Original Article

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Increasing doses of fiber do not influence short-term satiety or food intake and are inconsistently linked to gut hormone levels

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Abstract

Background: People who eat more fiber often have a lower body weight than people who eat less fiber. The mechanism for this relationship has been explained, in part, by increased satiety, which may occur as a result of changes in appetite-suppressing gut hormone levels, and decreases in food intake at subsequent meals.

Objective: We hypothesized that increasing doses of mixed fiber, consumed in muffins for breakfast, would proportionally influence satiety, gut hormone levels, and subsequent food intake.

Design: This was a randomized, double-blind, crossover study. Healthy men ($n = 10$) and women ($n = 10$) with a BMI of 24 ± 2 (mean $\pm$ SEM) participated in this study. Fasting subjects consumed a muffin with 0, 4, 8, or 12 g of mixed fibers and approximately 500 kcal. Visual analog scales rated hunger and satiety for 3 h; blood was drawn to measure ghrelin, glucagon-like peptide-1 (GLP-1), and peptide YY_{3-36} (PYY_{3-36}) at various intervals; and food intake was measured at an *ad libitum* lunch.

Results: Responses to satiety-related questions did not differ among treatments. However, despite lack of differences in satiety, gut hormone levels differed among treatments. Ghrelin was higher after the 12 g fiber dose than after the 4 and 8 g fiber doses. GLP-1 was higher after the 0 g fiber dose than after the 12 and 4 g fiber doses, and PYY_{3-36} did not differ among fiber doses. Food intake was also indistinguishable among doses.

Conclusion: Satiety, gut hormone response, and food intake did not change in a dose-dependent manner after subjects consumed 0, 4, 8, and 12 g of mixed fiber in muffins for breakfast.

Keywords: *fiber dose*; *fiber*; *ghrelin*; *GLP-1*; *PYY*; *appetite*; *hunger*; *visual analog scales*

Received: 12 March 2010; Revised: 26 May 2010; Accepted: 11 June 2010; Published: 29 June 2010

Observational studies suggest that fiber intake is inversely associated with body weight (1–3). For example, a study reported that in a 20-month period, every 1 g increase in total fiber consumed per day, decreased body weight by 0.25 kg (4). Improved satiety and decreased food intake are common theories used to describe why fiber intake may be associated with a lower body weight (5).

Fiber has well-documented effects on satiety (6); and because of this, it is often implied that consuming high-fiber foods will reduce food intake. Some studies have compared satiety and food intake after one dose of fiber compared to a control; however, few, if any, studies have evaluated how increasing doses of fiber actually influence food intake at subsequent meals.

Certain types of fiber may influence satiety more than others (7). For example, a large review suggests that viscous fibers, such as guar gum, pectin, and β-glucan may improve satiety more than less viscous fibers (6).

Gut hormones are also proposed as important factors for the control of appetite and satiety (8). Ghrelin has been shown to be positively correlated with hunger (9), while glucagon-like peptide-1 (GLP-1) and peptide YY_{3-36} (PYY_{3-36}) are believed to be inversely correlated

Citation: Food & Nutrition Research 2010, **54:** 5135 - DOI: 10.3402/fnr.v54i0.5135
(page number not for citation purpose)

(10, 11). However, most studies evaluate gut hormone changes after predominantly carbohydrate, protein, or fat intake; very few studies have evaluated how these three hormones change in response to fiber intake (12, 13). It is possible, that fiber decreases appetite by favorably influencing gut hormone levels.

At a time when food manufactures are adding fibers to everything from yogurt to snack foods, it is important to know more about the physiologic benefits of various fiber types and doses. Therefore, we hypothesized that a mixed-fiber muffin, fed at four practical doses (0, 4, 8, and 12 g), would increase satiety and decrease food intake in a dose-dependent manner. We also hypothesized that ghrelin, GLP-1, and PYY_{3-36} would change in proportion to fiber dose.

