# Effect of *Plantago ovata* (psyllium) husk and seeds on sterol metabolism: studies in normal and ileostomy subjects[1–3]

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**ABSTRACT** The diet of six normal and five ileostomy subjects was supplemented with 10 g/d *Plantago ovata* psyllium husk for 3 wk while six normal and four ileostomy subjects received 10 g/d psyllium seed. Fecal and ileostomy output, sterol excretion, serum cholesterol, and triglycerides were measured before and after supplementation. The husk had no effect on cholesterol or triglyceride concentrations in either normal or ileostomy subjects. Total and high-density-lipoprotein-cholesterol concentrations were reduced on average by 6.4% and 9.3%, respectively, in the normal group after seed supplementation. No effect on fecal bile acid excretion in the normal subjects was found after both regimes. Ileostomy bile acids were increased (on average 25%) after seed supplementation, whereas no effect on cholesterol concentrations was found. These results suggest that psyllium seed might be more effective than the husk in reducing serum cholesterol, that this cholesterol-lowering effect is not mediated by increased fecal bile acid losses, and increased ileal losses of bile acids might be compensated for by enhanced reabsorption in the colon. *Am J Clin Nutr* 1994;59:395–400.

**KEY WORDS** *Plantago ovata* husk, *Plantago ovata* seed, psyllium, ileostomy, serum cholesterol, high-density-lipoprotein cholesterol, triglycerides, bile acids, sterol excretion

## Introduction

The husk derived from *Plantago ovata,* also referred to as ispaghul or psyllium mucilloid, has been widely used as a stool bulking agent for the treatment of constipation. Psyllium husk is obtained by milling the seed of *P ovata,* and contains a high proportion of a hemicellulose that is composed of a xylan backbone linked with arabinose, rhamnose, and galacturonic acid units. Its laxative effect has been attributed to its ability to form a gel in water (1). More recently, psyllium husk has been recognized for its cholesterol-lowering properties. Studies in hamsters and monkeys have shown a significant lowering of serum total and low-density-lipoprotein (LDL) cholesterol (2, 3). In human subjects, both with normal and elevated cholesterol concentrations, significant reductions in total cholesterol (4–6), LDL (4, 5, 7), and high-density-lipoprotein (HDL) cholesterol (4) have been reported after daily supplementation with 10–30 g psyllium husk preparations for periods of 10 d to 4 mo.

An increase in fecal bile acid excretion has been proposed as a mechanism for the cholesterol-lowering action of some fibers (8). Psyllium husk has been shown to increase fecal bile acid excretion in rats (9) as well as in humans (10, 11). The results from a recent study in rats suggested that the psyllium seed may be as effective as the husk in lowering serum cholesterol concentrations (9). The seed includes the kernels as well as the husk and has a smaller proportion of soluble fiber (**Table 1**). The purpose of the present study was to compare the effects of a moderate dosage (10 g/d) of psyllium seed with a husk preparation on serum lipid concentrations. Fecal bile acid concentrations were measured to test the proposed mechanism of action. Normal subjects were studied together with subjects who had ileostomies because the ileostomy model gives insight into the small-intestinal phase of the enterohepatic circulation of bile acids.

## Subjects and methods

The effects of psyllium husk and seed were tested in two separate experiments with similar protocols.

### *Subjects*

For experiment 1, six male subjects were recruited from the laboratory and hospital staff after being informed of the study protocol. All were in good health and were not taking any medication at the time of the experiments. For experiment 2, four subjects from the first trial participated again, and two additional subjects were recruited. Patients with a diagnosis of ulcerative colitis and an ileostomy, treated at the Western General Hospital in Edinburgh, were contacted by letter. Those who expressed interest were visited at home and informed of the study protocol. Five ileostomy subjects were recruited. All had their colon removed between 16 mo and 13.5 y before the start of the study and were otherwise in good health. All five subjects participated in both experiments although one person had to withdraw during the second trial because of an unrelated illness. Subject characteristics are listed in **Table 2.** Both trials were reviewed and approved by the Lothian Health Board Medical Ethics Committee.

