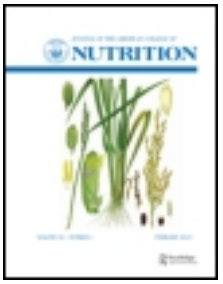

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Effects of Isomalto-Oligosaccharides on Bowel Functions and Indicators of Nutritional Status in Constipated Elderly Men

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Original Research

Effects of Isomalto-Oligosaccharides on Bowel Functions and Indicators of Nutritional Status in Constipated Elderly Men

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Key words: isomalto-oligosaccharide, bowel function, short-chain fatty acid, nutritional status, elderly

Objectives: To evaluate effects of isomalto-oligosaccharides (IO) on the bowel function and nutritional status of elderly men.

Methods: Seven older male subjects participated in this study that consisted of a 30-day control low fiber period followed by a 30-day IO-supplemented (10 g active components) experimental period. Bowel functions such as defecation, enema use and bloating were monitored daily. Fecal characteristics such as wet and dry stool weights, stool moisture, pH and short-chain fatty acid contents were determined on five-day fecal composites collected in each period. Feces were further fractionated into plant, bacterial and soluble fractions to determine the bases for the increase in stool weight. Nutritional status of subjects was assessed with anthropometric parameters, nutrient intake and biochemical measurements.

Results: Incorporation of IO significantly increased the defecation frequency, wet stool output and dry stool weight by twofold, 70% and 55%, respectively. Fecal acetate and propionate concentrations significantly increased by nearly two and a half fold with IO supplement. The increase in stool bulk was mainly attributed by increased bacterial mass. Mean serum sodium concentration decreased in the experimental period while other blood characteristics did not change significantly. Anthropometric parameters and nutrient intake remained constant throughout the study.

Conclusions: Consumption of IO effectively improved bowel movement, stool output and microbial fermentation in the colon without any adverse effect observed in this study. Therefore, supplementation of IO into ordinary low fiber diets may be practical in relieving constipation in the elderly population.

INTRODUCTION

Isomalto-oligosaccharide (IO) has been used as a sweetener in Japan for years. It is made from starch and consists mainly of oligomers with two to four degrees of polymerization, such as isomaltose, panose and isomaltotriose [1]. These oligomers contain α 1 $\rightarrow$ 6 glucosidic linkage [1] that resist endogenous digestion [2]. Biological effects of IO on defecation frequency and blood lipid levels have been shown in young adults and experimental rodents [3–5]. Administration of 10 g of active components of IO to healthy college men significantly improved defecation frequency and the feeling of incomplete defecation [3]. When IO replaced cellulose as the fiber source in experimental diets, rats fed an IO diet had lower plasma total lipids, cholesterol and triglyceride concentrations than the control group [4]. Although IO supplementation was shown to decrease serum cholesterol concentrations in healthy college men [5], effects of indigestible oligosaccharides on blood cholesterol concentrations have been inconsistent. Consumption of fructo-oligosaccharide (FOS) and inulin were unable to reduce serum cholesterol levels in normocholesterolemic subjects, but had a greater effect on hypercholesterolemic subjects [6,7]. Effect of IO on blood triglyceride levels has not been shown in previous studies [5–7]. Therefore, whether IO modulates blood lipid levels in the male elderly remains for further investigation.

The effect of IO on the blood glucose level has not yet been

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investigated. A previous study indicated that consumption of FOS effectively reduces fasting blood glucose levels [6,7]. Isomalto-oligosaccharides may also modulate serum electrolyte concentrations since calcium and magnesium absorption from the colon and rectum increased in rats fed FOS [8]. A mixture of short chain fatty acids (SCFA), the fermentation products of indigestible carbohydrates, have also been shown to promote calcium and phosphorus absorption in the intestine [9,10].

Abnormal bowel function, particularly constipation, is a common complaint of the ill or inactive elderly population [11]. Purified dietary fibers such as guar gum, oat fiber and soy fiber have been incorporated into commercial liquid formulas. However, the constipated elderly population still requires suitable dietary fiber supplements that could easily be incorporated into their ordinary diet for maintaining regular bowel movement. Therefore, it is important to explore the effects of IO supplements on the bowel function, as well as on other potential biological functions in the elderly population.

