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ORIGINAL ARTICLE

Oligofructose promotes satiety in healthy human: a pilot study

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Objective: The administration of a fermentable dietary fibre (oligofructose) in rats increases satietogenic gut peptides and lowered spontaneous energy intake. The aim of the study was to assess the relevance of those effects of oligofructose on satiety and energy intake in humans.
Design: Single-blinded, crossover, placebo-controlled design, pilot study.
Subjects: Volunteers included five men and five women aged 21–39 years, BMI ranging from 18.5 to 27.4 kg/m^2, were randomly assigned as described below.
Interventions: Subjects were included in two 2-week experimental phases during which they received either fibre (oligofructose (OFS)) or placebo (dextrine maltose (DM)); a 2-week washout period was included between crossover phases. In total, 8 g OFS or 8 g DM were ingested twice daily (16 g/day in total). Energy intake, hunger, satiety, fullness and prospective food consumption were assessed with analogue scales at the end of each experimental phase.
Results: During breakfast, OFS significantly increases the satiety ($P=0.04$) without any difference on other sensations as compared to DM treatment periods. After lunch, no significant differences are observed between treatment period. At dinner, OFS significantly increases satiety ($P=0.04$), reduces hunger ($P=0.04$) and prospective food consumption ($P=0.05$). The energy intake at breakfast and lunch are significantly lower ($P=0.01$, 0.03, respectively) after OFS treatment than after DM treatment. Total energy intake per day is 5% lower during OFS than in DM period.
Conclusion: Oligofructose treatment increases satiety following breakfast and dinner, reduces hunger and prospective food consumption following dinner. This pilot study presents a rationale to propose oligofructose supplements in the management of food intake in overweight and obese patients.
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Introduction

Dietary fibres would be of particular interest regarding their putative role in the management of metabolic syndrome; they are prone to modulate food intake, body weight, glucose homeostasis, plasma lipid profile and associated cardiovascular diseases. (Jenkins *et al*., 1999; Davy and Melby, 2003; Venn and Mann, 2004). Soluble dietary fibres, such as guar gum, pectin or mucilages, reduce postprandial glycemia by delaying gastric emptying, namely through their gel-forming effect (Nuttall, 1993). But other dietary fibres, which do not exhibit gel-forming properties, seem promising in the control of food intake and metabolic disorders associated with glucose intolerance and obesity. It is the case of dietary fructans, namely inulin-type fructans, which were recently recognized as dietary fibres (Delzenne *et al*., 2003; Delzenne, 2003). They are commonly found in several vegetables and cereals (onion, garlic, wheat, etc) and in food products in which they are added for their nutritional or organoleptic properties (fat or sugar replacer) (Van Loo *et al*., 1995; Roberfroid and Delzenne, 1998). Animal studies suggest that dietary consumption of oligofructose (OFS) – a short-chain fructan obtained from inulin – might enhance satiety, thereby resulting in greater reductions in energy intake in normal, Zucker fa/fa rats and

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streptozotocin-treated diabetic rats (Daubioul *et al*., 2002; Cani *et al*., 2005a). Although the mechanisms that might be responsible for such effects are not fully understood, OFS stimulates the release of a satiety-inducing gut hormone, GLP-1 (7–36) amide, and its precursor proglucagon mRNA in the proximal colon of rats (Cani *et al*., 2004, 2005a, b). Consistent with these studies, intravenous infusion of GLP-1 in humans enhances satiety and decreases energy intake during the period of infusion (Flint *et al*., 1998, 2001). One human study demonstrates that GLP-1 plasma level significantly increases after OFS treatment, but no study specifically analysed the putative effect of OFS on satiety and hunger sensations in humans (Piche *et al*., 2003).

We therefore performed a short-term pilot study to examine whether consumption of supplements of oligofructose would promote satiety and decrease energy intake in healthy subjects.

