Author's response to reviews

Title: Effects of Korean Red Ginseng (Panax Ginseng Meyer) on Bisphenol A Exposure and Gynecologic Complaints: Single blind, randomized clinical trial of efficacy and safety

Authors:

Mihi Yang (myang@sm.ac.kr)
Min-Woo Hwang (azure92@daum.net)
Mirim Jin (mirimj@dju.kr)
Eun Cho (eun-cho@sookmyung.ac.kr)

Version: 5 Date: 2 April 2014

Author's response to reviews: see over
April 02, 2014

**RE: Effects of Korean Red Ginseng (Panax Ginseng Meyer) on Bisphenol A Exposure and Gynecologic Complaints: Single blind, randomized clinical trial of efficacy and safety**

Dear Dr. Tom Rowles, BMC Complementary & Alternative Medicine,

We hope our response is not yet too late. We feel very sorry for the late response due to the unexpected email problems. However, we appreciate this opportunity to revise our manuscript.

We would like to submit our revised manuscript hereby. We appreciate the reviewers’ efforts for comments and believe they improve our manuscript.

Our answers toward each of reviewers’ questions and comments are followed below. We sincerely hope our revised version satisfies the reviewers’ comments for publication.

Thank you again. We are looking forward to hearing you soon again.

Yours sincerely,
Professor Mihi Yang, Ph. D. & D.A.B.T.
Department of Toxicology
Research Center for Cell Fate Control
College of Pharmacy, Sookmyung Women’s University
Cheongpa-ro 47-gil 100, Yongsan-gu, Seoul, 140-742, Republic of Korea
Tel. 82-2-2077-7179 / Fax. 82-2-710-9871 E-mail: myang@sookmyung.ac.kr
Reviewer 1: Dr. Jong Park

Comment 1: If the participants were compensated for this study, it needs to be described.

Answer: The participants were compensated not for the benefit but for time spent and inconvenience associated with participation in research activities. The IRB approved this appropriateness. (Please see the page 7)

Comment 2: In the Figure 4, one BPA value in control group appears to be an outlier. If this outlier was excluded, then the placebo group may show a similar pattern of the treated group.

Answer: Following this comment, we performed a regression analysis without the outlier and obtained -0.09 of the slope in the placebo group. It turned out that the control showed weak association with BPA levels, compared to the treatment (slope=-0.16). Therefore, we did not exclude the one subject.

Comment 3: SE group showed a better response from KRG than other treated groups. The authors may consider an intra-group analysis. Thus, QOL analysis between treated and control groups may be performed within same category determined by Sasang system.

Answer: When we compared effects of KRG to those of placebo in the same Sasang type, we found insomnia in the SE type and headache and menstrual pain in the TE type were significantly reduced by the KRG consumption (ps<0.05). We added these results in the text (page 13).

Comment 4: Application of KRG effect in Sasang constitutions is a novel and interesting approach. However, all humans cannot be categorized into 4 groups based upon questionnaire data. This may be described in the limitation section. Criteria for KRG Safety seem to be subjective. Description “there was no one who
quit the trial due to side effects of KRG” may not be enough to describe as “Safe”. Basic clinical blood analysis from representative participants may be helpful.

Answer: Taking this comment, we added these limitations regarding the Sasang constitutions in the manuscript and also revised the conclusion. (Please see page 15-16)

Reviewer 2: Dr. Ki-Chan Ha

Comment 1: The authors should explain the reason why 2.7 g/day of KRG has been determined as administration dosage.

Answer: This dose was based on the manufacturer’s (the Korean Ginseng Corp; Daejeon, Republic of Korea) suggested daily use. We added more information about this dose in the manuscript. (Please see page 6)

Comment 2: Authors should clarify primary outcomes and secondary outcomes in Abstract and main text, which should be the same as those in protocol. Currently, the description is vague.

Answer: As BPA is an endocrine disrupting chemical and suspected to induce toxicity on reproduction organs, we studied KRG effects on BPA and females’ QOL. Thus, the primary outcomes are chemopreventive effects of KRG for bisphenol A (BPA) and the secondary outcomes are KRG’s desirable effects for women’s quality of life (QOL) in terms of gynecological complains in our research.

In addition, we tested the Sasang types for optimal application of KRG and drove its safety. Following the reviewer’s comment, we revised the abstract and introduction by clarifying these outcome measures. (Please see highlighted parts in the abstract and page 5)

Comment 3: What is the safety outcome measure?
Answer: Regarding safety measure, we considered white ginseng-related side effects in QOL questionnaire consisted of 17 complaints, i.e. insomnia, face flushing, dipsosis (excessive thirst), headache, palpitation (abnormality of heartbeat), perspiration (sweating), nose-bleeding, and allergy. The subjects filled out the 5 scaled answers (head of page 7) and we analyzed their answers (such as highlighted on page 9-10).

Minor Essential Revisions
1. Fig3 the axis title (x, y-axis) Describe
Answer: The titles were on the figure-legends. Following the comment, we revised the fig.3.

2. The difference between group presented Fig 5, 6.
Answer: For Fig 6 A and B, we performed proper analyses for the comparison of 3 groups, i.e. Kruskal-Wallis test or ANOVA, rather than U- or T-tests for the comparison of two groups, and addressed the statistical differences in the legend. Please refer the highlighted part on the legend of fig 6.

When we analyzed the differences of the KRG effects on the above three complains between two groups (SY vs. SE; SE vs. TE; SY vs. TE), we found borderline significant alleviation of all of the three complains in the SE type, compared to that in the SY type (0.05<ps<0.1). However, there were no differences of the KRG effects between the SE and TE types and between the SY and TE types. We added these additional statistical results on the bottom of page 12.

We also revised English in the whole text and confirmed appropriateness of statistical analyses.