**ORIGINAL ARTICLE**

# Use of Psyllium Husk with new Pharmacokinetic and Pharmacodynamic Considerations

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## ABSTRACT

**Objective:** To see effects of Psyllium husk on specific lipid parameters like total cholesterol, LDL-cholesterol and triglycerides, which are important risk factors for development of CHD.
**Design:** It was single blind placebo-controlled study conducted at Department of Pharmacology, BMSI, JPMC-Karachi from March 2011 to June 2011.
**Results:** Consumption of 10 grams Psyllium husk/day lowered serum total cholesterol from 220.83±1.3 to 201.14±2.1, LDL-cholesterol from 180.77±1.1 to 130.11±1.0 and triglycerides from 233.22±5.8 to 188.13±3.1 mg/dl in three months. Changes in all these parameters are highly significant when analyzed biostatistically. Effects by placebo in all lipid parameters were non-significant (P>0.05).
**Conclusions:** Psyllium significantly lowered triglycerides, serum total and LDL-cholesterol concentrations in subjects consuming a low-fat diet. Psyllium is well tolerated and safe when used adjunctive to a low-fat diet in individuals with mild-to-moderate hypercholesterolemia.
**Key words:** Psyllium. Cholesterol. LDL cholesterol. Hypercholesterolemia. Fiber. Lipoprotein.

## INTRODUCTION

Thirty percent of normally looking individuals has undesirably high serum cholesterol concentrations. Although a low-fat diet is the primary intervention for these individuals, diet alone may not produce a sufficient response in the estimated 7% of these individuals with overt coronary heart disease or severe hyperlipidemia[1-4] Various studies has have proved that elevated serums total and low density lipoprotein (LDL) Cholesterol concentrations are powerful risk factors for CHD, with oxidation of LDL potentially playing a major role in atherogenesis and development of CHD.[2] Each 1% increase in the serum cholesterol concentration results in 2-3% increase in CHD risk (Anderson et al; 2000). The levels below 200 mg/dl are classified as desirable blood cholesterol, those 200 to 239 mg/dl as borderline high blood cholesterol and those 240 mg/dl and above as high blood cholesterol. The cut point that defines high blood cholesterol (240mg/dl) is a value above which risk of CHD rises steeply. The cut points recommended are uniform for adult men and women of all ages (Kostner GM; et al 1989)[5,7-10] In primary and secondary prevential trials, reduction in total and LDL cholesterol concentrations improved the function of the coronary endothelium and decreased the risk of CHD (Mayes, 1993)[11,12,14.] Psyllium husk has biphasic effects on gastrointestinal tract and cardiovascular system, determining its pharmacokinetic and pharmacodynamic considerations[15,16]. Soluble fiber has been shown to augment the cholesterol-lowering effects of low-fat diets in individuals with mild-to-moderate hypercholesterolemia. Psyllium is a source of natural and concentrated soluble fiber derived from the husks of blonde psyllium seed. Psyllium is well accepted as a safe and effective bulk laxative and is an adjunct to dietary intervention for individuals who do not adequately respond to a low-fat, low-cholesterol diet. When consumed as part of a low-fat diet, previous studies indicated that psyllium decreases serum total cholesterol concentrations an additional 3–6% and serum LDL-cholesterol concentrations an additional 5–9% relative to placebo, with no effect on serum HDL-cholesterol or triacylglycerol concentrations and inconclusive effects on serum apolipoprotein (apo) B concentrations. Psyllium has also been reported to reduce serum total cholesterol concentrations 5–15% and serum LDL-cholesterol concentrations 8–20% in hypercholesterolemic men consuming a typical, high-fat diet[6-9]. To more precisely determine psyllium's effects on serum lipids, we conducted placebo-controlled research, providing strength to statistical analysis of the effects of the drug.

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## PATIENTS AND METHODS

The research work was in single blind placebo-controlled design and was conducted at department of Pharmacology and therapeutics, Basic Medical

Sciences Institute, Jinnah Postgraduate Medical Centre, Karachi, from March to June 2011. Sixty patients of primary hyperlipidemia were initially enrolled in this study, selected from ward and OPD of National Institute of Cardiovascular Diseases, Karachi. Newly diagnosed and untreated primary hyperlipidemic patients of either sex, age range from 21 to 60 years were randomly selected. Patients with diabetes mellitus, peptic ulcer, renal disease, hepatic disease, hypothyroidism and alcoholism were excluded from the study. After explaining the limitations, written consent was obtained from all participants. The study period consisted of 90 days with fortnightly follow up visits. The required information like name, age, sex, occupation, address, previous medication, date of follow up visit and laboratory investigations, etc of each patient was recorded on a proforma. Detailed medical history and physical examination of all patients were carried out. All the base line assessments were taken on the day of inclusion (Day-0) in the study and a similar assessment was taken on Day-90 of research design. After fulfilling the inclusion criteria patients were randomly divided into two groups, i.e.Drug-1(Psyllium husk 10gm/day) and Drug-2 (placebo capsules, containing equal amounts of partly grinded wheat) groups. Patients of drug-1 group were advised to take Psyllium husk (ISPAGHOL) 10 gm daily in three divided times after or before each meal. Patients of drug-2 group were provided placebo capsules, i.e. one capsule, thrice daily, after meal for 90 days. Patients were called every 2 weeks for follow up to check blood pressure, weight, pulse rate and general appearance of the individual. Drug compliance to the regimen was monitored by interview and counseling at each clinical visits. Serum LDL-cholesterol was calculated by Friedwald formula (LDL-Cholesterol=Total Cholesterol-(Triglycerides/5+HDL-Cholesterol). Data were expressed as the mean ± SD and "t" test was applied to determine statistical significance as the difference. A probability value of <0.05 was considered as non-significancant and P<0.001 was considered as highly significant change in the results when pre and post-treatment values were compared.

