Author's response to reviews

Title: Essential oils purified from Schisandraceae semen inhibits tumor necrosis factor-alpha-induced matrix metalloproteinase-9 activation and migration of human aortic smooth muscle cells

Authors:

Jin-Woo Jeong (jinwooyo@nate.com)
Joo Wan Kim (warii@paran.com)
Sae Kwang Ku (gucci200@hanmail.net)
Sung Goo Kim (bioport@naver.com)
Ki Young Kim (bioportkorea@naver.com)
Gi-Young Kim (immunkim@cheju.ac.kr)
Hye Jin Hwang (lab301@nate.com)
Byung Woo Kim (bwm@deu.ac.kr)
Hae Young Chung (hyjung@pusan.ac.kr)
Cheol Min Kim (kimcm@pusan.ac.kr)
Yung Hyun Choi (choiyh@deu.ac.kr)

Version: 3 Date: 19 October 2014

Author's response to reviews: see over
Reversion Cover Letter

October 19, 2014

Ms. Ref. No.: MS: 1176694953137567

Manuscript Title: Essential oil purified from Schisandraceae Semen has an inhibitory effect on tumor necrosis factor-alpha-induced matrix metalloproteinase-9 activation and migration of human aortic smooth muscle cells

BMC Complementary and Alternative Medicine

Dear Editor

Thank you very much for your letter together with editorial and reviewer’s comments. We have completed the revision of our manuscript (MS: 1176694953137567). I would like to express my deep appreciation for your careful evaluation and suggestions. The comments and suggestions were highly valuable to revise and improve the quality of manuscript. As editor and reviewers have kindly suggested, we did our best for improvement of the manuscript, following their suggestions, as described below.

Therefore, I would like to resubmit our revised manuscript for consideration as a research article in the BMC Complementary and Alternative Medicine, and look forward to your reply. I’m looking forward to favorable response from you soon.

Authors of this paper are aware of and agree to the contents and to being listed as an author. This paper, or any similar paper, has not been and will not be submitted to or published in any other primary scientific journal.

Sincerely yours,

Yung Hyun Choi, Ph.D.
Department of Biochemistry
Dongeui University College of Korean Medicine
San 45-1, Yangjung-dong, Busanjin-gu, Busan 614-052, Republic of Korea
Tel.: 82-51-850-7413 FAX: 82-51-853-4036
E-mail: choiyh@deu.ac.kr
Response to Editor and Reviewers

Thank you very much for reviewing our manuscript (MS: 1176694953137567) contributed to the BMC Complementary and Alternative Medicine. As kindly suggested and commented, we would like to express my deep appreciation for the comments and agree with all the comments. We have tired to meet the cogent criticisms of the referees and believe it has been improved thereby. We hope you will now find it appropriate for publication. Specifically, the following changes have been made in blue font in the text.

: Thank you for your careful comment, and the content in the text was revised accordingly.

Response to the comments of Reviewers

Reviewer #1:
Reviewer's report:
The study submitted for publication entitled "Essential oil purified from Schisandraceae Semen has an inhibitory effect on tumor necrosis factor-a-induced matrix metalloproteinase-9 activation and migration of human aortic smooth muscle cells" describes the anti-atherosclerotic effects of Schisandraceae Semen essential oil in human aortic smooth muscle cells (HASMCs). The manuscript is written properly and is of interest to readers of the BMC Complementary and Alternative Medicine.

Minor Essential Revisions

1) The author wrote "Essential oils, which are concentrated hydrophobic liquids containing volatile aromatic compounds from plants". In fact, there are several products that get this concept, but are not essential oils. For example, some commercial products are synthetic flavoring oils containing volatile compounds from aromatic plants. A proposed concept is: "Essential oils, which are complex mixtures of volatile compounds produced by aromatic plants." : Thank you for your appropriate suggestion. I revised the text as you indicated.

2) In the description of the method of extraction of Schisandra chinensis essential oil was cited the reference 36. This reference is on pharmacological activities of Rosmarinus officinalis L. While the reference 35 reports a chemical study of Schisandra chinensis. Please check the citation of these references in the text.

: Although the paper 36 concerns the effects of essential oil of Rosmarinus officinalis L. on colitis, the references were cited in order to present proper references regarding the method for separating the essential oil. Paper 35 (This was changed to paper 40 due to addition of new
references) was replaced by the review paper below.


Major Compulsory Revisions
3) In the Introduction, the authors did not explain why to study the essential oil instead of vegetable alcoholic extract of the plant. Justify the choice of the essential oil for the study.

: Thus far, a lot of research has been conducted on complex extracts from Schisandra chinensis or single components with physiological activities contained in S. chinensis. However, research using essential oil contained in S. chinensis was relatively lacking compared to research on the efficacy of essential oil from other plants. The sentence below was added to the Introduction and four appropriate references were also presented.

"According to recent research, essential oil extracted from Schisandrae fructus has been found to have pharmacological activities such as antibacterial and antioxidant activities."