Subjects and methods

Subjects

In total, 10 healthy subjects (five men and five women) aged 21–39 year (mean $\pm$ s.e.m. 27.2 $\pm$ 1.6) with mean $\pm$ s.e.m. weight 67.5 $\pm$ 3.8 kg, mean $\pm$ s.e.m. height 173 $\pm$ 3 cm, BMI ranging from 18.5 to 27.4 kg/m^2 (mean $\pm$ s.e.m. 22.3 $\pm$ 0.7) were recruited by local advertisement, and were free from acute and chronic diseases or use of medications that might influence study outcomes. A diet evaluation consisting of both food-frequency questionnaires and a 2-day diet record was obtained to identify and exclude individuals with a usual fibre intake $>$30 g/day (22 subjects participated to the validation of food frequency questionnaire; 10 subjects were selected for the study). Throughout the study, subjects lived at home and prepared their own meals, while consuming oligofructose or placebo supplement – described in the protocol section – during the two 2-week experimental phases. Subjects were instructed to eat until they were comfortably full and to try to not gain or lose weight consciously. The study protocol was approved by the Ethical committee of Université catholique de Louvain and written informed consent was obtained from each subject.

Protocol

Subjects were randomly assigned in a single-blind, crossover, placebo-controlled design. Outpatient investigation consisted of two 2-week experimental phases when a fibre (Oligofructose-OFS) or placebo (Maltodextrin-DM) supplement was consumed, separated by a 2-week washout period. Five subjects first received the OFS supplement and five subjects received the DM supplement. Daily supplements were divided into two portions of 8 g each to be eaten during breakfast and dinner. To assess the compliance, subjects kept a preweighed bag (8 g) of daily supplement consumption and returned empty bags for monitoring. They were instructed to consume the entire amount of the two bags daily. Energy intake, hunger, satiety, fullness and prospective food consumption were measured at intervals during the study as described below. Potential adverse effects were monitored daily during each period of treatment (thirst, nausea, diarrhea, pain, flatulence, abdominal rumbling, gastric reflux). OFS consisted of Raftilose P95 (6.27 kJ/g) kindly provided by Orafti (Tienen, Belgium), which is the fully soluble and highly fermentable. Caloreen® (16.7 kJ/g) (Nestlé Clinical Nutrition, Brussels, Belgium) was used as fully soluble, totally absorbed and nonfermentable DM.

Free-choice buffet and diets

Before the study, the subjects were invited to participate in a day of acclimatization with three free choice buffet meals (breakfast, lunch, dinner); the objective was to define clearly the meaning of the appetite sensation scores, and to test the feasibility and adequacy of the appetite scale. The instructions for OFS or placebo ingestion (inclusion in food and/or adequate beverage) were given to the subjects. At the end of each 2 two-week period of OFS and DM treatment, subjects were invited to an excess day free-choice buffet meal (namely, breakfast, lunch and dinner). Food and drinking were weighed before and after meals, and caloric intake was calculated. Appetite ratings were made on 100 mm visual analogue scales (VAS) with text expressing the most positive and the negative rating anchored at each end. (A) Satiety: 'I cannot eat another bite'; (B) Hunger: 'I have never been more hungry'; (C) Fullness: 'I am totally full'; (D) Prospective food consumption: 'I can eat a lot'. (Raben *et al*., 1995). VAS were used to assess satiety, hunger, fullness and prospective food consumption of the test meals. Sensations were recorded at the beginning of each meal (time 0) and throughout the period after breakfast, lunch and dinner.

The subjects were instructed to abstain from alcohol and strenuous physical activity for the 2 days before the test days in order to ensure similar macronutrient balance on the test days. The subjects were invited to report food consumed between meals. Food consumption was recorded daily during the period test (OFS and DM) by the subjects and analysed by our dietitian; a food frequency questionnaire and 24 h recall were recorded on the days before test meals to validate the self-daily food record. Reported energy, macronutrients and fibre intakes were calculated using the program Diet-Expert 2000, and fructans intake was calculated taking into account the content reported in food stuff by Van Loo *et al*. (1995).

Statistical analysis

Results are expressed as mean $\pm$ s.e.m. The effects of OFS and placebo between test meals were compared by ANOVA using repeated measures model with fixed factors of treatment, time, treatment $\times$ time, and a random factor of patient. Energy intake and macronutrients between test meals were

compared using a paired *t*-test, SPPS 9.0.0 for Windows system (SPSS, Chicago IL, USA). The level of significance was set at $P<0.05$.

Results

The amount of fructans (including inulin and oligofructose) consumed before the study was not significantly different between men and women (10.3 ± 2.4 and 7 ± 0.8 g, for men and women, respectively; mean value $9.1\,g\pm1.3$ g/day). The total fibre and dietary energy and macronutrient intake (protein, carbohydrate, fat) during 2-week periods consuming OFS or DM supplements were equivalent and are presented in Table 1. Compliance was excellent; minor gastrointestinal disorders (abdominal rumbling, flatulence) were reported only on the first 3 days of oligofructose treatment.

