

Nutritional and Health Benefits of Inulin and Oligofructose

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Inulin, Oligofructose and Intestinal Function¹

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ABSTRACT Inulin and oligofructose have attracted much attention recently as nonabsorbable carbohydrates with prebiotic properties. When inulin and oligofructose were added to a controlled diet, significant increases were noted in colonic bifidobacterial populations, and it has been proposed that these changes promote both colonic and systemic health through modification of the intestinal microflora. Inulin and oligofructose are rapidly and completely fermented by the colonic microflora with the production of acetate and other short-chain fatty acids. As with lactulose, they may also result in the growth of the fecal biomass, and in doing so, entrap ammonia for bacterial protein synthesis or conversion to the ammonium ion. As with dietary fiber and other nonabsorbable carbohydrates, there is also interest in inulin and oligofructose from the standpoint of inhibition of colonic carcinogenesis, blood cholesterol reduction, immune stimulation and enhanced vitamin synthesis. In these areas, the influence of their molecular weight is also an issue, with the longer chain length providing a more sustained fermentation pattern. More human studies are now required, including studies on the long-term effects of inulin and oligofructose consumption on colonic health, in particular on markers of cancer risk such as reduction in colonic polyp recurrence. *J. Nutr.* 129: 1431S–1433S, 1999.

KEY WORDS: • *bifidobacteria* • *colon* • *inulin* • *carcinogenesis* • *ammonium*

In the latter half of this century, there has been a renewed interest in the relation between colonic function and health. The dietary fiber hypothesis of Burkitt and Trowell (1975) at the beginning of the 1970s was the stimulus to research in this area. Dietary fiber was initially defined as indigestible plant cell wall material that was predominantly carbohydrate in nature but included lignin, a polyphenol propane. Later the definition was enlarged to include all nonabsorbable carbohydrates of plant origin (Trowell et al. 1976). The debate continues over the status as fiber of purified gums and pectic substances, unavailable storage polysaccharides, resistant starch, nonabsorbable sugars of various kinds and associated oligosaccharides. The term non-starch polysaccharides is now preferred by some to refer to cell wall materials that do not include lignin (Cummings and Englyst 1995). Nevertheless, these nonabsorbable plant-derived materials share overlapping spectra of physiologic effects and potential preventive or therapeutic indications for incorporation into the diet. In this respect, the dietary fiber hypothesis and associated research continue to provide valuable insights relevant to the potential alterations in colonic function and systemic metabolism that these materials may induce.

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The dietary fiber hypothesis, inulin and oligofructose

The original dietary fiber hypothesis suggested that a deficiency of fiber in the diet increased the risk of development of colonic disorders, such as constipation, diverticular disease, hemorrhoids and colon cancer. Fiber deficiency was also implicated in systemic disorders including cardiovascular disease, diabetes, obesity and possibly certain nongastrointestinal cancers (Burkitt and Trowell 1975). Since the time of the original hypothesis, research has been carried out, initially defining some of the physiologic effects of fiber (Jenkins et al. 1997) and recently providing more support for the disease associations than was considered likely by most scientists at the time (DeCosse et al. 1989, Morris et al. 1977, Rimm et al. 1996, Salmeron et al. 1997). Much of the research on colonic function, colonic microbiology and short-chain fatty acid (SCFA) metabolism is relevant to the discussion of the effects of inulin and oligofructose. The potential importance of the changes they induce in colonic function led to the term “prebiotic” to indicate the ability of supplementation with nonabsorbed substances to induce favorable changes in colonic microflora and hence metabolism (Gibson and Roberfroid 1995).

Table 1 indicates some of the colonic and systemic physiologic effects that may relate to the disease entities, both colonic and systemic, indicated in **Table 2**. It is worth addressing the issues raised by Table 1 in relation to colonic function, inulin and oligofructose with mention of how these physiologic functions relate to the disorders in Table 2.

TABLE 1

Potential effects of nonabsorbable carbohydrates:
physiologic effects¹

Local	Systemic
↑ Fecal bulk	↓ (↑)Cholesterol
↑ Bacteria	↓ TG (↓ insulin; ↓ glucose)
Selective ↑ bacteria	↓ NH ₃
↑ SCFA production	↓ Urea
Selective ↑ in SCFA	↑ B vitamins
↑ Mineral absorption	↑ Immune function
↑ B vitamin synthesis	(↑ Glutamine?)

¹ Abbreviations: SCFA, short-chain fatty acids; TG, triglyceride.

Colonic events

Colonic microflora. Possibly the most widely accepted effect of inulin and oligofructose is to increase both the numbers and the proportion of fecal bifidobacteria. These studies raise the question of whether the increased vitamin B absorption associated with oligofructose results from increased small intestinal absorption or bacterial synthesis. However, there does not appear to be an increase in total bacterial numbers or a change in the anaerobe:aerobe ratio (Bouhnik et al. 1996, Gibson et al. 1995). Furthermore, pH reduction for the most part is not seen nor are increases in the fecal SCFA or their proportions (Gibson et al. 1995). However, more work is required in this area because in vitro studies indicate differences in SCFA proportions in relation to different substrates fermented.

SCFA have been shown to enhance the colonic absorption of calcium (Trinidad et al. 1997). In the absence of a change in fecal SCFA concentrations, the increased absorption of divalent cations seen with inulin and oligofructose supplementation is less readily explained. Nevertheless, the increased uptake of Ca, Mg, Zn and Fe in laboratory animals (Delzenne et al. 1995) can be seen as another potential health benefit if confirmed in humans.

What is of interest, however, is the fact that the bifidobacteria appear to displace potential pathogens by reducing their numbers selectively (Gibson et al. 1995). It has been implied that this is an "antibiotic-like" effect not related to changes in SCFA or pH. This is an obvious area for further research.

