Effects of psyllium on glucose and serum lipid responses in men with type 2 diabetes and hypercholesterolemia

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ABSTRACT

Background: Water-soluble dietary fibers decrease postprandial glucose concentrations and decrease serum cholesterol concentrations. This study examined the effects of administering psyllium to men with type 2 diabetes.

Objective: The objective was to evaluate the safety and effectiveness of psyllium husk fiber used adjunctively to a traditional diet for diabetes in the treatment of men with type 2 diabetes and mild-to-moderate hypercholesterolemia.

Design: After a 2-wk dietary stabilization phase, 34 men with type 2 diabetes and mild-to-moderate hypercholesterolemia were randomly assigned to receive 5.1 g psyllium or cellulose placebo twice daily for 8 wk. Serum lipid and glycemic indexes were evaluated biweekly on an outpatient basis and at weeks 0 and 8 in a metabolic ward.

Results: In the metabolic ward, the psyllium group showed significant improvements in glucose and lipid values compared with the placebo group. Serum total and LDL-cholesterol concentrations were 8.9% (P < 0.05) and 13.0% (P = 0.07) lower, respectively, in the psyllium than in the placebo group. All-day and postlunch postprandial glucose concentrations were 11.0% (P < 0.05) and 19.2% (P < 0.01) lower in the psyllium than in the placebo group. Both products were well tolerated, with no serious adverse events related to treatment reported in either group.

Conclusion: The addition of psyllium to a traditional diet for persons with diabetes is safe, is well tolerated, and improves glycemic and lipid control in men with type 2 diabetes and hypercholesterolemia.

INTRODUCTION

Psyllium husk fiber is a viscous, mostly water-soluble fiber prepared by mechanical removal of the husk from blonde psyllium seed (Plantago ovata). Early or uncontrolled studies suggested that psyllium improved glycemic and lipid control in individuals with type 2 diabetes (1–3). Although a more recent and carefully controlled study reported reduced postprandial glucose and insulin concentrations with psyllium supplementation in type 2 diabetes (4), other studies found no effect on glycemic control (5) or an effect only when psyllium was sprinkled onto or incorporated into a cereal meal (6).

Psyllium has been shown to significantly reduce postprandial serum glucose and insulin concentrations in nondiabetic individuals (7). Numerous studies of nondiabetic individuals indicate that psyllium significantly lowers both total and LDL-cholesterol concentrations (8–12). However, the safety and effectiveness of psyllium for individuals with type 2 diabetes and hypercholesterolemia has not been well documented. The Diabetes Control and Complications Trial convincingly showed that maintaining good glycemic control delayed the onset and slowed the progression of complications in individuals with type 1 diabetes (13). Many healthy individuals with type 2 diabetes may also benefit from improved glycemic control (14). Furthermore, type 2 diabetes dramatically increases the risk of atherosclerotic cardiovascular disease (15, 16) and reductions in atherogenic lipids could greatly reduce mortality and morbidity from cardiovascular disease in individuals with type 2 diabetes.

The purpose of this study was to investigate the safety and effectiveness of psyllium husk fiber consumed for 8 wk adjunctively to a standard diet for diabetes in the treatment of men with type 2 diabetes and mild-to-moderate hypercholesterolemia. Effects of psyllium on glycemic and serum lipid indexes were examined in both an outpatient and metabolic ward setting.

SUBJECTS AND METHODS

Subjects

A total of 56 men with type 2 diabetes and hypercholesterolemia were recruited initially. After a 2-wk dietary stabilization phase, 34 of these men qualified for random assignment to treatment. The Human Investigation Subcommittee of the

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University of Kentucky reviewed and approved the study and informed consent was obtained from each subject.