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TABLE 1
Fiber content of the experimental supplements

| | Total dietary fiber | Soluble fiber: nonsoluble fiber |
|---|---|---|
| | *g/kg* | *%:%* |
| *Plantago ovata* husk | 948 | 67:33 |
| *Plantago ovata* seed | 860 | 47:53 |

*Study protocol*

Both trials were divided into a control period and a test period. The first experiment also included a posttest period to study possible washout effects. The control period was of 1-wk duration. On the evening of day 0, the subjects ingested 40 radioopaque markers (given as 3 mm × 3 mm polythene cubes; Portex Ltd, Hythe, Kent, UK) for measurement of whole-gut transit time (normal group only). All stool or ileostomy effluent was collected for the next 5 d. On the mornings of days 2 and 5, fasting venous blood samples were taken. In addition, the subjects kept a 7-d diet diary starting on day 1, through to day 7.

The control period was followed by a 3-wk test period, during which the subjects consumed 3.3 g psyllium husk (Madaus AG, Cologne, Germany) in experiment 1 or seed (Madaus AG) in experiment 2, three times daily at mealtimes with ≈60 mL milk. The preparations were supplied to the subjects in individual packets. An excess number of packets was given and the remainder returned at the end of the study to gauge compliance. In the third test week, a similar protocol as in the control week was followed. Forty radio-opaque markers were ingested on day 0 (normal subjects only), feces and ileostomy effluent was collected on days 1–5, blood samples were collected on days 2 and 5, and a 7-d diet diary was completed from days 1 to 7.

The posttest period, conducted 3 wk after the end of the test period in experiment 1, followed the same protocol as the control week. During both trials, standing height of subjects was measured without shoes at the start of the experiment. Body weight was measured in the control and test periods (and posttest in experiment 1) on a set of portable scales, for subjects without shoes or heavy outer garments. The blood collections in experiment 2 were made on days 2 and 4.

*Background diet*

The subjects were asked to keep their background diet as constant as possible throughout the trials. Before the start of the experiments they were instructed on how to complete the 7-d diet diary. Recording sheets were supplied and quantities of food and drink consumed were estimated by the subjects in household measures (cups, spoons, items). The diaries were analyzed for average daily energy, fat, and fiber intake at the end of the experiments with the use of a computerized version (12) of the McCance and Widdowson's food composition tables (13).

*Serum lipid analysis*

All subjects except one came to the hospital for blood taking. One subject lived too far away and was visited at home on blood collection days. After collection, the blood samples were treated within 3 h. The serum was removed after clotting and centrifugation (at 900 × *g* for 10 min at 15 °C). Cholesterol and triglycerides were analyzed enzymatically with commercial kits (CHOD-PAP; Boehringer-Mannheim, Germany for cholesterol, and Merckotest 14360; Merck, Germany for triglycerides) by means of a Cobas-Bio centrifugal analyzer (Roche Diagnostica, Basel, Switzerland). HDL cholesterol was separated from serum by precipitation of very-low-density lipoprotein (VLDL) and LDL with magnesium-dextran (14).

LDL cholesterol was calculated according to Friedewald et al (15): LDL cholesterol (mmol/L) = total cholesterol − HDL cholesterol − (0.45 × triglycerides).

*Fecal and ileostomy collection*

The normal subjects were provided with sling bags (Trans Atlantic Plastics, Surrey, UK) and boxes for individual stool collection and were instructed to deliver all stool samples to the laboratory as soon as possible. They were asked to note date and time of defecation on each box. The ileostomy subjects were provided with plastic jars to collect ileostomy effluent and the jars were collected from the subjects' homes once a day. On delivery to the laboratory, all samples were weighed and frozen immediately at −20 °C until further processing. At the end of a 5-d collection period the stool samples (normal subjects) were radiographed to calculate whole-gut transit time. This was taken as the time between ingestion and recovery of 80% of the radioopaque markers (16). Stool and ileostomy samples were then thawed, pooled, and freeze-dried for calculation of daily dry weight.

