

Psyllium decreased serum glucose and glycosylated hemoglobin significantly in diabetic outpatients

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Abstract

Psyllium is a bulk-forming laxative and is high in both fiber and mucilage. The beneficial effect of dietary fiber in the management of type II diabetes, has not been totally demonstrated. The purpose of this study was to determine the plasma-lowering effects of 5.1 g b.i.d. of psyllium husk fiber, as an adjunct to dietary and drug therapy on lipid and glucose levels, in patients with type II diabetes. Patients were randomly selected from an outpatient clinic of primary care to participate in a double-blind placebo-controlled study in which *Plantago ovata* Forsk., or placebo was given in combination with their anti-diabetic drugs. Forty-nine subjects were included in the study that were given diet counseling before the study and then followed for 8 weeks in the treatment period. Fasting plasma glucose (FBS) was measured every 2 weeks, and total plasma cholesterol (TC), LDL-cholesterol (LDL-C), HDL-cholesterol (HDL-C), triglyceride (TG), and insulin levels were measured every 4 weeks. Glycosylated hemoglobin (HbA1c) was also measured at the beginning and ending of the study. The test products (psyllium or placebo) were supplied to subjects in identically labeled foil packets containing a 5.1 g dose of product, to consume two doses per day, half an hour before breakfast and dinner. Both products were well tolerated, with no serious adverse events related to treatment was reported in either. Better gastric tolerance to metformin was recorded in the psyllium group. FBS, and HbA1c, showed a significant reduction ($p < 0.05$), whereas HDL-C increased significantly ($p < 0.05$) following psyllium treatment. LDL/HDL ratio was significantly decreased ($p < 0.05$). Our results show that 5.1 g b.i.d. of psyllium for persons with type II diabetes is safe, well tolerated, and improves glycemic control.

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1. Introduction

Psyllium seeds from the *Plantago ovata* Forsk., belong to the plantaginaceae family, contain 10–30% mucilage. Psyllium is a common ingredient in over-the-counter bulk laxative products (Leung and Foster, 1996). Numerous double-blind trials have found that supplementation with

Plantago psyllium can lower total cholesterol (TC), and LDL-C (Anderson et al., 2000). Levels of HDL-C were shown to increase by psyllium supplementation (Oson et al., 1997). The cholesterol-lowering effect of psyllium has been reported in children (Davidson et al., 1996), as well as in adults (Florholmen et al., 1982). Psyllium supplementation has also improved blood sugar levels in some people with diabetes (Florholmen et al., 1982; Rodriguez-Moran et al., 1998; Anderson et al., 1999). The soluble fiber component of psyllium is believed to account for this effect. The

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Table 1
Demographic characteristics of the patients in the groups studied

Parameter	Psyllium (n = 21)	Placebo (n = 15)	p-Value
Age (year)	51.9 ± 2.2 ^a	53.6 ± 2.1	0.586
BMI (kg/m ²)	26.6 ± 1.0	27.5 ± 0.9	0.516
Glibenclamide (mg/day)	8.6 ± 1.3	9.8 ± 1.8	0.597
Metformin (mg/day)	759 ± 134	575 ± 155	0.375

^a Results are shown based on mean ± S.E. of mean for each group.

beneficial effect of psyllium is dose related (Fрати-Munari et al., 1989). Nevertheless, the side effects of psyllium are also dose related affecting the adherence (Tattersal and Mansell, 1990; Nuttall, 1993) so, the benefits of a high-fiber diet on reducing glucose levels are still controversial (Tattersal and Mansell, 1990; Nuttall, 1993) and has not been totally studied or appropriately shown in type II diabetes. Psyllium is nominated in Iran as ESFARZEH, and used mainly for its emollient effect. In Iranian folk medicine, there is a report on its anti-diabetic effect. The objective of this study was to determine the effects of 5.1 g b.i.d. of *Plantago ovata* Forsk., as an adjunct therapy, on fasting plasma glucose (FBS), glycosylated hemoglobin, cholesterol, and triglyceride levels, in patients with type II diabetes.