Individuals were eligible for the study if they were men aged 30–70 y; had a body mass index (in kg/m²) of ≤30; had a history of stable type 2 diabetes meeting the criteria of the National Diabetes Data Group (17), with a fasting blood glucose concentration of 8.33–11.10 mmol/L and a serum glycated hemoglobin (Hb A₁c) concentration of ≤9% (mean of values taken in weeks −2 and −1 of the study); and had mild-to-moderate hypercholesterolemia, with a stable serum total cholesterol concentration of 5.17–7.76 mmol/L and triacylglycerol concentration of ≤1.65 mmol/L (mean of weeks −2 and −1). Individuals whose diabetes was controlled with diet only or diet plus oral sulfonylurea agents were eligible for study. Individuals were excluded from the study if they had medical conditions or were taking medications or supplements that might have interfered with glucose, insulin, or lipid measurements. Individuals with a history of myocardial infarction or major surgical procedures within the previous 6 mo were excluded from the study, as were individuals with a history of alcohol abuse, allergy to aspartame or psyllium seed, or phenylketonuria.

Experimental design

This study was double-blind, placebo-controlled, and parallel. The study consisted of a 2–wk dietary stabilization phase during which subjects followed a diet for diabetes followed by an 8-wk treatment phase in which subjects continued the diet but were also randomly assigned to receive either 5.1 g psyllium (psyllium group) or cellulose placebo (control group) twice daily. Subjects were instructed to consume the test products 20–30 min before the morning and evening meals.

All subjects underwent 2-d metabolic ward studies at weeks 0 and 8. During these studies, standardized meals were used to more accurately measure the effects of psyllium on glycemic and lipid control. After an overnight insulin infusion, a random subset of 8 subjects in the psyllium group and 8 subjects in the placebo group underwent a euglycemic clamp procedure during the third day of each metabolic ward evaluation to more fully evaluate glucose metabolism and peripheral insulin sensitivity.

Diets and test products

During the dietary stabilization phase, subjects received instruction on a traditional weight-maintaining diabetes exchange diet providing ≤30% of total energy as fat, ≤10% of energy as saturated fat, and ≥55% of energy as carbohydrate. Diet was not the major focus of this intervention and the main goal of dietary instruction was to encourage subjects to maintain their same dietary patterns throughout the study. Subjects continued with this diet and received ongoing dietary counseling throughout the remainder of the study.

During the treatment phase, subjects in the psyllium group received an orange-flavored, sugar-free product (Metamucil, Procter & Gamble Co, Cincinnati); subjects in the placebo group received an insoluble fiber, microcrystalline cellulose (Avicel, PH-101; FMC Corp, Philadelphia). Both test products included the same psyllium-product excipients and were given in two 8.7-g doses daily; each dose provided 5.1 g of either psyllium or cellulose. Both products were orange-flavored powders and were packaged in identical foil packets. Subjects were instructed to mix each packet in 240 mL liquid and to drink the mixture immediately before (20–30 min) the morning and evening meals each day for 8 wk.

During the metabolic ward evaluations, subjects received standardized meals low in fiber to enhance detection of the effects of fiber on glucose and lipid metabolism, as described previously (8). Subjects consumed a low-fat, low-fiber meal (65% of energy as carbohydrate, 15% as protein, 20% as fat, and 50 mg cholesterol/MJ) on the evening of the first day of the metabolic ward evaluation. On day 2 of the metabolic-ward evaluation, subjects consumed 3 meals providing 40% of energy as carbohydrate, 15% as protein, 45% as fat, 50 mg cholesterol/MJ, and 0.8 g dietary fiber/kJ.

Measurements

Dietary compliance throughout the study was monitored by using 3-d food records collected at weeks −1, 4, and 8. Dietary data were analyzed for energy, total fat, polyunsaturated fat, saturated fat, carbohydrate, protein, total fiber, soluble fiber, and cholesterol contents by using a computerized nutrient database (18) with revised fiber values (19). Compliance with test product use was monitored by subject interviews and by counting unopened packets at follow-up visits. Reports of any treatment-related adverse experience were solicited at each follow-up visit. A brief physical exam, a complete serum lipid profile, and fasting blood glucose and glycated hemoglobin (Hb A₁c) concentrations were taken at week −2 to establish eligibility for the study and were repeated at weeks −1, 0, 2, 4, 6, and 8. Fasting glycated albumin concentrations were measured at weeks −1, 0, 2, 4, 6, and 8 of the study. Thyroid function tests were also measured at week −1 of the study. Clinic visits were scheduled in the morning after a minimum 12-h fast. Subjects were instructed not to take their test medication on the morning of the study visits.