Table 1 Dietary energy and nutrients intakes in healthy subjects during 2-week periods corresponding to oligofructose (OFS) supplement or placebo (DM) supplement[a]

	OFS	*DM*	P-*value*
Energy, kJ/day (kcal/day)	8937 ± 920 (2135 ± 220)	9440 ± 703 (2255 ± 168)	$P=0.05$
Protein, % energy	14.7 ± 1	13.9 ± 1	$P>0.05$
Carbohydrate, % energy	58.1 ± 2	58.1 ± 1.5	$P>0.05$
Fat, % energy	27.4 ± 1.5	27.2 ± 0.9	$P>0.05$
Dietary fiber (g/day)	22.4 ± 2.6	23.9 ± 3.2	$P>0.05$
Total fiber (g/day) (including supplements)	38.4 ± 2.6	23.9 ± 3.2	$P<0.05$

[a]Results are mean$\pm$s.e.m., $n=10$, statistical analysis are performed through a paired Student's *t*-test.

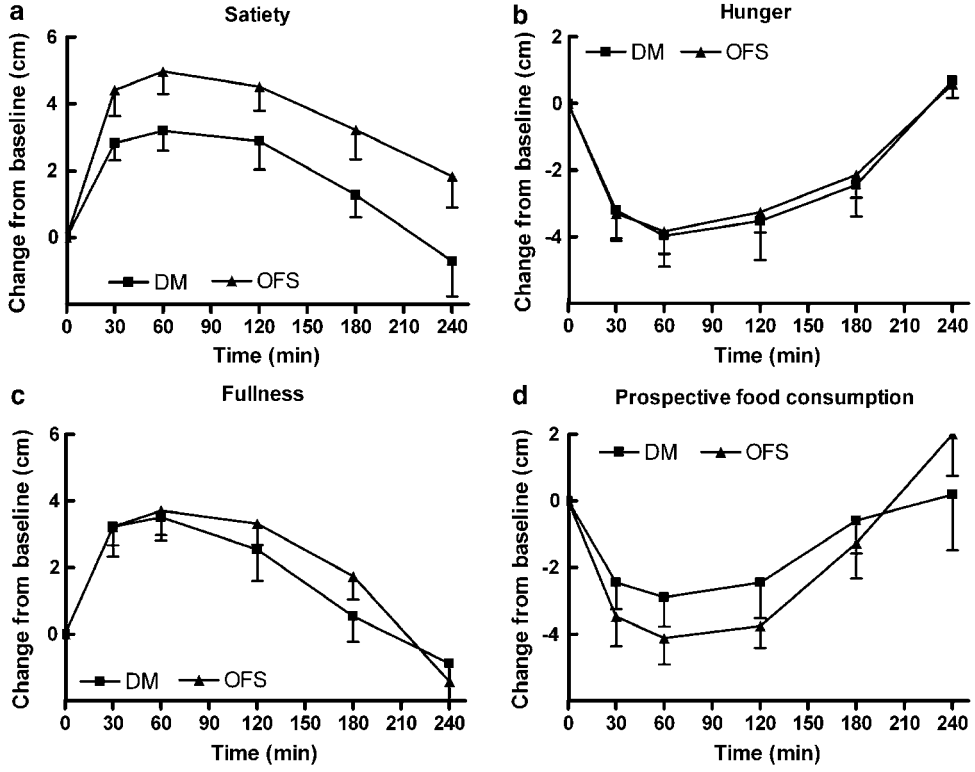

Figure 1 Breakfast visual analogue score (relative scale) (satiety, hunger, fullness and prospective food consumption) after 2 weeks of OFS (triangle) or DM (squares) supplements in healthy subjects. The results are presented as change from baseline scores and are mean$\pm$s.e.m. for all subjects. Visual analogue scale corresponds to (**a**) Satiety: 'I cannot eat another bite'; (**b**) Hunger: 'I have never been more hungry'; (**c**) Fullness: 'I am totally full'; (**d**) Prospective food consumption: 'I can eat a lot'. By ANOVA: *Satiety:* treatment effect, $P=0.045$; time effect, $P=0.002$; time $\times$ treatment interaction effect, $P=0.18$. *Hunger:* treatment effect, $P=0.88$; time effect, $P=0.001$; time $\times$ treatment interaction effect, $P=0.68$, *Fullness:* treatment effect, $P=0.58$; time effect, $P=0.05$; time $\times$ treatment interaction effect, $P=0.3$. *Prospective food consumption:* treatment effect, $P=0.23$; time effect, $P=0.17$; time $\times$ treatment interaction effect, $P=0.49$.