2. Methods

2.1. Trial organization

This was a 8-week, parallel group, double-blind, placebo controlled trial undertaken in an diabetes care clinic in the Shariati hospital during June 2003–April 2004. Overall coordination of the trial was from the Institute of Medicinal Plants, Tehran.

2.2. Participants

A total of 57 patients, age 35–70 years, whose diabetes were controlled with diet only or diet plus glibenclamide or metformin and volunteered to participate in the study were admitted initially (Table 1). Forty-nine of them qualified for random assignment to treatment. Patients were excluded from the study if they were receiving lipid-lowering drugs, corticosteroids, other soluble fiber treatment, lithium, carbamazepin, warfarin, digoxin or patients with clinically significant renal, hepatic, gastrointestinal, pulmonary, and thyroid disease. Individuals with a history of myocardial infarction or major surgical procedures within the previous 6 months, as well as, a history of allergy to aspartame or psyllium seed, or phenylketonuria were also excluded. The trial was carried out in accordance with the Declaration of Helsinki and subsequent revisions, and approved by the ethics committee at the Endocrinology and Metabolism Research Center of Tehran University of Medical Sciences. The patient provided written informed consent for participation.

FBS, total cholesterol and triglycerides more than 400, 300 and 500 mg/dl, respectively, were excluded from the study as well as HbA1c more than 13%.

2.3. Interventions

This study was double-blind, placebo-controlled, and parallel. The study consisted of an 8-week treatment phase in which subjects continued the diets and chemical drugs, but were also randomly assigned to receive either 5.1 g psyllium (psyllium group) or microcrystalline cellulose placebo (control group) twice daily. Subjects were instructed to consume the test product 20–30 min before the morning and evening meals, by stirring the content of one packet into 250 ml of water and drinking immediately. All patients completed a consent form, and all of these outpatients had been given diet counselling and were visited regularly in diabetes care clinic every 2 months at least for 1 year before the study. A questionnaire consisted of demographic, blood pressure, familial history of disease; concurrent disease, cigarette smoking and drug therapy were completed at the screening time. All participants were evaluated; blood pressure and weight were controlled and recorded in the screening period (at week 0) and in the treatment period at weeks 2, 4, 6, and 8. Samples of venous blood were taken for measurement of FBS, insulin, HbA1c, TC, LDL-C, HDL-C, and triglyceride levels.

2.4. Test products and dosages

The active medication was *Plantago ovata* Forsk. (Diamed[®], Iran Darouk Co., Tehran), containing by weight 5.1 g psyllium seed husk and inactive excipients that, in order of descending amount, were CMC, citric acid, artificial flavor, aspartame, and coloring agents. The placebo test article matched the active product except that it contained an inert bulk fiber purified from microcrystalline cellulose in place of psyllium. The test products (psyllium or placebo) were supplied to subjects in identically labelled foil packets containing a 5.1 g dose of product. Adherence to the dosing regimen was monitored by conducting interviews with the subjects on each visit, by counting the number of returned unopened packages, of psyllium or placebo, in each period of 2 weeks.

2.5. Outcomes

Parameters measured were body weight, blood pressure and fasting serum levels of glucose, HbA1c, insulin, and lipid profile. FBS, HbA1c, TC, HDL-C, LDL-C, and triglycerides levels were measured with commercial kits by Roche-hitachi 717 clinical chemistry autoanalyzer (Roche Diagnostics, Germany). Serum insulin and TSH levels were measured by radioimmunoassay (Immunotech, France). All of the measurements were done by Bahar clinical laboratory in Tehran. FBS was determined at weeks 0, 2, 4, 6, and 8; TC, HDL-C and LDL-C insulin, and triglycerides levels at weeks 0, 4, and 8; HbA1c at weeks 0 and 8.

2.6. Safety evaluation

All adverse events, reported or observed were recorded at each visit. Routine physical examination was conducted on each clinical visit.

