Fructo-oligosaccharide effects on serum cholesterol levels. An overview[1]

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ABSTRACT

PURPOSE: To address the effects of fructooligosaccharides (FOS) intake on serum cholesterol levels.

METHODS: We performed a search for scientific articles in MEDLINE database from 1987 to 2014, using the following English keywords: *fructooligosaccharides; fructooligosaccharides and cholesterol*. A total of 493 articles were found. After careful selection and exclusion of duplicate articles 34 references were selected. Revised texts were divided into two topics: "FOS Metabolism" and "FOS effects on plasma cholesterol."

RESULTS: The use of a FOS diet prevented some lipid disorders and lowered fatty acid synthase activity in the liver in insulin-resistant rats. There was also reduction in weight and total cholesterol in beagle dogs on a calorie-restricted diet enriched with short-chain FOS. Another study found that 2g FOS daily consumption increased significantly serum HDL cholesterol levels but did not ensure a significant reduction in levels of total cholesterol and triglycerides. Patients with mild hypercholesterolemia receiving short-chain FOS 10.6g daily presented no statistically significant reduction in serum cholesterol levels. However, when FOS was offered to patients that changed their lifestyle, the reduction of LDL cholesterol and steatosis was higher.

CONCLUSIONS: Fructooligosaccharides intake may have a beneficial effect on lipid metabolism and regulation of serum cholesterol levels in individuals that change their lifestyle. FOS supplementation use in diets may therefore be a strategy for lowering cholesterol.

Key words: Oligosaccharides. Dietary Fiber. Cholesterol. Dyslipidemias. Review.

Introduction

Fructooligosaccharides (FOS) are naturally occurring oligosaccharides consisted of glucose molecules and fructose joined by Beta 1,2 glycosidic linkages nondigestible at the brush border by enzymes of the small intestine, highly fermentable in the colon[1]. FOS passes intact through the upper digestive tract without being digested but is degraded in the colon by indigenous bacteria[2]. FOS can be found in many plant foods, such as bananas, onions, garlic, asparagus, wheat, rye, Jerusalem artichoke, and can also be produced enzymatically[3]. FOS act as prebiotics, defined as "food ingredients that affect the intestinal flora beneficially, by stimulating selectively the growth and / or activity of one or a limited number of bacteria in the colon"[4]. FOS digestive tolerance depends on the amount of FOS intake, on the presence of factors that reduce their osmotic load in the small intestine and on the degree of colonic microflora adjusting in the fermentation of these sugars[5]. The importance of the osmotic effect of these sugars is determined by the concentration of sugar which leaves the stomach and it obviously depends on the amount ingested, but also on factors that reduce the gastric emptying speed such as the energy, the meal content, the solid content and viscosity[5]. The fraction fermented in the large intestine provides 8.4 kJ/g; energy loss when a sugar is fermented is approximately 50%[5]. Part of this is due to the formation of SCFA and growth of bacteria, which in turn releases part of the energy as heat[6].

FOS recent use as a food ingredient has stimulated various researches on their effects on health, mainly concerning their bifidogenic nature[1]. Thus, their potentially beneficial actions have been discussed, in the prevention and control of increased health problems, particularly those associated with the metabolic syndrome[7]. Agheli *et al*.[8] studied the chronic effects of a short-chain fructo-oligosaccharide (FOS)-containing diet on plasma lipids and the activity of fatty acid synthase (FAS) in insulin-resistant rats and concluded that the addition of short-chain FOS prevented some lipid disorders, lowered fatty acid synthase activity in the liver[8]. Moreover, data on the effects of FOS on plasma lipids in humans are still conflicting[9].

The beneficial effects of FOS on glucose metabolism have been discussed in a previous review article[10].The aim of this review was to determine the current scientific knowledge on FOS specific role on serum cholesterol levels.

Methods

Pubmed medical database was searched for FOS articles from 1987 to 2014 without language restrictions. The search was limited to the following strings "fructooligosaccharides" and "fructooligosaccharides and cholesterol". Of the 493 initial results, including duplicates, 34 articles were selected for review. Older articles presenting similar results described in more recent papers were excluded. Revised texts were divided into two topics: "FOS Metabolism" and "FOS effects on plasma cholesterol."

FOS metabolism

Prebiotics such as FOS contribute to hypocholesterolemia via two mechanisms: decreasing cholesterol absorption accompanied by enhanced cholesterol excretion via feces, and the production of short-chain fatty acids (SCFAs) upon selective fermentation by intestinal bacterial microflora[5,11].

As FOS are not hydrolyzed by endogenous enzymes in the human small intestine. Upon reaching the cecum and intestinal colon they are fully metabolized by colonic microflora by means of fermentation, generating gases (carbon dioxide, hydrogen, methane) and reducing colonic pH by production of lactate and short-chain fatty acids (SCFA) such as acetate, propionate, methylmalonyl-CoA, succinyl CoA, and butyrate, which are rapidly absorbed by the colonic mucosa. The solubility of such oligosaccharides in water decreases the fecal content and increases the intestinal transit time[3,5,10,12-14] .The fraction fermented in the large intestine provides 8.4 kJ/g (kcal[2]); energy loss when a sugar is fermented is approximately 50%[11].Part of this is due to the formation of SCFA and growth of bacteria, which in turn releases part of the energy as heat[6]. The SCFA are rapidly absorbed from the lumen of the colon resulting in a lower concentration in the feces[12].