At weeks 0 and 8, all subjects were admitted to the metabolic ward for 2–3 d of evaluation. A complete physical examination, routine clinical chemistry and hematologic evaluations, and urinalyses were performed on day 1. Fasting serum lipid, C-peptide, Hb A₁c, and glycated albumin concentrations were some of the indexes measured.

On day 2 of the metabolic ward evaluation, serum lipids, glucose, insulin, fatty acids, apolipoproteins, and lipoprotein fractions by a vertical auto profile (VAP) were measured immediately before breakfast after a 14-h fast. Postprandial lipids, glucose, and insulin concentrations were measured at 9 intervals throughout the day; postprandial fatty acids were measured at 7 intervals; and postprandial apolipoproteins and VAP lipoproteins were measured at 3 intervals. A catheter was inserted into an antecubital vein to limit the number of venipunctures.

On the morning of day 3 of the metabolic ward evaluation, 16 randomly selected subjects also underwent a euglycemic hyperinsulinemic clamp procedure (20, 21). To standardize basal serum glucose concentrations, subjects received an overnight insulin infusion (W Duckworth, unpublished observations, 1992). Briefly, a 12-h intravenous insulin infusion (Novolin R in 1 L isotonic saline; Squibb & Co, Princeton, NJ) was started in these subjects on the evening of day 2. The insulin delivery rate was initiated and adjusted hourly according to a predetermined algorithm based on capillary blood glucose. Insulin was infused at $\approx 1$ mU·kg⁻¹·min⁻¹ for 3 h after an appropriate priming dose. Glucose (20% wt:vol, or 1.1 mol/L) was infused to maintain blood glucose at 5.55 mmol/L. Blood was drawn every 5 min throughout the procedure to monitor blood glucose concentrations, and 6 evaluations of serum...
insulin were made at regular intervals during the procedure. Subjects who underwent the euglycemic clamp were discharged after the postclamp meal. All other subjects were discharged after breakfast on day 3.

**Analytic methods**

Serum glucose concentrations were measured by using glucose oxidase (22). Serum insulin concentrations were measured with an insulin radioimmunoassay kit (ICN Micromedic Systems, Horsham, PA). Serum cholesterol, triacylglycerol, and HDL-cholesterol concentrations were determined with enzymatic methods by using the Abbott VP Analyzer (Abbott Laboratories, North Chicago). Serum cholesterol concentrations were measured with a sterol esterase–cholesterol oxidase assay (23). Serum triacylglycerol concentrations were determined by hydrolyzing the triacylglycerol and measuring the released glycerol (24). Serum HDL-cholesterol concentrations were measured with the same method used for serum cholesterol after removal of LDL and VLDL cholesterol by magnesium–dextran sulfate precipitation (25). Apolipoprotein A-I and B-100 concentrations were measured by radioimmunodiffusion with Tago-Diffu-Gen Kits (Tago, Burlingame, CA). Samples were sent to the University of Alabama Lipoprotein Laboratory (Birmingham) for VAP measurements (26). Other lipid measurements were done locally. Serum LDL-cholesterol, intermediate-density-lipoprotein (IDL), VLDL-cholesterol, HDL2, and HDL3 concentrations were available from VAP analysis. LDL cholesterol was also calculated with the Friedewald formula (27). Fasting serum C-peptide concentrations were measured as described previously (28). Glycated albumin was measured by using a boronated affinity column (Nichols Institute Reference Laboratories, San Juan Capistrano, CA), with expected values of 0.9–1.9%.

**Statistical analyses**

Two-sample \( t \) tests confirmed by Wilcoxon rank-sum tests were used to determine the comparability of values for the psyllium and placebo groups at baseline, to compare changes and percentage changes from baseline between treatment groups, and to compare dietary analyses indexes between groups. One-sample \( t \) tests were used to determine whether mean changes from baseline within each treatment group were significant. For the final values of body weight and each of the glycemic and lipid profile indexes, analysis of covariance was also completed with baseline values as covariates.

