Effects of soluble fiber (*Plantago ovata* husk) on plasma lipids, lipoproteins, and apolipoproteins in men with ischemic heart disease[1–3]

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ABSTRACT

Background: New dietary strategies to reduce cardiovascular disease (CVD) risk include the addition of fiber to the diet. The effect of soluble-fiber consumption derived from *Plantago ovata* husk on lipid risk factors in patients with CVD is unknown.

Objective: We compared the effects of soluble fiber (*P. ovata* husk) with those of insoluble fiber (*P. ovata* seeds) on plasma lipid, lipoprotein, and apolipoprotein (apo) concentrations within a CVD secondary prevention program.

Design: In a randomized, crossover, controlled, single-blind design, 28 men with CVD (myocardial infarction or stable angina) and an LDL-cholesterol concentration ≤3.35 mmol/L consumed for 8 wk, under controlled conditions, a low-saturated-fat diet supplemented with 10.5 g *P. ovata* husk/d or 10.5 g *P. ovata* seeds/d. Fasting plasma lipid concentrations and polymorphisms of genes involved in lipid metabolism, such as apo A-IV, apo E, and fatty acid–binding protein, were measured.

Results: Plasma triacylglycerol decreased (6.7%; $P < 0.02$), the ratio of apo B 100 to apo A-I decreased (4.7%; $P < 0.02$), and apo A-I increased (4.3%; $P < 0.01$) in the *P. ovata* husk consumers. Compared with the intake of insoluble fiber, the intake of *P. ovata* husk increased HDL-cholesterol concentrations by 6.7% ($P = 0.006$) and decreased the ratio of total to HDL cholesterol and of LDL to HDL cholesterol by 10.6% ($P = 0.002$) and 14.2% ($P = 0.003$), respectively.

Conclusion: In the secondary prevention of CVD, *P. ovata* husk intake induces a more beneficial effect on the cardiovascular lipid risk-factor profile than does an equivalent intake of insoluble fiber. *Am J Clin Nutr* 2007;85:1157–63.

KEY WORDS Dietary fiber, *Plantago ovata* (Ispaghula husk), psyllium, secondary prevention of cardiovascular disease, blood lipids, low saturated fat, FABP2 gene, apo A-IV gene, apo E gene, polymorphism

INTRODUCTION

Dietary fiber intake may reduce the risk of cardiovascular disease (CVD) (1). Consumption of diets high in fiber reduces the risk factors of CVD by acting, in part, on plasma lipid concentrations (2). Numerous studies have shown that soluble fibers are more effective in lowering blood cholesterol than are insoluble fibers (2–4).

Current advice is to increase the amount of dietary fiber, specifically of soluble (viscous) fiber, to 10–25 g/d to more effectively lower cholesterol concentrations (5, 6). Thus, an increased soluble fiber intake, within a therapeutic lifestyle, takes on an essential modality in the clinical management of CVD risk reduction (6–8). *Plantago ovata* husk is a source of natural, concentrated, soluble fiber obtained from the outer membranous green envelope of the *P. ovata* seed. *P. ovata* husk and *P. ovata* seeds, the latter often used as a source of control insoluble fiber, are well-accepted, safe, and effective bulk laxatives.

Differences in genetic background are known to affect lipid metabolism and the response to diet (9). Identifying common variations in genes involved in the intestinal absorption of lipids and, hence, in the dietary response to *P. ovata* husk is an attractive goal. These genes would include those affecting apolipoprotein (apo) (9–12) A-IV (9), apo E (10, 11), and fatty acid–binding protein (FABP2) (12).

The present study was completed before the results of recent clinical trials were assessed for their global implications concerning cholesterol management in the secondary prevention of CVD (7). The purpose of our study was to compare, in a crossover design protocol, the effects of soluble *P. ovata* husk fiber and an equivalent insoluble fiber as therapeutic measures in combination with a diet low in saturated fat and cholesterol. The target variables were plasma lipids, lipoproteins, and apolipoproteins in patients with

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established coronary heart disease and with plasma LDL-cholesterol concentrations ≤3.35 mmol/L (130 mg/dL). The potential interactions with genes involved in the response to dietary fiber therapy were explored as well.