The aim of this study was to evaluate if an IO supplement could modulate bowel movements, and if this supplement influenced the nutritional status indices in institutionalized constipated elderly men. This study was designed to compare the effects of IO supplementation with a low fiber control diet using a group of constipated nursing-home residents. Bowel function indices such as spontaneous defecation and enema use were recorded everyday while stool characteristics, such as wet and dry stool weights, fecal moisture, pH and fecal SCFA contents were analyzed in stools collected during the last five days of the control and experimental periods. Dried feces were further fractionated into plant, bacterial and soluble fractions to determine the bases for the changes in stool weight. Nutritional status such as blood biochemical measurements, food intake and anthropometric measurements were evaluated and determined for subjects in both periods of this study.

MATERIALS AND METHODS

Experimental Protocol

This study was designed to determine the effects of IO by comparing bowel function, fecal characteristics, blood biochemical measurements, nutrient intake and anthropometric parameters of a group of constipated older men during two consecutive periods: a 30-day control period followed by a 30-day IO-supplemented experimental period. Constipated subjects were recruited and selected from nursing home residents. Food served during both periods was kept constant while IO (ingredients as shown in Table 1) was incorporated into the afternoon dessert during the experimental period. The IO supplement dose was gradually increased from 8 g/day to 24 g/day (equal to 3.3 to 10 g of active component) during the first 10 days of the experimental period. Subjects continued consuming the final dose for the remainder of the experimental period.

Table 1. Composition of isomalto-oligosaccharides used in this study

Components	Content (%)
Moisture	25.00
Isomaltose[a]	9.00
Panose[a]	21.83
Isomaltotriose[a]	1.95
Isomaltotetraose[a]	7.42
Dextrin[a]	2.50
Fructose	0.38
Glucose	15.68
Maltose	11.55
Maltotriose	2.93
Maltotetraose	3.20

[a] Active components of the isomalto-oligosaccharide product used in this study.

Bowel functions, including spontaneous defecation, enema use, bloating and diarrhea, were monitored daily. No complaints about bloating and diarrhea were reported. Stools were individually collected on days 26 to 30 of each period to determine the fecal characteristics including wet and dry weights, pH and short chain fatty acid contents. Dry fecal composites were further fractionated, using physico-chemical methods, into plant, bacterial and soluble fractions. Fasting venous blood was collected in the early morning on the final day of each period after a 12-hour fast and analyzed for biochemical parameters. The anthropometric parameters were determined at the beginning and end of the control period, as well as on the final day of the experimental period. Dietary intake was assessed for three consecutive days in each period. This study did not employ a crossover design because existing evidence indicated the carry-over effects resulting from the diet change [12]. The experimental protocol was approved by the Committee on Human Study of the Taichung Municipal Aging Care Hospital.

Subjects

Residents living in the Aging Care Center of the Taichung Municipal Aging Care Hospital were recruited to participate in this study. The criteria for recruitment were: 60 years of age or older, history of chronic constipation, ability to chew soft or blended diets, physical inactivity in daily life, no tobacco use and not taking antibiotics. All subjects were free of hyperlipidemia, hyperglycemia and clinically terminal or wasting illness. The activity for daily life was assessed using the Barthel Index [13]. Eight subjects were recruited into this study. One dropped out during the control period for personal reasons unrelated to this study.

The basic characteristics of the subjects in this study are listed in Table 2.

Determination of Bowel Movement and Stool Characteristics

Spontaneous defecation (not including the bowel movement induced by enema) and administration of enema were recorded

Table 2. Selected characteristics of subjects participating in the Isomalto-Oligosaccharide (IO) Study[a]

Characteristics	IO
Number of subjects	7
Gender	male
Age (years old)	75.2 ± 4.0
Initial Body Weight (kg)	54.8 ± 3.5
Height (cm)	157.3 ± 3.5
Initial Body mass index	22.2 ± 1.5
ADL[b] (total points)	5.0 ± 1.8

[a] Data were expressed as mean ± SE.

