## EFFECT OF PSYLLIUM HYDROPHILIC MUCILLOID (HUSK) ON PRIMARY HYPERLIPIDEMIC PATIENTS

Shah Murad<sup>1</sup>, Amar Lal Ghurbakhshani<sup>2</sup>, Ghazi Mahmood<sup>3</sup>, Hasan Raza<sup>4</sup>, Saqib Sohail<sup>5</sup>

#### ABSTRACT

Background: Psyllium husk has been used for treating gastrointestinal upsets like diarrhea, constipation and irritable bowel disease in the past. Recent medical researches have shown remarkable effects of psyllium husk on all parameters of lipid profile, except triglycerides and very low density lipoproteins. Objective: This study was conducted to determine the effects of psyllium husk on lipid profile of primary hyperlipidemic patients. Patients and Methods: It was a single blind placebo controlled experimental study, conducted in Jinnah Hospital Karachi, from January 2009 to June 2009. Forty hyperlipidemic patients were included in this study. Twenty patients were on placebo as control group, and twenty were on psyllium husk, ten grams daily in three divided doses, for three months. Patients with hypothyroidism, alcoholism, renal and hepatic disease were excluded from the study. Serum total cholesterol and triglycerides were estimated by the enzymatic calorimetric method. Serum High Density Lipoprotein (HDL) was determined by direct method, at day one and on last day of the treatment. Low Density Lipoprotein, (LDL) was calculated by Friedwald formula (LDL-C= TC- (TG/5 + HDL-C). Data was analyzed as the mean  $\pm$  standard deviation. To determine statistical significance of results, paired t-test was applied and p < 0.05 was taken as significant. **Results:** Two patients withdrew from the study due to personal reasons. Psyllium decreased serum total cholesterol from 228.27±4.89 mg/dl to  $199.22 \pm 2.30 mg/dl$ , triglycerides from  $169.27 \pm 9.92 mg/dl$  to  $164.5 \pm 8.56 mg/dl$ , LDL from  $159.72 \pm 5.70$  to  $129.55 \pm 1000 mg/dl$ 2.81 mg/dl and increased serum HDL from 34.61±1.85 to 36.77±1.96 mg/dl in three months of treatment. Results of all parameters were significant, except triglycerides, when paired 't' test was applied for significance. Conclusion: From this experimental study, it was concluded that psyllium husk fibers are effective in maintaining lipid profile at normal limits in hyperlipidemic patients.

Key words: Cholesterol, Lipoproteins, Psyllium hydrophilic mucilloid

#### INTRODUCTION

Psyllium hydrophilic mucilloid is made from the husk of plants belonging to the Plantago family. These plants grow worldwide and a single plant can produce thousands of seeds. The husk of these seeds produce mucilage, that absorbs water in the intestines and adds bulk to the stool<sup>1</sup>. Psyllium hydrophilic mucilloid is also used to add fiber to the diet as it is a true fiber. The bulky stool then stimulates the intestines to produce a bowel movement.<sup>2</sup> This absorbing action of Psyllium makes it beneficial in diarrhea as well. Hence, Psyllium has a normalizing effect on the bowels in treating both constipation and diarrhea. Furthermore, a high-fiber diet may be beneficial in reducing cholesterol levels and balancing blood sugar levels as fiber helps reduce food transit time in the intestines. This may also help to reduce the incidence of colon cancer. Psyllium is available in

1. Pharmacology Dept. Lahore Medical and Dental College, Lahore.

- 2. Physiology Dept. Shaheed Benazir BhuttoUniversity, Larkana
- 3. Multan Medical and Dental College, Multan.