Fecal bulk and nitrogen excretion. In most studies, there is a small increase in fecal bulk upon inulin or oligofructose ingestion. When measured, there also appears to be an increase in fecal nitrogen. Despite the recorded absence of a change in total bacterial numbers (Bouhnik et al. 1996, Gibson et al. 1995) with inulin and oligofructose as assessed in log units, it is likely that an increase in the biomass occurs that accounts for the increase in fecal bulk because all of the fructo-oligosaccharide (FOS) is fermented in the colon. Furthermore, in the absence of a reduction in pH to convert free NH₃ to NH₄⁺ ion and thus reduce nitrogen elimination in the feces, it is likely that the increased fecal nitrogen comes from the increase in the protein nitrogen contained in the increased fecal biomass.

Relation of colonic events to systemic effects

Blood lipids. Studies in rats have demonstrated that feeding inulin or oligofructose as 10% of the diet reduced hepatic triglyceride synthesis and serum VLDL triglyceride (Fiordaliso et al. 1995, Kok et al. 1996a, Kok et al. 1996b). In addition, it

prevented the increase in hepatic triglyceride synthesis normally seen after fructose feeding. Lower levels of serum phospholipids and cholesterol were also seen. The exact mechanism is not clear because in the absence of small intestinal absorption of the intact oligofructose, a colonic explanation must be sought. SCFA have been shown to modulate cholesterol synthesis, with acetate as stimulator and propionate as inhibitor (Thacker et al. 1981, Wolever et al. 1989). Thus lactulose, which produces acetate, may raise serum cholesterol levels (Jenkins et al. 1991). Furthermore, antibiotic therapy, which may selectively alter microbial growth (Morgantein et al. 1981), may also reduce serum cholesterol (Samuel 1979). However, no effects have been reported for serum triglyceride, which could be linked to altered SCFA production. Because there is no clear evidence as yet in humans that SCFA proportions are altered by inulin or oligofructose, detailed studies in humans are necessary or an alternative explanation must be sought.

Blood NH₃ and serum urea. Dietary fibers and nonabsorbable sugars such as lactulose have long been known to reduce blood NH₃ and serum urea levels. These effects have been associated with the growth of the colonic biomass and nitrogen fixation by colonic bacteria, coupled with colonic acidification and conversion of diffusible NH₃ into the less diffusible NH₄⁺ ion. Increased fecal nitrogen elimination has been reported with inulin and oligofructose (Bouhnik et al. 1996, Gibson et al. 1995), and therefore these systemic effects would be expected.

Immune function enhancement. This has been proposed as a possible function of inulin and oligofructose. Studies have not been undertaken to assess systematically lymphocyte activity or other tests of immune function. However, lactulose administration raises serum glutamine levels (Jenkins et al. 1997) possibly as a result of its ability to spare glutamine as a substrate for the colonic mucosa by provision of increased SCFA. Because glutamine is a preferred substrate for lymphatic tissue, it is possible that this may improve immune function under some circumstances. Such an effect may also be relevant to inulin and oligofructose if SCFA production is increased in the proximal, even if not in the distal colon.

Disease prevention and therapy. Changes in colonic function induced by inulin and oligofructose may be relevant to both local and systemic disorders. Both would be expected to have preventive and treatment implications.

Colonic disorders. Inulin and oligofructose at doses of 10–20 g/d produce a small increase in fecal bulk. For example, in one study, oligofructose produced a 1.3-g increase in fecal weight for every gram fed compared with 2.0 g for inulin from chicory roots (Gibson et al. 1995).

No studies in which butyrate deficiency has been implicated appear to have been undertaken, for example, in patients with ulcerative colitis (Roediger 1980). However, in labora-

TABLE 2

Potential effects of nonabsorbable carbohydrates: disease prevention or therapy

Local	Systemic
Ulcerative colitis	Coronary heart disease-hyperlipidemia
Colon cancer	Uremia
Constipation	Hepatic encephalopathy
	Cancer risk
	Osteoporosis

tory animals, studies suggest that 10% oligofructose, possibly equivalent to an intake of 40–60 g in human terms, reduces the development of chemically induced aberrant crypt foci and the growth of transplanted tumors (Koo and Rao 1991, Pierre et al. 1997, Taper et al. 1997). Studies of fecal SCFA, nitroreductase and β -glucuronidase activity in humans have not provided an explanation for these potential anticancer effects (Bouhnik et al. 1996). Nevertheless, the data suggest that clinical trials of the effects of oligofructose on a precursor lesion such as polyp recurrence are appropriate in view of these data and the effect on the colonic microflora.

Systemic disorders. As mentioned in other articles in this proceeding, some studies have observed that inulin and oligofructose can reduce triglyceride and/or cholesterol concentrations. Dietary fibers may also reduce serum urea levels in renal disease (Reddy et al. 1994) and NH_3 levels in hepatic encephalopathy. The effects of inulin and oligofructose in these areas remain to be determined. Similarly, if further evidence surfaces that inulin and oligofructose can suppress tumor incidence and growth, it would have profound implications.

Conclusion. There is strong evidence in humans for an effect of inulin and oligofructose increasing fecal bulk and fecal nitrogen elimination and promoting the growth of bifidobacteria at the expense of other anaerobes. What is required now is the exploration of these changes in colonic function in relation to both colonic and systemic disorders for which laboratory studies have indicated possible benefits. These areas include colon cancer, ulcerative colitis, hyperlipidemia, renal and liver disease, and possibly osteoporosis and compromised immune function. In all of these areas, the importance of dose and molecular chain length also must be determined. A useful effect in any one of these situations would amply justify continued interest in inulin and oligofructose.

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