References

4) On the medicinal use of the plant by the population, is the essential oil used to therapeutic treatment? or tea? Please describe.

: Traditionally, the essential oil has been used in different ways. It has been applied to a wounded area or taken as a tea, or used in aromatherapy.
5) Please, write in the methodology the month and year of collection of plant seeds.
   : I added what you indicated.

6) In the methodology, describe the name of the method of extraction with 100% ethanol. For example, maceration?
   : I revised what you indicated.

Discretionary Revisions
7) The authors should comment on the chemical composition of the essential oil as well as if there are reports in the literature of pharmacological activities of components from oil related to the present pharmacological study.
8) Authors need to comment on some pharmacobotanical aspects of the study. For example, are there species of this plant genus or family with popular medicinal use related to this study? Is this pharmacological study related to the pharmacological studies of other species of the family?
   : The SSeo used in this study contained 45 g of carbohydrate, 31 g of fat, and 18 g of protein per 100 g. Please understand that data on the content of oleic acid, linoleic acid, and palmitic acid are presently being prepared to be presented in another paper. They will be used as additional data to compare the efficacy of essential oils from other plants.

We once again would like to thank you for your thorough advice in our paper.

Reviewer #2:
Reviewer’s report:
The manuscript entitled “Essential oils purified from Schisandrae Semen has an inhibitory effect on tumor necrosis factor-α-induced matrix metalloproteinase -9 activation and migration of human aortic smooth muscle cells” by Jeong et al. describes the antioxidative, anti-inflammatory and anti-migratory properties of essential oil purified from an oriental medicinal herb Schisandrae fructus. Authors reported that essential oil of Schisandrae fructus (SSeo) attenuated tumor necrosis factor-α (TNF-α)-induced migration of human aortic smooth muscle cells (HASMCs) by blocking the activation of matrix metalloproteinase-9 (MMP9) and suppression of inflammatory signaling through the blockade of ROS generation and nuclear factor-kappaB (NF-κB) activation. Since the herb Schisandrae fructus has long been used in traditional medicine as a remedy for inflammation and atherosclerosis, this study provides, for the first time, the mechanisms underlying its biological activity. The study has been well designed to address the objectives and the manuscript is well written. However, following issues
should be addressed prior to considering this manuscript for publication.

1. The title of the manuscript may be modified as “Essential oils purified from Schisandraceae fructus inhibits tumor necrosis factor-a-induced matrix metalloproteinase-9 activation and migration of human aortic smooth muscle cells”
   : Thank you for your appropriate suggestion. I revised the text as you indicated.

2. The results of the present study may be organized better as follows: Effects of SSeo on HASMCs migration; Effects of SSeo on the production/expression of inflammatory mediators; Effects of SSeo on the MMP-9 expression, production, activity; Effects of SSeo on ROS generation; Finally, addressing the effect of SSeo on NF-kB activation. In its current format of data organization, there is a lack of correlation between the effect of SSeo on MMP9 and inflammatory markers.
   : I slightly rearranged the order by referring to what indicated. However, in order to emphasize inhibition of MMP-9 activity, this part was mentioned first.

3. In the Introduction section, authors mentioned that the essential oil was purified from Schisandraceae fructus. However, the title shows Schisandraceae Semen. Will it be Semen or fructus?
   : It is semen and I revised the relevant parts.

4. In the Materials and methods section, authors should mention which plant parts was used to isolate essential oils and what are the components of the SSeo used in this study.
   : The experiment used dried seed parts and as components, SSeo contained 45 g of carbohydrate, 31 g of fat, and 31 g of protein per 100 g. Please understand that data on the content of oleic acid, linoleic acid, and palmitic acid are presently being prepared to be presented in another paper.

5. In Page 6, line 13-15: “Therefore, anti-inflammatory and …….. artery disease.” This sentence needs to be rewritten to improve the clarity.
   : I deleted what you indicated, considering that it was good to delete it for the whole context.

6. In Page 6, Line 18-19: “Essential oils from various plants have beneficial effects on various smooth muscle disorders” – this sentence may be rewritten as “Plant essential oils exert beneficial effects on various smooth muscle disorders” to avoid repeated use of the word “various”.
   : This suggested modification has been made.
7. Page 16, Line 5-16: The subtitle indicates that authors performed migration assay but in the text, authors talk about invasion assay. This paragraph should be carefully edited.
: I revised what you indicated.

8. Discussion section should be improved by minimizing simple description of experimental findings.
: I partially revised the Discussion by referring to what you indicated.

We once again would like to thank you for your thorough advice in our paper.

We would be grateful if the manuscript could be re-reviewed and considered for publication in the *BMC Complementary and Alternative Medicine*.

Very sincerely yours,

Yung Hyun Choi, Ph.D.
Department of Biochemistry
Dongeui University College of Korean Medicine
San 45-1, Yangjung-dong, Pusanjin-gu, Pusan 614-052, Republic of Korea
Tel.: 82-51-850-7413
FAX: 82-51-853-4036
E-mail: choiyh@deu.ac.kr