Author’s response to reviews

Title: Therapeutic Effects of Hydro-Alcoholic Extract of Achillea Wilhelmsii on Indomethacin-Induced Gastric Ulcer in Rats: A Proteomic and Metabolomic Approach

Authors:

Mehdi Koushki (mehdikoushki89@gmail.com)
Reyhaneh Yekta (rfyekta83@gmail.com)
Nasrin Amiri-Dashatan (nasrinamiri91@gmail.com)
Masoumeh Dadpay (dadpaym@gmail.com)
Fatemeh Goshadrou (fgoshadrou@yahoo.com)

Version: 2 Date: 24 May 2019

Author’s response to reviews:

Dear Dr. Karuppusamy Arunachalam

Associate Editor

BMC Complementary and Alternative Medicine

We are very excited to have been given the opportunity to revise and resubmit our manuscript entitled “Therapeutic Effects of Hydro-Alcoholic Extract of Achillea Wilhelmsii on Indomethacin-Induced Gastric Ulcer in Rats: A Proteomic and Metabolomic Approach” (BCAM-D-19-00414R1). We want to extend our appreciation for taking the time and effort to provide such insightful guidance. We carefully considered constructive comments and insightful queries raised by you and reviewers.

We hope that these revisions improve the paper such that you and the reviewers now deem it worthy of publication in the journal of BMC Complementary and Alternative Medicine. Next, we offer detailed responses to your comments.
RESPONSES TO THE REVIEWER’S COMMENTS

Before of all, we really thank you for your constructive and valuable comments. We also appreciate the time you devoted to reviewing our manuscript. In the revised version of this manuscript, we used highlighted items in order to highlighting our changes in the manuscript. We have addressed each of your concerns as outlined below.

Reviewers’ comments:

Ahmed Abdel Moneim (Reviewer 1):

- There are many English errors. The work should be revised by an English native speaker.

Response

Thank you for this point. we reviewed the manuscript and tried to correct all typographical and grammatical error. English writing was revised by an English native speaker in revised manuscript.

- Please use full names of abbreviations before using abbreviations.

Response

Thank you for your valuable comment. The full names of abbreviations were all added to be used before using the abbreviations in the whole manuscript and highlighted as yellow in revised manuscript.

- Exposure to indomethacin does not induce typical gastric ulcers- please, correct this expression in the manuscript to e.g. gastric damage, gastric lesions or gastric erosion.

Response

Thank you for your valuable and insightful suggestion. We have changed “gastric ulcer” to “gastric lesion” in the whole of revised manuscript that highlighted as yellow.
- Different doses of the extract should be used rather than one dose.

Response

You raised a good point. We demonstrated in one study that dose of 800 mg/kg of Achillea wilhelmsii is the better than doses of 200 and 400 mg/kg for the therapy of indomethacin – induced gastric lesions. In this study, we assessed the possible anti-ulcerative activity of Achillea wilhelmsii extract by measuring the protective index, mucus secretion, NP-SH (non-protein sulfhydryl compounds) and lipid peroxidation in gastric tissue in addition to examination macroscopic features and histopathological markers. In this study, Achillea wilhelmsii decreased the extend of ulcers compared to control group. Moreover, the results were revealed that Achillea wilhelmsii extract significantly reduced acid secretion in doses of 400 and 800 mg/kg compared with indomethacin control group. A statistically significant difference in acid secretion and ulcer index was observed by Achillea wilhelmsii extract 800 mg/kg in comparison to control group. Meanwhile, we have added a sentence “We selected dose of 800 mg/kg of Achillea wilhelmsii extract based on the findings of our previous studies on Achillea wilhelmsii” to Plant extract: hydro-alcoholic extraction in method section (lines 88-89) in revised manuscript and highlighted as yellow.

Finally, we selected the dose of 800 mg/kg of Achillea wilhelmsii for present study.

- The extract should be compared with a standard drug to prove the efficacy of the extract.

Response

Thank you for your attention to this point. As mentioned in answer the above comment, we performed two pilot studies that in these studies we used ranitidine as standard drug to prove the efficacy of the extract. Ranitidine is an H2 histamine receptor antagonist that works by blocking histamine and thus decreasing the amount of acid released by cells of the stomach. In Our previous study, the rats wistar were divided into elven groups (each 8), rats in group 1 received indomethacin with single dose of indomethacin as gavage, rats in group 2 received carboxymethyl cellulose 1% as drug control and rats in group 3 received indomethacin single dose 45 mg/kg and ranitidine with dose 150 mg/kg as a standard drug to prove the efficacy of the extract. Therefore, we did this in previous pilot studies and approved the efficacy of the extract. The findings from the pilot studies showed that both the Achillea wilhelmsii extract and ranitidine (150 mg/kg) for three days after single dose of indomethacin increased the therapeutic indexes relative to group receiving indomethacin alone. Meanwhile, the human dosage of ranitidine used in market as medicine is 150 mg/kg body weight.
- Some references are old references and there are new versions of the manuscript. Please use the new papers instead of the old papers. May the authors cite the new version of papers like: doi:10.1016/j.biopha.2017.04.069.

Response

Thank you for valuable suggestion. Based on your advice, we have added above mentioned reference and new references to revised manuscript that highlighted as yellow.

- Histopathology quality is too poor.

Response

Thank you for this point. The resolution of the histopathology picture (Figure 3) was improved in revised figure 3.

- What about inflammation and oxidative stress pathways??

Response

Thank you for your valuable and insightful question. We have added sentences associated with inflammation and oxidative stress in gastric lesions pathways in discussion section and highlighted as yellow (lines 281-286, 351-356).

Salmon Adebayo, PhD (Reviewer 2):

- The changes made to the revised manuscript were not highlighted, so it was difficult to re-assess the resubmission. Inconsistent font style and sizes used in the manuscript.

Response

Thank you for your attention to this points. We highlighted all of points listed in lines (438-463) as yellow in revised manuscript as well as we corrected font style and size in revised manuscript.
Again, we appreciate the opportunity to revise our manuscript for consideration in your journal. We hope our revision meet with your approval.

Fatemeh Goshadrou,

Best Regards