Methods and materials

The University of Minnesota Institutional Review Board Human Subjects Committee approved all aspects of this research. Twenty subjects were recruited in the fall of 2007 by flyers placed around the University of Minnesota campus. They were chosen based on power calculations (80% power with $\alpha = 0.05$) calculated from the differences in visual analog scale (VAS) scores.

Subjects were screened over the phone and subject eligibility was determined in accordance with all inclusion and exclusion criteria. Included subjects were English-speaking, healthy men and women between 18 and 65 years of age. They were non-smoking; not taking medications; non-dieting (weight stable over last 3 months); had a BMI between 18 and 27; and were normoglycemic. Subjects also had to be able to give blood through an IV. Subjects were excluded if they: did not regularly consume breakfast; had a distaste for muffins; had any history of disease or significant past medical history; were vegetarians or consumed more than approximately 15 g of fiber per day; were pregnant or lactating; or if they had irregular menstrual cycles.

Screening and study visits

Prior to any procedures the study coordinator obtained a signature on informed consent. After formal acceptance into the study, each subject received instructions for the day before study visits. In the 24 h prior to each visit, subjects followed a low-fiber, lead-in diet, which prohibited use of fiber supplements and alcohol. Subjects were required to maintain their body weight and activity level throughout the study period; specifically, they had to avoid excessive exercise 24 h before each visit.

Fasted subjects arrived at the General Clinical Research Center (GCRC) on the University of Minnesota campus between 7:00 and 9:00 am on weekdays. All visits were held in a quiet room, which allowed subjects to read, use laptops, work quietly, or listen to music. Visits were scheduled at least 1 week apart. However, women participated only during the follicular phase of their menstrual cycle so some visits were more than a week apart.

Upon arrival at the GCRC, a registered nurse inserted an antecubital IV that was used for blood drawing purposes only. The IV was left in place for 10 min before drawing the baseline blood sample; this was done in attempt to reduce the possibility of elevated hormone levels after venipuncture stress (14).

After 10 min of rest, subjects were given instructions for completing the computerized VAS and proceeded to complete their baseline appetite assessment. Immediately after, fasting blood samples were drawn to evaluate ghrelin, GLP-1, and PYY_{3-36}. Subjects then consumed either a low-fiber control muffin or one of three fiber-containing muffins for breakfast. The muffin and 250 ml of water were consumed within 10 min.

Appetite sensations were rated by VAS at 15, 30, 45, 60, 90, 120, and 180 min after baseline. Ghrelin samples were drawn at 15, 30, 60, and 90 min, and GLP-1 and PYY_{3-36} were drawn at 30 and 60 min. The IV was removed at the end of the 180-min period and subjects were given a buffet lunch of pre-selected, pre-weighed pizzas, and 1 l of water. Subjects were told to eat until comfortably satisfied. After 30 min, the remaining pizza and water were weighed, and energy intakes were calculated. Pizza has been successfully used as an *ad libitum* meal in previous studies (15–17). Before subjects were discharged from the GCRC they were instructed to keep a detailed food record for the remainder of the day.

Treatment muffins

In a randomized fashion subjects received the four treatment muffins containing: 0, 4, 8, and 12 g of mixed fiber for breakfast. The mixed fiber was presented in equal proportions in each muffin: pectin (Apple Pectin SF 50-LV, Herbstreith & Fox, Neuenbürg/Württ, Germany), barley β-glucan (Barliv, Cargill, Hammond, IN), guar gum (Guar, TIC Gums, White Marsh, MD), pea fiber (Centara Dietary Pea Fibre, Norben, Willoughby, OH), and citrus fiber (Citri-Fi 100FG, Fibrestar, Inc., Willmar, MN). These fibers were chosen based on a literature review of fiber and satiety, which suggested that viscous fibers were more likely to affect appetite, and for their ability to be baked uniformly into muffins (6). The muffins were spice flavored and commercially made (Nestlé R&D Center; Solon, OH). Attempts were made to balance macronutrient content; however, disguising viscous fiber in products is extremely difficult and some variances in macronutrient content were inevitable (Table 1).

