

## Short communication

### The effect of ingestion of inulin on blood lipids and gastrointestinal symptoms in healthy females

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The effect of a daily intake of 14 g inulin added to a low-fat spread on fasting blood lipids and gastrointestinal symptoms was investigated in sixty-four young healthy women in a randomized double-blind crossover study involving two periods of 4 weeks. The test spread with and without inulin replaced habitual spread during the test periods. No significant differences between the test periods in plasma total cholesterol, HDL-cholesterol, LDL-cholesterol and triacylglycerol concentrations were observed. Gastrointestinal symptoms assessed with questionnaires showed that in the inulin period there was a significantly ( $P < 0.05$ ) higher degree of discomfort from flatulence and other gastrointestinal symptoms than in the control period. In general, there was no indication of intestinal adaptation to this level of intake of inulin.

**Fructo-oligosaccharides: Blood: Flatulence**

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Non-digestible oligomers of fructose and other saccharides, usually not included in the dietary fibre concept, are found in many plant foods, such as artichokes, onions, asparagus and chicory (Dysseler & Hoffem, 1995). Daily intakes vary from 2 to 12 g in Western populations (Roberfroid *et al.* 1993). In addition, oligosaccharides are used as a food ingredient. They display gelling and thickening properties without interfering with texture or appearance, and in particular inulin, a fructo-oligosaccharide, is currently used in various food items such as bread, baked goods, dairy and cheese products. The content of inulin in these products varies from 50 to 100 g/kg (Dysseler & Hoffem, 1995).

Lipid-lowering effects of oligosaccharides have been proposed (Roberfroid, 1993) and in studies with rats, the addition of fairly high (50–200 g/kg) amounts of fructo-oligosaccharides to the diet have led to reductions in blood lipids (Levrat *et al.* 1991; Delzenne *et al.* 1993). The number of studies of the effect of oligosaccharides on blood lipids in human subjects is limited. Indications of a lipid-lowering ability have been observed in hyperlipidaemic and diabetic patients (Yamashita *et al.* 1984; Hidaka *et al.* 1991). Oligosaccharides are rapidly and completely fermented in the colon and the most common hypothesis for a lipid-lowering mechanism is that the fermentation products, especially propionate reaching the liver by the portal vein, could modulate cholesterol synthesis (Chen *et al.* 1984). A recent study in rats supported this hypothesis by showing that the decrease in blood lipids after daily administration of an oligofructose-rich diet was

associated with a reduction in plasma VLDL particles, and a reduced capacity of isolated hepatocytes to synthesize triacylglycerols (Fiordaliso *et al.* 1995).

In the present study the effects of daily consumption of a significant amount (14 g/d) of the oligofructose inulin on blood lipids in young normolipidaemic women were investigated. A low-fat spread was used as a realistic vehicle for the inulin. As the colonic fermentation of oligosaccharides leads to gas production which may induce gastrointestinal discomfort in human subjects (Roberfroid, 1993), an additional objective was to assess whether a high daily consumption of inulin would lead to noticeable gastrointestinal disturbances, and if so, to determine to what extent adaptation to inulin intake occurred.

## SUBJECTS AND METHODS

### *Subjects*

Seventy-two healthy normolipidaemic women aged 20–36 years were recruited for the study by local advertisement. Average BMI was 21.9 (SD 2.6) kg/m<sup>2</sup>. Six subjects dropped out within the first week because they found the ascribed amount of spread too large, one became ill and one subject dropped out due to an event unrelated to the study. The aim of the study was explained to the subjects who gave their written consent. The study was approved by the Scientific Ethics Committee of the municipalities of Copenhagen and Frederiksberg (01-115/94).

### *Experimental design*

The study was performed as a double-blind randomized crossover experiment with two periods of 4 weeks without any washout period. The women replaced their usual spread with 40 g of two different low-fat spreads (30 g fat/kg). The spreads had an identical fat composition, but differed in the content of inulin (average degree of polymerization 11–12; Raftilin LS; Raffinerie Tirlemontoise (ORAFTI), Tienen, Belgium), which was incorporated into one of the spreads (360 g/kg). The spreads were produced at the Unilever Research Laboratorium (Vlaardingen, The Netherlands), repacked into cups containing 40 g each and kept at 2–4° until the day of consumption.

Gastrointestinal symptoms were assessed by a health questionnaire before the experiment and at days 2, 4, 8, 16 and 24 in each period. Fasting blood samples were taken once at baseline, once at week 3 and twice at week 4 in each period. Dietary intakes were monitored for 3 d in the last week of each experimental period. Once weekly the subjects collected a ration of spread, reported the actual consumption of the spread to a research assistant, and delivered the empty cups; the contents of those not fully emptied was determined by weighing.