-----

5. Physiology Dept Lahore Medical and Dental College, Lahore.

**Correspondence:** Prof. Dr. Shah Murad, Prof of Pharmacology Lahore Medical and Dental College, Lahore

Cell No . 0314-2243415 Email: shahmurad65@gmail.com some breakfast cereal products and some commercially prepared laxative products also contain it. Psyllium is easily available in bulk at many herbal or natural food stores.<sup>3,4</sup>

It has been proved by various lipid research clinics in US and UK that psyllium fibres reduce serum total cholesterol and LDL-cholesterol if 10 grams are used daily. Psyllium fibre has lesser effect on triglycerides and HDL-cholesterol. Elevated lipids and lipid carrying lipoproteins cause atherosclerosis, eventually leading to myocardial infarction. Elevation of LDL-cholesterol is particularly associated with risk of coronary artery disease.<sup>5</sup> Prevention and treatment of hyperlipidemia include elimination of risk factors, in conjunction with treatment of the specific lipid disorder. For treating primary hyperlipidemia, HMG-CoA reductase inhibitors, fibric acids, niacin or vitamin B-3, bile acid binding resins including psyllium hydrophilic mucilloid are the main drugs used.<sup>6</sup>

Psyllium fibers bind with bile acids in the gastrointestinal tract (GIT), thereby interrupting the enterohepatic circulation of bile acids and increasing the conversion of cholesterol into bile acids in the liver. The bile acids formed pass into the gut in the bile and are largely reabsorbed at the terminal ileum. The total bile acid pool is only 3 to 5 grams but, because such enterohepatic recycling takes place 5

<sup>4.</sup> Biochemistry Dept. Lahore Medical and Dental College, Lahore.

to 10 times a day, on average, 20-30 grams of bile acid are delivered into the intestine every 24 hours. Bile acids bound to psyllium fibers are lost in the feces and the depletion of the bile acid pool stimulates conversion of cholesterol to bile acid: The result is a fall in intracellular cholesterol in hepatocytes, and an increase or up regulation of LDL receptors leading to an increase in cholesterol synthesis. LDL-cholesterol falls 20 to 25 % by up-regulation of LDL-receptors. In many patients there is some compensatory increase in hepatic triglyceride output. Psyllium husk fibers therefore may be used as first line for hypercholesterolemia but not when there is significant hypertriglyceridemia, which may be aggravated in such patients.<sup>7,8</sup>

This study was conducted to determine the effects of psyllium husk on lipid profile of primary hyperlipidemic patients.

## **PATIENTS AND METHODS**

It was a single blind placebo controlled experimental study, conducted in Jinnah Hospital Karachi, from January 2009 to June 2009. Forty adult patients of primary hyperlipidemia were initially enrolled in this study, selected from wards and OPD of Jinnah Hospital. Patients with diabetes mellitus, peptic ulcer disease, renal disease, hepatic disease, hypothyroidism and alcoholism were excluded from the study by clinical examination, laboratory investigations and medical history. Consent was obtained from all participants on designed proforma and was approved by Ethical Committee for Research of Jinnah Hospital, Karachi.

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. In it ially, medical history and physical examination of all participating patients was carried out.

All the base line assessments were taken on the day of inclusion, i.e. Day-0 in the study and a similar assessment was taken on Day-90. After fulfilling the inclusion criteria, patients were randomly divided into two groups i.e.Group-1(Psyllium husk 10gm/day) and Group-2 (placebo capsules, containing equal amounts of partly grinded wheat). Patients of Group-1 were advised to take psyllium husk 10 grams daily, in three

divided doses, before or after each meal. Patients of Group 2 were provided placebo capsules i.e. one capsule, thrice daily, after meals for 90 days. Patients were called every 2 weeks for follow up to check general appearance, blood pressure, weight and pulse rate. Serum total cholesterol and triglycerides were estimated by the enzymatic calorimetric method. Serum LDL-cholesterol was calculated by Friedwald formula (LDL-Cholesterol = Total Cholesterol-(Triglycerides/5 +HDL-Cholesterol). Serum HDLcholesterol was determined by direct method at day-0 and day-90.<sup>3,5,7-9</sup> Data was expressed as the mean  $\pm$ SD and "t" test was applied to determine statistical significance as the difference in results. A p-value < 0.05 was the limit of significance in this research study.

