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Chicory Fructooligosaccharides and the Gastrointestinal Tract

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Chicory fructooligosaccharides are fructans extracted on a commercial basis from the chicory root. These materials are called *inulin* or *oligofructose*, and they are widely used in Europe in a variety of foods, especially as dietary fiber. This editorial examines the composition and source of inulin and oligofructose, the physiologic effects of their consumption, and how these materials relate to the concept of dietary fiber.

CHICORY FRUCTOOLIGOSACCHARIDES: IDENTITY AND OCCURRENCE

Chicory fructooligosaccharides are fructans. *Fructan* is a general term used for any carbohydrate in which fructosyl–fructose links constitute the majority of glycosidic bonds. The plant species currently used by the food industry to produce inulin belongs to the Compositae family; it is chicory (*Cichorium intybus*).[1] In chicory inulin, both GpyFn (α-D-glucopyranosyl-[β-D-fructofuranosyl]*n*-1-D-fructofuranoside) and FpyFn (β-D-fructopyranosyl-[β-D-fructofuranosyl]*n*-1-D-fructofuranoside) compounds are considered to be included under the same nomenclature, and the number of fructose units differs from 2 to more than 70. Native inulin is processed by the food industry to produce either short-chain fructans, namely oligofructose (DP 2–10; average DP 4), as a result of partial enzymatic (endoinulinase EC 3.2.1.7) hydrolysis or long-chain fructans by applying industrial physical-separation techniques. Chicory fructooligosaccharides are present in significant amounts in several edible fruits and vegetables. Average daily consumption has been estimated to be between 1 and 4 g in the United States[3] and between 3 and 11 g in Europe,[2] the most common sources being wheat, onion, banana, garlic, and leek.[2] Chicory inulin and oligofructose are officially recognized as natural food ingredients and are classified as dietary fiber in almost all European countries. An analytical method has recently been developed to quantify inulin and oligofructose in plants and food products.[4]

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METABOLISM AND PHYSIOLOGIC EFFECTS OF CHICORY FRUCTOOLIGOSACCHARIDES

Non-Digestibility in the Upper Gastrointestinal Tract

Because of the β-configuration of the anomeric C2 in their fructose monomers, inulin and oligofructose are resistant to hydrolysis by human digestive enzymes (α-glucosidase, maltase-isomaltase, sucrase) specific for α-glycosidic linkages. These carbohydrates have indeed been classified as "non-digestible" oligosaccharides.[5,6] Both in vitro[7,8] and in vivo[9–11] data have supported this classification. Knudsen and Hessov[10] and Ellegärd et al.[11] used the ileostomy model, and both studies have shown that between 86% and 88% of the ingested dose (10, 17, or 30 g) of inulin and oligofructose are recovered in the ileostomy effluent, supporting the conclusion that chicory fructooligosaccharides are practically indigestible in the small intestine of humans. Moreover, there is no evidence that they are absorbed to any significant extent.[9,12,13] Thus, it has been proposed to classify them as "colonic food," i.e., a "food entering the colon and serving as substrate for the endogenous bacteria, thus indirectly providing the host with energy, metabolic substrates and essential micronutrients."[14]

