactitol.

The effects of isomalt consumption have been compared to those of sorbitol, lactitol, maltitol, and polyglycitol. As cited above, the gastrointestinal effects have been shown to be less for isomalt compared to sorbitol (Lee et al., 1994) and lactitol (Koutsou et al., 1996) at an amount of about 30 g. However, Koutsou reported intakes of 30 g and 40 g maltitol were tolerated

better than equivalent intakes of isomalt, and, compared to 25 g polyglycitol syrup, 25 g isomalt was associated with a significant increase in the frequency of watery bowel movements and reports of colic in adults (Lee et al., 2002).

Maltitol has been shown to be tolerated better than similar amounts of sorbitol, lactitol, and isomalt (Koizumi et al., 1983a; Koutsou et al., 1996). Only one study compared the effects of maltitol to those of polyglycitol (Beaugerie et al., 1990), but since the amounts of the two treatments were different (57 g maltitol and 69 g polyglycitol), it can only be concluded that these sugar alcohols are tolerated equally well (no diarrhea or other effects) at the respective intakes.

As cited above, the effects of polyglycitol consumption have been compared to the effects of sorbitol (Abraham et al., 1981; Beaugerie et al., 1990), isomalt (Lee et al., 2002), and maltitol (Beaugerie et al., 1990). In general, it is better tolerated than sorbitol and isomalt, but there is not enough data to draw a conclusion about the relationship between maltitol and polyglycitol.

### **CHILDREN AND LOW-DIGESTIBLE CARBOHYDRATES**

Due to the relatively few published clinical studies of children and adolescents and LDCs, the focus of this review has been on studies reporting laxative and other gastrointestinal effects associated with the consumption of LDCs by adults. Saavedra and Tschernia (2002) reviewed clinical trials for prebiotics with children and found that the average daily intake of 1.1 g oligofructose in cereal was well-tolerated in young children ages 4 to 24 months; this amount was associated with less abdominal discomfort during bowel movements compared to the control treatment (cereal without the oligofructose supplement). Other studies indicated that infants and young children could tolerate up to 0.8 g oligofructose per kg body weight without symptoms (such as flatulence) when the oligofructose is incorporated into semi-solid foods such as cereal (Saavedra and Tschernia, 2002). Authors of another review article reported school-age children can tolerate up to 9 g/day and incorporation in solid food is better tolerated than in beverages (Carabin and Flamm, 1999).

Most of the published studies in this field have concerned sugar alcohols. Studies from forty years ago investigated the tolerance of sorbitol in children. In a parallel control study (sorbitol,  $n = 143$ ; or no treatment,  $n = 62$ ) with children at a summer diabetic camp, with increasing, divided intakes of sorbitol reaching up to 41 g/d (with three meals), diarrhea was reported in 12.5% of the sorbitol group and 21% of the control group; abdominal cramps were reported in 10% of the sorbitol group and 6% of the control group (Steinke et al., 1961).

In another study, children ages 20–36 months and 5–6 years, who had previously consumed mints with sorbitol and developed diarrhea, were given 1 dose of 9.3 g sorbitol in dietetic mints; in the stool samples that were collected for 24 h, there were no changes in the bowel movements of the older children,

but the younger group had soft to diarrheal stools (Gryboski, 1966).

More recently, the results of a survey of 221 parents of young children (ages 1–5 years) concerning the use of sugar-free gum, breath mints, and dietetic candies showed a significant correlation between sorbitol use and the incidence of diarrhea only in the three-year-old group; all children who consumed at least 0.5 g/kg body weight/day had diarrhea (Payne et al., 1997).