## RESULTS

In Group 1, out of twenty, eighteen hyperlipidemic patients continued to take psyllium hydrophilic mucilloid for the period of 3 months. Two patients discontinued it due to its metallic taste.

When results were compiled after completion of research, mean total serum cholesterol decreased from 228.2±4.8 mg/dl on day-0 to 199.2±2.3 mg/dl on day-90 in 18 patients. This reduction in total cholesterol was highly significant (p < 0.001), when levels on day-0 and those on day-90 were compared. The average percentage reduction in total cholesterol was 12.7%. In these 18 primary hyperlipidemic patients, their mean serum LDL level at day-0 was 159.7±5.7 mg/dl. This level reduced to 129.5±2.8 mg/dl at day-90. When compared, this change was also highly significant (p<0.001). The percentage change was -18.88%. Furthermore, the mean HDL at day-0 was 34.6±1.8 mg/dl, which increased to  $36.7\pm1.9$  mg/dl on day-90. In these 18 patients the result was highly significant (p<0.001). The percentage increase in HDL from day-0 to day-90 was +6.24%. Result of all parameters are shown in Tables I, II and III.

Placebo Group (n=20)				Psyllium Group (n=18)			
Parameter	Baseline	Post Treatment	p-Value	Baseline	Post Treatment	p-Value	% Difference in groups
Triglyceride (TC)	215.95 ±2.47	$208.70 \pm 5.38$	>0.05	$228.27 \pm 4.89$	199.22 ±2.30	< 0.001	9.37%
Low Density Lipoprotein (LDL)	150.75 ±2.67	148.80 ±2.28	>0.05	$159.72 \pm 5.70$	$129.55 \pm 2.81$	<0.001	17.59%
High Density Lipoprotein (HDL)	35.50 <b>±</b> 13	35.75 ±07	>0.05	34.61 <u></u> ±85	36.77 <u>+</u> <b>±</b> .96	< 0.001	5.54%

Table no: I: Comparison of changes in lipid profile parameters between Psyllium husk and Placebo group of patients in 3 months of treatment

#### Table no: II

Changes in lipid profile in psyllium husk group of patients (n=18)

Parameter	At day-0	At day-90	change
Triglyceride (TC)	228.27	199.22	-12.72%
Low Density	159.72	129.55	-18.88%
Lipoprotein(LDL)			
High Density	34.61	36.7	+6.24%
Lipoprotein (HDL)			

#### Table no: III Changes in lipid profile of patients on placebo group (n=20)

Parameter	At day-0	At day-90	change
Triglyceride (TC)	215.95	208.70	-3.35%
Low Density	150.75	148.80	-1.29%
Lipoprotein(LDL)			
High Density	35.50	35.75	+0.70%
Lipoprotein (HDL)			

# DISCUSSION

In this research work, in 18 primary hyperlipidemic patients, ten grams of psyllium hydrophilic mucilloid reduced Low Density Lipoprotein cholesterol by 18.88% and serum total cholesterol by 12.72% in treatment period, ie three months. High density lipoprotein cholesterol was increased by 6.24%. Results of our research work match with a previous research study which also observed almost same changes in lipid profile of 26 male patients when they were treated with 3.4 gram of psyllium thrice daily for eight weeks.<sup>10</sup> They observed a 19.66% and 13.54% reduction in LDL-C and serum total cholesterol respectively in two months. HDL-C was raised by 4.89% in their research. Our results also match with the study of Krista A Varady and Peter JH Jones in all parameters of lipid profile except change in LDL-

cholesterol level which was higher than ours.<sup>11</sup> This difference may be due to genetic variation in patients suffering from primary hyperlipidemia. Results are also comparable with those of Inar A Castro et al, in which 46 primary hyperlipidemics were treated by psyllium husk 12 gram daily in divided doses for 4 months.<sup>12</sup> In their observation, triglyceride reduction was 3.71%, LDL was reduced upto 20.1%. HDL increased from  $36.12\pm1.73$  to  $40.11\pm3.33$  mg/dl and serum total cholesterol reduction was 14.81%.