Fermentation in the Large Bowel: The Prebiotic Effect

That inulin and oligofructose are fermented by bacteria colonizing the large bowel is supported by a large number of in vitro and in vivo studies that also have confirmed the production of lactic and short-chain carboxylic acids as endproducts of the fermentation.[15,16] Furthermore, human in vivo studies have demonstrated that this fermentation leads to the selective stimulation of growth of the bifidobacteria population, making inulin and oligofructose the prototype prebiotic.[15,17–19] Compared with most other malabsorbed carbohydrates (e.g., resistant starch and other dietary fibers), the colonic fermentation of chicory fructooligosaccharides is acompanied by a significant change in the composition of the colonic microbiota due to selective proliferation of bifidobacteria and a concomittent reduction in the number of other bacteria such as bacteroides, fusobacteria, or clostridia. This effect has been identified as "a prebiotic effect" and a prebiotic has been defined as "a non-digestible food ingredient that beneficially affects the host by selectivley stimulating the growth and/or the activity of one or a limited number of bacteria in the colon and thus improves host health."[14] Based on the results of well-designed human studies that have shown significant changes in the composition of human fecal flora, it can be concluded that chicory fructooligosaccharides (3 to 15 g/d for a few weeks) are prebiotic.[20–22] However, even though some studies have shown a significant reduction in the number of clostridia, the health benefits (e.g., reducing the risk of intestinal infections) of such a change in the compostion of the colonic microbiota still need to be established. A recent report by Hunter et al. has shown that, at a daily dose of 6 g (2 × 3 g), oligofructose had no therapeutic value in patients with irritable bowel syndrome.[23] Conversely, in an experimental model of necrotising enterocolitis in quails, Catala et al. reported data that support the hypothesis that oligofructose may prevent the overgrowth of bacteria known to play a role in this pathology in preterm neonates.[24]

The colonic fermentation of inulin and oligofructose produces short-chain fatty acids and lactate plus gases as products of the anerobic metabolism. Concerning the pattern of production of short-chain fatty acids, in vitro fermentation and animal studies have demonstrated that supplementing the diet with inulin and oligofructose decreases the cecal pH and increases the size of the cecal pool of short-chain fatty acids. Due to the selective fermentation of these chicory fructans, the relative proportion of the three main short-chain fatty acids is changed. Typically, the molar ratio of butyrate is increased as compared with rats that received a typical starch-rich standard diet without added oligosaccharides.[25–29] Possibly related to this increase in the pool of short-chain fatty acids is the effect of inulin and oligofructose on the intestinal tissue, leading to hyperplasia of the mucosa and increased wall thickness in both the small intestine[29] and the cecum.[27]

Other Physiologic Effects

Besides the properties reviewed above concerning their role as fiber in the diet, inulin and oligofructose have been shown to induce interesting physiologic and nutritional effects. These effects relate to improved calcium bioavailability, the reduction of risk in developing precancerous lesions in the colon, hypotriacylglycerolemia, and hypoinsulinemia in experimental models. These effects have been reviewed recently.[30,31]

One of the most promising physiologic consequences of the consumption of chicory fructooligosaccharides is an increased bioavailability of calcium. Such an effect has extensively been studied in rats and hamsters.[32–34] These studies have led to the conclusion that, most probably because of their malabsorption and their colonic fermentation, these food ingredients facilitate calcium absorption from the large bowel comparment, thus complementing the process that takes place in the small bowel. Change in colonic pH, production of short-chain fatty acids, and increase in mucosal concentration of the calbindin protein in the colon have been proposed as hypotheses to explain that effect. In addition to increased calcium bioavailability, it has been shown in both rat and hamster that feeding *fructoligosaccharides* increases calcium concentration and improves structure in the bones.[33,34] More recently, two human trials (one in *adolsecents* and one in *adults*) have shown that supplementing the diet with either 16.8 g of oligofructose[35] or 40 g of inulin[36] significantly increases the apparent absorption of calcium by 12% and 11%, respectively. The first study used the calcium-balance measurement, whereas the second used the double-stable isotope technique.

Over the past 2 y, reports have been published that have repeatedly demonstrated that feeding chicory fructooligosaccharides to rats previously treated with a colon carcinogen (i.e., dimethylhydrazine or azoxymethane) reduces the incidence of the so-called aberrant crypt foci in the colon.[37,38] In one of these studies, the synbiotic approach that combines oligofructose (prebiotic) and bifidobacteria (probiotic) was reported to be more active than either the prebiotic or the probiotic alone.[38] Even though still experimental, these data suggest that chicory fructooligosaccharides may play a role in reducing the risk of developing preneoplastic lesions in the colon.