## RESULTS

Results of the research work are biostatistically highly significant (P<0.001) in case of drug effects and non significant (P>0.05) in case of placebo effects. Out of 60 patients, 58 completed the overall study period. Two patients withdrew from one group (Psyllium husk group) due to non-compliance of Psyllium. Their complaint was bizarre (actually metallic) taste of the drug Psyllium husk. When results were summed up and test parameters were compared, it was seen that, after 90 days of treatment with Psyllium husk, total cholesterol decreased from 220.83 mg/dl to 201.14 mg/dl, LDL-cholesterol decreased from 180.77±1.1 mg/dl to 130.11±1.0 mg/dl, biostatistically change in both parameters are highly significant (P<0.001). When difference between Psyllium and placebo effect were compared it was 15.18 % in total cholesterol and 17.15 % in LDL-cholesterol. Triglycerides at baseline were 233.22±5.8 mg/dl which reduced to 188.13±3.1 mg/dl, which is again highly significant change in the parameter. Difference between drug and placebo effect is 17.15 %. In placebo group at day-0, LDL-Cholesterol level was 144.68±1.22 mg/dl, which decreased to 141.00±1.11 mg/dl, which is non-significant (P>0.05). Total cholesterol in this group at day-0 was 209.11±3.11 mg/dl which reduced to 207.21±1.00 mg/dl, which is again non significant change in the parameter. Triglycerides at baseline was 216.12±3.01 mg/dl which reduced to 215.77±2.14 mg/dl which is non significant change (P>0.05).

Table 1: Comparisons of effects of Psyllium husk and placebo on various lipid parameters

| Type of Lipid | Before treatment | After treatment | P-value | Difference between drug and placebo effect |
|---|---|---|---|---|
| Total cholesterol | 220.83±1.3 | 201.14±2.1 | <0.001 | 15.18 % |
| LDL-cholesterol | 180.77±1.1 | 130.11±1.0 | <0.001 | 17.15 % |
| Triglycerides | 233.22±5.8 | 188.13±3.1 | <0.001 | 9.31 % |

Note: all lipid parameters are measured in mg/dl, sample size is 60, ± are indicating standard error of mean, <0.001 means highly significant result in biostatistics

## DISCUSSION

Suggested mechanisms of Psyllium to reduce cholesterol and triglycerides are that Psyllium stimulated bile acid synthesis (7-hydroxylase activity). Second mechanism is diversion of hepatic cholesterol for bile acid production. Effects of Psyllium on absorption of cholesterol and fat appeared minimal but may make a small contribution to cholesterol lowering. All these effects are due to drug's pharmacokinetic peculiarities. Additional mechanisms such as inhibition of hepatic cholesterol synthesis by propionate and secondary effects of slowing glucose absorption may also play a role[14,15]. This study proves that significant changes occurred in serum total cholesterol, LDL-Cholesterol and serum triglycerides as a result of administration of Psyllium husk for the period of three months. LDL-Cholesterol is reduced highly significantly (P<0.001).

Our study matches with the study of Petchettil et al[16] who observed almost same changes in LDL-Cholesterol of 26 male patients, treated with 3.4 gm of Psyllium thrice daily for eight weeks. These results also match with two other research studies conducted by Saper RB et al[17] and Sartore G et al[18]. Our study results are in contrast with the study results of Shrestha S et al[19] and Theuwissen E and Mensik RP[20] who observed less percentile changes in lipid profile of hyperlipidemic patients. They observed that Psyllium decreased LDL- Cholesterol 10.2% in 70 male patients when treatment period was 4 weeks. This contrast may be due to increased sample size and lesser duration of treatment in their study. Our research work also contradict the results in reduction of serum lipids in two other research studies conducted by Wei ZH et al[21] and Giacosa A and Rondanellim[22] who observed significant changes in serum lipids of placebo group of patients, i.e., cholesterol and triglycerides with use of 13 grams of psyllium husk in 22 and 15 grams of psyllium in 50 hyperlipidemic patients for three months and four months respectively. Both of these results are in contrast with our inference due to their different design of research work and higher dose of drug psyllium husk