Appetite scores

After breakfast, OFS significantly increases satiety ($P=0.04$), without any significant difference in hunger, fullness and prospective food consumption as compared to that in the DM treatment period (Figure 1). After lunch, no significant differences were observed between OFS and DM treatment period (Figure 2). After dinner, OFS significantly increases and maintains a higher satiety ($P=0.04$), and OFS treatment reduces hunger ($P=0.04$) and prospective food consumption ($P=0.05$) (Figure 3).

Energy Intake during ad libitum free choice buffet

The energy intake at breakfast and lunch, expressed as % from energy intake observed at DM period buffet, were significantly lower (by about 10%) ($P=0.01$ and 0.03, respectively) after OFS treatment as compared to that after DM treatment (Table 2). At dinner, there was no difference in the energy intake between OFS and DM. The total energy intake during the 24-h period of the buffet was significantly lower corresponding to 95% ($P=0.05$) of the total energy intake recorded during DM treatment period (Table 2).

Discussion

Previous research has suggested that increasing total fibre intake could help to reduce energy intake by decreasing hunger and/or increasing satiety and be helpful in the management of type 2 diabetes (Howarth *et al*., 2001; Venn and Mann, 2004). Dietary fibres have thus been proposed as key food components taken into account in the control of the current high prevalence of obesity and overweight. Nowadays, there is little information on the putative effects of fermentable fibres on food intake and energy regulation. In the present study, oligofructose or maltodextrin (as placebo) were given twice daily, 8 g at breakfast and 8 g at dinner. The observation of food intake related sensations and behaviour was measured for several hours following breakfast, lunch and dinner proposed as controlled buffet. Tolerance towards oligofructose was good and explains the excellent compliance observed. Interestingly, we found that oligofructose promotes satiety following breakfast and dinner, and reduces hunger and prospective food consumption after the dinner. During oligofructose feeding, breakfast, lunch and total energy intake were moderately (by about