### *Analytical methods*

*Assessment of gastrointestinal symptoms by a health questionnaire.* The health questionnaire contained ten specific questions on gastrointestinal symptoms. The main question was: 'Did you suffer from any of the gastrointestinal symptoms mentioned below during the past 24 h?' The listed symptoms were: rumbling stomach, rumbling in gut, belching, nausea, stomach cramps, gut cramps, bloatedness, acid reflux, flatulence,

diarrhoea, vomiting. The degree of discomfort was ranked in one of four categories (0 absent, 1 mild, 2 moderate or 3 severe; van Munster *et al.* 1994).

*Dietary intakes.* On the same three weekdays in the last week in each period the participants weighed (electronic scales, Soehnle, 1 g intervals) and recorded all food and drink. The energy intake and the composition of the diet were calculated from the food records using a national computer database (DanKost; Danish Catering Centre, Denmark). The energy value of the inulin was set to zero and inulin was included in the fibre value.

*Blood sampling and analysis.* Blood was drawn in the morning after supine rest for 10 min. Blood samples (EDTA-blood) were immediately placed on ice and centrifuged before storage of plasma at  $-20^{\circ}$ . All samples from each subject were analysed within a single run.

Plasma total cholesterol, HDL-cholesterol and triacylglycerol concentrations were determined by enzymic methods (CHOD-PAP, GPO-PAP; Boehringer Mannheim GmbH, Mannheim, Germany) on an autoanalyser (Cobas Mira; Hoffmann-La Roche, Basel, Switzerland). HDL-cholesterol concentration was determined after precipitation of apolipoprotein-B-containing lipoproteins by phosphotungstic acid-MgCl<sub>2</sub> reagent. LDL-cholesterol was calculated according to the Friedewald procedure (Friedewald *et al.* 1972). Control serum (K89; Nycomed Pharma A/S, Oslo, Norway) was used for quality control of the analyses. The CV for plasma total cholesterol, HDL-cholesterol and triacylglycerol concentrations were 2.0, 5.6 and 1.3% respectively.

#### *Statistical methods*

Data analysis was performed using the SPSS-PC+ package (Statistical Package for the Social Sciences Inc., Chicago, IL, USA). A two-tailed paired *t* test was used for the blood lipid and food record values. For the analysis of the questionnaires one-way ANOVA was used for each test period to determine whether the symptoms experienced during the study were time-dependent. The questionnaires were analysed for the presence of a period or a carry-over effect according to Armitage & Berry (1987). When there were no time dependency and no carry-over effects, average values for the degree of discomfort were calculated for each subject, and a paired *t* test was used for comparisons between the groups (habitual diet, control test period, inulin test period). For the discomfort coming from flatulence there was a carry-over effect and consequently a *t* test for independent samples was used for comparison within the periods 1 and 2 for this particular symptom. Results were considered to be significant at  $P < 0.05$ . Power calculations (power 0.85, significance level  $P < 0.05$ ) showed that with a total sample size of sixty-four subjects it should be possible to detect a difference in plasma cholesterol concentration of 0.24 mmol/l, in plasma HDL-cholesterol concentration of 0.11 mmol/l and in plasma triacylglycerol concentration of 0.16 mmol/l (Altman, 1991).

## RESULTS

### *Blood lipids*

Blood lipid concentrations of the subjects at baseline and at the end of each test period are shown in Table 1. There were no significant differences between the two test periods ( $P > 0.1$ ). However, if compared with the habitual diet HDL-cholesterol concentration was significantly higher ( $P = 0.02$  for both test periods) and the LDL-cholesterol:HDL-cholesterol ratio was significantly lower ( $P = 0.006$  for the control period,  $P = 0.003$  for the inulin period) during the experimental periods.

Table 1. Total, LDL- and HDL-cholesterol and triacylglycerol concentrations (mmol/l) and reported gastrointestinal symptom scores in sixty-four young healthy women consuming their habitual diet and after 4 weeks of daily intake of 40 g low-fat control spread or 40 g low-fat spread containing 14 g inulin†‡§

(Mean values and standard deviations)