*Bile acid and neutral sterol analyses*

Bile acids and neutral sterols were analyzed in freeze-dried feces and ileostomy effluent by flame-ionization gas chromatography (model CP9000; Chrompack, Middelburg, The Netherlands), by using a capillary column (25 m × 0.32 mm internal diameter) with modified 5% phenyl, 95% methyl siloxane as stationary phase (Scientific Glass Engineering Pty Ltd, Milton Keynes, UK) and nitrogen as carrier gas (split ratio 60). Initial oven temperature was 260 °C, increasing to 330 °C at 5 °C/min. Bile acids were prepared from the freeze-dried material according to Evrard and Janssen (17). After hydrolysis and removal of neutral sterols, the bile acids were extracted, methylated, and oxidized to prepare methyl ketone derivatives for gas chromatography. 23-Nordeoxycholic acid (Maybridge Chemicals Co, Cornwall, UK) was used as the internal standard, and a composite standard of cholic acid, chenodeoxycholic acid, deoxycholic acid, and lithocholic acid (Sigma Chemical Co, Dorset, UK) was analyzed in each run for calculation of response

TABLE 2
Characteristics of the subjects*

| | Normal subjects | Ileostomy subjects |
|---|---|---|
| Experiment 1—husk | | |
| Age (y) | 36.8 ± 9.0 | 47.6 ± 17.0 |
| BMI† | 24.4 ± 1.0 | 21.0 ± 2.8 |
| Experiment 2—seed | | |
| Age (y) | 36.3 ± 9.8 | 41.8 ± 8.5 |
| BMI | 26.2 ± 3.9 | 21.9 ± 1.4 |

* $\bar{x}$ ± SD; $n$ = 6 normal subjects; $n$ = 5 ileostomy subjects in experiment 1, $n$ = 4 in experiment 2.
† In kg/m$^2$.

factors. Linearity was established up to 8 mg bile acid per sample. The CV for multiple determinations in a fecal sample ($n = 6$) was 2.3% for the total bile acid value.

Neutral sterols were prepared according to Miettinen et al (18) by using 5-$\beta$-cholestane (Sigma) as the internal standard. A composite standard containing coprostanol, cholesterol, coprostanone, and cholestanol (Sigma; Steraloids Inc, Wilton, NH) was used for determination of response factors. Linearity was assessed up to 16 mg sterol per sample. The CV, established in a similar fashion as for bile acids, was 1.8% for the total sterol value ($n = 6$). All chemical analyses were carried out at the end of the experiments to minimize batch-to-batch variation.

### *Statistics*

Paired Student's $t$ tests were performed to detect differences between the study periods (19). A statistical computer software package was used to perform all comparisons (20). A $P$ value $< 0.05$ (two-tailed) was considered significant. Data are expressed as mean ± SD.

## Results

The consumption of psyllium estimated from the number of packets returned by the subjects, was on average 99% for the husk (range 97–103%) and 99% for the seed (range 85–110%). Both supplements were well tolerated and no adverse effects were reported. The average number of radioopaque markers recovered from the 5-d fecal collection was 39 (range 31–40) in the first experiment and 39 (range 34–40) in the second experiment, indicating that there was good compliance by the normal subjects.

The average daily energy, fat, and fiber intake of the subjects (**Table 3**) was unchanged after psyllium husk supplementation. A significantly greater fat intake was measured after seed supplementation compared with the baseline period ($P < 0.05$). A small but significant reduction in body weight was found after consumption of the seed in the normal group ($P < 0.05$). Body weight was reduced by 1.5 kg (baseline 82.0 ± 8.3, test 80.5 ± 8.3 kg).

After psyllium husk supplementation the average stool weight and transit time were unchanged in the normal subjects (**Table 4**). However, stool weight measured in the posttest period was significantly lower than the test value ($P < 0.05$). No effect was seen on total and HDL cholesterol, LDL cholesterol, triglycerides, and fecal bile acid excretion. All indexes equaled their initial baseline values after the posttest period.

After psyllium seed supplementation, total cholesterol values were reduced by an average of 6.4% ($P < 0.05$; Table 4). HDL cholesterol was also significantly reduced ($P < 0.005$). This reduction, on average 9.3%, was seen in all six subjects. The average estimated LDL-cholesterol value was reduced by 10.1% but this reduction was not statistically significant. The HDL-LDL ratio remained unchanged (0.31 ± 0.12 for both baseline and test period). No difference in fecal bile acids was found and all other indexes remained unchanged. The diet diaries of the normal group were analyzed for dietary cholesterol and ratio of polyunsaturated to saturated fatty acids (P:S; 21) to assess whether the cholesterol-lowering effect of the seed coincided with a change in these indexes. No change was found in either cholesterol intake (baseline 290 ± 82 mg/d, test period 273 ± 76 mg/d) nor P-S ratio (baseline 0.44 ± 0.15, test period 0.48 ± 0.12).