2.7. Statistical analysis

A one-way repeated measures analysis of variance with a two-tailed post hoc Tukey mean comparison test was undertaken on the change in FBS, TC, LDL-C, HDL-C, TG, and insulin from baseline. To compare the change in FBS, TC, LDL-C, HDL-C, TG, and insulin at week 8 in relation to week 0, a paired two sided Student's *t*-tests, was used. Kruskal–Wallis test was employed to compare the baseline data and frequency of side effects between two groups.

3. Results

From 57 patients admitted, 49 diabetic patients were included in the study, 27 and 22 in psyllium and placebo group, respectively. Thirty-six of them completed the study and 13 were dropout (Fig. 1). Demographic characteristics for both groups, at the week 0 without statistical differences between them, were shown in Table 1. There was no significant difference between glibenclamid and metformin dosage in two groups (Table 1).

Counting their unopened psyllium or placebo foils, checked patients' compliance. Patients did not modify the composition of their diets and drug regimen along the study. Subjects in the treatment group completed the study, with excellent tolerance to psyllium. Gastric tolerance to metformin was recorded in the psyllium group. No significant changes were observed in the patient's weight at the begin-

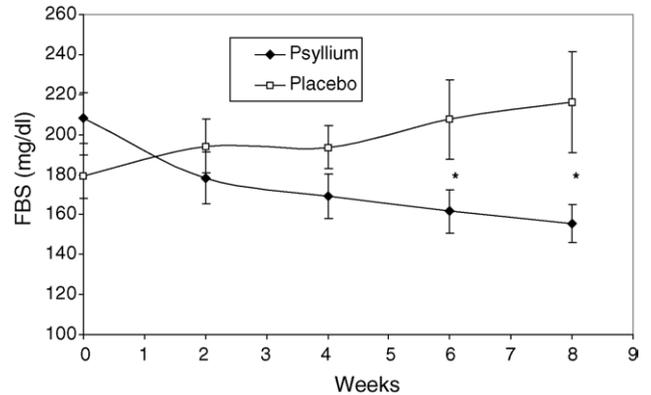


Fig. 2. Mean (\pm S.E.M.) of FBS levels in psyllium and placebo groups. FBS decreased significantly in the psyllium group and in the weeks 6 and 8 the difference between psyllium and placebo groups were significant, $*p < 0.05$.

ning and end of the study, in psyllium and placebo group, respectively.

3.1. Glucose profile

There were no significant differences between the two groups at the baseline (week 0) on the FBS ($t = 1.617$, d.f. = 34, $p = 0.115$). A one way repeated measures analysis of variance showed a significant change from week 6 on the FBS ($p < 0.05$). The changes at the end point compared to baseline were (mean (SD)): -52.77 (52.33) and 31.36 (85.74) for psyllium and placebo, respectively (Fig. 2 and Table 2).

Insulin was not changed between and within the study groups.

Glycosylated hemoglobin measured, as HbA1c was significantly different between the groups ($p < 0.05$). It was significantly decreased from 10.5 (± 0.73) to 8.9% (± 0.23) in the psyllium group ($p < 0.001$) and increased from 9.1 (± 0.51) to 10.5% (± 0.59) in the placebo group ($p < 0.05$) (Table 2).