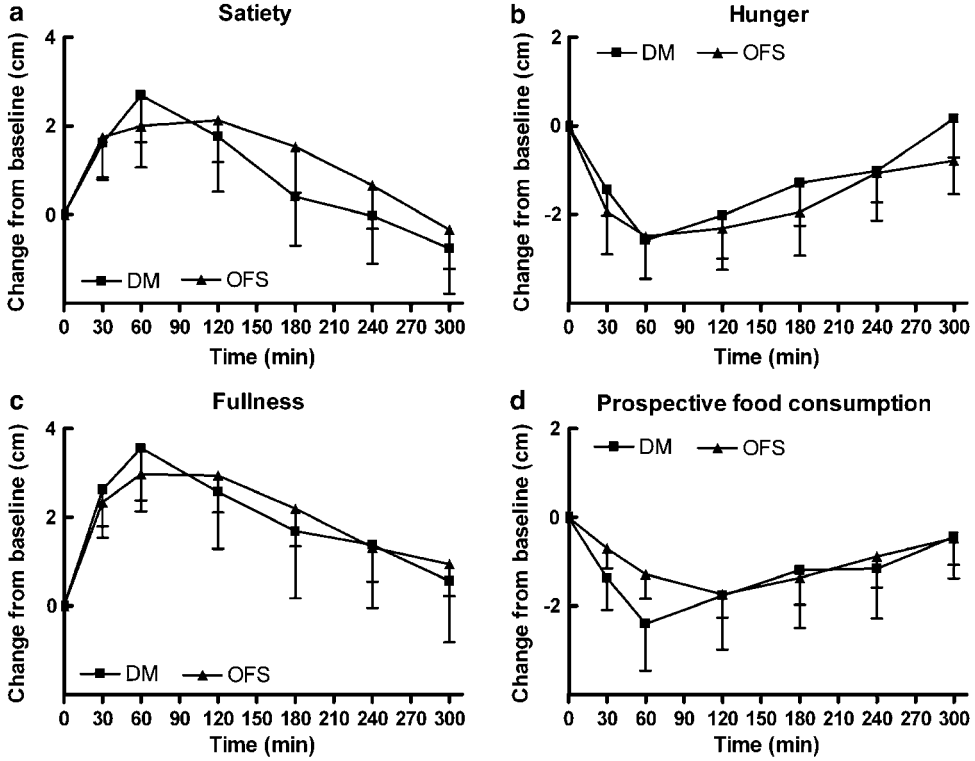

Figure 2 Lunch visual analogue score (relative scale) (satiety, hunger, fullness and prospective food consumption) after 2 weeks of OFS (triangle) or DM (squares) supplements in healthy subjects. The results are presented as change from baseline scores and are mean $\pm$ s.e.m. for all subjects. Visual analogue scale corresponds to (**a**) Satiety: 'I cannot eat another bite'; (**b**) Hunger: 'I have never been more hungry'; (**c**) Fullness: 'I am totally full'; (**d**) Prospective food consumption: 'I can eat a lot'. By ANOVA: *Satiety:* treatment effect, $P=0.92$; time effect, $P=0.25$; time $\times$ treatment interaction effect, $P=0.36$. *Hunger:* treatment effect, $P=0.84$; time effect, $P=0.83$; time $\times$ treatment interaction effect, $P=0.44$. *Fullness:* treatment effect, $P=0.98$; time effect, $P=0.77$; time $\times$ treatment interaction effect, $P=0.78$. *Prospective food consumption:* treatment effect, $P=0.35$; time effect, $P=0.64$; time $\times$ treatment interaction effect, $P=0.88$.

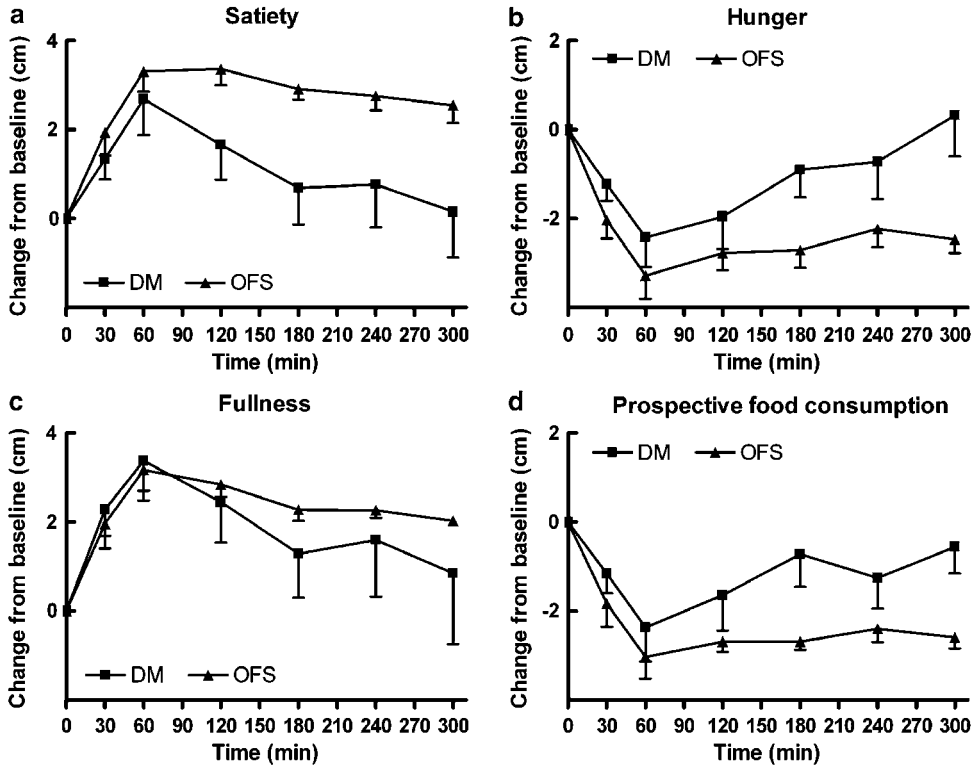

Figure 3 Dinner visual analogue score (relative scale) (satiety, hunger, fullness and prospective food consumption) after 2 weeks of OFS (triangle) or DM (squares) supplements in healthy subjects. The results are presented as change from baseline scores and are mean ± s.e.m. for all subjects. Visual analogue scale corresponds to (**a**) Satiety: 'I cannot eat another bite'; (**b**) Hunger: 'I have never been more hungry'; (**c**) Fullness: 'I am totally full'; (**d**) Prospective food consumption: 'I can eat a lot'. By ANOVA: *Satiety:* treatment effect, $P=0.04$; time effect, $P<0.001$; time × treatment interaction effect, $P=0.03$. *Hunger:* treatment effect, $P=0.04$; time effect, $P=0.001$; time × treatment interaction effect, $P=0.06$. *Fullness:* treatment effect, $P=0.62$; time effect, $P=0.004$; time × treatment interaction effect, $P=0.21$. *Prospective food consumption:* treatment effect, $P=0.05$; time effect, $P=0.001$; time × treatment interaction effect, $P=0.02$.