After baking and cooling, the muffins were frozen at $-20°C$. Muffins were removed from the freezer 2 h before each subject visit and were thawed at room temperature.

Table 1. Composition of treatment muffins[a]

Mixed fiber dose (g)	Total fiber (g)	Soluble fiber (g)	Insoluble fiber (g)	kcal	Total fat (g)	Total carbohydrate (g)	Protein (g)	Moisture content (g)	Ash (g)	Serving size (g)
0	<1	n/a	n/a	502	19.5	74	11	24	1	144
4	5.7	2.5	3.2	488	13	81	12	68	3	176
8	8.9	4.0	4.9	493	10	89	12	62	3	175
12	12.8	6.1	6.7	544	13	93	13	81	3	204

[a]Content listed per serving. Fiber, fat, protein, moisture, and ash analyses were determined by AOAC Methodology. Carbohydrate and calorie content were estimated by US Department of Agriculture calculations. Fiber was assigned 0 kcal/g in the calculations. This analysis was completed at Covance Labs, Madison, WI, USA.

Visual analog scales (VAS)

Questions were taken directly from previously validated 100 mm VAS (18). The appetite-related questions assessed hunger, satisfaction, fullness, and prospective food intake.

Dietary intake analysis

The post-intervention food records were analyzed using the dietary analysis program, Nutrition Data System for Research (NDSR, version 2007, Nutrition Coordinating Center, Minneapolis, MN). NDSR provided detailed nutrient information, including: total energy, carbohydrate, fat, protein, and fiber intake.

Sample collection and analysis

Gut hormones were analyzed with commercially available RIA and ELISA kits from Millipore, St. Charles, MO (Total Ghrelin, Cat. # GHRT-89HK; Active Glucagon-Like Peptide-1, Cat. # EGLP-35K; and Human PYY_{3-36}, Cat. # PYY-67HK). Plasma samples were prepared and stored according to manufacturer's instructions. Intra- and inter-assay coefficients of variation are available on the manufacturer website.

Statistical analysis

Every subject who consented to the study completed all four visits. Appetite-related responses and gut hormone levels are expressed as change from baseline and were compared using area under the curve (AUC). AUC was calculated by the trapezoidal rule. Change from baseline AUC for appetite questions; change from baseline AUC for gut hormones; and *ad libitum* food intake in the post-intervention period were compared among treatments using a mixed effects linear model with a random subject effect (Proc Mixed). Proc Mixed calculated treatment means, standard error, and statistical differences between treatment means. Data are presented as mean ± SE when appropriate. Statistical significance was determined at $p < 0.05$. Carryover, treatment sequence, and interaction terms were tested in each model, but were omitted because they were not significant at $p < 0.05$. All final models included fiber dose and visit number only. Spearman correlation coefficient tests were performed to assess associations between select variables. All analyses were carried out with SAS 9.1.2 (SAS Institute, Cary, NC).

Results

Subject characteristics

Twenty racially diverse subjects (10 men and 10 women) participated in this study. The mean age and BMI were 26 ± 7 years and 24 ± 2 kg/m^2, respectively. Age and BMI did not differ between genders or among the treatment sequence groups (data not shown).

Baseline responses on VAS and fasting gut hormone levels were not statistically different among treatments. All data were normally distributed and, therefore, were not transformed.

Appetite sensations

AUC hunger and prospective food intake did not differ among fiber doses; AUC satisfaction and fullness varied slightly among treatments (Fig. 1). Subjects were more satisfied and more full after consuming the 4 g fiber muffin than after consuming the 0 g fiber muffin ($p < 0.01$); the remaining treatments were indistinguishable. Appetite sensations did not change in a clear dose-dependent manner (p for trends > 0.11).

Food intake

Food intake at the lunch buffet and in the post-intervention period did not differ among fiber doses (Fig. 2). Total fiber (g), total fat (g), total carbohydrate (g), total protein (g), and total food weight (g) consumed were also indistinguishable (data not shown).