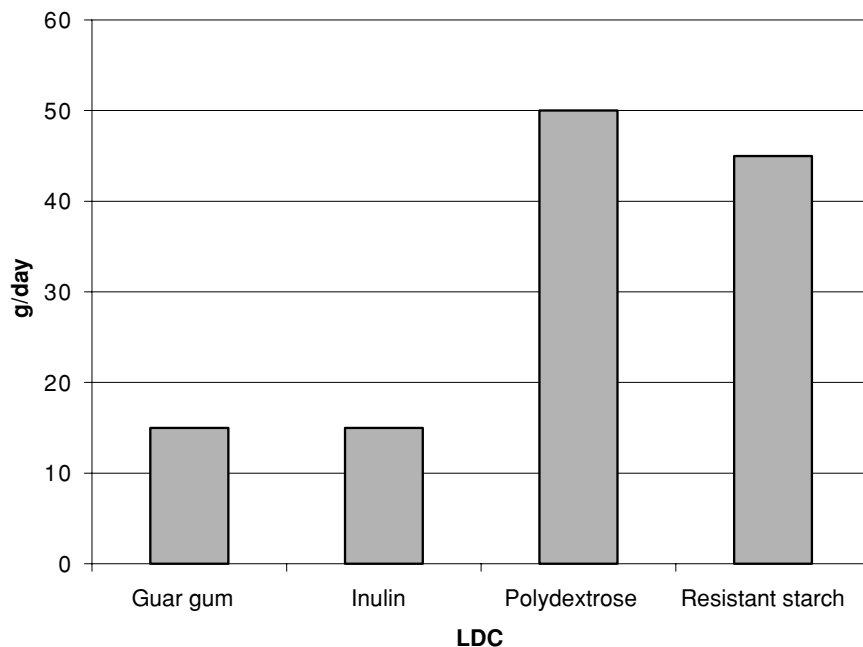
Most of the recent research with children has been limited to sugar alcohols: xylitol (Uhari et al., 1988; Uhari et al., 1996) and isomalt and polyglycitol (Lee et al., 2002; Paige et al., 1992; Storey et al., 2002). These five studies are summarized in Table 9.

Two controlled studies with focus on the prevention of acute otitis media in children suggest that daily intakes of 8–10 g xylitol in gum are generally well-tolerated (Uhari et al., 1988; Uhari et al., 1996). An increased incidence of abdominal discomfort occurred when xylitol was incorporated into lozenges or syrup, perhaps because children tend to ingest these forms at a faster rate than gum (Uhari et al., 1988); these authors concluded the tolerance level in children is lower than that of adults (about 8–10 g) and is affected by the rate of ingestion.

Studies of isomalt consumption by children have yielded inconsistent results with regard to laxation and other gastrointestinal effects (Lee et al., 2002; Paige et al., 1992). Twenty-five g isomalt increased significantly the number of watery bowel movements and frequency of bowel movements in children ages 6–9 years (Lee et al., 2002), though this effect was not significant in the adults from this and a similar study (Storey et al., 2002). In another study, however, the differences in the development of diarrhea in children (ages 8–18 years) consuming 15–35 g isomalt compared to sucrose were not significant (Paige et al., 1992). Concerning other gastrointestinal effects, Paige et al. (1992) reported no significant differences in children's symptom reports within 24 hours after consuming 15–35 g isomalt compared to sucrose, but Lee et al. (2002) reported a significant increase in bloating and borborygmi, and colic for children consuming 25 g isomalt for two days compared to sucrose. It should be noted that the population studied by Lee et al. (2002) was younger (ages 6–9) than that studied by Paige et al. (1992) (ages 8–18).

Although Lee et al. (2002) did not report a difference in the mean number of watery bowel movements, the number of gastrointestinal responses or the mean symptom score after children consumed 25 g polyglycitol and sucrose, this amount of polyglycitol was associated with a significant increase in borborygmi. In addition, the authors noted that most of the reports of symptoms were rated as "a little."

Based on these studies, daily intakes of 8–10 g sorbitol and xylitol and 25 g isomalt or polyglycitol may contribute to a mild laxative effect yet may be acceptable for school-age children and adolescents, but the consumption of sugar alcohols by younger children should be more limited. More clinical studies of sugar alcohols as well as the other LDCs should be conducted with children. Future studies could assess the effects of LDCs incorporated into beverages and various foods consumed with meals.



**Figure 2** Estimated acceptable daily intakes of nonstarch polysaccharides and resistant starch.

## RECOMMENDATIONS

Despite great variety in study designs, protocol, and types of results, some recommendations and generalizations can be made for consuming LDCs (Figs. 2–3). Although these amounts may appear conservative, when consumer gastrointestinal acceptability is of concern, it is better to be more conservative than liberal.

The non-starch polysaccharides guar gum and inulin fructans may cause mild symptoms such as flatulence with intakes below 10 g per day, but most individuals would be able to tolerate daily intakes of 10–15 g with an increase in the occurrence and severity of symptoms with 20 or more grams per day. Consuming at least 40 g FOS would likely increase fecal volume to meet the definition of clinical diarrhea; studies of inulin and guar gum at higher levels would be needed to estimate such a threshold for these non-digestible carbohydrates. The tolerance for polydextrose appears to be higher than guar gum and inulin. Individuals may be able to consume 50 g without experiencing diarrhea, whereas 88 g was calculated as a mean laxation threshold (Flood et al., 2004). Polydextrose appears to be more similar to resistant starch than the other NSPs as far as levels of acceptability when gastrointestinal effects are considered.

