Author’s response to reviews

Title: Anti-hyperalgesic properties of a flavanone derivative Poncirin in acute and chronic inflammatory pain models in mice

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BMC-Pharmacology and Toxicology

Editorial Office

RE: Revision PHAT-D-18-00110R7

Dear Editor,

We have revised our manuscript seven times (R7) for publication in BMC-Pharmacology and Toxicology. We highly appreciate for providing the valuable comments which help us to improve our manuscript greatly. This times again we have addressed the entire shortcoming in
our study in earnest, in the revised manuscript. All the changed/corrected parts have been highlighted in the text of the revised manuscript.

All the points raised by the editor are appended below.

Comments and Response

I am extremely sorry to send this manuscript back to you for further revision but as part of our commitment to reproducibility, we encourage authors to include information about their study design that ensures compliance with our minimum set of standards: randomisation, blinding, sample size calculation and inclusion/exclusion criteria, where appropriate. We feel that is also very important for the authors to be clear about any limitations of their methods used so that their research can be fully utilized. Please note that non-compliance will not necessarily determine the outcome of the article.

The exclusion and inclusion criteria:

The inclusion and exclusion criteria was followed as reported previously and highlighted in the revised manuscript as per recommendation.


Limitation of the study

No limitation of the current study were found.

1. Randomization

In the Methods section, please describe how samples/animals were allocated to experimental groups. If randomization was not done, please explain in the methods why this was not possible or was not appropriate.

Response:

In the present study the animals were assigned to various groups by using randomization and animal of the same age, sex and weight were assigned to different groups randomly to achieve the non-bias distribution of animals to all groups. The randomization was adopted according to the previously described protocols and the changes were highlighted in the revised manuscript as per recommendation and highlighted.

2. Blinding

In the Methods section, please describe whether the investigators were blinded to group allocation during the experiments and/or analysis. If blinding was not performed, please explain in the methods section why this was not possible or was not appropriate.

Response:

The double blindness was maintained during the whole study from the experiment to analysis of the data in order to avoid any biasness. The double blindness method was followed as reported.


The statement regarding the double blindness assignment was added into the revised manuscript as per recommendation and the changes were highlighted.

3. Sample size calculation

In the methods section, please describe how sample size was determined. If the sample size was based on a related study, please make this clear in your writing, citing the relevant publication reference. If a sample size calculation was not performed, please explain in the methods section why it was not possible or was not appropriate.

Response:

The sample size was calculated based on previously established methods and also considered ethical issues concerned with the animals care and handling, institutional guidelines in mind. We have used “resource equation” for the calculation of sample size. The calculation of E value was made, which is the degree of freedom of analysis of variance (ANOVA). The value of E should be between 10 and 20 to be considered acceptable (Arifin and Zahiruddin 2017). The formula used are highlighted in the reference provided and also cited.


4. Please clarify the methods used to reduce bias when assigning animals to groups (randomization, allocation concealment and/or others).

Response:

The randomization was adopted during the assignment of animals to various groups to avoid study biasness. The statement regarding the randomization was added into the revised manuscript as per recommendation and highlighted.

5. Can you also clarify the timeline for the experiments; i.e., which animal groups were used for which experiments and what happened to each group of animals after each experiment. Please include this information in the methods and in the cover letter.

Response:

During each experiment separate set of animals were used for different experiments and were used once. At the end of the experiments the animals were euthanized using CO2 chamber.

We are grateful for your efforts for the improvement of our manuscript and are hopeful for a positive decision this time, on our manuscript.

The final version of the manuscript was edited by the native speaker (www.aje.com).

We would be pleased to consider our manuscript for publication in BMC-Pharmacology and Toxicology.

Sincerely yours

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