Gut hormones

AUC ghrelin was higher after the 12 g fiber dose than after the 4 and 8 g fiber doses (Fig. 3). This was unexpected since ghrelin is known to be the hunger

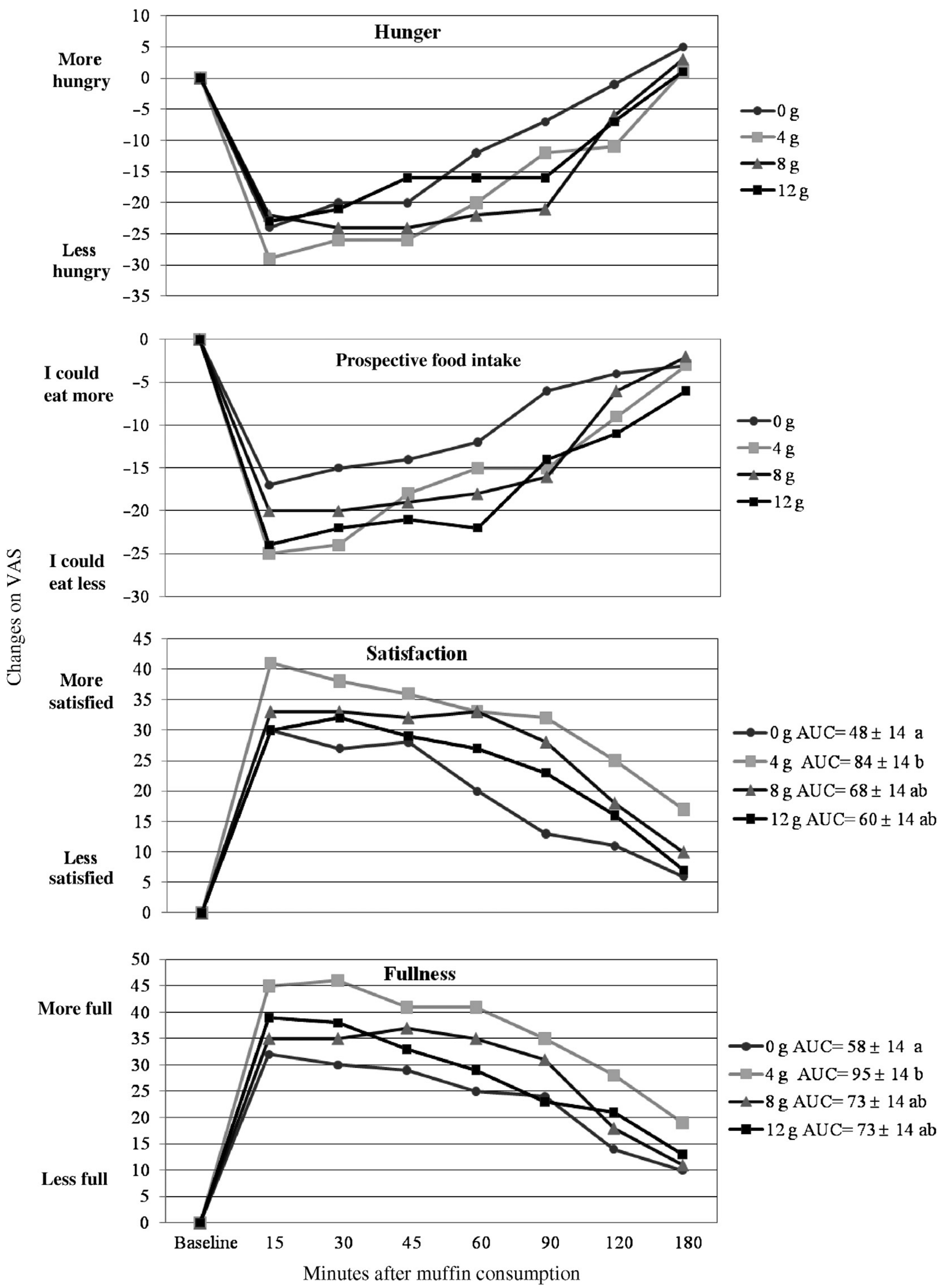

Fig. 1. AUC changes for satiety-related questions (expressed as change from baseline). In the legend, the numbers after each fiber dose represent the AUC score ± SEM. The treatments with different letters have statistically different AUC; $p < 0.05$. AUC is not specified unless the fiber doses provoked significantly different responses.