	Habitual diet		Control spread period		Inulin spread period	
	Mean	SD	Mean	SD	Mean	SD
Total cholesterol	4.28	0.76	4.25	0.63	4.24	0.75
LDL-cholesterol	2.48	0.72	2.39	0.56	2.38	0.67
HDL-cholesterol	1.32	0.28	1.37†	0.30	1.38†	0.30
LDL-cholesterol : HDL-cholesterol	1.97	0.73	1.83†	0.63	1.82††	0.69
Total triacylglycerols	0.95	0.31	0.98	0.42	0.97	0.39
Rumbling in stomach	0.3	0.5	0.1†	0.2	0.4***	0.3
Rumbling in gut	0.3	0.5	0.2†	0.2	0.6***††	0.3
Stomach cramps	0.1	0.2	0.1	0.2	0.3***††	0.3
Gut cramps	0.2	0.4	0.1	0.2	0.5***††	0.3
Bloatedness	0.4	0.4	0.3	0.2	0.6***	0.4
Flatulence	0.3	0.4	0.4	0.3	1.2***††	0.5

Mean values were significantly different from those for the control spread: \*\*\*  $P < 0.001$ .

Mean values were significantly different from those for the habitual diet: †  $P < 0.05$ , ††  $P < 0.005$ .

† For habitual diet values are based on a single blood sample; for the intervention periods values are the mean of three separate blood samples for each individual in each period, one sample after 3 weeks and two samples after 4 weeks.

§ The degree of discomfort over the past 24 h was ranked in one of four categories (0 absent, 1 weak, 2 moderate, 3 severe). For habitual diet, scores are from one evaluation; for the intervention periods, scores are mean values for each individual of rankings at days 2, 4, 8, 16 and 24 in each period.

### Dietary intakes

The intakes of energy and macronutrients did not differ in the two experimental periods, except the expected difference in dietary fibre intake due to the inulin (Table 2).

### Health questionnaires

The degrees of discomfort from the gastrointestinal variables, rumbling in stomach, rumbling in gut, stomach cramps, gut cramps, bloatedness and flatulence were all ranked significantly higher in the inulin test period compared with the control test period ( $P < 0.001$ ; Table 1). The discomfort from flatulence was the most profound symptom throughout the experiment (Table 1; Fig. 1). This discomfort was ranked as severe by 12% of the volunteers when consuming the inulin spread (Fig. 2).

There were in general no indications of adaptation to consumption of 14 g inulin daily for any symptoms (effect of time,  $P > 0.05$ ).

### DISCUSSION

This study was designed to evaluate the effects of daily consumption of 14 g inulin on blood lipids and gastrointestinal disturbances in normolipidaemic women. Apart from replacing habitual spreads with a test spread, the women were not given any other dietary instructions. The dietary records confirmed a virtually identical dietary intake in the two

Table 2. Daily energy, nutrient and dietary fibre intakes in sixty young healthy women consuming a low-fat (control) spread or an inulin-containing spread calculated from 3 d weighed food records

(Mean values and standard deviations)

Intake of:	Control spread period		Inulin spread period	
	Mean	SD	Mean	SD
Energy (MJ)	9.2	2.1	9.0	1.9
Fat (g)	72	24	72	23
Saturated fatty acids (g)	27	11	26	11
Monounsaturated fatty acids (g)	19	8	21	14
Polyunsaturated fatty acids (g)	9	4	11	5
Protein (g)	73	17	76	17
Carbohydrate (g)	284	70	294	77
Alcohol (g)	6	10	7	10
Dietary fibre (g)	26.3	11.8	38.5***	10.1

Mean value was significantly different from that for control spread: \*\*\*  $P < 0.001$ .

periods, with no differences in fat consumption that could have interfered with any effect of inulin on blood lipids.

Earlier studies of dietary interventions in subjects with similar or lower cholesterol concentrations as those in the present study have shown significant lowering of blood-lipid concentrations (Marckmann *et al.* 1990; Sandström *et al.* 1992; Tholstrup *et al.* 1994). Thus, the lack of effect of inulin on blood lipid concentrations observed in the present study is not likely to be due to the selection of subjects. In accordance with our results, there were no changes in blood lipid concentrations in a study involving twelve young healthy males who ingested 20 g fructo-oligosaccharides daily for 4 weeks in a randomized crossover experiment (Luo *et al.* 1996).