SUBJECTS AND METHODS

Patients

Adult men with ischemic heart disease (myocardial infarction and stable angina) were selected from among those attending the University Hospital Sant Joan, Reus, Spain. We contacted those outpatients who were currently not receiving any hypolipidemic drug therapy.

Eligible patients were those with fasting plasma LDL-cholesterol concentrations ≤3.35 mmol/L (130 mg/dL) and triacylglycerol concentrations ≤2.84 mmol/L (250 mg/dL). The subjects were <75 y of age, were clinically stable, and had no medical or social conditions that would impair their ability to participate in the trial. Patients being treated with antiplatelet drugs ($n = 28$), β blockers ($n = 12$), calcium-channel-blocking drugs ($n = 6$), angiotensin-converting enzyme inhibitors ($n = 6$), nitrates ($n = 7$), and diuretics ($n = 3$) were included. Neither the drugs that the patients were receiving nor the doses of the drugs were altered during the study. There was no evidence of alcohol, tobacco, or recreational-drug abuse.

The criteria for exclusion, derived from the medical history and a complete physical examination, were diabetes mellitus, congestive heart failure, renal insufficiency, thyroid or other endocrine disease, blood pressure >140 (systolic)/90 (diastolic) mm Hg, and the current use of lipid-lowering drugs. Of 50 eligible patients, 31 met the inclusion criteria and were randomly assigned to 2 different dietary supplement sequences. There was no monetary inducement to participate in the trial.

The study was approved by the Clinical Research Ethical Committee of Hospital Universitari Sant Joan de Reus and by the Spanish Agency for Drug Monitoring. The study protocol was fully explained to the patients and they gave their written informed consent on enrollment.

Study design

In a controlled, single-blind, crossover study (**Figure 1**) consisting of a 4-wk dietary adaptation period, the patients were randomly assigned to 2 different fiber-supplement periods of 8 wk each (4, 13). We incorporated a washout period of 8 wk between the first and second periods of the study to test possible interactions between treatment and sequence order (carryover effect).

The participants were randomly assigned, per a computer-generated random number sequence, to consume either the *P. ovata* husk or an equivalent amount of insoluble fiber (Figure 1). Allocation was concealed in sealed study folders that were held in a central, secure location until informed consent had been obtained. The dietitian who scheduled the study visits and the laboratory personnel responsible for the analyses were blinded to the patient-group assignment.

The patients attended the outpatient clinic, where a full clinical history was recorded and anthropometric measurements were made. To reinforce the dietary requirements of the study, each subject received expert dietary counseling from the dietitian twice during the adaptation period and at weeks 4, 8, 12, 16, 20, and 24 of the study. Blood was extracted for laboratory measurements, as described below.

Diet and fiber treatments

Since the time of their CVD diagnosis, all patients had been advised to follow a low-fat diet. From the start of the adaptation period of the present trial, the subjects consumed the recommended low-fat diet and cholesterol under strictly controlled conditions in which compliance was assessed by a research dietitian.

The diet was isocaloric and contained 30% of total energy as fat (<7% of energy as saturated fatty acids) and <300 mg cholesterol daily. The diet followed the consensus recommendations of several expert committees for the prevention of CVD (5–8, 14). On weekdays, lunches were prepared by the nutrition research kitchen of the Sant Joan University Hospital and were consumed in the hospital's restaurant. All breakfasts, dinners, and weekend lunches were consumed on the premises under the supervision of the research dietitian. Three-day food records (a total of 7 records per patient) were maintained to monitor dietary compliance during the study. The nutrient composition of the diet was calculated with the Répertoire Géneral Des Aliments database (15).

P. ovata husk (Plantaben; Madaus SA, Barcelona, Spain) is manufactured as a palatable orange-flavored, sugar-free product. The insoluble fiber used as control additive was hemicellulose and lignin klason obtained from *P. ovata* seeds (Madaus SA). The 2 products are obtained from the same *P. ovata* plant; *P. ovata* husk consisted of only the epidermis and collapsed adjacent layers removed from the dried ripe *P. ovata* seeds.

The patients received three 5-g sachets daily, of which ≈70% (3.5 g) was the soluble fiber (test additive) or an equivalent insoluble fiber (control additive). The patients were instructed to mix each sachet of soluble fiber in 150 mL water or, in the case of the insoluble fiber, to consume it directly with a spoon if convenient. In both cases, the participants were encouraged to drink 250 mL water. The sachets were consumed 15 min before the 3 main meals.