With regard to the effect of chicory fructooligosaccharides on the metabolism of triacylglycerols, experimental data have led to formulation of the hypothesis that feeding such non-digestible oligosaccharides may reduce the hepatic-lipogenic capacity by inhibiting the expression of lipogenic enzymes either by the production of short-chain fatty acids or by modulating insulinemia through still-unknown mechanisms that are presently under extensive investigation.[30]

CALORIC VALUE

Several studies have estimated the caloric value of inulin and oligofructose in human subjects using various methodologies. In summary, because only a part of the energy of these dietary carbohydrates is salvaged, their available energy content is only 40–50% that of a digestible carbohydrate, for an energy value of 1.5 to 2.0 kcal/g.[39]

SAFETY

Inulin and oligofructose are natural food ingredients present in edible plants and are part of the traditional diet. Based on data from the U.S. Department of Agriculture, it was estimated that the average per-capita daily intake of chicory fructooligosaccharides ranges between 1 and 4 g/d, with the 90th percentile consuming 2 to 8 g/d.[3] Their current and proposed uses in multiple food categories could lead, in principle, to increased consumer exposure to dietary fiber in general and to inulin and oligofructose in particular. This may have some desirable effects on colonic function and health. The daily reference value for fiber (soluble or insoluble) is 25 g/d. The average daily intake of inulin or oligofructose, naturally present in food, is estimated be 1 to 4 g/d in the United States[3] and 3 to 11 g/d in Europe.[2] The extensive available data indicate that safety, as traditionally defined, is not an issue in the case of inulin and oligofructose.[40] This notion is supported by the critical review of the toxicologic studies showing that chicory fructooligosaccharides do not increase morbidity or mortality or cause reproductive or target-organ toxicity. These fibers are not mutagenic, carcinogenic, or teratogenic.[40,41]

Numerous animal and human investigational studies have been performed to identify the physiologic and potential health benefits of these fructans and to assess possible intolerance. The only biological effects observed have been attributed to their action as non-digestible, fermentable carbohydrates causing self-limited gastrointestinal distress. Symptoms range from flatulence (the most common), to borborygmi and bloating, to laxation (the most severe). As demonstrated by various studies, the ensuing gastrointestinal symptoms are dose dependent.[42,43] Results indicate that these fructans are well tolerated at amounts up to 20 g/d; diarrhea can develop with intakes of 30 g/d or more.[44]

CONCLUSION: CHICORY FRUCTOOLIGOSACCHARIDES AS DIETARY FIBER

As is the case with other dietary fibers, inulin and oligofructose are resistant to digestion in the upper part of the intestinal tract and are subsequently fermented in the colon. They also have a bulking effect due to the increase in the microbial biomass that results from their fermentation. From a quantitative point of view, that bulking effect, expressed as the increase in daily fecal mass, has been reported to range between 1.5 and 2 g/d of ingested inulin or oligofructose,[17,31,44] which is of the same order of magnitude as pectin. Another typical dietary fiber effect is the increase in stool frequency, as was recently observed when inulin was incorporated into the diet of healthy but chronically, slightly constipated human volunteers.[19,44] Thus, inulin and oligofructose fit well within the current concept of those classes of materials referred to as dietary fiber. Their nutritional properties agree very well with the accepted definition of dietary fiber put forth by Trowell et al.[45] None of the molecules of fructose and glucose that form inulin and oligofructose appears in the portal blood. These materials share the basic common characteristics of dietary fibers, i.e., saccharides of plant origin, resistance to digestion, absorption in the small intestine, and fermentation in the colon to produce short-chain fatty acids that are absorbed and metabolized in different parts of the body. Moreover, this fermentation induces a bulking effect. Chicory fructooligosaccharides also show beneficial effects on calcium absorption, on the biochemical mechanisms controlling triacylglyerol metabolism, and possibly on the reduction of risk in developing precancerous lesions in the colon.

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