Compared to other non-glycemic carbohydrates, resistant starch has a high laxation threshold since reports of diarrhea were rare, even at levels as high as 80 g/day. The main side effect, excessive flatulence, is related to colonic fermentation and is significantly greater at intakes above 45 g/day.

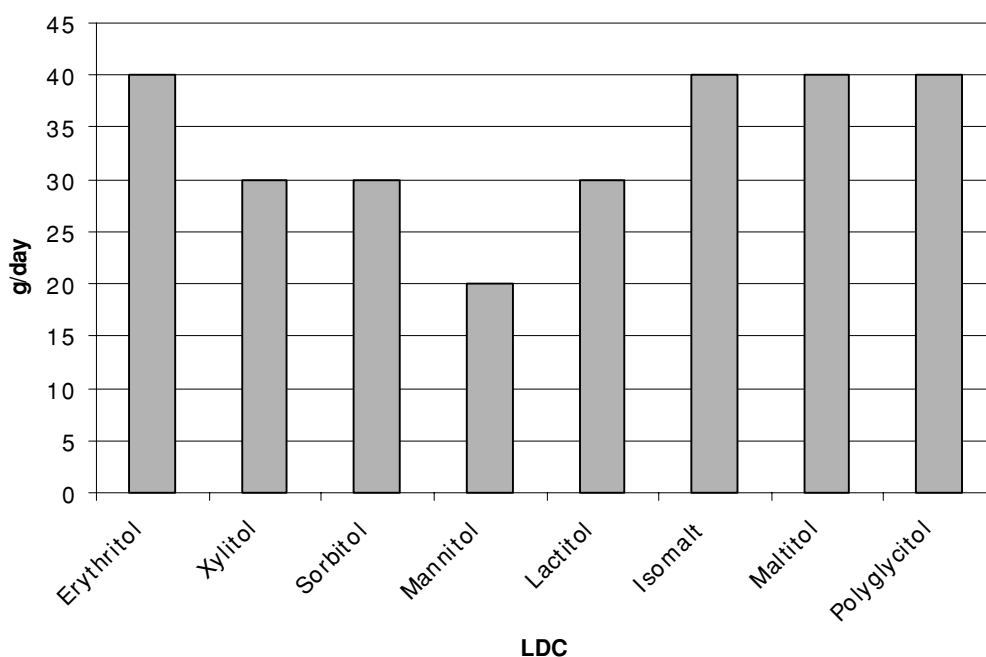
Daily intakes of 20–40 grams may be well-tolerated, depending on the sugar alcohol and intake conditions (Fig. 3). Higher single or daily amounts may be acceptable if consumers grad-

ually increase their intake. Daily amounts of 40 g erythritol, isomalt, maltitol, and polyglycitol and 30 g of xylitol, sorbitol, and lactitol should be acceptable to most people. Mannitol intake should be limited to 20 g per day.

When evaluating recommendations for acceptable intakes of LDCs for individuals, it is important to consider dietary conditions (as well as other factors that affect tolerance, as discussed previously and presented in Fig. 1). The following trends concerning dietary conditions were noted during the review process. First, gastrointestinal effects tend to increase in a dose-dependent manner. Second, when compared to similar amounts of a particular LDC in hydrated forms, solid forms have better gastrointestinal acceptability. Third, large intakes of LDCs have better gastrointestinal acceptability if the amount is increased gradually over days or weeks and divided into several portions throughout the day. As noted by Livesey (2001), the tolerance of individuals to LDCs may increase with time because their large intestines adapt to the fermentation due to improvement of water retention in the small and large intestines, greater fermentation of the low-digestible carbohydrate, or the reduced placebo effect of laxation. Livesey (2001) recommends regulations should consider doses for unadapted people.

