Psyllium fiber reduces rise in postprandial glucose and insulin concentrations in patients with non-insulin-dependent diabetes[1-3]

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ABSTRACT The ability of psyllium fiber to reduce postprandial serum glucose and insulin concentrations was studied in 18 non-insulin-dependent diabetic patients in a crossover design. Psyllium fiber or placebo was administered twice during each 15-h crossover phase, immediately before breakfast and dinner. No psyllium fiber or placebo was given at lunch, which allowed measurement of residual or second-meal effects. For meals eaten immediately after psyllium ingestion, maximum postprandial glucose elevation was reduced by 14% at breakfast and 20% at dinner relative to placebo. Postprandial serum insulin concentrations measured after breakfast were reduced by 12% relative to placebo. Second-meal effects after lunch showed a 31% reduction in postprandial glucose elevation relative to placebo. No significant differences in effects were noted between patients whose diabetes was controlled by diet alone and those whose diabetes was controlled by oral hypoglycemic drugs. Results indicate that psyllium as a meal supplement reduces proximate and second-meal postprandial glucose and insulin concentrations in non-insulin-dependent diabetics. *Am J Clin Nutr* 1991;53:1431–5.

KEY WORDS Psyllium, dietary fiber, postprandial glucose, postprandial insulin, non-insulin-dependent diabetes, second-meal effects

Introduction

Studies indicate that plant fibers can moderate postprandial glucose and insulin concentrations in non-insulin-dependent diabetic patients if administered with meals (1–4). In particular, water-soluble fibers including guar, soy, psyllium, and pectin were reported to be more effective than insoluble fibers such as wheat bran (5). Some researchers, however, failed to detect significant postprandial glucose blunting when soy (6) or psyllium fiber (7) was administered to non-insulin-dependent diabetic patients or when pectin was administered to nondiabetic patients (8). These discrepant findings may be due in part to the type of test meal given with the fiber. In two trials where no effect was observed, the fiber was administered with a liquid test meal (6, 7). However, when the fiber was given as a supplement to, or as a component of, a conventional solid-food meal, beneficial effects were found (2–4).

In addition to reducing acute rises in serum glucose and insulin concentrations when administered with a meal, soluble fibers may have residual or second-meal effects that blunt the postprandial glucose rise after meals eaten several hours after the fiber ingestion (9). Several studies in nondiabetic subjects demonstrated such effects with both soluble-fiber supplements and high-fiber foods (9–11). Little evidence of soluble fiber's second-meal effect exists to date in diabetic patients.

To resolve some of the ambiguities of these findings, we studied the ability of psyllium to reduce postprandial serum glucose and insulin concentrations in non-insulin-dependent diabetic patients. To determine whether psyllium's ability to alter postprandial glucose concentrations depends on the mode of diabetic therapy, postprandial effects were investigated separately in patients controlled by diet alone or in patients controlled by oral hypoglycemic agents.

Subjects and methods

Protocol

In this placebo-controlled, crossover trial, 18 non-insulin-dependent diabetic patients were randomly assigned to receive either psyllium or placebo as their first treatment. To ensure an overnight fast, patients were admitted to the General Clinical Research Center, University of Virginia, the previous evening. The following morning, a sampling catheter was placed in a peripheral vein and patency was maintained with a saline drip. Three blood samples were drawn at 15-min intervals (−30, −15, and 0 min before psyllium or placebo were administered) and assay results were averaged to obtain a fasting glucose value. Patients then took the psyllium or placebo followed immediately (within 2 min) by a standardized breakfast. Patients were instructed to consume this entire meal within 15 min. Serum glucose concentrations were determined during the next 5 h from samples drawn at 15-min intervals between 30 min and 2 h,

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TABLE 1
Food composition of meals

Food	Amount
	g
Breakfast	
Egg, scrambled	50
Corn flakes	21
Orange juice	249
Milk, 2% fat	244
Margarine, corn oil	5
Bread, white	24
Lunch	
Tuna, water packed	92
Mayonnaise	14
White bread	48
Tomato soup	122
Applesauce, unsweetened	122
Graham crackers	21
Dinner	
Baked chicken breast	86
Potato, boiled without skin	150
Margarine, corn oil	15
Roll, dinner	28
Green beans, canned	75
Pineapple rings, juice packed	83

then at 2.5, 3, 4, and 5 h. Serum insulin concentrations were also measured for the first 3 h of this period.

