**ORIGINAL ARTICLE**

# Single Blind and Placebo Controlled Research Study of Effects of Ispaghula on Serum Lipids

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## ABSTRACT

Coronary heart disease is main cause of morbidity and mortality throughout world. When serum lipids rise from their normal limits, they tend to deposit at vascular walls, causing narrowing of blood vessels and ultimately to development of coronary heart disease. Ispaghula husk have had been used as house hold remedy for constipation and diarrhea. Husk of Ispaghula is being used frequently now days to decrease serum lipids after vigilant, single-blind, double-blind placebo-controlled and closely monitored research studies. Objective of research was to see effects of Ispaghula on serum lipids in primary hyperlipidemia. The Research conducted at Jinnah Hospital Karachi, Pakistan, from January 2008 to June 2008. 40 hyperlipidemic patients were included in the study. 20 patients were on placebo as control/compare group, and twenty were on psyllium husk, ten gram daily, in divided doses for the period of 12 weeks. Hyperlipidemic patients with other diseases were excluded from the study. Serum cholesterol and triglycerides were estimated by the enzymatic calorimetric method. Serum HDL-Cholesterol was determined by direct method, at day zero and at last day of the treatment. LDL-Cholesterol was calculated by Friedwald formula (LDL= Tc- (TG/5 + HDL-C). Data were expressed as the mean ± SD and "t" test was applied to determine statistical significance of results. P value lesser than 0.05 was the limit of significance. When results were compiled, it was observed that two patients discontinued taking drug given, due to metallic taste of psyllium husk. Psyllium decreased serum total cholesterol from 228.27±4.89 mg/dl to 199.22±2.30 mg/dl, triglycerides from 169.27± 9.92 mg/dl to 164.5±8.56 mg/dl, LDL-Cholesterol from 159.72±5.70 to 129.55±2.81 mg/dl, and increased serum HDL-Cholesterol from 34.61±1.85 to 36.77±1.96 mg/dl in 90 days of treatment. Results of all parameters were significant when paired't' test was applied for result analysis. Psyllium is an effective agent to reduce lipid profile parameters in hyperlipidemic patients.

**Key words:** Triglycerides, Coronary heart disease. High-density lipoprotein cholesterol.

## INTRODUCTION

The chief risk factors for cardiovascular disease include fatty diet, sedentary life style, alcohol intake, cigarette smoking. When these risk factors occur in combination with hyperlipidemia and low serum HDL concentrations, early cardiovascular disease is likely to occur. Wise expert medical advice for prevention and treatment are the elimination or modification of risk factors, if possible, in conjunction with treatment of the specific lipid disorder. For treating primary hyperlipidemia, nicotinic acid, statins, bile acid binding resins, psyllium husk and fibric acids are main drug groups used[1]. Blond psyllium seed husk or seed added to food or as a separate supplement in a dose of approximately 10-12 grams daily, in combination with a low-fat or a high-fat diet, can reduce levels of total cholesterol by 3% to 14% and low density lipoprotein (LDL) cholesterol by 5% to 10 after 7 weeks or more of treatment. Blond psyllium also does not seem to lower other blood fats called triglycerides[2]. In children with high cholesterol, taking psyllium can further decrease LDL cholesterol levels by 7% to 15% when added to a low-fat, low-cholesterol diet such as the National Cholesterol Education Program (NCEP) Step 1 diet. Interestingly, taking blond psyllium along with a stricter low-fat, low-cholesterol diet such as the NCEP Step 2 diet may have less of an additional effect in lowering LDL cholesterol.[3] Some evidence suggests that psyllium seed might be more effective than the seed husk for lowering cholesterol[4]. Blond psyllium seems to be most effective when taken with foods at mealtime. Breakfast cereal containing blond psyllium can decrease total cholesterol and LDL cholesterol by 5% and 9%, respectively[5-9,11]. Psyllium husk binds bile acids in the intestine, thereby interrupting the enterohepatic circulation of bile acids and increasing the conversion of cholesterol into bile acids in the liver. Hepatic synthesis of cholesterol is also increased, which in turn increases the secretion of

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VLDL into the circulation, raises serum triglyceride concentrations, and limits the effect of the drug on LDL cholesterol concentrations[12-13]. HDL-Cholesterol concentrations increase by about 0.5mg/dl, when psyllium is added to the treatment regimen of patients who are already receiving niacin (nicotinic acid), fibrates and/or HMG-CoA reductase inhibitors[14,16]. The husks of the psyllium seed absorb water and form a large mass[17]. In people with constipation, this mass stimulates the bowel to move. In people with diarrhea, it can slow down the bowel and reduce bowel movements[18-20]. Psyllium husk contains a high proportion of hemicellulose, composed of a xylan backbone linked with arabinose, rhamnose, and galacturonic acid units (arabinoxylans). The seed consists of 35-percent soluble and 65-percent insoluble polysaccharides (cellulose, hemicellulose, and lignin)[21]. Psyllium is classified as a mucilaginous fiber due to its powerful ability to form a gel in water. This ability comes from its role as the endosperm of the P ovata seed, where it functions to retain water in order to prevent the seed from drying out[22]. Blond psyllium is an herb. The seed and the outer covering of the seed (husk) are used to make medicine[23]. Blond psyllium is used as a laxative and for softening stools in people with hemorrhoids, anal fissures, and after anal surgery. It is also used for diarrhea, irritable bowel syndrome, ulcerative colitis, and dysentery. Other uses include high cholesterol, high blood pressure, diabetes, cancer, weight control, and serious renal disease[24].