When FOS was added to the diet of young Western subjects the oligosaccharide was recovered in feces and the total concentration of short-chain fatty acids, the pH and the fecal weight did not change[13]. The researchers concluded that FOS are fully metabolized in the large intestine[13].

Similar to indigestible fibers, soluble indigestible prebiotics have been postulated to increase the viscosity of the digestive tract and increase the thickness of the unstirred layer in the small intestine, and thus inhibiting the uptake of cholesterol[14].

FOS effects on plasma cholesterol

The percentage of total cholesterol as high density lipoprotein cholesterol, was significantly higher with Konjac-glucomannan (KGM) powder (Konjac root fiber) supplementation than with the other diets after 9 wk. Liver cholesterol concentration was 31-34% lower with KGM and propionate diets than with the unsupplemented diet[15].

Kim and Shin[16]. used hypercholesterolemic-induced Sprague-Dawley rats (n = 32) and found that the administration of inulin for 4-weeks decreased serum LDL-cholesterol and increased serum HDL-cholesterol levels ($p<0.05$) compared to the control. Rats fed with inulin also showed higher excretions of fecal lipid and cholesterol compared to the control ($p<0.05$), mainly attributed to reduced cholesterol absorption[16].

Long-term (16 week) administration of oligofructose decreased total serum cholesterol concentrations in rats, but did not influence either the absorption of dietary cholesterol or the excretion of cholesterol or bile acids in ileostomy subjects[17].

When evaluating supplementation with short-chain FOS 10.6g daily consumption in patients with mild hypercholesterolemia, there was no statistically significant reduction in serum cholesterol levels[9]. The same happened when there was this carbohydrate supplementation in patients with type 2 Mellitus Diabetes[3].

Apparently, the type of FOS ingested has a different impact on the lipid metabolism in humans. As a matter of fact most studies have observed a reduction of plasma triglyceride and/or cholesterol in humans[18-20] when longchain FOS, such as inulin were used. Nevertheless, another study showed opposite results. Pedersen *et al*.[21] investigated the effect of a daily intake of 14 g inulin added to a low-fat spread on fasting blood lipids in sixty-four young healthy women in a randomized double-blind crossover study involving two periods of four weeks and did not find any significant differences between the test periods in plasma. On the contrary, studies utilizing short-chain FOS, like Actilight®, were not effective in improving lipid metabolism[22-23].

A Chinese study showed no change in intestinal lipase activity with 2-4g/kg FOS supplementation in the diet of chickens[24].

Nakamura *et al*.[25] studied the effects of dietary FOS and concluded that it suppresses high-fat diet-induced body fat accumulation and inhibits intestinal absorption of dietary fat in mice.

A randomized, double-blind, placebo-controlled study found that 2g FOS daily consumption increased significantly serum HDL levels, although it has not shown significant reduction in levels of total cholesterol and triglycerides[26].

Another study compared a randomized group of patients who, in addition to FOS supplementation had a change of lifestyle, with physical exercise practice and a balanced diet, with another group that only had changes in lifestyle. The result was that the reduction of LDL and steatosis was higher in the group that besides changing the lifestyle, made dietary FOS supplementation[27].

Rats on a FOS diet decreased abdominal fat and serum levels of total cholesterol[28]. There was also reduction in weight and total cholesterol in beagle dogs on a calorie-restricted diet enriched with short-chain FOS[29]. OS supplementation also reduced the accumulation of liver triglyceride in mice[30].

Delgado *et al*.[31] reviewed the potential of yacon, a tuberous Andean plant that presents high content of fructooligosaccharides and inulin[32-33], and concluded that the consumption of FOS and inulin improves the growth of bifidobacteria in the colon, enhances mineral absorption and gastrointestinal metabolism and plays a role in the regulation of serum cholesterol[31].

Rajkumarl[34] studied the effects prebiotic FOS administration (10 g/d) used alone or in a ‘‘symbiotic’’ blend of putative *L salivarius* preparation and observed that the blend exhibited superior influence on serum lipid profiles for 6 weeks compared with FOS alone. HDL levels were lower than 40 mg/dL among few participants from both experimental groups. Interestingly, the total cholesterol and LDL in the symbiotic group were found to be more reduced ($p<.05$), when compared to the end point values of the probiotic group[34].

Merino-Aguilar *et al*.[35] treated obese rats with FOS fraction extracted from *Psacalium decompositum* for 12 weeks and found decreased body weight, cholesterol, triglycerides, and significantly reduced cytokines IL-6, IFN-γ, MCP-1, IL-1β and VEGF levels ($p<0.05$)[35].

Conclusions

Fructooligosaccharides intake may have a beneficial effect on lipid metabolism and regulation of serum cholesterol levels in individuals that change their lifestyle. FOS supplementation use in diets may therefore be a strategy for lowering cholesterol.

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