[b] ADL denotes for activity for daily life.

everyday throughout the study. Glycerin enema was used only if spontaneous defecation was incomplete or did not occur in three days, in order to prevent complications. Stools collected on days 26 to 30 of both periods were stored at 4°C, weighed within eight hours of collection and blended with sufficient deionized water to form uniform homogenates. The acidities of the feces were determined by inserting a glass pH electrode into the slurries. Aliquots of fecal homogenates were stored in a freezer at −20°C until analysis for SCFA. The rest of the fecal homogenates were weighed again and lyophilized to determine dry weight and fecal moisture.

Fractionation of Dry Feces

Fractionation scheme was modified from a previous study [14]. Aliquots of five-day fecal composites (2 g) were blended (Stomacher Lab Blender 400, Tekmar Co., Cincinnati, OH, USA) with 60 mL saline (containing 0.1% SLS) for five minutes. The material was filtered through a nylon screen apparatus (350-μm and 35-μm dual screen) to separate plant material from the other material. The first filtrate through the screen apparatus was centrifuged at 20,000 g for 15 minutes. The supernatant was the soluble fraction and recovered by lyophilization while the pellet was the bacterial fraction. The residue on the 350-μm screen was stomached and filtered two more times. The residue on the 35-μm screen was then blended two more times. The filtrate through the screens was pooled and centrifuged at 20,000 g for 15 minutes. The final residue on the screens was the plant fraction. The combined pellets were the bacterial fraction. Plant and bacterial pellets were rinsed with distilled water and lyophilized to obtain the weights of each fraction.

Analysis of Fecal SCFA

Fecal samples were analyzed for acetate, propionate, *i*-butyrate, *n*-butyrate, *i*-valerate, *n*-valerate, caproic and heptanoic acids as described previously [15,16]. Samples were extracted by the method of Remsey and Demigne [16] and injected onto a gas chromatography (Hewlett-Packard 5890, Hewlett-Packard, Palo Alto, CA, USA) fitted with a glass capillary column (0.25 mm, 30 m Stabilwax-DA, Restek Corp., Bellefonte, PA, USA) and a flame ionization detector. The initial temperature of oven was 100 °C and raised to 200 °C at 6 °C/min. The temperature of the detector and injection ports was 250 °C. The carrier gas was N_2 at a flow rate of 1 mL/min.

Assessment of Dietary Intake

Three-day cycle menus of Chinese foods were provided to subjects in the ward throughout the study. These diets provided 14.8 g dietary fiber in the average of three days. To assess the nutrient intake of subjects, meals served to and left over by the subjects were weighed and recorded for three consecutive days in each period. The amount of nutrients consumed was calculated using local food composition tables [17] and compared to the recommended daily nutrient allowance (RDNA) in Taiwan [18].

Anthropometric and Blood Biochemical Measures

Anthropometric parameters were obtained by trained personnel. Weight was determined with a lifter equipped with a digital scale (Vander lift, VanCare Inc., OH, USA). Height was measured with a leather ruler. Body fat was determined by infrared wave body fat scale (Futrex 5000, Futrex Inc., MD, USA). Upper arm circumference (AC) and triceps skinfold (TSF) were measured with an insertion tape and caliper, respectively. Arm muscle circumference (AMC), upper arm muscle area (AMA) and upper arm fat area (AFA) were calculated by the computation described previously [19]. Venous bloods collected on the final day after a 12-hour fast was analyzed for serum total protein, albumin, triglyceride, total cholesterol, HDL-cholesterol, sodium, potassium, calcium and phosphorus concentrations using an automatic analyzer (CX5 Synchron, Beckman Instrument Inc., Fullerton, CA, USA). The coefficient of variation for intra-assays and inter-assays were 4.5% and 5.0%, respectively.

Statistics

All data were expressed as means ± SE and were analyzed with a commercial package (SPSS, Version 7.0, Chicago, IL). Effects of time on anthropometric measures were analyzed with repeated measures analysis of variance. Frequencies of defecation and enema use and percentage weights of fecal plant, bacterial and soluble materials were analyzed using the Wilcoxon signed-rank test. Effects of IO supplement on stool characteristics, fecal SCFA concentrations, dietary intake and blood measures were compared using paired Student's *t* test. Effect was considered significant as $p < 0.05$.