For outpatient evaluations, baseline values were defined as the average of all values taken at weeks $-2$, $-1$, and 0. Final values were defined as those measured at week 8. For metabolic ward evaluations, baseline and final values were defined as an average of values taken on day 2 of the metabolic ward evaluation at weeks 0 and 8, respectively. Values measured during the euglycemic clamp procedure were analyzed separately from other metabolic ward evaluations. Mean and peak serum glucose and insulin values were calculated separately for the postprandial periods after breakfast, lunch, and dinner.

All subjects were included in the safety analyses, whereas only subjects meeting all inclusion and exclusion criteria were included in the efficacy analyses. Two-tailed \( P \) values $<0.05$ were considered statistically significant, whereas \( P \) values between 0.05 and 0.10 were considered to be nearly significant. All analyses were performed by using the SAS package (29).

**RESULTS**

Of the 56 men who entered the dietary stabilization phase, 19 failed to meet study inclusion and exclusion criteria and 3 withdrew their consent to participate. Of the 34 subjects randomly assigned to treatment (18 to the psyllium group and 16 to the placebo group), 29 (15 in the psyllium group and 14 in the placebo group) completed the study and were considered evaluable. In the psyllium group, one subject withdrew consent, one subject was discharged by the study investigator because of back pain due to a spinal infection unrelated to treatment, and one subject was deemed unevaluable because of a baseline fasting blood glucose concentration in violation of the study protocol. In the placebo group, one subject withdrew consent and one subject was discharged by the study investigator because of noncompliance. On the basis of the number of returned, unopened packages and subject interviews, compliance was determined to be excellent. Subjects consumed 99.6% of the psyllium and 95.3% of the placebo given.

**Baseline characteristics**

Baseline characteristics of subjects in the psyllium and placebo groups are summarized in Table 1. Subjects were well matched according to age, height, body weight, and body mass index. Baseline C-peptide concentrations were not significantly different between groups.

**Baseline and final dietary nutrient intakes in the psyllium and placebo groups** are shown in Table 2. Except for the significantly higher total energy intake in the psyllium group than in the placebo group at baseline, dietary intakes did not differ significantly between groups throughout the study. The low energy intakes reported by both the psyllium and placebo groups in this study indicated that subjects substantially underreported their food intakes. More intensive training of subjects is required to ensure accurate self-reported intakes for careful dietary studies.

**Outpatient responses**

Changes from baseline in the glycemic and lipid indexes of the 2 groups during the outpatient and metabolic ward portions of the study are summarized in Table 3. At week 8, serum LDL-cholesterol concentrations decreased 4.9% in the psyllium group but increased 2.8% in the placebo group. This 7.7% difference in serum LDL-cholesterol concentrations was nearly significant (\( P = 0.09 \)). The change in serum HDL-cholesterol concentrations was significantly different between the psyllium and placebo groups at week 8, although the change in the ratio of LDL to HDL cholesterol was significantly different. Other than these exceptions, there were no significant differences in the change in glycemic and lipid indexes between the psyllium and placebo groups during outpatient evaluations.

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**Table 1**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control (( n = 14 ))</th>
<th>Psyllium (( n = 15 ))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>63.8 ± 1.6</td>
<td>62.0 ± 1.6</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>178.6 ± 2.0</td>
<td>176.8 ± 1.4</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>87.1 ± 3.3</td>
<td>89.6 ± 2.4</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>27.4 ± 1.1</td>
<td>28.7 ± 0.9</td>
</tr>
<tr>
<td>C-peptide (nmol/L)</td>
<td>1.16 ± 0.10</td>
<td>1.32 ± 0.10</td>
</tr>
</tbody>
</table>

\( \pm \) SEM of values taken at weeks $-2$, $-1$, and 0 during the dietary stabilization phase. There were no significant differences between groups.
All subjects maintained their body weights within ±5% during the study. As shown in Table 3, body weight decreased 0.3% in the psyllium group but increased 1.5% in the placebo group at week 8. Although this 1.8% difference in change in body weight between the psyllium and placebo groups was significant at week 8, no consistent trends in body weight were seen during the study. Changes in body weights did not differ significantly between groups at weeks 2, 4, or 6.