Five hours after breakfast a standard lunch was eaten but no psyllium or placebo was given. Serum glucose concentrations were again determined during the next 5 h by use of similar blood-sampling intervals as those used after breakfast. Ten hours after breakfast, patients took a second dose of psyllium or placebo followed immediately by a standard dinner meal. Serum glucose concentrations were once more determined during the next 5 h at the same intervals as those after lunch. After a washout period (median 7 d), patients crossed over to the opposite treatment and the protocol was repeated. Body weight was monitored during the course of participation with a mean weight reduction of 0.6 kg occurring between the first and second visit.

Subjects

Eighteen patients, 6 men and 12 women, meeting the National Diabetes Data Group criteria for non-insulin-dependent diabetes were enrolled in this trial. All patients had diabetes diagnosed ≥ 2 y before the trial and none had additional medical conditions or were receiving medications that might have confounded their glucose or insulin concentrations. Patients ranged from 29 to 71 y of age (53.6 ± 2.89, $\bar{x}$ ± SD) and weighed from 10 to 100% more than their desirable body weight (12, 13). Patient medical records indicated fasting blood glucose concentrations ranging from 6.7 to 12.3 mmol/L and hemoglobin A_{1c} ($HgbA_{1c}$) concentrations between 8 and 12%. Six patients treated their condition with diet alone whereas twelve took oral hypoglycemic agents. All patients provided informed consent. The University of Virginia's Human Investigation Committee and Clinical Research Center Committee both reviewed and approved the study protocol.

Test meals and medications

Standard test meals in this study were designed to meet the American Diabetes Association's 1986 nutritional recommendations (14) and to be similar to what patients might normally consume. Each meal contained ~2301.25 kJ (~550 kcal) with an average of 53% of calories as carbohydrates, 27% as fat, and 20% as protein. These meals provided a daily total of 14 g dietary fiber. **Tables 1 and 2** show the menu and composition of each of the meals, respectively. Nutritional analysis was calculated by using the *Auto-Nutritionist II* software program (N-Squared Computing, Salem, OR), with the exception of dietary and soluble fibers (Table 2).

Each patient took two doses of psyllium or placebo during each crossover period, one dose before breakfast and the other before dinner. No lead-in dosing period was used. Each premeal psyllium dose consisted of 6.8 g psyllium hydrophilic mucilloid as sugar-free, orange-flavored Metamucil (Procter & Gamble, Cincinnati). The psyllium was dispensed as two 3.4-g packets, each mixed into a 240-mL glass of water. The placebo consisted of fiber-free excipients of Metamucil (colorings, flavorings, and citrate) in the same ratio as in the active treatment. Each placebo dose was also divided with each half mixed into a 240-mL glass of water. Hence, patients drank 480 mL water before breakfast and dinner with each treatment. Ten patients received placebo and eight patients received psyllium as their first treatment. All subjects were questioned to assess subjective gastrointestinal side effects of the fiber, if any.

Clinical measurements

Serum glucose concentrations were determined by glucose oxidase methods by using a Beckman Glucose Analyzer II.

TABLE 2
Nutrient composition of meals*

	Daily total	Breakfast	Lunch	Dinner
Energy [kJ(kcal)]	6920.50 (1654)	2100.42 (502)	2284.52 (546)	2209.20 (528)
Carbohydrate (g)	219 [53]	73 [56]	76 [53]	70 [50]
Protein (g)	84 [20]	20 [15]	32 [22]	32 [23]
Fat (g)	50 [27]	17 [29]	16 [25]	17 [27]
Dietary fiber (g)†	13.05	1.7	5.1	6.25
Soluble fiber (g)‡	4.34	0.53	1.5	2.31

* Percentage of nutrient in brackets.
† Reference 15.
‡ References 16 and 17.

TABLE 3
Postprandial glycemic response after breakfast and dinner

	Psyllium (n = 18)	Placebo (n = 18)	P
Breakfast			
Peak glucose elevation (mmol/L)	6.03 ± 0.65 [−14]*	7.02 ± 0.62	0.08
Time to peak (min)	97.5 ± 6.7 [+9]	89.2 ± 7.7	0.26
Area under glucose curve (mmol · h⁻¹ · L⁻¹)	13.0 ± 2.6 [−13]	14.9 ± 2.4	0.37
Dinner			
Peak glucose elevation (mmol/L)	2.98 ± 0.42 [−21]	3.76 ± 0.42	0.06
Time to peak (min)	90.8 ± 7.8 [+9]	83.3 ± 7.3	0.35
Area under glucose curve (mmol · h⁻¹ · L⁻¹)	4.9 ± 2.0 [−41]	8.3 ± 1.7	0.07

* $\bar{x}$ ± SEM. Values calculated as the percent difference between mean values for psyllium and placebo. Percent difference is in brackets.