hormone and our subjective appetite measures indicated that there were no differences in hunger among the 4 fiber doses. In addition, AUC ghrelin did not correlate with AUC hunger for any of the fiber doses (Spearman Correlation Coefficients; $p > 0.05$). Ghrelin did not change in a clear dose-dependent manner (p for trend $= 0.24$).

AUC GLP-1 was higher after the 0 g fiber dose than after the 4 and 12 g doses; it was also higher after the 8 g dose than after the 12 g dose (Fig. 4). GLP-1 did

Citation: Food & Nutrition Research 2010, 54: 5135 - DOI: 10.3402/fnr.v54i0.5135

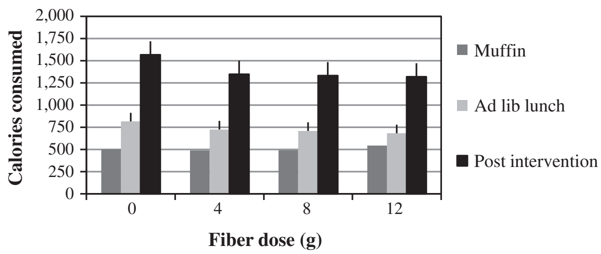

Fig. 2. Mean (±SEM) calorie intake during 24-h intervention day. There were no statistical differences among treatments for intake at the lunch buffet or during the post-intervention period.

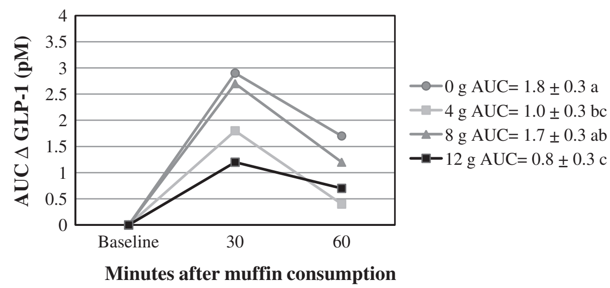

Fig. 4. AUC GLP-1 (expressed as change from baseline). In the legend, the numbers after each fiber dose represent the AUC score ± SEM. The treatments with different letters have statistically different AUC; $p < 0.05$.

not change in a clear dose-dependent manner (p for trend = 0.08).

AUC PYY_{3-36} did not differ among treatments, but approximately 65% of samples fell below the assay detection level of 21.1 pg/ml (data not shown). Levels less than detection were included in the analysis as 21 pg/ml.

Discussion

The purpose of this study was to compare the effects of four practical doses of mixed fiber on satiety, gut hormone levels, and food intake. Surprisingly, none of our endpoints changed in a dose-dependent manner.

Our findings are inconsistent with previous reviews suggesting that fiber intake is positively associated with satiety (5, 6). To the best of our knowledge, only two crossover studies have evaluated how various doses of the same fiber influence satiety in the same subject population. In each of these studies, the higher fiber dose was more satiating than the low- or no-fiber dose. Mathern et al. (19) studied the effects of 0, 4, and 8 g of viscous fenugreek fiber on a variety of appetite sensations. They found that 8 g of fenugreek mixed into orange juice was significantly more satiating than 0 or 4 g. Similarly, Gustafsson et al. (20) found that portions of carrots containing 6 and 9 g of fiber were significantly more satiating than portions containing 3 g of fiber, when incorporated into a mixed meal. It is difficult to explain why our results are incongruous with these two studies; however, it is likely related to the type of fiber administered. Certain types of fiber have been found to be more satiating than others (7). The fibers used in this study were chosen because of their viscous characteristics and their previous association with appetite suppression (6). Our results, however, suggest that a combination of fibers may not be as effective as one fiber given in isolation.