In each treatment period, the sachets were provided before the start and in the middle (at 4 wk) of each of the 2 periods. Compliance was monitored by interviewing the patients and counting the unopened sachets returned at each follow-up visit. We defined noncompliance as any deviation from instructions of >20% regarding diet and fiber supplement consumption.

Safety

Information on adverse events possibly related to the supplement products was solicited at each visit to the clinic during the dietary supplement period. The patients were asked an open-ended question regarding any unusual symptoms, or discomfort, or side effects such as more defecation, bloating, flatulence, fullness, or any other events over the previous 4 wk.

We evaluated vitamin and mineral salt status before and after treatment to monitor any potential adverse effects of *P. ovata* husk or of the control insoluble fiber. Serum analyses included magnesium, iron, ferritin, hemoglobin, calcium, prothrombin time (as indirect measure of vitamin K status), and vitamins A and E.

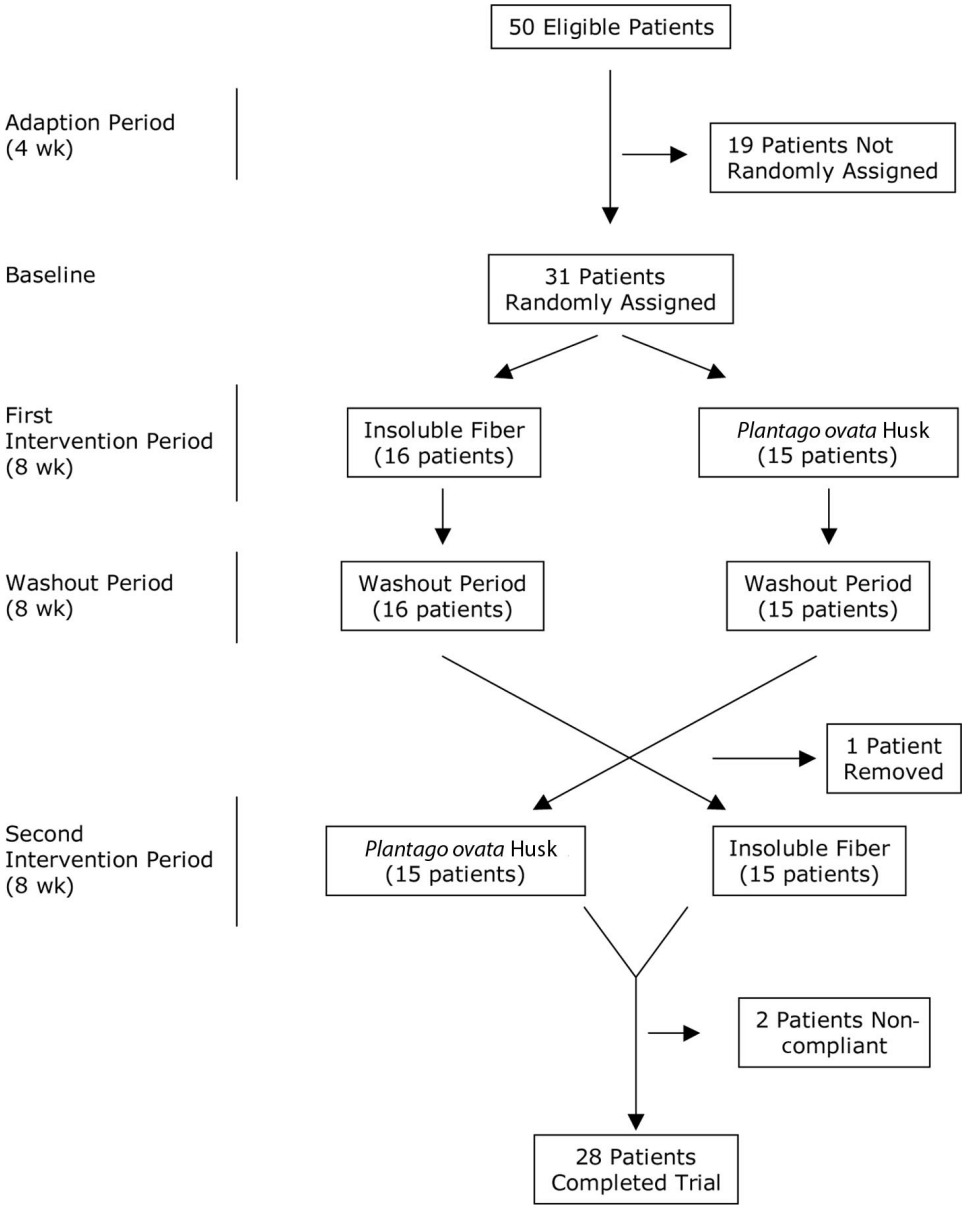

FIGURE 1. Study flow.

Laboratory measurements

Blood was drawn from each patient after an overnight fast. To reduce intraindividual day-to-day variability, the blood sampling was performed on 2 separate days before (days −32 and −30) and at the end of the adaptation period (days −4 and −2). The measurements were recorded as baseline values. Additional blood samples were obtained at the beginning and at the end of each supplement period.

Plasma total cholesterol and triacylglycerol concentrations were measured with enzymatic kits (Boehringer Mannheim, Mannheim, Germany) adapted for a Cobas Mira centrifugal analyzer (Roche Pharmaceuticals, Basel, Switzerland) with Precilip EL and Precinorm (Boehringer Mannheim) as quality controls. Immunoturbidimetry was used for the measurement of apo A-I and apo B with the use of specific antiserum purchased from Boehringer Mannheim. Apo A-IV was determined by enzyme-linked immunosorbent assay (16).