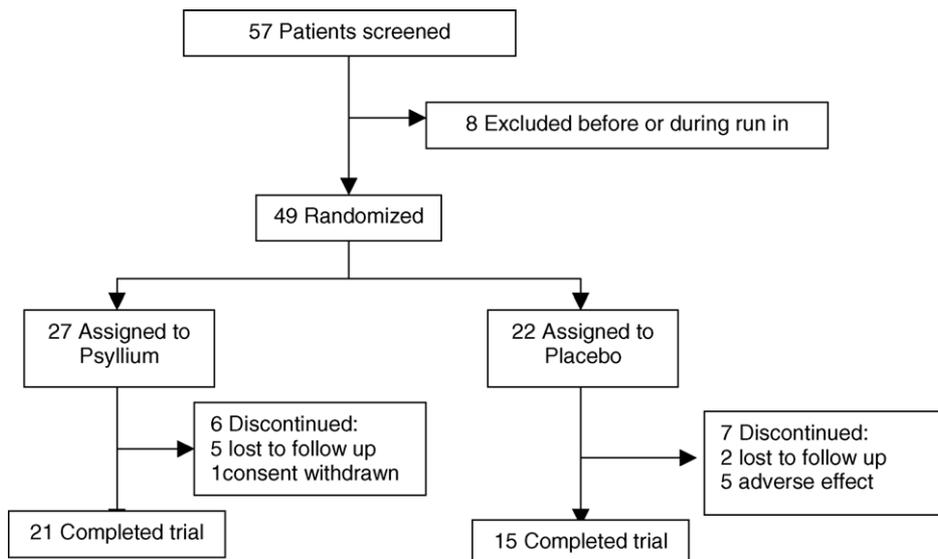


Fig. 1. Trial profile.

Table 2
Glucose and lipid profiles in the study groups

	Week 0 ^a		Week 2		Week 4		Week 6		Week 8	
	Psyllium	Placebo	Psyllium	Placebo	Psyllium	Placebo	Psyllium	Placebo	Psyllium	Placebo
FBG (mg/dl)	208.2 ± 12.7	179.1 ± 10.8	178.4 ± 12.7	194.1 ± 13.4	169.3 ± 11.0	193.6 ± 10.9	161.6 ± 10.7 [*]	207.5 ± 19.8	155.6 ± 9.5 [*]	216.2 ± 25.3
Total Cholesterol (mg/dl)	207.2 ± 8.5	224.3 ± 15.4	193.9 ± 7.2	204.4 ± 9.7	39.8 ± 1.9	40.2 ± 2.5	42.9 ± 2.0 [*]	216.5 ± 11.3	216.2 ± 8.3	216.5 ± 11.3
HDL-C (mg/dl)	40.2 ± 2.1	48.9 ± 3.9	108.3 ± 6.8	119.2 ± 9.7	8.0 ± 0.7	8.9 ± 0.8	7.4 ± 1.1	142.1 ± 10.4	131.3 ± 8.1	36.2 ± 2.4
LDL-C (mg/dl)	126.0 ± 8.2	131.8 ± 11.6	207.6 ± 18.6	239.3 ± 25.3	2.8 ± 0.2	3.1 ± 0.3	3.2 ± 0.3 [*]	193.4 ± 20.9	186.0 ± 22.4	142.1 ± 10.4
Triglycerides (mg/dl)	217.6 ± 20.2	219.0 ± 17.0	8.0 ± 0.7	8.9 ± 0.8	2.8 ± 0.2	3.1 ± 0.3	3.2 ± 0.3 [*]	193.4 ± 20.9	186.0 ± 22.4	142.1 ± 10.4
Insulin (μU/ml)	7.5 ± 0.8	8.3 ± 1.2	8.0 ± 0.7	8.9 ± 0.8	2.8 ± 0.2	3.1 ± 0.3	3.2 ± 0.3 [*]	193.4 ± 20.9	186.0 ± 22.4	142.1 ± 10.4
HbA1c (%)	10.5 ± 0.7	9.1 ± 0.5	8.0 ± 0.7	8.9 ± 0.8	2.8 ± 0.2	3.1 ± 0.3	3.2 ± 0.3 [*]	193.4 ± 20.9	186.0 ± 22.4	142.1 ± 10.4
LDL/HDL	3.24 ± 0.2	2.8 ± 0.2	2.8 ± 0.2	3.1 ± 0.3	2.8 ± 0.2	3.1 ± 0.3	3.2 ± 0.3 [*]	10.5 ± 0.6	8.9 ± 0.2 [*]	10.5 ± 0.6

^a Results are shown based on mean ± S.E. of mean for each group.

^{*} $p < 0.05$ significant difference between placebo and psyllium groups.