Another study was conducted by Charland SL and Malone DC on placebo based trials in which 13 primary hyperlipidemic patients of either sex were treated with 10 gram psyllium husk in divided doses, thrice daily for the period of two months.<sup>13</sup> Results of the trial are in concordance with with our results. In their study, total-cholesterol reduction was 17.1%, triglycerides reduced from  $162.73\pm0.72$  mg/dl to  $149\pm9.71$  mg/dl. In percentage, it was - 4.87%. Observed LDL-C reduction was 17.83%.

Our study results are in contrast with the results of the study conducted by Pereira MA et al, who observed less percentile changes in LDL-C, HDL-C and total cholesterol.<sup>14</sup> This difference may be due to selection of both diabetic and non-diabetic patients. We excluded diabetic patients, as we were working on primary hyperlipidemics. In our observation, serum cholesterol and lipoprotein response is different in primary and secondary hyperlipidemia. For primary hyperlipidemia, one of the cholesterol reduction mechanisms is that psyllium stimulates bile acid synthesis through 7á-hydroxylase activity. Another mode of action of psyllium fibers in reducing cholesterol is diversion of hepatic cholesterol synthesis to bile acid production. Other modes of action of psyllium include inhibition of hepatic cholesterol synthesis by propionate and secondary effects of slowing glucose absorption from GIT. Results of our study are in contrast with research work results of Moreyra AE et al, who observed much more increase in HDL-cholesterol and very less decreased levels of plasma total cholesterol, LDL-Cholesterol.<sup>15</sup> They observed a 10.03% increase in levels of HDL-C. Total cholesterol and LDL-C and triglycerides were reduced by 19.23%, 30.01% and 5.01% respectively. This difference may be due to large sample size and long period of drug trial in their study. In that study, sample size was 98 male and female primary hyperlipidemic patients who used psyllium husk 7 grams daily, in two divided doses, daily for one year. Large sample size, research study design, well controlled follow up, counseling on psyllium husk intake and compliance to drug may change the results in different research works. Reid R et al researched the use of psyllium hydrophilic mucilloid in 30 male primary hyperlipidemic patients, with age range from 30 to 70 years for the period of five weeks.<sup>16</sup> They used psyllium husk 12 grams daily, in divided doses with regular exercise and low calorie diet. They observed that psyllium husk reduced LDL-cholesterol by 21.03% and serum total cholesterol by 20.72%. HDL-Cholesterol was increased too much as compared to our observations. In their study, HDL-Cholesterol increased by 7.68%. These results do not match with our results. The reason may be ethnic selection of patients, age difference, and only male patients.

These are proved facts that geographic selection of patients may change results in same type of research in two different geographical areas. Gender also affects the results in same type of research work, especially nutrition-based research. Our results do not match the results of research conducted by Blackwood et al, who observed less increase in HDL-C, when 5 grams of psyllium was added in regular diet of 16 hyperlipidemic patients for the period of 2 months.<sup>17</sup> The obvious reason for this difference, might be due to lesser dose of drug used for two months only. Sample size, dose and duration of drug used may affect results of research work.

## CONCLUSION

We conclude from the results of this research work that psyllium hydrophilic mucilloid is very effective dietary fiber to reduce serum total and low density lipoprotein cholesterol. These dietary fibers also increase high density lipoprotein cholesterol significantly. All these facts suggest that psyllium husk is very important dietary fiber which can prevent cardiovascular risk in development of atherosclerosis.

#### Acknowledgment

We are thankful to Hamdard Laboratories (WAKF) Pakistan, to provide psyllium hydrophilic mucilloid for the whole period of our research work. We are also thankful to administration of Jinnah Hospital, Karachi, to provide us all laboratory facilities for the research.