A cholesterol-lowering effect of intakes of inulin has so far only been observed in a group of eighteen middle-aged non-insulin-dependent diabetic patients (Yamashita *et al.*

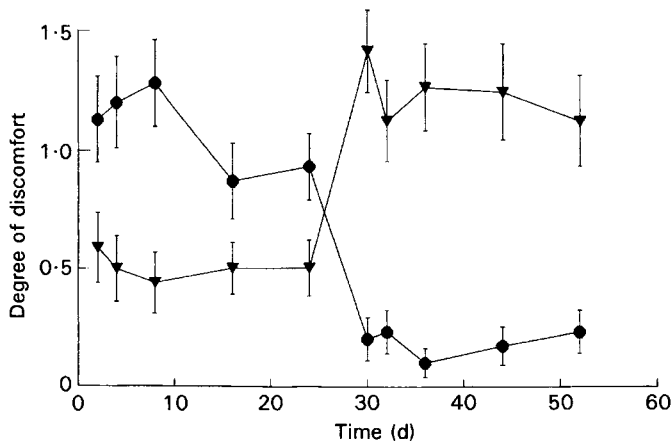


Fig. 1. The degree of discomfort from flatulence in sixty-four young healthy women randomly assigned to daily consumption of 40 g spread containing 14 g inulin on days 1–26 and 40 g control spread on days 27–52 (●), or daily consumption of the control spread on days 1–26 and the inulin spread on days 27–52 (▲).

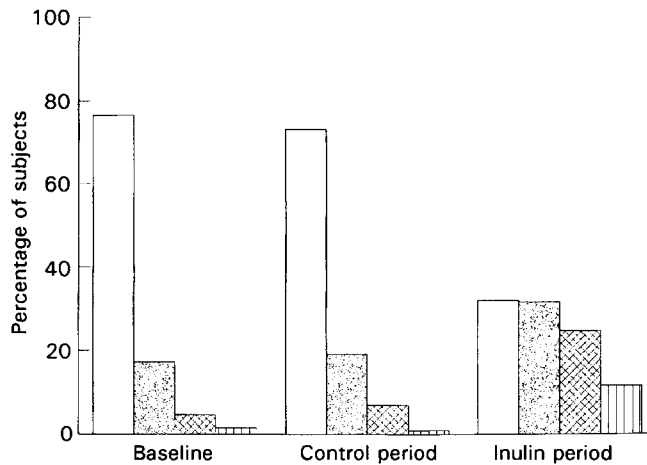


Fig. 2. Percentage of subjects experiencing absent (□), mild (▨), moderate (▩) or severe (▧) discomfort from flatulence at baseline, after 4 weeks daily intake of 40 g control spread, and after 4 weeks daily intake of 40 g spread containing 14 g of inulin ( $n$  64).

1984), and in a group of twenty hyperlipidaemic adults (Hidaka *et al.* 1991). These two studies were conducted in a parallel design with an intervention and a control group, and consequently had a lower statistical power than the present study.

In the present study there was a significantly higher degree of gastrointestinal discomfort during the inulin test period compared with the control period. Although the average judgment of discomfort arising from flatulence in the inulin test period was 'mild', 12% of the subjects ranked this particular symptom as severe and unacceptable (Fig. 2). The change from period 1 to period 2 caused a more profound difference in the rankings between the two groups for all symptoms (Fig. 1). This phenomenon probably reflects the fact that the change from the inulin spread to the control spread was experienced as a relief by some of the subjects.

From studies performed in human subjects using the  $H_2$  breath test it has been concluded that oligofructoses are completely unabsorbed in the upper intestinal tract (Stone-Dorshow & Levitt, 1987; Rumessen *et al.* 1990). In rats inoculated with a human whole faecal flora, inulin consumption led to higher levels of  $H_2$  and a fourfold greater caecal concentration of butyrate than other fibres such as carrot, cocoa, wheat, pea and oats (Roland *et al.* 1995). Another study in rats showed that this malabsorption was not modified after chronic exposure to high doses for 6 weeks (Oku *et al.* 1984). In the present study there was no indication of digestive adaptation to consumption of inulin (Fig. 1). This is in accordance with results reported by Stone-Dorshow & Levitt (1987), where daily ingestion of fructo-oligosaccharides for 12 d resulted in a 50% increase in breath  $H_2$  production and no improvement in gaseous symptoms was noted.

Although most of the symptoms experienced in the present study were of a rather innocent nature, clinicians should be aware of the currently rather widespread use of oligosaccharides in processed foods, which in some subjects can give rise to unwanted side-effects. On the other hand, oligosaccharides fermented in the colon might have beneficial health effects by changing the gut microflora. Ingestion of 15 g oligosaccharides has resulted in increased colonic growth of bifidobacteria with potential health-promoting consequences (Gibson *et al.* 1995).

In conclusion, daily consumption of 14 g inulin for 4 weeks did not affect blood lipids in young normolipidaemic women but led to various gastrointestinal symptoms. In general, there were no indications of intestinal adaptation to this level of inulin intake. Thus, while a role for inulin in the treatment of hypercholesterolaemia remains to be shown, the present study does not support more general claims for a lipid-lowering effect of inulin.

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