RESULTS

Bowel Function and Stool Characteristics

Bowel function and stool weights are shown in Table 3. The mean frequency of spontaneous passage was low, only

Table 3. Frequencies of defecation and enema use, stool weights and moisture contents of stools collected on days 26 to 30 of control and experimental periods*

	Control	Experimental
Defecation (times/5 days)	0.5 ± 0.2	1.5 ± 0.4[a]
Enema (times/5 days)	2.3 ± 0.9	1.1 ± 0.6
Wet wt/day (g)	47.7 ± 4.4	81.1 ± 1.5[b]
Dry wt/day (g)	9.2 ± 1.4	14.3 ± 2.2[b]
Wet wt/stool (g)	119.2 ± 10.9	202.8 ± 28.8[b]
Dry wt/stool (g)	23.1 ± 3.6	35.8 ± 5.5[b]
Moisture (%)	80.0 ± 2.8	80.6 ± 2.5

* Data were expressed as mean ± SE (n = 7).

[a] $p < 0.05$ as analyzed using Wilcoxon signed-rank test between the control and experimental periods.

[b] $p < 0.05$ as analyzed using paired Student's *t* test between the control and experimental periods.

(mean ± SE) 0.5 ± 0.5/5-day period in the control period. Supplementation of IO for 30 days significantly increased the defecation frequency by nearly threefold and, accordingly, tended to decrease the use of glycerol-enema. Mean fecal wet weight per day and per passage were both enhanced by IO supplement for 70%. Mean dry weight per day and per passage were also increased significantly (55%, respectively). However, mean fecal moisture contents of subjects were not different between the control and experimental periods.

Fecal Fraction Weight and SCFA Concentrations

Stool composites from the last five-day period were fractionated, and results are shown in Table 4. The mean percentage weight of bacterial fractions increased significantly from approximately 53% to almost 70%, while the mean percentage weight of soluble fractions decreased significantly by 10%. In other words, consumption of IO significantly increased the fecal bacterial mass from (mean ± SE) 5.0 ± 0.4 g/day to 9.9 ± 1.2 g/day. However, the weights of fecal plant and soluble fractions were not significantly different between control and experimental periods.

The effect of IO supplement on fecal SCFA concentrations is shown in Table 5. Consumption of IO significantly increased fecal acetate and propionate concentrations by two and a half fold; this contributed to a significant increase in total SCFA concentration. However, fecal pH was not influenced by IO supplement.

Table 4. Plant, bacterial and soluble fractions of fecal composites collected on days 26 to 30 of the control and experimental periods* (%)

	Control	Experimental
Fractions		
Plant (%)	9.2 ± 0.4	6.4 ± 0.3
Bacterial (%)	52.8 ± 1.8	69.8 ± 2.1[a]
Soluble (%)	33.2 ± 1.1	21.6 ± 0.6[a]

* Data were expressed as mean ± SE (n = 7).

[a] $p < 0.05$ as analyzed using Wilcoxon signed-rank test between the control and experimental periods.

Table 5. Short-chain fatty acid concentrations and pH of stools collected on days 26 to 30 of control and experimental periods*

	Control	Experimental
pH	6.5 ± 0.1	6.4 ± 0.1
Acetate (mg/g wet feces)	2.4 ± 0.3	6.2 ± 0.4[a]
Propionate (mg/g wet feces)	1.0 ± 0.3	3.8 ± 0.4[a]
i-Butyrate (mg/g wet feces)	0.5 ± 0.1	0.8 ± 0.2
n-Butyrate (mg/g wet feces)	0.7 ± 0.2	2.0 ± 0.6
i-Valerate (mg/g wet feces)	0.6 ± 0.1	1.0 ± 0.4
n-Valerate (mg/g wet feces)	0.6 ± 0.1	0.5 ± 0.1
Caproic acid (mg/g wet feces)	0.7 ± 0.1	0.4 ± 0.1
Heptanoic acid (mg/g wet feces)	0.8 ± 0.1	0.5 ± 0.1
Total (mg/g wet feces)	7.3 ± 1.1	15.6 ± 2.6[a]

* Data were expressed as mean ± SE (n = 7).

[a] $p < 0.05$ as analyzed with paired Student's *t* test between the control and experimental periods.