Measurements at each time point were determined in triplicate from a single blood sample, immediately after blood sampling. These triplicate readings were averaged for statistical analysis. Serum insulin concentrations were determined by radioimmunoassay techniques modified from Freedlander et al (18). The interassay CV was ±3% for glucose and ±6% for insulin.

Statistical methods

Changes in serum glucose and insulin concentrations were calculated separately for each postmeal period by using the serum concentration at each mealtime as the baseline. Treatments were compared for maximum increase, time to peak increase, and incremental area under the glucose and insulin curves for each meal according to standard crossover analysis of variance techniques (19). As part of this analysis, order and time effects were investigated and found to be negligible. Area increments under the curves for a given meal were determined for the 5-h period after the meal. Differences in response between modes of diabetes therapy (diet alone vs oral hypoglycemics) were investigated by two-way analysis of variance testing for interaction (19). All statistical analyses were done with the *SAS* statistical software package (Statistical Analysis System, release 5.16, SAS Institute Inc, Cary, NC). Two-tailed P values ≤ 0.05 were considered statistically significant whereas P values between 0.05 and 0.10 were considered supportive of the effect.

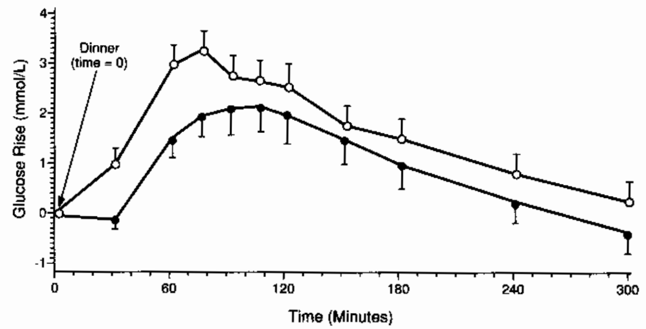

FIG 2. Effect of psyllium fiber (●; n = 18) or placebo (○; n = 18) on postprandial glucose concentrations after a dinner test meal. $\bar{x}$ ± SEM.

Results

The proximate hypoglycemic effects of psyllium (administered with a meal) are demonstrated by comparing postprandial serum glucose concentrations for both breakfast and dinner. The response to psyllium was generally greater after dinner than after breakfast, suggesting a possible cumulative effect (**Table 3**). Five-hour profiles displaying the rise and decline in glucose are shown in **Figures 1 and 2** for breakfast and dinner, respectively. Psyllium produced a significant ($P < 0.05$) decrease in peak postprandial glucose concentrations for up to 90 min after breakfast and for up to 75 min after dinner. Average glucose elevations with psyllium were 14% lower after breakfast (P = 0.08) and 20% lower after dinner (P = 0.06), and area under the glucose curve was lower after dinner (P = 0.07) although not lower after breakfast. The increase in time to peak glucose elevations was not statistically significant.

Serum insulin concentrations were also significantly ($P < 0.05$) lower with psyllium ingestion for the first 90 min after breakfast (**Fig 3**). The area under the curve for insulin was significantly lower (17%, P = 0.02) with psyllium, supported by a 12% reduction in peak insulin elevations (P = 0.09) with psyllium (**Table 4**).

Second-meal effects of psyllium on glucose concentrations are shown in **Figure 4.** This graph displays glucose elevations after a standard lunch eaten 5 h after psyllium administration at breakfast. Psyllium reduced postprandial peak glucose concentrations by 31% (P = 0.01) and area under the curve by 65% (P = 0.02) (**Table 5**).