Table 3
Study of side effects in psyllium and placebo group

Effect	Psyllium	Placebo	<i>p</i> -Value
Flatulence	4	13	0.000
Diarrhoea	1	1	0.809
Constipation	1	1	0.809
Reduced flushing	11	0	0.002

3.2. Lipid profile

Total serum cholesterol levels, low-density lipoprotein fraction, and triglycerides levels showed no significant changes. The high-density lipoproteins decreased significantly in the placebo group and increased non-significantly in the psyllium group, but overall it was different in the week 8 between the study groups (Table 2). LDL/HDL ratio was also significantly different in week 8.

3.3. Safety and tolerance

Adverse effects were recorded in each visit, which are shown in Table 3. Flatulence was significantly high in the placebo group. Psyllium group tolerated metformin better than placebo and hot flushing was significantly abolished in the psyllium group.

4. Discussion

High-fiber supplements, such as psyllium (Florholmen et al., 1982; Rodriguez-Moran et al., 1998) guar gum (found in beans) (Landin et al., 1992) pectin (from fruit) (Schwartz et al., 1988) oat bran (Hallfrisch et al., 1995), and glucomannan (Doi et al., 1979; Vuksan et al., 2000) have improved glucose tolerance in some studies. Psyllium fiber as a meal supplement reduces proximate and second meal postprandial glucose and insulin concentrations in NIDDM (Pastors et al., 1991). *Plantago psyllium* and acarbose, both significantly reduce glycemic index of carbohydrate food (Fрати Munari et al., 1998). Our results showed that 8 weeks treatment with 5.1 g psyllium (*Plantago ovata*) two times daily half an hour before breakfast and dinner, could reduce FBS, and control glucose fluctuations by reducing HbA1c significantly. It also reduced TG non-significantly but had no effect on the total cholesterol and LDL-C. HDL-C was reduced in placebo group while it increased in psyllium group, and overall HDL-C changed significantly between two treatment groups. In calculation, LDL/HDL ratio decreased significantly. In a double-blind trial, men with diabetes type II took 5.1 g of psyllium (*Plantago psyllium*) twice daily for 8 weeks. HDL-C increased significantly in the outpatients and glucose, HbA1c, TC, LDL-C and TG didn't change any, but in metabolic ward they showed significant improvement in glucose and lipid profile compared to the placebo group (Anderson et al., 1999). In one study, 6 weeks treatment with 14 g/day psyllium, glucose absorption significantly decreased, and HbA1c

decreased non-significantly, that may be due to short time of the treatment (Sierra et al., 2002). In another clinical study 5 g psyllium (*Plantago psyllium*) t.i.d. decreased TC, TG, and LDL-C, as well as, increased HDL-C significantly in week 12 (Rodriguez-Moran et al., 1998). In another crossover study on only hypercholesterolemic patients, 12 g psyllium for 6 weeks caused significant decrease in TC and LDL, but no significant changes in HDL-C or TG (Roberts et al., 1994). In a longer period study for 90 days in 24 patients, psyllium 3.5 g twice daily caused TC, LDL-C, and TG decrease, as well as HDL-C increased significantly (Gupta et al., 1994). So the beneficial effect of dietary fiber on glucose serum and cholesterol levels varies according to the dosage and period used and we can conclude that the glucose and cholesterol lowering effects of psyllium in low doses and long term are equal to high doses in short term (Leatherdale et al., 1982; Smith and Holm, 1982; Ray et al., 1983; Jarjis et al., 1984; Bell et al., 1989; Hunt et al., 1993; Sprecher et al., 1993; Gupta et al., 1994; Bennet and Cerda, 1996) Considering that ingestion of soluble fiber before regular meals could be a factor to improving the customary diet content; this study was conducted to evaluate the efficacy and tolerability of psyllium (*Plantago ovata*) as an adjunct therapy in diabetic outpatients in comparison to placebo, and all patients needed to treat for their hypercholesterolemia (LDL-C > 100 mg/dl in diabetic patients must be treated) (Third Report of the National Cholesterol Education Program, 2002) Significant reduction in FBS and HbA1c in psyllium group shows that 5.1 g psyllium twice daily can control blood glucose effectively. Significant decrease in LDL/HDL ratio by psyllium shows the usefulness of this product in hypercholesterolemia. Not only no adverse effects were investigated in the psyllium group, but also it increased gastric tolerance to metformin. In the placebo group, most noticed adverse effect was flatulence. Lack of significant TC, LDL-C and TG changes in our study may be due to the short period of treatment (8 weeks), which has caused a non-significant lipid profile change, or it may be related to plant species difference between our trial with other trials (Frati Munari et al., 1998; Rodriguez-Moran et al., 1998; Anderson et al., 1999). There were no significant changes in BMI whether or not the subjects were on psyllium or placebo during the study, so weight loss or reduced food intake did not explain effects of psyllium on the glucose and lipid levels.