HDL cholesterol was measured subsequent to the precipitation of the apo B–containing lipoproteins by using polyethylene glycol (Immuno AG, Vienna, Austria). LDL was calculated by using the Friedewald algorithm [LDL-cholesterol = total cholesterol − (triacylglycerols/2.2 + HDL cholesterol)] (17). The interassay CVs ranged from 2.5% to 3.0% for total plasma cholesterol, 2.4% to 3.1% for HDL cholesterol, and 2.6% to 4.8% for total plasma triacylglycerols.

Vitamins A and E were determined with an HPLC system (model 1050; Hewlett-Packard, Palo Alto, CA) equipped with an ultraviolet-visible detector. Retinol acetate and tocopherol acetate were used as internal standards. The column used was a Spherisorb ODS (125 × 4 mm, 5 μm), and the mobile phase

TABLE 1
Characteristics of the patients at baseline and after the 2 fiber-treatment periods[1]

	Baseline	Po husk	Insoluble fiber	P^2
Age (y)	61.4 ± 8.6[3]	—	—	—
Weight (kg)	77.30 ± 8.70	77.35 ± 9.46	76.98 ± 9.15	0.24
BMI (kg/m^2)	28.22 ± 3.18	28.24 ± 3.49	28.16 ± 3.32	0.54
Waist circumference (cm)	95.3 ± 3.0	93.6 ± 6.1	93.3 ± 3.2	0.61
WHR	0.962 ± 0.057	0.940 ± 0.053	0.940 ± 0.055	1.00
SBP (mm Hg)	123.3 ± 10.0	125.4 ± 9.6	125.4 ± 8.5	1.00
DBP (mm Hg)	79.8 ± 8.1	79.5 ± 7.0	78.1 ± 7.1	0.31

[1] $n = 28$. Po, *Plantago ovata;* insoluble fiber is *P. ovata* seeds; WHR, waist-to-hip ratio; SBP, systolic blood pressure; DBP, diastolic blood pressure. There were no significant differences between the means of all variables at the start of each of the 2 fiber-treatment periods by paired *t* test.
[2] Po husk compared with insoluble-fiber treatment by using paired *t* test.
[3] $\bar{x}$ ± SD (all such values).

was methanol:water (100% for vitamin E and 98% for vitamin A) (18).

Gene polymorphisms

The apo A-IV variants Gln360His and Thr347Ser were genotyped by polymerase chain reaction with the following primers: forward, 5′-GCT TCC TGG AGA AGG ACC TGA GGG ACA AGG-3′; and reverse, 5′-CAT CTG CAC CTG CTC CTG CTG CTG CTC CAG-3′. A mismatch in the reverse primer forced a PvuII restriction site that allows detection of the 360 variant. The 347 variant was determined by digestion with the Hinf-I restriction enzyme.