Psyllium husk supplementation resulted in a significant increase in ileostomy dry weight ($P < 0.05$), which returned to the baseline value after the posttest period (**Table 5**). No increase in ileostomy wet weight was found. The main bile acids present in ileostomy fluid were cholic and chenodeoxycholic acid, which are of primary origin. Only trace amounts of the secondary bile acids deoxycholic and lithocholic acid were found, indicating that no bacterial degradation had occurred. Total bile acid excretion tended to increase in all five ileostomy subjects but was not statistically significant ($P = 0.088$). Total cholesterol, HDL and LDL cholesterol, and triglycerides remained unchanged. A significant difference was found between baseline and posttest neutral sterol output as well as test and posttest LDL-cholesterol values. After psyllium seed supplementation, a significant increase in bile acid output was found in the ileostomy effluent ($P < 0.05$, Table 5). Although not statistically significant ($P = 0.15$), ileostomy dry weight tended to increase in all four subjects. Total cholesterol, HDL and LDL cholesterol, and triglycerides remained unchanged.

## Discussion

Psyllium husk preparations have been studied in many trials for their effects on constipation and cholesterol concentrations. Study results are difficult to compare because of the many different preparations used. Comparison is further impeded by the use of nonstandardized nomenclature. Ispaghul, psyllium, and oral hydrophilic mucilloid are some of the names used to describe the *P ovata* preparations tested. Sometimes only commercial product names are given without any further description or information concerning the composition of the product. In the present study, purified psyllium husk and seed preparations were used, of which the proportions of soluble and insoluble fiber was determined previously (9).

Psyllium husk supplementation was shown to reduce serum cholesterol concentrations in hypercholesterolemic subjects (5–7) as well as in subjects with normal cholesterol concentrations (4). For this study, in which the diet of six normal and five ileostomy subjects was supplemented with a moderate amount of psyllium husk for 3 wk, no effect was found on total, HDL, or LDL cholesterol. The dosage of 10 g psyllium husk/d was chosen because larger doses may be unpleasant to consume (6) and therefore affect compliance. A similar dosage was used by Anderson et al (5), who supplemented the diet of a group of 26 mildly to moderately hypercholesterolemic men with Metamucil, a commercial psyllium preparation, and found a reduction in total and LDL-cholesterol concentrations. Larger dosages have been used by others. Abraham and Mehta (4) studied seven men with normal baseline cholesterol concentrations and found a reduction in total as well as HDL and LDL cholesterol after supplementing a low-fiber diet with 21 g psyllium husk/d. Miettinen and Tarpila (7) supplemented the diet of a group of hyperlipidemic subjects with 30 g psyllium mucilloid/d and found a reduction in total, HDL, and LDL cholesterol. The results of this study indicate that a larger dosage of psyllium husk might be required to achieve a significant drop in cholesterol in subjects with normal baseline cholesterol concentrations. However, in the present study the same dosage of psyllium seed resulted in a significant reduction of total and HDL cholesterol in a small group of men with normal baseline cholesterol concentrations. Psyllium seed is a less well-

TABLE 3
Composition of background diet of normal and ileostomy subjects before and after 3-wk *Plantago ovata* (psyllium) husk or seed supplementation*

| | Husk | | | Seed | |
|---|---|---|---|---|---|
| | Baseline | Test | Posttest† | Baseline | Test |
| Normal subjects | | | | | |
| Energy (kJ/d) | 9331 ± 3140 | 8032 ± 1892 | 8882 ± 2670 | 9072 ± 4318 | 8945 ± 3087 |
| Fat (g/d) | 89 ± 35 | 78 ± 21 | 82 ± 32 | 80 ± 29 | 87 ± 26‡ |
| Fiber (g/d) | 16 ± 9 | 18 ± 8 | 18 ± 10 | 18 ± 7 | 18 ± 5 |
| Ileostomy subjects | | | | | |
| Energy (kJ/d) | 10341 ± 1959 | 10532 ± 3010 | 10978 ± 2187 | 11785 ± 878 | 11276 ± 1858 |
| Fat (g/d) | 102 ± 16 | 107 ± 35 | 110 ± 17 | 122 ± 24 | 111 ± 11 |
| Fiber (g/d) | 20 ± 8 | 20 ± 7 | 21 ± 7 | 22 ± 4 | 22 ± 1 |