Blood Measurement

The mean serum biochemical measures and electrolyte concentrations of older men observed in this study were in the normal range for both the control and experimental periods (Table 6). Pre-prandial serum glucose, total protein, albumin, triglyceride, total cholesterol and HDL-cholesterol concentrations remained constant between the control and experimental periods (Table 6). However, mean serum sodium concentration decreased by 58 mg/dL (2.4 mEq/dL, 1.8%) while IO was supplemented (Table 6).

Dietary Intakes

Energy and nutrients consumed are shown in Table 7. Dietary intake remained constant between the two periods

Table 6. Serum sugar, total protein, albumin, triglycerides, total cholesterol (total-chol), HDL-cholesterol (HDL-chol), Ca, P, Na and K concentrations of subjects on day 30 in control and experimental periods*

	Control	Experimental
Glucose (mg/100 mL)	81.2 ± 5.6	80.0 ± 3.6
Total Protein (g/100 mL)	7.2 ± 0.2	7.0 ± 0.1
Albumin (g/100 mL)	3.6 ± 0.1	3.5 ± 0.1
Triglycerides (mg/100 mL)	45.8 ± 7.9	44.3 ± 9.7
Total-Chol (mg/100 mL)	162.3 ± 11.5	165.1 ± 12.6
HDL-Chol (mg/100 mL)	35.4 ± 3.8	34.7 ± 2.9
Ca (mg/100 mL)	9.2 ± 0.2	9.2 ± 0.1
P (mg/100 mL)	3.2 ± 0.2	3.1 ± 0.2
Na (mg/100 mL)	3269.2 ± 2.3	3210.8 ± 11.5[a]
K (mg/100 mL)	179.8 ± 6.2	162.6 ± 6.6

* Data were expressed as mean ± SE (n = 7).

[a] $p < 0.05$ as analyzed with paired Student's *t* test between the control and experimental periods.

Table 7. Daily dietary intakes of subjects during the control and experimental periods*

	Control	Experimental
Energy (Kcal)	1956.7 ± 98.2 (108.7)[a]	1948.1 ± 88.6 (108.2)[a]
Carbohydrate[b] (g)	278.1 ± 20.9	276.0 ± 20.6
Protein (g)	71.7 ± 3.1 (110.3)	71.7 ± 6.4 (110.3)
Fat[b] (g)	60.2 ± 3.2	59.9 ± 1.9
Dietary fiber[b] (g)	11.2 ± 0.7	11.6 ± 0.5
Calcium (mg)	525.2 ± 69.7 (87.5)	483.3 ± 47.4 (80.6)
Phosphorus (mg)	816.1 ± 38.3 (136.0)	820.3 ± 34.2 (136.7)
Iron (mg)	9.5 ± 0.5 (95.0)	9.4 ± 0.3 (94.0)
Vitamin A (R.E.)	1379.4 ± 110.7 (229.9)	1248.2 ± 96.5 (208.0)
Vitamin B_1 (mg)	1.0 ± 0.1 (111.0)	1.0 ± 0.1 (111.0)
Vitamin B_2 (mg)	0.7 ± 0.0 (70.0)	0.8 ± 0.1 (80.0)
Niacin (mg)	12.9 ± 0.6 (107.5)	12.7 ± 0.4 (105.8)
Vitamin C (mg)	109.5 ± 11.3 (182.5)	110.7 ± 13.2 (184.5)

* Data were the average of three consecutive days and were expressed as mean ± SE (n = 7).

[a] Data in the parenthesis indicated the percentage of the recommended daily nutrient allowances (RDNA) in Taiwan [18].

[b] RDNA in Taiwan have not been established.

(Table 7). Carbohydrate, protein and fat contributed approximately 58%, 15% and 28% of the total energy intake (Table 7). Mean dietary fiber intake (excluding IO) remained at 11–12 g/day throughout the study (Table 7). The amount of nutrients consumed generally met the recommended RDNA in Taiwan except for calcium, iron and vitamin B_2 while the vitamin A and C intake was nearly twofold the recommended amount (Table 7).

Anthropometric Measurement

The anthropometric parameters of the subjects during the control and experimental periods are summarized in Table 8. Consuming the control diet *per se* or in combination with IO supplement did not influence the anthropometric parameters of the subjects as analyzed using repeated measures ANOVA (Table 8).