The FABP2 Ala54Thr variant was genotyped with the following primers: forward, 5′-ACA GGT GGT AAT ATA GTG AAA AG-3′; and reverse: 5′-TAC CCT GAG TTC AGT TCC GTC-3′ followed by restriction with HhaI.

The primers used for apo E genotype determination were as follows: forward, 5′-ACA GAA TTC GCC CCG GCC TGG TAC AC3′; and reverse, 5′TAA GCT TGG GCA CGG CTG TCC AAG GA3′. Digestion was with HhaI.

Statistical analyses

All lipid values represent the mean of measurements conducted on 2 separate days. Descriptive values are expressed as means ± SDs. The analyses were made according to a crossover design (19). The statistical analyses included paired *t* tests for the comparison of anthropometric measures and biochemical and lipid concentrations in response to treatment and treatment sequence for a 2-period crossover design and by chi-squared test for categorical variables. The possible interaction between the treatments and the treatment sequence (carryover effect) and the differences between the means at the start of each of the 2 fiber treatment periods was also tested by paired *t* tests. All analyses were performed with the SPSS package (version 12.0; SPSS Inc, Chicago, IL).

RESULTS

Characteristics of patients

The subjects were recruited from September 2002 to February 2003, during which time 50 patients were considered eligible. Of these, 19 were excluded because they did not meet the lipid criteria at the end of the adaptation period. The flow of patients throughout the study is depicted in Figure 1. Of the 31 patients recruited, 1 withdrew for personal reasons after the first dietary supplement period, and 2 were excluded for noncompliance. Thus, 28 men (age: 61.4 ± 8.6 y; range: 48–70 y) completed both periods of the study.

The baseline characteristics of the 28 patients who completed the 2 treatment periods are presented in **Table 1**. Of the 28 men, 26 had survived a myocardial infarction and 2 had had stable angina. Individual treatments remained essentially unchanged throughout the study.

Dietary and fiber treatments, compliance, and body weight

The nutrient content of the patients' current diet is shown in **Table 2**. The composition was similar to that of the prescribed diet; except for the intake of polyunsaturated fatty acids, which was lower than that recommended (4.2% compared with <7%; $P < 0.01$). Compliance with the diet and treatments was excellent (92% for insoluble fiber and 90% for *P. ovata* husk supplements). No significant differences in compliance were observed between the 2 fiber-supplement groups.

Body weight was stable throughout the 2 treatment periods (Table 1). Both fibers produced a significant reduction in waist circumference (93.6 ± 6.1 cm in the *P. ovata* husk period and 93.3 ± 3.2 cm in the insoluble-fiber period) compared with baseline (95.3 ± 3.0 cm; $P < 0.01$). The waist-to-hip ratio decreased significantly (0.94 ± 0.05 in both fiber periods) from baseline (0.96 ± 0.05; $P < 0.01$).

Effects on plasma lipids, lipoproteins, and apolipoproteins

Lipid values before and after the 8-wk treatment periods, and the different effects of the treatments, are presented in **Table 3**. No carryover effect between the periods was observed. *P. ovata* husk intake significantly decreased the plasma triacylglycerol concentration by −0.17 mmol/L (−6.7%; $P < 0.02$) and the ratio of apo B to apo A-I (apo B:apo A-I) by −0.04 (−4.7%; $P < 0.02$) and increased the apo A-I concentration by 0.05 g/L (4.3%; $P < 0.01$).

Conversely, insoluble fiber intake increased plasma concentrations of total cholesterol by 0.18 mmol/L (3.8%; $P < 0.05$), plasma concentrations of LDL cholesterol by 0.25 mmol/L (8.5%; $P < 0.01$), plasma concentrations of apo A-I by 0.04 g/L (3.0%; $P < 0.01$), the ratio of total to HDL cholesterol in plasma by 0.41 (8.7%; $P < 0.01$), and the ratio of LDL to HDL cholesterol in plasma by 0.41 (14.0%; $P < 0.01$) and decreased the

TABLE 2
Composition of prescribed and observed diets of the patients at 8 wk of the study[1]