## FURTHER RESEARCH

Most Americans do not meet the recommendations for dietary fiber (25 g/day for women and 38 g/day for men); based on data from the CSFII, men consume 16.5–17.9 g/day and women consume 12.1–13.3 g/day, which is about half of the recommendation for total fiber (IOM, 2005). However, these average



**Figure 3** Estimated acceptable daily intakes of sugar alcohols.

intakes do not include carbohydrates formerly excluded from the definition of fiber (oligosaccharides and resistant starch) as well as sugar alcohols. Thus, this data do not estimate total daily LDC intake. Total daily LDC intake is more useful for predicting potential gastrointestinal effects than considering only a single component of the total intake. As the use of LDCs by the food industry rises, total LDC intakes will likely increase, but it is likely that many different LDCs from many food sources will contribute to this amount. Therefore, recommendations for acceptable intake levels of a single category of LDCs like dietary fiber are of limited value.

Future research should examine the effects of consuming particular LDCs in combination with other LDCs and in the setting of the normal dietary patterns of the subjects. Diet is a complex exposure for which investigators try to control, but when that is done by removing all LDCs from the diet with the exception of a test LDC, then the results are not necessarily applicable to the general public in normal living conditions. Investigators should develop protocols that include various amounts of LDCs in the background diet and study the effects of particular LDCs consumed in combination with other identified LDCs in order to determine if interactions between different LDCs affect gastrointestinal acceptability or if adding another LDC has only an additive effect.

The results of Livesey et al. (1993) illustrate the importance of investigating the combination of multiple low-digestible carbohydrates. Compared to sugar alcohols such as lactitol and isomalt, the hydrogen breath expiration is significantly lower with polydextrose (Livesey et al., 1993), perhaps indicating that the fermentation of polydextrose would cause reduced symptoms related to fermentation, such as flatulence, compared to

sugar alcohols. The results of the tolerance tests discussed in Flood et al. (2004) compared to those discussed below for the sugar alcohols, the tolerance threshold for polydextrose is much higher than that for sugar alcohols. In addition, when lactitol and polydextrose were combined, the increase in breath hydrogen expiration increased greater than would be expected based on the data for each substance taken separately, which demonstrates an interaction between the metabolism of these carbohydrates (Livesey et al., 1993). Although the relationship between the results of hydrogen breath tests and gastrointestinal symptoms is tenuous, the results of Livesey et al. (1993) indicate the need for further studies investigating the interactions between non-glycemic carbohydrates.

Researchers need to come to a consensus concerning study design and protocol for assessing the gastrointestinal effects and acceptability of consuming all LDCs. Investigations using standardized designs and methods would contribute to a body of literature that could be used for a meta-analysis to make quantitative recommendations for LDC intake. A summary of the suggested study protocol is provided in Table 11.

Studies should be designed as randomized, double-blind, placebo-controlled crossover studies with washout periods (at least 2–3 weeks has been recommended by Marteau and Flourié, (2001)) between treatments. In addition, there are many factors that should be considered to assess gastrointestinal acceptability of LDC consumption. Study design affects results of individual studies and their application. Many published studies excluded subjects based on the following characteristics: gastrointestinal diseases, surgeries or other similar problems, and antibiotic and laxative use within the last 1–6 months. These are necessary exclusions because these conditions affect gastrointestinal

**Table 11** Suggested study design and protocol.

N	Large enough to have adequate power for statistical analysis
Exclusionary criteria	GI diseases/problems, laxatives/antibiotics *may want to do studies specifically with these groups
Subject characteristics to control or balance	Gender, age, weight
Study design	Double-blind, randomized placebo-control cross-over study (with 2 or more LDC)
Washout period between treatments	2–3 weeks, depending on length of treatment
Treatment period duration	1 day; extended periods (several weeks)
Conditions	Fasting; non-fasting conditions Within food; drink; hard candy Meal; snack
Dosing	Adapted/gradual increase and single dose; increasing doses to threshold Divided and non-divided doses
Measurements	- usual LDC intake (food frequency questionnaire) and LDC intake in background diet during study (food diaries) - usual fluid intake and intake during study - stool frequency, consistency, composition - symptoms (with mutual understanding of definitions) compared to usual baseline symptoms (rated from none to severe)
Statistical analysis	Detect significant difference between two or more groups with multiple factors
Reporting	- study conditions - subjects actual intake (treatment; total LDC) - statistically significant differences between control (sucrose) and LDC(s) for measurements - % subjects or absolute numbers experiencing all/total symptoms/stool frequency/consistency - any significant increase/decrease in symptoms with increasing doses and/or over time threshold or ED <sub>50</sub> dose if applicable - statistical analysis

function; however, it may be useful to conduct studies with these populations (especially those on antibiotics) in order to apply results to these common populations.