* $\bar{x}$ ± SD.
† Three-week washout study.
‡ Significantly different from seed baseline, $P < 0.05$.

known fiber source. Furthermore, it has a smaller proportion of soluble fiber compared with the husk, making these results unexpected because soluble fibers are generally thought to be more effective in lowering cholesterol than insoluble fibers (22).

The reduction in cholesterol concentrations in the normal group coincided with an average weight loss of 1.5 kg, posing the question that the weight loss was responsible for the drop in cholesterol concentrations, independent of psyllium seed supplementation. Kromhout (23) predicted that a weight reduction of 1 kg would results in a 0.052 mmol/L (2 mg/dL) fall in total cholesterol. Based on this estimation, only 21% of the drop in cholesterol found in the present study can be accounted for by the reduction in weight. The cause of this weight loss is unknown. Stevens et al (24) found a reduction in ad libitum energy intake after supplementing the diet of 12 women with either psyllium or a combination of psyllium and wheat bran. They concluded that a dosage as small as 10.5 g psyllium/d could decrease energy intake. The dietary intake data in the present study do not support this finding. However, the validity of the dietary data needs to be questioned because the total energy and fat intake of both normal groups were low compared with British average values (energy 10.26 MJ/d, and fat 102 g/d; 25), and there were large variations within the groups. HDL-cholesterol concentrations were also significantly reduced after psyllium seed supplementation. However, the HDL-LDL ratio was unchanged and therefore the clinical relevance of this reduction in HDL cholesterol is questionable. A similar effect was found by Abraham and Mehta (4) after psyllium husk feeding. They reported a significant reduction in HDL-cholesterol concentrations whereas the HDL-LDL ratio actually increased for the majority of their subjects.

The cholesterol-lowering action of psyllium seed did not coincide with increased fecal bile acid excretion. However, both supplements tended to increase the amount of bile acids excreted in the ileostomy effluent. Bile acids are actively reabsorbed in the terminal ileum and reexcreted into the bile. A small amount

TABLE 4
Fecal and serum indexes of normal subjects after 3-wk *Plantago ovata* (psyllium) husk and seed supplementation*

| | Husk | | | Seed | |
|---|---|---|---|---|---|
| | Baseline | Test | Posttest† | Baseline | Test |
| Fecal indexes | | | | | |
| Stool output (g/d) | | | | | |
| Wet | 137 ± 44 | 175 ± 42 | 126 ± 31‡ | 159 ± 58 | 166 ± 35 |
| Dry | 35.3 ± 10.6 | 39.3 ± 9.1 | 34.5 ± 9.2 | 39.8 ± 12.6 | 44.5 ± 10.1 |
| Transit time (h) | 73.4 ± 20.8 | 51.0 ± 14.0 | 69.2 ± 29.3 | 63.9 ± 29.7 | 59.1 ± 8.9 |
| Fecal bile acids (mmol/d) | 0.72 ± 0.12 | 0.89 ± 0.19 | 0.72 ± 0.14 | 1.15 ± 0.63 | 1.44 ± 0.96 |
| Fecal sterols (mmol/d) | 1.34 ± 0.32 | 1.42 ± 0.62 | 1.36 ± 0.58 | 2.02 ± 0.77 | 2.25 ± 0.58 |
| Serum indexes | | | | | |
| Total cholesterol (mmol/L) | 5.51 ± 1.06 | 5.43 ± 1.05 | 5.46 ± 1.20 | 5.75 ± 0.91 | 5.38 ± 0.92§ |
| HDL cholesterol (mmol/L) | 1.20 ± 0.31 | 1.22 ± 0.32 | 1.22 ± 0.37 | 1.17 ± 0.32 | 1.06 ± 0.30‖ |
| LDL cholesterol (mmol/L) | 3.77 ± 0.96 | 3.63 ± 1.01 | 3.71 ± 1.08 | 3.97 ± 0.85 | 3.57 ± 0.80 |
| Triglycerides (mmol/L) | 1.21 ± 0.37 | 1.30 ± 0.55 | 1.19 ± 0.51 | 1.35 ± 0.51 | 1.66 ± 0.86 |

* $\bar{x}$ ± SD; $n = 6$.
† Three-week washout study.
‡ Significantly different from husk test, $P < 0.05$.
§‖ Significantly different from seed baseline: §$P < 0.05$, ‖$P < 0.005$.