	Prescribed	Po husk observed	Insoluble fiber observed	P^2
Energy (kcal/d)	1990 ± 543[3]	1989 ± 442	1989 ± 443	0.99
Protein (% of energy)	19.4 ± 3.4	18.5 ± 3.4	18.5 ± 3.5	0.99
Total carbohydrates (% of energy)	46.5 ± 6.7	45.5 ± 5.7	45.5 ± 5.8	0.99
Fiber (g/d)	20.5 ± 5.3	20.7 ± 5.0	20.8 ± 5.1	0.83
Total fat (% of energy)	30.7 ± 4.4	31.7 ± 4.4	31.6 ± 4.5	0.96
PUFA (% of energy)	5.2 ± 0.9	4.2 ± 0.9	4.1 ± 1.1	0.76
MUFA (% of energy)	15.3 ± 3.1	15.8 ± 3.1	15.3 ± 3.2	0.62
SFA (% of energy)	8.8 ± 1.1	8.4 ± 2.1	8.4 ± 2.4	1.00
Cholesterol (mg/d)	156.0 ± 128.3	146.4 ± 130.1	147.0 ± 132.2	0.62

[1] $n = 28$. Patients followed a crossover design protocol for the 2 fiber treatments. Po, *Plantago ovata;* insoluble fiber is *P. ovata* seeds; SFA, saturated fatty acids; PUFA, polyunsaturated fatty acids; MUFA, monounsaturated fatty acids. There were no significant differences between the means for all variables at the start of each of the 2 fiber-treatment periods by paired *t* test.
[2] Comparison of dietary compliance in the 2 treatments groups by paired *t* test.
[3] $\bar{x}$ ± SD (all such values).

HDL-cholesterol concentration by −0.03 mmol/L (−3.3%; $P < 0.05$).

Compared with the insoluble fiber supplement, the *P. ovata* husk supplement increased HDL-cholesterol concentrations by 6.7% (*P*: 0.006), decreased the ratio of total to HDL cholesterol by 10.6% (*P*: 0.002), and decreased the ratio of LDL to HDL cholesterol by 14.2% (*P*: 0.003).

Safety evaluation

No statistically significant or clinically meaningful changes were observed in blood chemistry, hematology, or mineral-status results between the *P. ovata* husk and insoluble-fiber groups. The patients reported no difference between the 2 supplement fibers with respect to bloating, flatulence, or abdominal pain. The number of bowel movements was 11.6/wk in the insoluble-fiber period and 12.3/wk in the *P. ovata* husk period.

Vitamin E (13.64 ± 2.72 μg/dL in the *P. ovata* husk period and 13.41 ± 2.10 μg/dL in the insoluble-fiber period) and vitamin A (542.90 ± 113.40 μg/L in the *P. ovata* husk period and 522.90 ± 117.40 μg/L in the *P. ovata* insoluble-fiber period) concentrations did not vary significantly from baseline in either treatment period. Similarly, there were no adverse effects on clinical vital signs in patients receiving either *P. ovata* husk or insoluble fiber.

Genotype-fiber treatment interaction and FABP2 genotypes

The genotype-fiber treatment interaction was not statistically significant. After the *P. ovata* husk consumption, the carriers of the Thr54 allele (11 patients) had significantly higher (8%; 0.11 mmol/L) HDL-cholesterol concentrations (1.32 ± 0.27 mmol/L) than did those who consumed insoluble fiber (1.21 ± 0.14 mmol/L; $P < 0.05$).

The FABP2 Thr54 variant (11 patients) was associated with a 5.7 mg/dL (20%) greater plasma apo A-IV concentration in the *P. ovata* husk period than in the insoluble-fiber period: 24.67 ± 5.88 compared with 18.97 ± 4.87 mg/dL ($P < 0.05$).