### REFERENCES

- 1. Leon AS, Bronas UG Dyslipidemia and Risk of Coronary Heart Disease: Role of Lifestyle Approaches for Its Management. American Journal of Lifestyle Medicine. 2009; 3(4):257-273.
- Sprecher DL, Massien C, Pearce G, Billin AN, Perlstein I, Willson TM, Hassall DG, Ancellin N, Patterson SD, Lobe DC, Johnson TG. Triglyceride:High-Density Lipoprotein Cholesterol Effects in Healthy Subjects Administered a Peroxisome Proliferator Activated Receptor Agonist. Arteriosclerosis, Thrombosis, and Vascular Biology 2007; 27:359.
- 3. Plaisance EP, Grandjean PW, Mahurin AJ. Independent and combined effects of aerobic exercise and pharmacological strategies on serum triglyceride concentrations: a qualitative review. Phys Sportsmed 2009; 37(1): 11-19.
- 4. Otles S, Cagindi O. Cereal-based functional foods and nutraceuticals. Acta Sci. Pol. Technol. Aliment 2006; 5:107-112.
- Regmi PR, Sauer WC, Zijlstra RT. Prediction of in vivo apparent total tract energy digestibility of barley in grower pigs using an in vitro digestibility technique. J. Anim. Sci. 2008; 86:2619-2626.
- 6. Grant WB. A Multicountry Ecological Study of Riskmodifying Factors for Prostate Cancer: Apolipoprotein E {varepsilon}4 as a Risk Factor and Cereals as a Risk Reduction Factor. Anticancer Res. 2010; 30(1): 189-199.
- Chen CW, Cheng HH. A Rice Bran Oil Diet Increases LDL Receptor and HMG-Co A Reductasem RNA Expressions and Insulin Sensitivity in Rats with Streptozotocin/Nicotinamide-Induced Type 2 Diabetes. J. Nutr. 2006; 136(6): 1472 - 1476.
- 8. Singaraja RR, James ER, Crim J, Visscher H, Chatterjee A, Hayden MR. Alternate transcripts expressed in response to diet reflect tissue-specific

regulation of ABCA1. J Lipid Res. 2005; 46: 2061-2071.

- 9. Petersen KF, Shulman GI. Etiology of insulin resistance. Am J Med. 2006; 119: 10-16.
- 10. Most M, Tulley R, Morales S, Lefevre M. Rice bran oil, not fiber, lowers cholesterol in humans. Am J clin Nutr. 2005; 81(1): 64-68.
- 11. Varady KA, Jones P. Combination diet and exercise interventions for the treatment of dyslipidemia: an effective preliminary strategy to lower cholesterol levels? J. Nutr. 2005; 135: 1829-35.
- 12. Castro IA, Barroso LP, Sinnecker P. Functional foods for coronary heart disease risk reduction: a meta-analysis using a multivariate approach American J of Clini Nutrition. 2005; 82(1): 32-40.
- 13. Charland SL, Malone DC. Prediction of cardiovascular event risk reduction from lipid ranges associated with high potency dyslipidemia therapy. Curr Med Res Opin 2010; 26(2): 365-75.
- 14. Pereira MA, O'Reilly E, Augusstsson K, et al.

Dietary fiber and risk of coronary heart disease. A pooled analysis of cohort studies. Arch Intern Med. 2004;164:370-6.

- 15. Moreyra AE, Wilson AC, et al. "Effect of combining psyllium fiber with simvastatin in lowering cholesterol."Arch InternMed. 2005;165(10):1161-6.
- 16. Reid R, Fodor G, Lydon-Hassen K, D'Angelo MS, McCrea J,Bowlby M, Difrancesco L. Dietary counselling for dyslipidemia in primary care: results of a randomized trial. Can J Diet Pract Res. 2002 Winter; 63(4):169-75.
- 17. Blackwood et al. Dietary fibre, physicochemical properties and their relationship to health. The Journal of the Royal Society for the Promotion of Health. 2000; 120:242-247.