**Metabolic ward responses**

Changes from baseline in serum glucose with treatment are illustrated in Figure 1. During the first 180 min of treatment, values for subjects in the placebo group did not differ significantly from baseline, but values were consistently higher than baseline beginning at 270 min and beyond, being significantly different at 420 and 480 min. In contrast, values for psyllium-treated subjects were consistently below baseline values and differed significantly from values in the placebo group at 420 and 480 min.

Changes from baseline in glycemic and lipid indexes in the metabolic ward and outpatient evaluations are also shown in Table 3. There were significant differences in changes from baseline between the 2 groups for both glycemic and lipid indexes, with the psyllium group showing improved metabolic control compared with subjects in the placebo group. Of the glycemic indexes measured in all subjects in the metabolic ward, the percentage change in all-day postprandial serum glucose concentrations and postlunch serum glucose concentrations differed significantly between the psyllium and placebo groups. Compared with baseline concentrations, all-day postprandial serum glucose concentrations declined 4.2% in the psyllium group but rose 6.8% in the placebo group \( (P < 0.05) \). Postlunch serum glucose concentrations declined 6.5% in the psyllium group but rose 12.7% in the placebo group \( (P < 0.05) \). Thus, all-day and postlunch postprandial glucose concentrations were 11.0% and 19.2% lower, respectively, in the psyllium than in the placebo groups. Although mean baseline and peak serum insulin concentrations were significantly different between the psyllium and placebo groups, percentage changes from baseline in insulin did not differ significantly between groups (data not shown).

Glycemic indexes measured during the insulin clamp studies were not significantly different before and after treatment in the psyllium and placebo groups. After an overnight insulin infusion, baseline serum glucose values averaged 7.6 ± 0.6 and 7.5 ± 0.5 mmol/L in the psyllium and placebo groups, respectively; these values did not differ significantly between groups after the 8-wk treatment period. Mean serum glucose concentrations during the baseline insulin clamp procedure were 6.2 ± 0.1 and 6.1 ± 0.2 mmol/L in the psyllium and placebo groups, respectively; these values did not differ significantly between groups after treatment. Mean serum insulin concentrations during the baseline insulin clamp procedure were 517.4 ± 17.4 pmol/L (74.5 ± 2.7 mU/mL) and 470.2 ± 38.9 pmol/L (67.7 ± 5.6 mU/mL) in the psyllium and control groups, respectively; these values did not differ significantly between groups at baseline and did not change significantly after treatment. Glucose infusions during the baseline insulin clamp procedure averaged 2.3 ± 0.7 and 2.4 ± 0.5 mg·kg\(^{-1}\)·min\(^{-1}\) in the psyllium and control groups, respectively; these values decreased by 4.4 ± 5.3% and 4.2 ± 13.8%, respectively, during treatment. Thus, there were no significant differences in these glycemic indexes nor in percentage changes in these indexes between the psyllium and control groups at baseline or after treatment.

Of the lipid indexes measured in the metabolic ward, percentage changes in serum total cholesterol concentrations differed significantly between the psyllium and placebo groups \( (P = 0.012) \). Differences in percentage changes between groups were nearly significant for calculated LDL-cholesterol concentrations \( (P = 0.068) \) and VAP LDL-cholesterol concentrations \( (P = 0.068) \). Serum total cholesterol concentrations declined 2.1% from baseline in the psyllium group but increased 6.9% in the placebo group, resulting in a net difference in serum total cholesterol concentrations of 9.0% between the 2 groups.

### Safety analyses

Safety analyses were performed on all 34 subjects randomly assigned to treatment. Test products were well tolerated by most subjects. There were no significant differences between treatment groups in the incidence of adverse events or in the type of event reported. Respiratory system disorders were the most commonly reported adverse event. No serious adverse events related to treatment were reported by either the placebo or psyllium group.

