Author's response to reviews

Title: Does Glycine max leaves or Garcinia Cambogia promote weight-loss or lower plasma cholesterol in overweight individuals: A randomized control trial

Authors:

Ji-Eun Kim (jek8604@hanmail.net)
Seon-Min Jeon (smjeon@knu.ac.kr)
Ki Hun Park (khpark@gsnu.ac.kr)
Woo Song Lee (wslee@kribb.re.kr)
Tae-Sook Jeong (tsjeong@kribb.re.kr)
Robin A McGregor (robinmcgregor@gmail.com)
Myung-Sook Choi (mschoi@knu.ac.uk)

Version: 2 Date: 31 August 2011

Author's response to reviews: see over
Reviewer's report
Title: Does Glycine max leaves or Garcinia Cambogia promote weight-loss or lower plasma cholesterol in overweight individuals: A randomized control trial
Version: 1 Date: 20 July 2011
Reviewer: Carlos Vasques

Reviewer's report:
1. Is the question posed by the authors new and well defined?
   Although the theme is not new, the clinical-pharmacological evaluation using controlled studies of soybean and Garcinia extracts, in order to verify the effectiveness as useful herbal medicines for the treatment of obesity, is relevant facing the lack of conclusive studies.
   The problem of the study is well defined.
   Thank you for your kind comments.

2. Are the methods appropriate and well described, and are sufficient details provided to replicate the work?

Minor Essential Revisions:
The exclusion criteria did not indicate if it was excluded subjects who were in hypocaloric diet or using hypolipemiant or anorexic drugs. Thus, considering that weight and lipid profile are key variables analyzed in this study, it is important to evidence if the subjects who used other methods for weight reduction or control of lipids were included in the study.
Thank you, we have now clarified this in the methods section by adding the following:
“No subjects were actively using any other methods for weight reduction or control of blood lipids, including hypocaloric diet, anorexic drugs or lipid-lowering drugs.”

To describe the equation used to determine body composition from the data of electrical impedance.
We have now clarified the equation used to determine body composition by adding the following:
“The X-Scan plus II software automatically calculates body composition based on tetrapolar bioelectrical impedance [23] with a proprietary formula: Total body water = A × Height²/Impedance + B × Weight + C × Age + D × Gender + E. Constants were derived from a validation study using the isotope dilution method.”

The soy extract is standardized? If so, indicate the phytochemical marker and its percentage in the extract, as was done for hydroxycitric acid in relation to the extract of G. cambogia.
We have now indicated the polyphenol content of the soy extract by adding.
“The total polyphenol content of EGML determined by HPLC (Shimadzu Corp., Japan) was 44.5±2.1 mg gallic acid equivalents/g of EGML.”

Discretionary Revisions:
Considering that the sample consists of subjects of both sexes, it would be
Interestingly to adjust the sex-dependent variables. For example, to adjust to the sex the WHR (Waist to Hip Ratio), BFP, Body fat percentage, leptinemia, HDL-cholesterol, between others. The same could be done about the variables dependent of the adiposity level, adjusting them to BMI or% BF. For example, lipid profile variables and adipokines.

You make an interesting suggestion. It is true these factors may contribute additional variability and make it more difficult to detect a true change in adiposity given the same sample size. In the discussion we argue the significant difference we observed in %body fat is of little clinical relevance. The lack of any change in the primary outcome measure body weight and the low variability in the change in body weight (+/- 0.3 kg) across groups suggests additional statistical correction would be of little benefit. Furthermore, adjustment of variables to %body fat would introduce additional measurement error given the reported intra-individual variability of bioelectrical impedance monitors is ~5% [Ref #30].