TABLE 5
Ileostomy effluent and serum indexes of ileostomy subjects after 3-wk *Plantago ovata* (psyllium) husk and seed supplementation*

| | Husk | | | Seed | |
|---|---|---|---|---|---|
| | Baseline | Test | Posttest† | Baseline | Test |
| Ileostomy effluent | | | | | |
| Output (g/d) | | | | | |
| Wet | 1013 ± 585 | 1120 ± 496 | 1005 ± 554 | 975 ± 480 | 1031 ± 428 |
| Dry | 78.7 ± 26.2 | 94.4 ± 24.7‡ | 78.1 ± 26.5 | 73.0 ± 11.4 | 96.6 ± 33.9 |
| Bile acids (mmol/d) | 2.80 ± 2.65 | 4.26 ± 4.01 | 3.43 ± 3.15 | 4.15 ± 4.36 | 5.18 ± 4.70‡ |
| Sterols (mmol/d) | 1.43 ± 0.27 | 1.38 ± 0.13 | 1.21 ± 0.30‡ | 1.42 ± 0.17 | 1.77 ± 0.58 |
| Serum indexes | | | | | |
| Total cholesterol (mmol/L) | 5.44 ± 2.09 | 5.29 ± 1.90 | 5.67 ± 2.02 | 5.16 ± 2.01 | 5.06 ± 1.67 |
| HDL cholesterol (mmol/L) | 1.57 ± 0.67 | 1.56 ± 0.65 | 1.58 ± 0.80 | 1.24 ± 0.46 | 1.21 ± 0.39 |
| LDL cholesterol (mmol/L) | 3.41 ± 1.79 | 3.21 ± 1.65 | 3.58 ± 1.71§ | 3.45 ± 1.80 | 3.37 ± 1.51 |
| Triglycerides (mmol/L) | 1.02 ± 0.33 | 1.16 ± 0.48 | 1.14 ± 0.32 | 1.07 ± 0.47 | 1.09 ± 0.50 |

* $\bar{x}$ ± SD; $n$ = 5 for husk, $n$ = 4 for seed.
† Three-week washout study.
‡ Significantly different from baseline, $P < 0.05$.
§ Significantly different from test, $P < 0.05$.

escapes this mechanism and can be passively reabsorbed in the colon (26). It has been suggested that fibers may alter sterol metabolism by increasing ileal and fecal losses of bile acids by their sequestration (27). In the present study, no reduction in serum cholesterol in the ileostomy group was found despite an increase in ileal loss of bile acids. It is possible that increased ileal losses are compensated for by increased reabsorption of bile acids in the colon. The results of the present study do not support the suggestion that the mechanism of action is through an enhanced flow of bile acids into the colon followed by excretion into the feces.

An alternative mechanism for the cholesterol-lowering action of psyllium husk was suggested recently by McCall et al (28). They measured the metabolism of apolipoprotein B in African green monkeys after long-term addition of psyllium husk to the diet and suggested that the cholesterol-lowering effect was due to a reduction in LDL synthesis. After supplementation with psyllium seed in the present study, no significant decrease in LDL-cholesterol concentrations was found, which may have been due to the compounded errors associated with the derived LDL-cholesterol values. Significant differences may be achieved with a more accurate and precise measurement of LDL cholesterol and more subjects.

In conclusion, a moderate dosage of psyllium husk (10 g/d) had no effect on cholesterol concentrations in a small group of normal subjects, whereas the same dosage of psyllium seed significantly reduced total and HDL-cholesterol concentrations. Furthermore, the reduction in cholesterol did not coincide with an increase in fecal bile acid excretion, which indicates that the cholesterol-lowering action of psyllium seed is not mediated by this mechanism. Ileostomy bile acid output was higher, suggesting that increased ileal losses may be compensated for by reabsorption in the colon.

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