Except for increased total protein and γ-glutamyltransferase concentrations and significant changes in some of the leukocyte indexes in the placebo group compared with baseline, no
TABLE 3
Serum glycemic and lipid responses in metabolic ward and outpatient settings in subjects in the psyllium and control groups

<table>
<thead>
<tr>
<th></th>
<th>Control (n = 14)</th>
<th>Percentage change</th>
<th>Baseline Percentage change</th>
<th>Psyllium (n = 15)</th>
<th>Percentage change</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td></td>
<td></td>
<td>Baseline</td>
<td></td>
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<tr>
<td><strong>Outpatient</strong></td>
<td></td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>Body weight (kg)</td>
<td>87.1 ± 3.3</td>
<td>1.5 ± 0.7</td>
<td></td>
<td>89.6 ± 2.4</td>
<td>−0.3 ± 0.4²</td>
</tr>
<tr>
<td>Glucose (mmol/L)</td>
<td>10.74 ± 0.56</td>
<td>2.8 ± 0.6</td>
<td></td>
<td>10.02 ± 0.41</td>
<td>−6.1 ± 4.5</td>
</tr>
<tr>
<td>Hb A\textsubscript{1c}</td>
<td>0.075 ± 0.002</td>
<td>−0.8 ± 0.3</td>
<td></td>
<td>0.073 ± 0.003</td>
<td>−6.3 ± 3.1</td>
</tr>
<tr>
<td>Glycated albumin</td>
<td>0.0222 ± 0.0010</td>
<td>−5.6 ± 6.2</td>
<td></td>
<td>0.020 ± 0.001</td>
<td>−3.1 ± 4.1</td>
</tr>
<tr>
<td>Total cholesterol (mmol/L)</td>
<td>5.89 ± 0.15</td>
<td>2.8 ± 2.3</td>
<td></td>
<td>6.08 ± 0.18</td>
<td>−2.3 ± 2.2</td>
</tr>
<tr>
<td>LDL cholesterol (mmol/L)</td>
<td>3.80 ± 0.17</td>
<td>2.8 ± 3.4</td>
<td></td>
<td>4.00 ± 0.23</td>
<td>−4.9 ± 2.4</td>
</tr>
<tr>
<td>HDL cholesterol (mmol/L)</td>
<td>0.94 ± 0.05</td>
<td>8.8 ± 2.3</td>
<td></td>
<td>0.97 ± 0.07</td>
<td>−0.9 ± 3.0²</td>
</tr>
<tr>
<td>Triacylglycerols (mmol/L)</td>
<td>2.50 ± 0.20</td>
<td>−0.4 ± 5.3</td>
<td></td>
<td>2.71 ± 0.35</td>
<td>−7.0 ± 13.3</td>
</tr>
<tr>
<td><strong>Metabolic ward</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Glucose (mmol/L)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Postbreakfast</td>
<td>13.54 ± 0.95</td>
<td>3.8 ± 4.7</td>
<td></td>
<td>13.44 ± 0.82</td>
<td>−3.0 ± 4.6</td>
</tr>
<tr>
<td>Postlunch</td>
<td>10.43 ± 0.83</td>
<td>12.7 ± 5.6</td>
<td></td>
<td>10.75 ± 0.69</td>
<td>−6.5 ± 4.2²</td>
</tr>
<tr>
<td>Postdinner</td>
<td>10.89 ± 0.61</td>
<td>2.2 ± 3.9</td>
<td></td>
<td>11.80 ± 0.75</td>
<td>−5.7 ± 4.5</td>
</tr>
<tr>
<td>All day</td>
<td>11.53 ± 0.76</td>
<td>6.8 ± 3.9</td>
<td></td>
<td>11.90 ± 0.70</td>
<td>−4.2 ± 3.3²</td>
</tr>
<tr>
<td>Total cholesterol (mmol/L)</td>
<td>5.39 ± 0.17</td>
<td>6.9 ± 2.4</td>
<td></td>
<td>5.69 ± 0.20</td>
<td>−2.1 ± 2.3²</td>
</tr>
<tr>
<td>LDL cholesterol (mmol/L)</td>
<td>3.39 ± 0.17</td>
<td>8.3 ± 5.3</td>
<td></td>
<td>3.81 ± 0.19</td>
<td>−4.7 ± 4.3</td>
</tr>
<tr>
<td>HDL cholesterol (mmol/L)</td>
<td>0.85 ± 0.05</td>
<td>2.0 ± 2.2</td>
<td></td>
<td>0.88 ± 0.07</td>
<td>0.6 ± 3.1</td>
</tr>
<tr>
<td>Triacylglycerols (mmol/L)</td>
<td>2.50 ± 0.23</td>
<td>13.7 ± 7.3</td>
<td></td>
<td>2.54 ± 0.31</td>
<td>6.5 ± 6.8</td>
</tr>
<tr>
<td>VAP lipoprotein cholesterol (mmol/L)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LDL</td>
<td>3.39 ± 0.14</td>
<td>2.7 ± 3.5</td>
<td></td>
<td>3.70 ± 0.20</td>
<td>−7.0 ± 3.7</td>
</tr>
<tr>
<td>HDL</td>
<td>0.86 ± 0.05</td>
<td>−2.6 ± 3.6</td>
<td></td>
<td>0.85 ± 0.07</td>
<td>−0.1 ± 4.2</td>
</tr>
<tr>
<td>HDL\textsubscript{2}</td>
<td>0.14 ± 0.02</td>
<td>−19.2 ± 9.2</td>
<td></td>
<td>0.12 ± 0.04</td>
<td>8.7 ± 15.9</td>
</tr>
<tr>
<td>HDL\textsubscript{3}</td>
<td>0.72 ± 0.03</td>
<td>1.4 ± 4.3</td>
<td></td>
<td>0.72 ± 0.05</td>
<td>−3.1 ± 4.2</td>
</tr>
<tr>
<td>Apolipoprotein B (g/L)</td>
<td>1.45 ± 0.08</td>
<td>5.7 ± 2.3</td>
<td></td>
<td>1.46 ± 0.08</td>
<td>−1.5 ± 3.7</td>
</tr>
<tr>
<td>Apolipoprotein A (g/L)</td>
<td>1.064 ± 0.032</td>
<td>2.5 ± 3.0</td>
<td></td>
<td>1.047 ± 0.079</td>
<td>2.2 ± 4.4</td>
</tr>
</tbody>
</table>