In conclusion, our results show that 5.1 g b.i.d. of psyllium (*Plantago ovata* Forsk.), a natural soluble fiber supplement, is useful as an adjunct to dietary therapy in patients with type II diabetes, to reduce glucose, with excellent tolerance.

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References

- Anderson, J.W., Allgood, L.D., Turner, J., 1999. Effects of psyllium on glucose and serum lipid response in men with type II diabetes and hypercholesterolemia. *American Journal of Clinical Nutrition* 70, 466–473.
- Anderson, J.W., Davidson, M.H., Blonde, L., 2000. Long-term cholesterol-lowering effects of psyllium as an adjunct to diet therapy in the treatment of hypercholesterolemia. *American Journal of Clinical Nutrition* 71, 1433–1438.
- Bell, L.P., Hectorne, K., Reynolds, H., Balm, T., Hunninghake, D.B., 1989. Cholesterol-lowering effects of Psyllium hydrophilic mucilloid. *Journal of American Medical Association* 261, 3419–3423.
- Bennet, W.G., Cerda, J.J., 1996. Benefits of dietary fiber. *Postgraduate Medicine* 99, 153–175.
- Davidson, M.H., Dugan, L.D., Burns, J.H., 1996. A psyllium-enriched cereal for the treatment of hypercholesterolemia in children: a controlled, double-blind, crossover study. *American Journal of Clinical Nutrition* 63, 96–102.
- Doi, K., Matsuura, M., Kawara, A., Baba, S., 1979. Treatment of diabetes with glucomannan (konjac-mannan). *Lancet* 1, 987–988.
- Florholmen, J., Arvidsson-Lenner, R., Jorde, R., Burhol, P.G., 1982. The effect of metacul on postprandial blood glucose and plasma gastric inhibitory peptide in insulin-dependent diabetics. *Acta Medica Scandinavia* 212, 237–239.
- Frati Munari, A.C., Benitez Pinto, W., Raul Ariza Andraca, C., Casarubias, M., 1998. Lowering glycemic index of food by acarbose and plantago psyllium mucilage. *Archives of Medical Research* 29, 137–141.
- Frati-Munari, F.A., Flores, G.M., Ariza, A.R., Islas, A.S., 1989. Chavezo Efecto de diferentes dosis de mucilago de plantago psyllium en la prueba de tolerancia a la glucosa. *Archives of Investigational Medicines* 20, 147–152.
- Gupta, R.R., Agrawal, C.G., Singh, G.P., Ghatak, A., 1994. Lipid lowering efficacy of psyllium hydrophilic mucilloid in non-insulin dependent diabetes mellitus with hyperlipidaemia. *Indian Medical Research* 100, 237–241.
- Hallfrisch, J., Scholfield, D.J., Behall, K.M., 1995. Diets containing soluble oat extracts improve glucose and insulin responses of moderately hypercholesterolemic men and women. *American Journal of Clinical Nutrition* 61, 379–384.
- Hunt, R., Fedorak, R., Frohlich, J., McLennan, C., 1993. Pavlanis therapeutic role of dietary fiber. *Canadian Family Physician* 39, 897–910.
- Jarjis, H.A., Blackburn, N.A., Redfern, J.S., Read, N.W., 1984. The effect of ispaghula (fybogel and metacul) and guar gum glucose tolerance in man. *British Journal Nutrition* 51, 371–378.
- Landin, K., Holm, G., Tengborn, L., Smith, U., 1992. Guar gum improves insulin sensitivity, blood lipids, blood pressure, and fibrinolysis in healthy men. *American Journal of Clinical Nutrition* 56, 1061–1065.
- Leatherdale, B.A., Green, D.J., Harding, L.K., Griffin, D., 1982. Bailey Guarind gastric emptying in non-insulin dependent diabetes. *Acta Diabetologica Lat* 19, 339–343.
- Leung, A.Y., Foster, S., 1996. *Encyclopedia of Common Natural Ingredients Used in Food, Drugs, and Cosmetics*, second ed. John Wiley & Sons, New York, pp. 427–429.
- Nuttall, F.Q., 1993. Dietary fiber in the management of diabetes. *Diabetes* 42, 503–508.
- Oson, B.H., Anderson, S.M., Becker, M.P., 1997. Psyllium-enriched cereals lower blood total cholesterol and LDL cholesterol, but not HDL cholesterol, in hypercholesterolemic adults: results of a meta-analysis. *Journal of Nutrition* 127, 1973–1980.
- Pastors, J.G., Blaisdell, P.W., Balm, T.K., Asplin, C.M., Pohl, S.L., 1991. Psyllium fiber reduces rise in postprandial glucose and insulin con-