3. Are the data sound and well controlled?
Although there is no standardized diet prescription, which would allow a better methodology control, the study appears to be well conducted.
Thank you for your comments

4. Does the manuscript adhere to the relevant standards for reporting and data deposition?
Minor Essential Revisions:
The presentation and description of the results seems appropriate, showing the data needed to meet the problem proposed by the study. However, it should be pointed out if the increase of total caloric intake and nutrient analysis (such as carbohydrates, fats and dietary cholesterol) was significant for groups (show p values), comparing pre- and post-treatment.
We have now clarified that only cholesterol intake was significantly increased pre- post-treatment within each group (p<0.05). The variability in energy, carbohydrate, protein and fat intake within each group no doubt contributed to the lack of significant difference pre- and post-treatment. But at baseline and post-treatment there were no significant differences in nutrient intake between groups.

Line 196: “Subjects were instructed to maintain their habitual diet, however, 24 h diet recalls conducted during the trial revealed significantly higher cholesterol (p<0.05) within each group pre- (Table 2) to post-supplementation (Table 3). Nevertheless there was no significant difference in energy, protein, carbohydrate, fat or cholesterol intake between the EGML, GCE and placebo groups at baseline or after 10 weeks supplementation (Table 2 and Table 3).”

5. Are the discussion and conclusions well balanced and adequately supported by the data?
The conclusions are supported by the results.
Thank you for your comments.
Minor Essential Revisions:
Although it is mentioned in the discussion and abstract of the study a significant increase in HDL-C for EGML and GCE groups when compared to placebo after 10 weeks of treatment, the results only describe the significant difference for the group EGML versus placebo. In fact, comparing visually the post-treatment graphics between GCE and placebo it is not noticed the difference (Figure 1B). It is important to highlight this difference in the presentation of the results if it actually exists; if it does not, rephrase the statement in the abstract and discussion.
Thank you for pointing out the discrepancy! The figure and results are correct. We only observed a significant difference in HDL-C in the EGML group compared to placebo. We have now rephrased the statement in the abstract and discussion.
“EGML appears to be effective for increasing plasma HDL-C levels in overweight individuals. In contrast, GCE supplementation appeared to be ineffective for raising HDL-C compared to placebo in overweight individuals.”

6. Do the title and abstract accurately convey what has been found?
Yes, both the title and the abstract convey what has been found.
Thank you for your comments.

7. Is the writing acceptable?
Needs some language corrections before being published.
Thank you, we have now carefully checked language.

Level of interest: An article of importance in its field
Quality of written English: Needs some language corrections before being published
Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests: 'I declare that I have no competing interests.
Reviewer's report

Title: Does Glycine max leaves or Garcinia Cambogia promote weight-loss or lower plasma cholesterol in overweight individuals: A randomized control trial
Version: 1 Date: 30 June 2011

Reviewer: Carol DeNysschen

Reviewer's report:

Major compulsory revisions:
1. Background: Lines 33 & 34: Strike this comment or better substantiate. This reference does not adequately support your statement "Garcinia cambogia is a plant species......reported to promote weight-loss". We have revised as requested. Now it is clearer we direct the interested reader to the recent meta-analysis on the effects of *Garcinia cambogia* on weight-loss. “The effects of *Garcinia cambogia* have been largely attributed to its rich (-)-hydroxycitric acid (HCA) content. A recent meta-analysis of nine trials suggested *Garcinia cambogia* /HCA supplementation may cause short-term weight-loss, but the clinical relevance still remains to established [14].”

2. Background: Line 36- I have reservations about this reference (#15)- it is a vague study with a potential conflict of interest in the funding source. We have deleted reference (#15) as requested. The following references (#16 #17) provide examples of how HCA may alter energy metabolism and appetite.

3. Background: Line 40 - reference studies that "report improved blood lipid profiles in hypercholesterolemia". We have revised to make the distinction between evidence from animal and human studies clear as follows: “*Garginia cambogia* is also reported to suppress cholesterol and triglycerides accumulation in high fat diet fed mice [19]. However, evidence that *Garcinia cambogia* can improve blood lipid profiles or has antioxidant activity in humans is lacking [20].”