Table 8. Anthropometric parameters of subjects on the first day of the control period, and the final days of each period*

	Initial Day of the Control Period	End of the Control Period	End of the Experimental Period
Weight (kg)	54.8 ± 3.5	55.0 ± 4.2	56.1 ± 3.7
AC (mm)[a]	252.1 ± 10.0	246.4 ± 7.1	252.9 ± 11.7
AMC (mm)[a]	220.3 ± 6.4	219.8 ± 8.5	227.7 ± 9.9
AMA (mm^2)[a]	3883.2 ± 216.1	4056.2 ± 279.8	4176.4 ± 359.4
AFA (mm^2)[a]	1315.8 ± 269.8	1088.5 ± 96.7	1078.8 ± 220.5
TSF (mm)[a]	10.1 ± 1.7	8.5 ± 1.2	8.0 ± 1.4
Body fat (%)	18.1 ± 3.6	18.3 ± 2.6	20.7 ± 2.6

* Data were expressed as mean ± SE (n = 7) and were analyzed using repeated measures ANOVA. No significant effect of time was shown.

[a] AC, AMC, AMA, AFA, and TSF denote midarm circumference, arm muscle circumference, arm muscle area, arm fat area and triceps skinfold, respectively.

DISCUSSION

The addition of 10 g/day of active components of IO exerted significant effects on bowel function without adverse influence on the nutritional status in our constipated elderly subjects. After consuming the IO supplement for 30 days, the frequency of spontaneous defecation significantly increased, and the use of glycerol enema tended to decrease (Table 3). Daily stool output and stool weight per passage increased significantly with the supplement (Table 3). The increases in wet stool weight per day and per passage were about 70%, respectively. That equaled to a 3.34 ± 0.54 g (mean ± SE) increase in wet weight per day for every g of active IO ingredient consumed. The bulking effect of IO in this study was greater than that in a previous study in which there was a nearly two-gram increase of stool for each gram of oligofructose (three to eight degrees of polymerization) consumed [20].

In this study, dry mass excreted per day and per passage increased for 55%, respectively, as IO was consumed (Table 3). This meant that each gram of IO caused a 0.51 ± 0.07 g (mean ± SE) increase in dry fecal mass. Recent studies demonstrated that ingestion of nondigestible oligosaccharides might preferentially stimulate colonic bacteria [21–22]. We therefore examined how indigestible plant material and colonic bacteria contributed to the dry stool mass. We found that the bacterial fraction significantly increased after IO was consumed (Table 4). Fecal total SCFA, acetate and propionate concentrations also significantly increased when IO was consumed (Table 5). However, the increase in fecal SCFA was unable to decrease the pH significantly (Table 5).

Supplementation of IO failed to modulate blood lipid levels in our normocholesterolemic older subjects (Table 6). This result agrees with previous studies in which indigestible oligosaccharides were unable to reduce serum cholesterol concentration in normocholesterolemic subjects, but were able to reduce hypercholesterolemia [5,6].

Addition of isomaltulose-based oligomers has been shown to increase calcium or phosphorus absorption in rats [23]. The mechanism for these effects can be attributed to the fermentation products of indigestible carbohydrate, SCFA, since previous studies suggest a mixture of SCFA can stimulate cecocolonic calcium and phosphorus absorption in humans and rats [9,10]. Although consumption of IO significantly increased fecal acetate and propionate concentrations in our study, the concentrations of other SCFA and fecal pH did not change significantly (Table 5). This is probably the reason why serum calcium and phosphorus concentrations were unaffected by IO consumption (Table 6).

In conclusion, IO acted similarly to dietary fiber in several ways. A daily supplement of 10 grams of active components of IO was useful in normalizing bowel movement, increasing stool bulk and colon microbial activity as assessed by the SCFA concentration and fecal bacterial mass. However, IO

intake was unable to decrease fasting serum glucose, triglyceride and cholesterol concentrations in our non-diabetic, normolipidemic subjects. Consuming IO for 30 days did not adversely influence the anthropometric parameters and nutrient intake of the subjects. Therefore, application of IO to the elderly population with chronic constipation could be helpful in normalizing bowel function.

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