Table 2 Dietary energy intake in healthy subjects during 2-week periods corresponding to oligofructose (OFS) supplement or placebo (DM) supplement[a]

Meals	*DM*	*OFS*	P-*value*
Breakfast (% from DM)	100	91 ± 3.3	$P<0.01$
Lunch (% from DM)	100	89.5 ± 3	$P<0.05$
Dinner (% from DM)	100	95 ± 6.8	$P>0.05$
Total energy intake (% from DM)	100	94.6 ± 1.8	$P<0.05$

[a]Values are mean ± s.e.m., $n=10$. Statistical analysis is performed through a paired Student's *t*-test.

5–10%), but significantly lower than those observed during DM period. The significant increase of satiety observed following breakfast could explain the decrease of energy intake during the following meal, that is lunch. In contrast, this observation, the similar satiety observed following lunch could predict the same energy intake during the following meal, that is dinner. Two questions may arise from this study: (1) by which mechanism could oligofructose modulate food intake behaviour? (2) Could this effect also be relevant for other fermentable dietary fibres? In rats, oligofructose supplementation decreases food intake – with interesting effects on fat mass development, steatosis and hyperglycemia – namely through the promotion of intestinal synthesis and portal release of GLP-1 (7–36) amide (Cani *et al*., 2004, 2005a, b). GLP-1 (7–36) amide is a satiety hormone causing weight loss in humans when administered exogenously at levels ranging from physio to supraphysiologic doses (Flint *et al*., 1998, 2001; Verdich *et al*., 2001). An increase in serum GLP-1 (7–36) amide by oligofructose has been reported in one interventional study performed in patients presenting gastric reflux, but this results has not been related to food intake and satiety (Piche *et al*., 2003). The authors suggest that the 'kinetics' of fermentation – assessed by hydrogen breath test – is important to take into account when assessing the influence of fermented nutrients on circulating peptides. The increase in expired hydrogen (marker of fermentation) correlates with the modulation of serum GLP-1 (7–36) amide level, which could explain the link between intestinal fermentation and this peptide secretion. Thus, on the basis of these results, it is reasonable to suggest a role of oligofructose in enhancing satiety and reducing energy intake in humans consuming a diet *ad libitum*. Recently, Archer *et al*. (2004) have demonstrated that another fermentable fructans dietary fibre – inulin – added in

food as fat-replacer was able to induce a lower energy intake during a test day, despite no effect on satiety at breakfast, suggesting, as mentioned by the authors, a late postabsorptive satiety trigger related to the complete fermentation of this fibre (Archer *et al*., 2004). Nevertheless, all fermentable dietary fibres do not have the same potency to increase satietogenic peptides, at least in rats: long-chain inulin, which is largely fermented in the distal colon, whereas oligofructose is fermented in the proximal colon, was not able to produce the same effects of oligofructose in terms of GLP-1 (7–36) amide and proglucagon mRNA modulation (Cani *et al*., 2004). Besides, other authors have compared the putative effects of fermentable fibres (pectin and β-glucan, ratio 2:1) and nonfermentable fibres (hydroxypropyl methylcellulose) on satiety, hunger and body weight and have found no effect of these two fibres (Howarth *et al*., 2003). The last observation leads us to think that the place (proximal or distal colon) and the pattern of fermentation (in terms of short-chain fatty acids (SCFA) production) (Van Loo *et al*., 1999) of fermentable fibre would be important, but this remains speculative.

In conclusion, 2 weeks of oligofructose treatment increases satiety following breakfast and dinner, reduces hunger and prospective food consumption following dinner. Breakfast, lunch and total energy intake were significantly reduced as compared to that in the DM treatment. These results suggest a role of oligofructose in promoting a moderate negative energy balance in humans consuming a diet *ad libitum*. These results remain to be confirmed in a longer period of time and assessed in obese and type 2 diabetes patients.

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