- centrations in patients with non-insulin-dependent diabetes. *American Journal of Clinical Nutrition* 53, 1431–1435.
- Ray, T.K., Mansell, K.M., Knight, L.C., Malrnud, L.S., Owen, O.E., Boden, G., 1983. Long-term effects of dietary fiber on glucose tolerance and gastric emptying in non-insulin dependent diabetic patients. *American Journal of Clinical Nutrition* 37, 376–381.
- Roberts, D.C., Truswell, A.S., Bencke, A., Dewar, H.M., Farmakalidis, E., 1994. The cholesterol-lowering effect of a breakfast cereal containing psyllium fibre. *Medical Journal of Austria* 161, 660–664.
- Rodriguez-Moran, M., Guerrero-Romero, F., Lazcano-Burciaga, G., 1998. Lipid- and glucose-lowering efficacy of plantago psyllium in type II diabetes. *Journal of Diabetes and its Complications* 12, 273–278.
- Schwartz, S.E., Levine, R.A., Weinstock, R.S., 1988. Sustained pectin ingestion: effect on gastric emptying and glucose tolerance in non-insulin-dependent diabetic patients. *American Journal of Clinical Nutrition* 48, 1413–1417.
- Sierra, M., Garcia, J.J., Fernandez, N., Diez, M.J., Calle, A.P., 2002. Therapeutic effects of psyllium in type II diabetic patients. *European Journal of Clinical Nutrition* 56, 830–842.
- Smith, U., Holm, G., 1982. Effect of a modified guar gum preparation on glucose and lipid levels in diabetic and healthy volunteers. *Atherosclerosis* 45, 1–10.
- Sprecher, D.L., Harris, B.V., Goldberg, A.C., Anderson, E.C., Bayuk, L.M., Rusell, B.S., 1993. Efficacy of psyllium in reducing serum cholesterol levels in hypercholesterolemic patients on high- or low-fat diets. *Annals of Internal Medicines* 119, 545–554.
- Tattersal, R., Mansell, P., 1990. Benefits of fiber itself are uncertain. *British Medical Journal* 300, 1136–1137.
- Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III), Final report. U.S. Department of Health and Human Services, Public Health Service National Institutes of Health National Heart, Lung, and Blood Institute. NIH Publication No. 02-5215, September 2002. <http://www.nhlbi.nih.gov/guidelines/cholesterol>.
- Vuksan, V., Sievenpiper, J.L., Owen, R., 2000. Beneficial effects of viscous dietary fiber from konjac-mannan in subjects with the insulin resistance syndrome: results of a controlled metabolic trial. *Diabetes Care* 23, 9–14.