Researchers must decide if they want to create ideal consumption conditions that would yield the highest tolerance level or if they want to mimic real-life consumption conditions. Ideal conditions would include: low/restricted LDC in background diet, LDC in food within a meal, adequate fluid intake, period of adaptation with gradual increases in intake, and divided intakes. Real-life conditions would include: various amounts of LDC in the background diet; LDC in food and beverages within a meal or snack; LDC in beverages on an empty stomach; various levels of fluid intakes; single dose without adaptation period, period of adaptation with gradual increase, and period of adaptation with constant amount; and divided and single daily intakes. It

is important for these factors to be considered in the analysis of results and reported in published studies as they affect the application of the results. Both acute studies and chronic studies with and without adaptation periods are needed. In long-term studies, when adaptation might occur, the measurement of tolerance should be taken and analyzed in order to identify any significant differences between the beginning of administration and at various time points throughout the study. Studies that increase the intake until subjects experience a given symptom (such as flatulence or diarrhea) in order to determine a threshold should also be conducted. In addition, it is also useful to study tolerance to LDC under fasting and non-fasting conditions.

Regardless of the choice of real-life or ideal conditions, the following factors should be reported and considered in the statistical analysis: assessment of the usual LDC and probiotic (yogurt) intake and intake as background diet by subjects during the study (as well as usual intake of the treatment LDC in the study); assessment of their usual fluid intake and intake during the study; and their gender, age, and physical activity.

Measurements of laxative and other gastrointestinal effects should be objective and subjective and include fecal collections to analyze stool consistency, composition, and weight as well as subject questionnaires or diaries to assess laxation frequency and gastrointestinal effects. The reporting of symptoms should be standardized between studies. Some studies provide a list of specific symptoms with detailed explanations/definitions, and others ask subjects to write down any symptoms they have. Over-reporting may be more likely with the first method, but open-ended reporting tools may result in discrepancies between the symptoms subjects experienced and those defined by the researchers. A compromise would be to provide subjects with a list of gastrointestinal effects and stool consistencies accompanied by definitions and descriptions and then ask them to note the occurrence of these symptoms in a daily diary (that does not have the symptoms listed). Or, subjects could be asked to write down symptoms with a detailed description of what they mean by them and then discuss the symptoms with the study staff. Most studies require subjects to score the degree of their symptoms. In addition to rating the symptoms from none to severe, subjects should also be asked to compare their symptoms to their usual experience: usual, slightly more than usual, noticeably more than usual, or considerably more than usual. In addition, the subjects could be asked to describe their “usual” (baseline) experience as none, mild, moderate, or severe.

Statistical analysis should be conducted and reported for all gastrointestinal parameters. In order to have adequate power, investigators will have to recruit enough subjects. Specifically asking subjects if they perceive the degree of their experiences as acceptable would assist investigators in determining whether effects associated with LDC consumption are not only statistically significant but also clinically significant. For example, a study might demonstrate a statistically significant increase in the number of reports of an effect such as mild flatulence, but some subjects might find this change acceptable while others might find it unacceptable. Ideally, recommendations should be

made based on results that are not only statistically significant but also clinically significant according to subjects.

Standardized designs and procedures for assessing gastrointestinal acceptability will make it more plausible to compare the results of studies and conduct a meta-analysis in the future.

## CONCLUSION

Although the prevalence of low-digestible carbohydrates in the food supply is increasing, it appears that normal intakes of foods with these added carbohydrates are below the levels that would cause significant gastrointestinal effects. Future studies should consider the effect of other total fiber in the background diets of subjects. Many of the reviewed studies reported that the protocol included food records, but most published accounts did not report the total fiber during the study or the intake of total fiber in the normal diets of subjects.

In addition to comparing the gastrointestinal effects of LDCs in single studies, as these carbohydrates continue to be used in more and more food products, it will be increasingly important to study how individuals respond to mixed intakes of these carbohydrates, within and between different categories of LDCs (NSP, RS, and sugar alcohols). Future research should follow standardized procedures.

Given the potential for gastrointestinal side effects, it would be prudent for food manufacturers to consider the amount of LDCs in a single serving of a product, including all categories of LDC. Although some LDCs may be consumed at high amounts without undesirable effects, typical serving sizes of solid foods should limit total LDCs to 10–15 g; this amount should be less in beverages or foods often consumed on empty stomachs in order to reduce the likelihood that average consumers will experience side effects.

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