TABLE 3
Plasma lipid, lipoprotein, and apolipoprotein (apo) concentrations before and after the 2 fiber-treatment periods[1]

	Po husk		Insoluble fiber			
	Before	After 8 wk	Before	After 8 wk	Change between groups	P^2
					%	
Total cholesterol (mmol/L)	5.06 ± 0.67[3]	5.06 ± 0.68	4.91 ± 0.48	5.09 ± 0.65[4]	−3.76	0.57
Triacylglycerols (mmol/L)	1.62 ± 0.91	1.45 ± 0.83[5]	1.59 ± 0.90	1.50 ± 0.88	−2.79	0.46
Apo B (g/L)	0.92 ± 0.17	0.90 ± 0.18	0.88 ± 0.13	0.91 ± 0.16	−5.24	0.24
Apo A-I (g/L)	1.21 ± 0.16	1.26 ± 0.15[6]	1.20 ± 0.12	1.23 ± 0.13[4]	1.22	0.21
Apo B:apo A-I	0.77 ± 0.19	0.73 ± 0.19[5]	0.74 ± 0.15	0.74 ± 0.16	5.83	0.15
LDL cholesterol (mmol/L)	3.22 ± 0.61	3.26 ± 0.67	3.10 ± 0.45	3.35 ± 0.61[7]	−6.90	0.18
HDL cholesterol (mmol/L)	1.12 ± 0.27	1.15 ± 0.27	1.10 ± 0.20	1.06 ± 0.23	6.71	0.006
Total:HDL cholesterol	4.78 ± 1.41	4.65 ± 1.33	4.63 ± 1.09	5.05 ± 1.43[7]	−10.61	0.002
LDL:HDL cholesterol	3.04 ± 0.98	3.01 ± 1.02	2.91 ± 0.70	3.33 ± 1.09[7]	−14.24	0.003

[1] $n = 28$. Patients followed a crossover design protocol for the 2 fiber-treatment periods Po, *Plantago ovata;* insoluble fiber is *P. ovata* seeds There were no significant differences between the means of all variables at the start of each of the 2 fiber-treatment periods by paired *t* test.
[2] Comparisons between treatments were tested by using a paired *t* test.
[3] $\bar{x}$ ± SD (all such values).
[4,7] Significantly different from before insoluble-fiber treatment (paired *t* test): [4] $P < 0.05$, [7] $P < 0.01$.
[5,6] Significantly different from before Po husk treatment (paired *t* test): [5] $P < 0.05$, [6] $P < 0.01$.

Apo E and apo A-IV variant genes

In the *E2* genotype group (5 patients), vitamin A was significantly lower after *P. ovata* husk consumption than after insoluble-fiber consumption (461.6 ± 172.9 and 526.8 ± 175.3 μg/L; $P < 0.01$). The Apo A-IV 360 and 347 variants did not show any significant association with lipid or apolipoprotein changes in relation to either of the treatments.

DISCUSSION

Our results indicate that soluble *P. ovata* husk consumption induced a more favorable effect on the lipoprotein profile (ie, reduction in CVD risk factors) than did a comparable insoluble fiber.

In our study, in men with coronary heart disease after a low-saturated-fat, low-cholesterol diet, the incorporation of *P. ovata* husk significantly reduced plasma triacylglycerol concentrations by 6.7% and apo B:apo A-I by 4.7% and increased the apo A-I concentration by 4.3%.

The triacylglycerol reduction observed with the *P. ovata* husk supplement was approximately half that of the reduction (between 10% and 16%) observed with statin therapies (the most widely used LDL-cholesterol-lowering drugs) and was similar to that of ezetimibe (7% triacylglycerol reduction). With this modest hypotriglyceridemic effect, *P. ovata* husk can be considered as an adjuvant treatment in patients with moderate hypertriglyceridemia (7, 8).

Apo B:apo A-I has been shown to be the best marker of atherogenic and antiatherogenic particles in plasma. The INTERHEART study showed this ratio to be a marker of risk of myocardial infarction, irrespective of the geographic regions of the populations studied (20). Recently, apo B:apo A-I was linked to the risk of fatal stroke (21) in a similar manner to that of myocardial infarction and other ischemic events (20, 21).

In our study, *P. ovata* husk intake reduced this ratio by ≈5%, which was mainly due to a moderate (statistically nonsignificant) reduction in apo B and a statistically significant increase in apo A-I. This could be clinically relevant in view of the results of the INTERHEART study, in which differences in mean apo B:apo A-I between CVD cases (0.85) and controls (0.80) was 6%..

P. ovata husk significantly increased HDL-cholesterol concentrations (6.7%) relative to the insoluble fiber. This finding is of considerable clinical relevance because studies of the secondary prevention of CVD have shown that the recommended LDL-cholesterol lowering diets (low in saturated fat and cholesterol) also have the detrimental effect of decreasing HDL-cholesterol concentrations. This applies to the Step I National Cholesterol Education Program prudent diet (22) and other recommended diets.

