

**Author's response to reviews**

**Title:** Serum lipid responses to psyllium fiber: differences between pre- and post-menopausal, hypercholesterolemic women

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**Author's response to reviews:** see over

**Explanation of revisions**

**Reviewer 3**

**Reviewer's report:**

Minor Essential Revisions

1. The number of subjects may not be enough to detect true significance. It is my opinion that there is need for sample size estimation that will allow for the determination of numbers of subjects required for a study such as this. This point was earlier addressed by the authors in their response to previous reviewer.

**Response/Revision:** Yes, we have addressed this (Line 192-195).

2. In addition, nuts (eg, almonds), viscous fibers (eg, fibers from oats, apple and barley), soy proteins, and plant sterols, reduce serum lipids. How much of these did subjects incorporate as part of their daily habitual diet intakes? What was done to assess individual pattern of intake in order to avoid complication of extra fiber from unintended sources? Points could be clarified.

**Response/Revision:** Yes, it is possible that subjects may have changed their dietary habits during the study inspite of our instruction not to do so. This is mentioned as a potential limitation in Lines 195-197.

3. Clinical trials also showed that psyllium helps to lower LDL cholesterol when taken with a low-fat diet, more than a low-fat diet alone. Because of this, the US Food and Drug Administration (FDA) allows marketers to claim that using psyllium along with a low-fat diet may reduce risk of heart disease. Thus, knowing the level of fat intake of subjects may enhance the design of this study.

This trial, has merit and the questions raised above could be included in a follow up research which I believe is the purpose of the pilot study.

**Response/Revision:** We appreciate these recommendations and these points will certainly be incorporated into the follow up research.

**Reviewer 1**

**Reviewer's report:**

This is a small pilot study comparing the lipid/lipoprotein responses of pre- and post menopausal women to 6 weeks of consuming 15g psyllium daily in the form of cookies containing 5g each, one with each meal. The main result reported is that the decrease in total cholesterol is observed in post menopausal, but not pre-menopausal women - and that it is due primarily to an effect on lowering HDL-cholesterol. It is of note that the post-fiber concentration of Apo A-I (the major apolipoprotein of HDL) increased in both groups of women.

There may be a real phenomenon at play here - in our study of 40 men 28 women in which we added psyllium to simvastatin, we observed a reversal of the

HDL-increase due to statin therapy. However the interaction of estrogen and dietary psyllium supplementation in HDL-cholesterol/triglyceride changes is not clear.

#### Major Compulsory Revisions

1. Notwithstanding this being a pilot study, it is under-powered and the number of subjects should be increased - consult your local statistician to estimate the appropriate number, but it should be at least 20 in each group.

**Revision/Response:** Yes, we agree that the sample size smaller and this is mentioned as a limitation and caution should be used in interpreting these findings. Limitation section is new in the revised manuscript. Revision appears in Lines 192-195.

2. State in the limitations of the study, that all the women in the post-menopausal group were Asian.

**Revision/Response:** Yes, we have added this to the limitation section. Please refer to Line 200-201.

3. The problem with all cholesterol studies of this type is that the magnitude of the effect is close in value to the analytical error. In other words - the combination of individual, biological, sampling, and measurement errors can reach 6%. If they are still available, the authors should consider re-analysis of the samples and use the averaged results.

**Revision/Response:** Yes, we agree with the Reviewer that the magnitude of effect is close the analytical error. Unfortunately, we have no access to the samples. Hence we are unable to perform re-analysis.

#### Minor Essential Revisions

1. On page 4, line 102 - change serum to plasma - You indicate that anticoagulant tubes were used.

**Revision/Response:** Infact, there was an error on our part. The measurements were made in serum samples not on plasma. Revision appears in Line 102-103.

2. On page 9, line 194 - include the clause beginning "Because" into the previous sentence.

**Revision/Response:** Yes, we have changed this. Revision appears in Line 204-207.

## Reviewer 2

### Reviewer's report:

This paper by Kuo et al investigated the differences in serum lipid responses to psyllium fiber between pre- and post-menopausal hypercholesterolemic women in San Francisco and its neighbouring communities. The key finding in this study is that consumption of 15g/day of psyllium fiber for 6 weeks was able to achieve

a significant reduction in serum total and HDL-cholesterol only in the post-menopausal but not in the pre-menopausal group.

The research question posed by the authors regarding the effect of menopausal status on the lipid-lowering properties of psyllium fiber is a good one but not original. A similar study in greater detail and in a larger sample size was earlier conducted by Vega-Lopez et al (Ref 15).

#### Major Compulsory Revisions

In my opinion, there are 3 shortcomings in this paper:

1. Smoking is a well known modulator of lipid levels. However, the authors did not provide any information on whether any of the subjects were smokers and for those who are, whether they were advised to keep their smoking habit consistent during the period of the study.

**Revision/Response:** Yes, we agree that the smoking status affects the serum lipid levels. Actually, we have excluded individuals who smoked from the study. This is mentioned in Line 72-74.

2. The lack of association for the pre-menopausal group and for lipids other than total and HDL-cholesterol might be due to type II error, ie insufficient number of subjects recruited to observe statistically significant differences. Did the authors carry out a sample size estimation prior to the study to determine how many subjects are required to observe a similar effect size as those seen in ref 15? In the absence of such power analysis, it would not be appropriate to make a conclusion regarding the differential effectiveness of psyllium fiber in the pre- and post-menopausal group.

**Revision/Response:** Yes, we agree that the sample size may have affected the power. We have added a new paragraph on limitations. This is mentioned as a limitation of our study. Please refer to Line 192-195.

3. In the light of point 2, I am not too convinced by the authors' statement that "our study did not reveal that psyllium fiber reduced serum total cholesterol without lowering HDL-cholesterol." because a larger sample size might reveal significant total cholesterol and/or LDL-cholesterol reduction. Based on the conclusion in the Abstract, "In post-menopausal women, the observed change in response to psyllium fibre in total cholesterol was due to change in HDL-cholesterol", it ironically implies that the outcome of consuming psyllium is undesirable since lowering of total cholesterol was due to lowering of the good HDL-cholesterol. I am sure this is not what the authors are trying to convey to the readers.

**Revision/Response:** Yes, we are under the same predicament. It may imply that cholesterol-lowering effect of psyllium is due to changes in HDL rather than LDL. As the reviewer pointed out that the larger sample might reveal LDL-lowering effect of psyllium. We have indicated this in the limitation section (Line 192-195) and we have cautioned the readers on this issue (Line 195).

4. The conclusion in the abstract is not consistent with that found at the end of

the text.

**Revision/Response:** We have changed the conclusion a bit to reflect our findings.