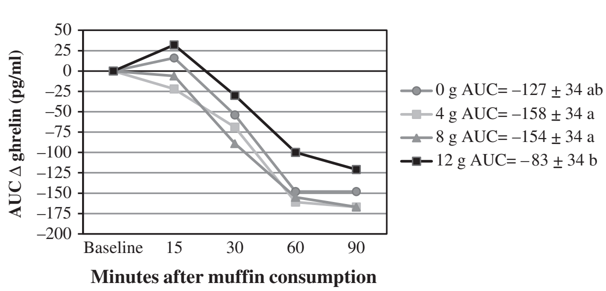

Fig. 3. AUC ghrelin (expressed as change from baseline). In the legend, the numbers after each fiber dose represent the AUC score ± SEM. The treatments with different letters have statistically different AUC; $p < 0.05$.

Studies that use lower doses of fiber generally find no effect on satiety. For example, Mattes et al. (21) found no difference in satiety when subjects consumed a snack bar with 4 g of mixed fiber and a bar with 1 g of fiber. Similarly, Hlebowicz et al. (22) found no differences in appetite ratings after subjects consumed a control cereal and cereals with 1.5–7 g of fiber. Lastly, a third study found snack bars with 4–10 g of added fiber had no influence on appetitive sensations compared to a 2 g fiber control (23). Although, our study included up to 12 g of fiber, it is possible that this dose still was not large enough to influence appetite. Collectively, the results of these studies suggest that higher fiber doses may be needed to induce satiety.

It should also be noted that the water content increased and the caloric density decreased slightly with each dose of fiber. It is possible that these differences could have influenced our satiety results. However, this is unlikely since research suggests that an increased water content and increased caloric density should improve satiety (6); and this was not the case in our study. In fact, the 12 g fiber muffin (with the highest water content and lowest caloric density) was no more satiating than any of the other muffins. Also of note, we recognize that the 0 g fiber muffin contained more fat than the other muffins. We do not, however, feel this influenced our findings since the satiety-related results for this muffin were not significantly different from the other muffins with less fat.

A large dietary fiber review reported that subjects tend to eat less at subsequent meals (and over time) if they are fed higher fiber foods compared to lower fiber foods (5). Our data contradict this association. Food intake at the *ad libitum* pizza lunch, and in the post-intervention period, was indistinguishable among our fiber doses. This, however, was somewhat expected since appetite sensations were not significantly different among our fiber doses. If subjects' hunger and prospective food intake levels were not different then we would not expect food intake to differ at a subsequent meal or for the remainder of the day. Mattes (21) reported similar findings after feeding subjects a combination of viscous fibers in a breakfast bar.

Many reviews have suggested that gut hormones – like ghrelin, GLP-1, and PYY_{3-36} – play influential roles in appetite regulation and food intake (8, 24–27). However, it is clear that different macronutrients exert different post-prandial effects (28, 29).

Research suggests that digestible carbohydrates or proteins are more effective for suppressing post-prandial ghrelin than fat (25, 28, 30). However, the effect of consuming a predominantly fiber food, or consuming fiber as part of a mixed meal, is rarely described.

Elevated ghrelin is typically correlated with hunger and stimulation of food intake, while ghrelin suppression is correlated with satiety (25, 31, 32). In our study, AUC ghrelin was higher after the 12 g fiber dose than after the 4 and 8 g doses. This finding was unexpected, since there were no differences in hunger or satiety among these doses. There is some evidence, however, that fiber intake may inhibit ghrelin suppression. For example, ghrelin suppression was inhibited when comparing meals that had little or no fiber, to meals that contained high doses of psyllium (33), viscous fibers (34), and wheat fiber (35).