¹SEM. Baseline values were measured at weeks −2, −1, and 0; final values were measured at week 8. VAP, verticle auto profile; Hb A\textsubscript{1c}, glycated hemoglobin.

²Significantly different from control group: ²P < 0.05, ³P = 0.01.

clinically significant changes occurred in clinical chemistry, hematology, or urinalysis indexes as a result of treatment in either group. Although the changes in glycemic and lipid indexes were significant for total protein, γ-glutamyltransferase concentrations, and some leukocyte indexes, none of these indexes changed significantly from baseline in the psyllium group.

**DISCUSSION**

This study was designed to evaluate the safety and effectiveness of psyllium compared with a cellulose placebo used adjunctively to a traditional diabetes diet in men with type 2 diabetes and mild-to-moderate hypercholesterolemia. Significant differences in changes from baseline between treatment groups were seen in both glycemic and lipid indexes evaluated in the metabolic ward, with the psyllium group showing improved metabolic control compared with the placebo group. Although most changes in glycemic and lipid indexes during the outpatient evaluations were not significantly different between treatment groups, directional changes also suggested improved metabolic control in the psyllium group.

The magnitude of serum total and LDL-cholesterol reductions seen in this study were similar to reductions reported in studies of nondiabetic individuals. Sprecher et al (10) reported significant net decreases (psyllium minus placebo) in total and LDL cholesterol-concentrations of 3.5% and 5.1%, respectively, after 8 wk of psyllium treatment (5.1 g twice daily) in subjects consuming a low-fat diet. In a similar study with an 8-wk dietary stabilization phase, Bell et al (12) reported significant net decreases in total and LDL-cholesterol concentrations of 4.8% and 8.2%, respectively, after psyllium and placebo supplementation.