4. Background: Lines 46-48- the meta-analysis mentioned points out many flaws of studies reviewed and the effect size of those studies was small (1% change in body weight). The review of results of this meta-analysis do not do support your statement well. We have revised the statement as follows: “Furthermore, a recent meta-analysis based on nine RCTs concluded HCA supplementation results in only a small short-term weight-loss, which appears to be of limited clinical relevance [14].”

5. Results: starting line 214: Effect of EGML and GCE on plasma toxicity and
erythrocyte antioxidant enzyme activity: this is a well stated summary and although it is only a secondary aim of your study you should reflect importance of this issue more in your background section. Readers need to realize the importance of this and why you included it as an aim (just a few sentences would provide insight to the reader).

We have now highlighted the potential relationship between both supplements and potential antioxidant activity as follows:

Line 41: “Other bioactive components of Garginia cambogia including benzophenones are reported to reduce oxidative stress levels based on in-vitro experiments in human plasma, hence may protect against diseases associated with oxidative stress [18].

6. Discussion: Line 329: should mention what other contributors to a lower HDL might have been involved (such as participants may have exercised more knowing they were in a clinical study).

We have already included a lengthy section on limitations. Modification of physical activity was not part of the study design. Subjects were randomized into groups, supplement was administered in a double-blind fashion. Individuals were free-living, subjects were advised to maintain their usual physically activity levels. If the Garcinia Cambogia or soy supplemented group had increased their physically activity levels, you really would expect some major changes in other blood parameters measured, not only HDL-C.

7. Discussion: Line 350: There are quite a few studies that support soy’s antioxidant effect in humans. I suggest deleting the animal reference and including more good human studies as references.


8. Discussion: overall comment- I noticed placebo participants had a lower baseline fiber intake. Comment on this in your discussion.

Thank you for your careful observation, the placebo participants did indeed have apparently lower average baseline fiber intake, but also consider the variability (standard deviation) within the placebo, GCE and EGML groups (± 4g). How much do individuals need to modify fiber intake to effect satiety, is ~3-5 g/day extra fiber sufficient? Also at the end of 12 weeks, you could argue the fiber intake was the same in the placebo and EGML group (22.5±4.5 v 23.4±0.6 g/day). We have already commented in the limitations section about regression to the mean and learning effects in dietary recall. We really wanted to avoid over interpreting the diet data, given the inherent variability in dietary recall.

Minor Essential Revisions:
1. Table 5 was difficult to read with current format structure.
   We have changed Table 4, 5, 6, 7, 8 to landscape orientation to make it easier to read.

2. Methods: Line 74 and 75 - should write out these measures before you use abbreviations.
Thank you, we have corrected.

3. Noted that 1 group of the participants had a different number of capsules to take each day - this could provide insight into what group participants were in if they were in touch with each other. Just a comment.
We agree, although any effects due to capsule number would presumably lead to greater effects in the GCE group (8 capsules) v the placebo (4 capsules) or EMGL groups (4 capsules), but we found changes in HDL-C were not limited to solely the GCE group. Certainly, in future such nutritional intervention studies it would be prudent to make sure equal capsule numbers are prepared.

4. Report in the discussion that participants did not keep exercise logs so unable to determine if change in physical activity could have contributed to HDL changes.
As stated earlier this study did not involve any physical activity intervention, we primarily investigated whether in free-living individuals simply consuming a soy or *Garcinia cambogia* supplement without any additional lifestyle modification (e.g. dietary restriction or physical activity) can lower body weight or cholesterol. There is plenty of evidence to suggest a physical activity intervention of sufficient intensity and duration with improve plasma lipid profiles and may lead to weight-loss, similar carefully controlled calorie restriction or indeed Orlistat are effective weight-loss interventions. However, many individuals consume supplements alone, based on their purported health benefits demonstrated in animals. Hence the need for this type of free-living study.

**Level of interest:** An article of importance in its field  
**Quality of written English:** Acceptable  
**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.  
**Declaration of competing interests:**  
I declare that I have no competing interests below.