It is possible that the viscous nature of our fibers inhibited ghrelin suppression by altering gastric emptying and changing patterns of digestion and absorption (36, 37). However, if this were true then we should have expected to see the most ghrelin suppression after the 0 g fiber dose, which we did not. Further research is needed to better understand the role ghrelin plays in appetite after fiber intake.

GLP-1 is typically very low in the fasting state, but rises quickly after food intake, especially after carbohydrates (10). The rise of GLP-1 has been correlated with increased satiety and less hunger (38, 39). In our study, AUC GLP-1 was highest after the 0 g fiber treatment and lowest after the 12 g dose. GLP-1 was also significantly higher after the 0 g fiber dose than after the 4 g fiber dose. This is contrary to what we would expect, since the 4 g fiber dose produced greater feelings of satisfaction and fullness compared to the 0 g fiber treatment.

Again, we hypothesize that gastric emptying time and overall nutrient absorption may have been slower after our fiber treatments; thus, fewer stimuli (nutrients) were available to promote GLP-1 release. It is conceivable that nutrients interfaced with intestinal cells and nerve fibers more rapidly after the 0 g fiber dose, which subsequently produced a greater GLP-1 response. This theory is supported by Juvonen et al. (36). They compared high- and low-viscosity beverages with equivalent fiber content and found that the high-viscosity beverage significantly slowed gastric emptying and suppressed GLP-1 release compared to the equivalent low-viscosity beverage. Miholic et al. (40) also report that gastric emptying time is positively correlated with GLP-1 levels. Specifically, they state that faster gastric emptying time was related to higher GLP-1 concentrations. This is contrary to the findings of others, who have reported that GLP-1 is inversely associated with gastric emptying time (38, 41, 42). However, these studies have evaluated gastric emptying after GLP-1 infusions or GLP-1 stimulated by fiber-free meals.

Similar to GLP-1, PYY_{3-36} concentrations are expected to increase shortly after food intake (11). The change in PYY_{3-36} concentration is believed to reflect calorie content and the macronutrient composition of a meal. However, there are no published human studies evaluating changes in PYY_{3-36} after fiber is consumed as part of a mixed meal. Several studies have indicated that satiety increases in proportion to plasma levels of PYY_{3-36}; however, this is most often seen after exogenous administration and not by way of endogenous production after food intake (43–45).

PYY_{3-36} did not rise substantially after any of our muffins were consumed. However, the majority of our subjects' blood samples remained below the assay detection range for PYY_{3-36}. We have no reason to believe this was an assay error, since preparation and analysis techniques were the same as those previously described in the literature (46, 47). PYY_{3-36} was consistently detectable in seven of our 20 subjects; though, there was significant variability in the baseline values among subjects and among test days (22–161 pg/ml). This suggests that basal levels of PYY_{3-36} are highly variable within, and between, individuals, and that this study was not powered appropriately to determine statistical differences in PYY_{3-36}.

In conclusion, increasing doses of a practical dose of mixed fiber did not influence satiety, gut hormone levels, or food intake in a dose-dependent manner. Despite common notions that fiber may improve satiety, this does not appear true for all types and doses of fibers. Therefore, blanket statements between fiber and satiety should be made with caution, and should be specific to a particular fiber type and dose. As well, three commonly accepted objective appetite markers (ghrelin, GLP-1, and PYY_{3-36}) were not consistent with the subjective satiety ratings of our subjects. This emphasizes the complexity of appetite and gut hormone signaling in the setting of fiber intake.

Citation: Food & Nutrition Research 2010, **54**: 5135 - DOI: 10.3402/fnr.v54i0.5135

Acknowledgements

This research was sponsored by the Nestlé Research Center, a Doctoral Dissertation Fellowship from the University of Minnesota, and Grant No. M01 RR00400 from the National Center for Research Resources.

Conflict of interest and funding

ALE, LH, and HG are employees of Nestlé but have no conflicts of interest. Authors HJW, WT, and JLS have no conflicts of interest.

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