## MATERIAL AND METHODS

This study was conducted at Basic Medical Sciences Institute, Jinnah Hospital, Karachi, from January 2008 to June 2008. Forty patients with increased serum lipids were initially registered in this study, selected from ward and OPD of Cardiovascular Diseases Center, Karachi, Pakistan. Hyperlipidemic male and female patients, age range from 20 to 60 years, were randomly selected. Patients with diabetes mellitus, peptic ulcer, renal disease, hepatic disease, hypothyroidism, and alcoholism were excluded from the study by available laboratory investigations, history and clinical examination. 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 such as name, age, sex, occupation, address, previous medication, date of follow up visit and laboratory investigations, etc of each patient was recorded on a Performa, especially designed for this study. Initially a 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 (ISPAGHULA) 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. 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 the limit of significance. 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).18-20 Serum HDL-cholesterol was determined by direct method, at start of and at the end of the treatment.

## RESULTS

When results were complied, at the end of the research work, it was observed that mean serum total cholesterol decreased from 228.2±4.8 mg/dl on day-0 to 199.2±2.3 mg/dl on day-90. 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 18 patients treated with psyllium husk, the mean HDL-C at day-0 was 34.61±1.85mg/dl, which increased to 36.77±1.96mg/dl on day-90. The result was highly significant (P<0.001) when values were compared at day-0 to day-90. The percentage increase in HDL-C from day-0 to day-90 was +6.24. The mean serum triglycerides level of 18 patients treated with psyllium husk was 169.27±9.92 mg/dl on day-0 which reduced to 164.5±8.56 mg/dl on day-90. The mean value differences were highly significant (P <0.001) when levels on day-0 and those on day-90 were compared. The percentage change between day-0 to day-90 was -2.81. In 18 primary hyperlipidemic patients, when started treatment with psyllium husk, their mean serum LDL-C level at day-0 was 159.72±5.70 mg/dl. This level reduced to 129.55±2.81 mg/dl at day-90. When compared between day-0 to day-90, this change was highly significant (<0.001). The percentage change was -18.88, as shown in the table below:

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Table, Effects of psyllium on placebo and test groups

| Effects of Placebo (n=20) | | | | Effects of Psyllium (n=18) | | | |
|---|---|---|---|---|---|---|---|
| **Parameter** | **Baseline** | **Post Treatment** | **P Value** | **Baseline** | **Post Treatment** | **P Value** | **% Difference in groups** |
| T-C | 215.95±2.47 | 208.70±5.38 | <0.05 | 228.27±4.89 | 199.22±2.30 | <0.001 | -9.37 |
| TG | 148.45±4.80 | 146.20±4.20 | >0.05 | 169.27±9.92 | 164.50±8.56 | <0.001 | -1.30 |
| LDL-C | 150.75±2.67 | 148.80±2.28 | >0.05 | 159.72±5.70 | 129.55±2.81 | <0.001 | -17.59 |
| HDL-C | 35.50±1.13 | 35.75±1.07 | >0.05 | 34.61±1.85 | 36.77±1.96 | <0.001 | +5.54 |

Key: Baseline means at the start of treatment, ± is standard error of mean values, + and – means increased and decreased values of the parameters, T-C means total cholesterol, TG means triglycerides, LDL-C means low density lipoprotein cholesterol, HDL-C stands for high density lipoprotein cholesterol, P-Value >0.05 indicates non significant, P-Value <0.05 indicates significant, P-Value <0.001 indicates highly significant.

## DISCUSSION

Results of our research work are in close resemblance with results of work conducted by Vijay Ganji and Jennifer Kuo[25] who observed almost same changes in lipid profile of 26 hyperlipidemic patients, treated with 3.4 gram of psyllium thrice daily for eight weeks. Results also match with the study of Petchetti L et al[26] in all parameters of lipid profile except change in triglyceride level which was higher than ours. Reason for this difference may be the genetic variation in patients suffering from primary hyperlipidemia. Various types of primary hyperlipidemia could respond in different manners with different drug regimen and duration of the treatment. Results of the study also match with results of placebo controlled study conducted by Chan MY and Heng CK et al[27] in which 60 primary hyperlipidemic patients were treated by psyllium husk 8 gram daily in divided doses for the period of 4 months. Triglycerides reduction was -2.9%, LDL-C was reduced to -24.1%. They did not calculate HDL-C and total cholesterol. Another study was conducted by Hokanson JE et al[28] on placebo based trials, in which 15 male children were treated with 6 gram psyllium husk in divided doses, thrice daily for a period of 8 weeks. Results of the trial almost match with our results. In their results total-cholesterol reduction was 13.1%, triglycerides reduced from 171.12±7.77 mg/dl to 165±2.12 mg/dl (P value <0.001). In percentage it was -3.4%. Observed LDL-C and VLDL-C reduction was -20.01% and -11.11%, respectively. Parameter of VLDL-C was not included in our study and HDL-C was not included in their trial. Our study results do not match with results of study work conducted bySartore G et al[29] who observed less percentile changes in LDL-C, HDL-C, and total cholesterol. Only change in triglycerides match with our study. They even observed 0.3% increase in HDL-C in placebo group but by psyllium treatment, HDL-C was decreased up to 1.2%. They did not mention the mechanism of action of psyllium to decrease high density lipoprotein cholesterol. Results of our study do not agree with results of placebo controlled study conducted by Shrestha S et al[30] who observed much more increase in HDL-Cholesterol and very less decreased levels of plasma total cholesterol, LDL-Cholesterol and triglycerides. They observed 9.12% increase levels of HDL-C. Total cholesterol, LDL-C and triglycerides reduced -21.23%, -36.21%, and -6.81% respectively. This remarkable difference may be due to large sample size and long period of drug trial in their study. In that study, sample size was 110 male and female primary hyperlipidemic patients who took psyllium husk 6 gram daily, in divided doses, twice daily for the period of 12 months.

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