In large-scale studies of nondiabetic individuals with hypercholesterolemia, 8–16 wk of psyllium treatment after a dietary stabilization phase reduced serum total cholesterol concentrations by 3.5–5.6% and serum LDL-cholesterol concentrations by 5.1–8.8% compared with placebo treatment (8, 10–12). This smaller-scale study may not have had sufficient statistical power to detect all significant treatment effects of psyllium. Additional larger-scale studies are needed to confirm the preliminary results of this study.

Earlier studies reported that psyllium reduced fasting serum glucose concentrations (1) or decreased postprandial serum glucose concentrations (30) in individuals with type 2 diabetes. In another study, psyllium reduced the glycemic response of diabetic individuals to a flaked bran cereal test meal only when psyllium was incorporated into or sprinkled onto the cereal (6). In a carefully controlled crossover study of the effects of psyllium taken immediately before breakfast and dinner compared with the effects of cellulose placebo supplementation in individuals with type 2 diabetes, postprandial serum glucose values were 14% lower after breakfast, 31% lower after lunch, and 20% lower after dinner with psyllium (4). The ability of soluble fibers to reduce the postprandial glucose response to meals eaten...
several hours after fiber ingestion (eg, the so-called second meal effect) was shown previously in nondiabetic individuals (31, 32).

The second-meal effect of psyllium was also evident in the present study. Two doses of psyllium taken immediately before breakfast and dinner resulted in significantly lower metabolic ward measurements of all-day postprandial glucose and postlunch serum glucose concentrations in the psyllium than in the placebo group. All-day and postlunch postprandial glucose concentrations were 11.0% and 19.2% lower, respectively, in the psyllium than in the placebo group.

It is unlikely that the steady improvements in metabolic indexes seen in the psyllium group in this study were due to weight changes. Although body weights were 1.8% lower in the psyllium group than in the placebo group at week 8 \( (P < 0.05) \), no consistent trends in body weight were seen during this study.

Except for higher energy intakes in the psyllium group at baseline, dietary intakes were not significantly different between groups during the study. The low energy intakes reported by both groups indicated that subjects underreported their food intakes, as was documented in other clinical studies (33). The present study was not intended to be a careful dietary study but, rather, the purpose of dietary instruction and monitoring in this study was to ensure that dietary intake did not change significantly and that there were no significant differences in dietary intake between treatment groups during the study. Careful dietary studies require intensive instruction and monitoring beyond the scope of this study.

Psyllium is a viscous water-soluble fiber that has long been used as a bulk laxative with a good safety record. Although the role of dietary fiber in nutrition therapy for type 2 diabetes remains controversial (34, 35), several studies indicate that high-fiber diets (36–40) or diets supplemented with soluble fibers such as guar gum (41), soy (42), or pectin (43) improve metabolic control in many individuals with type 2 diabetes. The practical applications for some soluble fiber sources, however, are limited because of the lack of palatable forms. In this study, psyllium was well tolerated, was associated with no serious adverse events, and improved metabolic control compared with a cellulose placebo.

Medical nutrition therapy in type 2 diabetes must be individualized to reflect personal lifestyle and management goals (44). Because type 2 diabetes markedly increases the risk of atherosclerosis and its complications (45), achievement and maintenance of normal serum lipid concentrations is a primary goal of diabetes treatment.  

FIGURE 1. Mean (±SEM) changes (final values at week 8 — initial values at week 0), in serum glucose concentrations before and after meals for subjects in the placebo (▲) and psyllium (■) groups. *Significant difference between groups, \( P < 0.05 \).
management that could greatly reduce death and disability in this population. Results of this study suggest that the addition of psyllium to a standard diet for diabetes is safe, is well tolerated, and offers an additional dietary tool to improve metabolic control in individuals with type 2 diabetes and hypercholesterolemia.

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REFERENCES