The present results support the use of *P. ovata* as a supplement that can stabilize HDL-cholesterol concentrations and can be used as part of several dietary recommendations, such as those applying to monounsaturated fatty acid intakes and moderate alcohol consumption (23).

The present study describes new beneficial lipid-redistribution effects resulting from *P. ovata* husk consumption; effects that are different from those of other soluble fibers (2–4, 9). However, the mechanism by which *P. ovata* husk modifies lipid, lipoprotein, and apolipoprotein concentrations remains, as yet, undefined.

In our study, *P. ovata* husk did not produce an LDL-cholesterol-lowering effect, as has been observed with other soluble fibers. This may have been due to several factors. For example, our patients consumed a more palatable and more tolerable low dose (10.5 g/d) than did the subjects in the study by Sierra et al (24), in which the dose of the same *P. ovata* husk preparation was higher (14 g/d). The high dose was observed to induce significant reductions in total and LDL cholesterol (7% and 9%, respectively) in patients with type 2 diabetes.

Reports indicate that the initial concentration of cholesterol is predictive of the subsequent reduction in cholesterol concentrations induced by some soluble fibers. As described in the meta-analyses (4, 25) and observed in our study, the low-moderate basal LDL-cholesterol concentration of the patients (mean: 3.04 mmol/L; maximum: 3.36 mmol/L) was highly predictive of the failure of dietary *P. ovata* husk supplementation to lower LDL-cholesterol concentrations. This could explain why patients with moderate-to-high LDL-cholesterol concentrations, such as those with type 2 diabetes (mean LDL cholesterol of 3.97 mmol/L) in the study by Sierra et al (24), would be more responsive to supplementation with *P. ovata* husk soluble fiber than were the patients in the present study.

It would be of interest to analyze the effects of a higher *P. ovata* husk intake in patients with low or moderate total plasma cholesterol and LDL-cholesterol concentrations.

Of note is the finding that both fibers (soluble and insoluble) significantly reduced the patients' waist circumference and waist-to-hip ratio. This aspect has not been previously reported. Hence, supplementing a low-fat diet with fiber may have an additional benefit on risk factors (2) by reducing abdominal fat without appearing to have a significant effect on the BMI.

One limitation of this study was that an intention-to-treat analysis was not performed. Another limitation of this study, probably due in part to the small sample size of our study population, was that an influence of the proposed genes (FABP2, apo A-IV, and apo E) and their variants on the response to the fiber intervention in the diet cannot be ruled out.

Guidelines from the National Cholesterol Expert Program Adult Treatment Panel III suggest an increase in the intake of 20–30 g total dietary fiber, particularly of viscous or soluble fiber, to 10–25 g/d to achieve a more effective lowering of LDL cholesterol and of a consequent reduction in the risk of heart disease (5, 6). It remains to be determined whether treatment with a soluble fiber, such as *P. ovata* husk, can contribute to these beneficial effects of diets that are protective against CVD. Whether the benefits would be additive when used in combination with statins and other drugs used in the secondary prevention of CVD (7) remains to be determined.

In conclusion, *P. ovata* husk treatment in combination with a low-saturated-fat, low-cholesterol diet results in a more beneficial lipoprotein profile (ie, one considered to be protective against CVD) than does the addition to the diet of an equivalent amount of insoluble fiber.

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RS (principal investigator) was responsible for the original study design; recruitment and monitoring of the patients; data collection, analysis, and interpretation; and manuscript construction and revision. GG was responsible for monitoring the study, management of the dietary data, and manuscript

construction. JR was responsible for the data analyses, interpretation of data, manuscript construction, and manuscript revision. J-CV was responsible for the data analyses, interpretation of data, and manuscript construction. JG was responsible for the statistical analyses, manuscript construction, and manuscript revision. AA was responsible for the original study design, data interpretation, and manuscript construction. MAO was responsible for the data analyses and data interpretation. DR, JS, and MC were responsible for the data analyses and data interpretation. FM-L was responsible for the recruitment of patients, monitoring of the study, manuscript construction, and manuscript revision. JS-S and LM were involved in the conception of the study and critical revisions of the manuscript. None of the authors had a conflict of interest.

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