## REFERENCES


1. Wolever, T.M.S., V. Vuksan, H. Eshuis, P. Spafadora, R. Peterson, E. Chao, M. Storey, and D. Jenkins.. Effect of method of administration of psyllium on glycemic response and carbohydrate digestibility. J. Am. Coll. Nutr. 1991; 10(4):364-371.
2. S. A. Sorrentino, C. Besler, L. Rohrer, M. Meyer, K. Heinrich, F. H. Bahlmann, M. Mueller, T. Horvath, C. Doerries, M. Heinemann, *et al.* Endothelial-Vasoprotective Effects of High-Density Lipoprotein Are Impaired in Patients With Type 2 Diabetes Mellitus but Are Improved After Extended-Release Niacin Therapy Circulation 2010; 121(1): 110 - 122.
3. Singh B. Psyillium as therapeutic drug delivery agent. *Int J Pharm* 2007;334(1-2):1-14.
4. Uehleke B, Ortiz M, Stange R. Cholesterol reduction using psyllium husks - do gastrointestinal adverse effects limit compliance? Results of a specific observational study. *Phytomedicine.* 2008;15(3):153-9.
5. Ziai SA, Larijani B, Akhoondzadeh S, Fakhrzadeh H, Dastpak A, Bandarian F, et al. Psyllium decreased serum glucose and glycosylated hemoglobin significantly in diabetic outpatients. *J Ethnopharmacol*. 2005 Nov 14;102(2):202-7.
6. Chang HY, Kelly EC, Lembo AJ. Current gut-directed therapies for irritable bowel syndrome. *Curr Treat Options Gastroenterol*. 2006 Jul;9(4):314-23.
7. Fernandez-Banares F. Nutritional care of the patient with constipation. *Best Pract Res Clin Gastroenterol*. 2006;20(3):575-87. Review.
8. Karira KA, Shah SMA et al (2000). Incidence of lipid disorders in offspring of patients with premature myocardial infarction. Medical Channel; 6: 9-12
9. Chan, J.K.C. and V. Wypyszyk. 1988. A forgotten natural dietary fiber: psyllium mucilloid. Cereal Foods World 33(11):919-922.
10. Mayes PA, (1993). Cholesterol synthesis, transport and excretion. In: Harper's Biochemistry. Murray RK, Granner DK, Mayes PA, Rodwell VW. Eds. (23rd edition) Appleton and Lange, Connecticut,pp. 266-278.
11. Alberts DS, Martínez ME, Roe DJ, et al. Lack of effect of a high-fiber cereal supplement on the recurrence of colorectal adenomas. *N Eng J Med*. 2000; 342(16): 1156-1162.
12. L. Yvan-Charvet, J. Kling, T. Pagler, H. Li, B. Hubbard, T. Fisher, C. P. Sparrow, A. K. Taggart, and A. R. Tall. Cholesterol Efflux Potential and Antiinflammatory Properties of High-Density Lipoprotein After Treatment With Niacin and Psyllium**.** Arterioscler Thromb Vasc Biol 2010; 30(7): 1430 - 1438.
13. Burke V, Hodgson JM, Beilin LJ, et al. Dietary protein and soluble fiber reduce ambulatory blood pressure in treated hypertensives. Hypertension 2001;38:821-6.
14. Cicero AF, Derosa G, Manca M, Bove M, Borghi C, Gaddi AV. Different effect of psyllium and guar dietary supplementation on blood pressure control in hypertensive overweight patients: a six-month, randomized clinical trial. *Clin Exp Hypertens.* 2007; 29(6):383-94.
15. Chan MY, Heng CK. Sequential effects of a high-fiber diet with psyllium husks on the expression levels of hepatic genes and plasma lipids. *Nutrition.* 2008; 24(1): 57-66.
16. Petchetti L, Frishman WH, Petrillo R, Raju K. Nutriceuticals in cardiovascular disease: psyllium. *Cardiol Rev.* 2007 May-Jun;15(3):116-22. Review.
17. Saper RB, Eisenberg DM, Phillips RS. Common dietary supplements for weight loss. *Am Fam Physician.* 2004 Nov 1;70(9):1731-8. Review.
18. Sartore G, Reitano R, Barison A, Magnanini P, Cosma C, Burlina S, Manzato E, Fedele D, Lapolla A. The effects of psyllium on lipoproteins in type II diabetic patients. *Eur J Clin Nutr.* 2009;63(10):1269-71.
19. Shrestha S, Freake HC, McGrane MM, Volek JS, Fernandez ML. A combination of psyllium and plant sterols alters lipoprotein metabolism in hypercholesterolemic subjects by modifying the intravascular processing of lipoproteins and increasing LDL uptake. *J Nutr*. 2007 May;137(5):1165-70.
20. Theuwissen E, Mensink RP. Water-soluble dietary fibers and cardiovascular disease. *Physiol Behav* 2008; 94(2):285-92.
21. Wei ZH, Wang H, Chen XY, Wang BS, Rong ZX, Wang BS, Su BH, Chen HZ. Time and dose dependent effect of psyllium on serum lipids in mild to moderate hypercholesterolemia: a meta analysis of controlled clinical trials. *Eur J Clin Nutr.*2009;63(7):821-7.
22. Giacosa A, Rondanelli M. The right fiber for the right disease: an update on the psyllium seed husk and the metabolic syndrome. *J Clin Gastroenterol.* 2010;44 Suppl 1:S58-60.