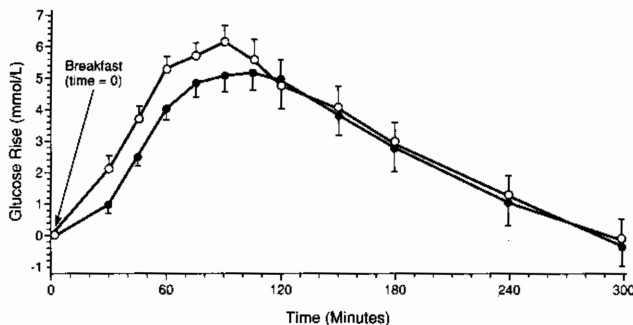

FIG 1. Effect of psyllium fiber (●; n = 18) or placebo (○; n = 18) on postprandial glucose concentrations after a breakfast test meal. $\bar{x}$ ± SEM.

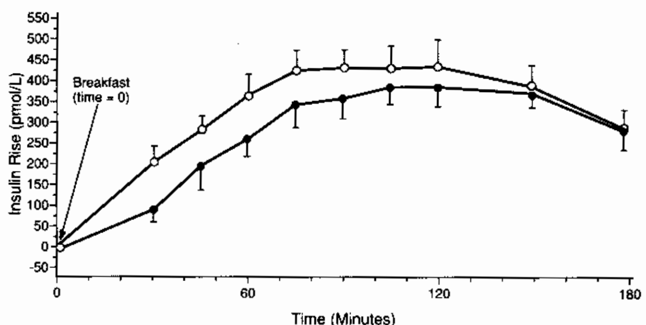

FIG 3. Effect of psyllium fiber (●; n = 18) or placebo (○; n = 18) on postprandial insulin concentrations after a breakfast test meal. $\bar{x}$ ± SEM.

TABLE 4
Postprandial insulin response after breakfast

	Psyllium (n = 18)	Placebo (n = 18)	P
Peak insulin elevation (pmol/L)	486.2 ± 48.1 [−12]*	551.3 ± 57.1	0.09
Time to peak (min)	112.1 ± 6.3 [+12]	100.0 ± 6.8	0.15
Area under insulin curve ($pmol \cdot h^{-1} \cdot L^{-1}$)	840.9 ± 105.5 [−17]	1008.2 ± 113.0	0.02

* $\bar{x}$ ± SEM. Values calculated as percent difference between mean values for psyllium and placebo. Percent difference is in brackets.

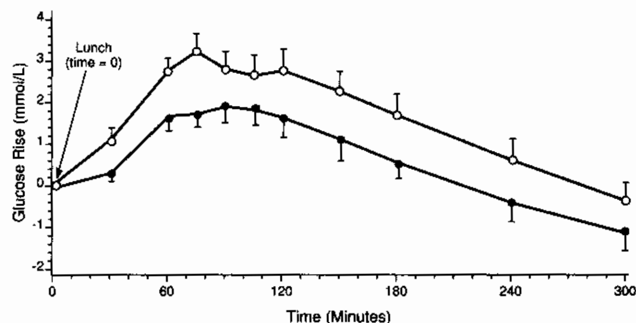

FIG 4. Effect of psyllium fiber (●; n = 18) or placebo (○; n = 18) on postprandial glucose concentrations after a lunch test meal eaten 5 h after test medication. $\bar{x}$ ± SEM.

The patient's mode of diabetic therapy had no apparent effect on psyllium's ability to reduce blood glucose concentrations. In patients treated by only dietary therapy, peak glucose elevation decreased 18% after breakfast, 32% after lunch, and 19% after dinner. Similarly, glucose elevation decreased 13% after breakfast, 31% after lunch, and 22% after dinner in patients receiving oral hypoglycemic therapy. No significant adverse reactions were reported for either psyllium or placebo during the study.

Discussion

Findings of this study indicate that psyllium reduces postprandial glucose and insulin concentrations in non-insulin-dependent diabetic patients both when taken with meals and after a second meal eaten up to 5 h after fiber ingestion. Psyllium appears to be equally effective in patients receiving either diet or oral hypoglycemic-agent therapy. These effects were achieved by a relatively modest fiber supplement to the diet and by meals that diabetic patients might reasonably be expected to consume outside the clinic.

In nondiabetic subjects, studies demonstrated the ability of guar or high-fiber foods to reduce the postprandial glucose rise of meals eaten several hours after fiber ingestion (9–11). Data from this study indicate that psyllium has a similar effect in diabetic patients. This second-meal result shows that the effect of psyllium given with one meal carries over to the next.

Psyllium's mechanism of action for glucose reduction in diabetic patients is probably similar to that of other soluble fibers. Several closely related mechanisms have been proposed. First, because psyllium forms a viscous gel in aqueous solution, it may slow the access of glucose to the small intestine's absorptive epithelium, thereby blunting postprandial glucose peaks. This has been postulated for guar (20, 21). Second, soluble fibers may delay gastric emptying, slowing carbohydrate uptake (22). Other researchers, however, did not confirm this correlation between delayed gastric emptying and reduced postprandial glucose concentrations (23). A third mechanism that may contribute to the postprandial effect is the sequestration of carbohydrates ingested with the meal, retarding carbohydrate access to digestive enzymes (24). The design of this study does not allow these mechanisms to be distinguished.

A different mechanism may underlie psyllium's second-meal effect. Recent research indicates that soluble fiber may evoke a lower postprandial rise in insulin concentrations with a corresponding smaller counterregulatory response to a meal (9, 10). A counterregulatory response is elicited by an undershoot of blood glucose. When fiber is administered with a meal, a reduced insulin response may cause a smaller undershoot of the blood glucose, which in turn might result in a reduced counterregulatory response producing less insulin resistance at the time of the second meal. Thus, soluble fiber may smooth the large fluctuation in postprandial glucose concentrations typical of diabetic patients, resulting in an improved response to later meals.

In this study psyllium caused a reduction in insulin after the test breakfast as well as a subsequent reduction in postprandial glycemic response after lunch. However, the glucose profile for placebo does not exhibit the theorized decline of serum glucose to concentrations below the initial fasting concentration, and measurements of glucagon, catecholamine, and other counterregulatory hormone concentrations would be needed to confirm such a mechanism. Clearly, additional work is needed to probe the importance of this or other mechanisms underlying the second-meal effect demonstrated in this research.

Whichever mechanism is responsible for psyllium's effect, oral hypoglycemic agents do not appear to affect the outcome. This finding is indicated by the lack of difference in postprandial glucose response demonstrated by patients receiving either dietary therapy alone or oral hypoglycemic agents. Differences between psyllium and placebo in peak glucose elevations and times to peak were not statistically different for the two groups. Soluble fibers such as psyllium may alter either counterregulatory or gut hormone responses, blunting the postprandial glucose rise. However, further research is needed to understand soluble fiber's effect on these activities.

If the short-term benefits psyllium demonstrated in non-insulin-dependent diabetic patients in this study can be extended by regular intake of the fiber, long-term glycemic control could

TABLE 5
Second-meal postprandial glycemic response after dinner

	Psyllium (n = 18)	Placebo (n = 18)	P
Peak glucose elevation (mmol/L)	2.58 ± 0.41 [−31]*	3.76 ± 0.42	0.01
Time to peak (min)	110.0 ± 13.0 [+16]	95.0 ± 8.0	0.13
Area under glucose curve ($mmol \cdot h^{-1} \cdot L^{-1}$)	2.76 ± 1.58 [−64]	7.57 ± 1.96	0.02

* $\bar{x}$ ± SEM. Values calculated as percent difference between mean values for psyllium and placebo. Percent difference is in brackets.

be improved. Lipid concentrations in these patients might also be reduced, as seen in a large-base trial in which psyllium was administered to hypercholesterolemic, nondiabetic patients (25). Preliminary studies in diabetic patients demonstrated reductions in fasting glucose and $HgbA_{1c}$ concentrations as well as lowered lipid concentrations (26–28). However, interpretation of these studies is complicated by lack of a placebo control (26), the presence of other diseases (27), patient weight loss, and small base sizes (28). Thus, trials confirming the ability of long-term psyllium administration to improve diabetic patients' $HgbA_{1c}$ and lipid concentrations are needed.

It would also be valuable to determine the effects of long-term psyllium use on the postprandial glucose and insulin response during such a trial. Changes psyllium may potentially elicit in peripheral insulin sensitivity, counterregulatory response, and intestinal morphology could become manifest. In this regard, a trial in nine non-insulin-dependent diabetic patients given psyllium for 1 wk indicated an improvement in postprandial response over the course of the study, but not enough patients were assessed to obtain statistical significance (3).

In conclusion, results from this trial indicate that the use of psyllium as a meal supplement reduces postprandial glucose and insulin elevations in non-insulin-dependent diabetic patients. This effect appears to be independent of diabetic therapy because similar results are seen in patients treated with diet alone and in patients on a diet and taking oral hypoglycemic agents. The results also indicate that psyllium can exert these effects hours after its administration and can produce a significant reduction in glucose after a second meal.

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