Author's response to reviews

Title: Gene expression profiling reveals underlying molecular mechanism of hepatoprotective effect of Phyllanthus niruri on thioacetamide-induced hepatotoxicity in Sprague Dawley rats

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Author's response to reviews: see over
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Dear Editor in Chief,

Thank you for your kind handling of our recently submitted manuscript entitled “Gene expression profiling reveals the underlying molecular mechanism of the hepatoprotective effect of *Phyllanthus niruri* on thioacetamide induced hepatotoxicity on Spargue Dawely rats”. We appreciate your consideration of the manuscript and the thoughtful comments of the reviewers. We are pleased to know that you would reconsider it for publication in the BMC Complementary and Alternative Medicine after we have revised the manuscript according to comments of the reviewers.

We thank the reviewers for reading the original manuscript thoroughly and providing their critiques, which were constructive and improved the MS. We responded each criticism point by point below and indicated the changes made in the MS by highlighting the relevant text with yellow color wherever possible. As suggested by the reviewers, an extensive rewriting of some parts was required.

We received help from a native-English speaker with scientific expertise at Edanz (www.edanzediting.com/bmc1), as recommended by the BioMed Central for proofing the English grammar and style of the revised MS.

We hope that you will find our manuscript now appropriate for publication in the BMC Complementary and Alternative Medicine.

Thank you for your consideration of this MS.

Sincerely Yours,

Prof. Mahmood Ameen Abdulla
Responses to comments of the reviewer Madhavan G. Nampoothiri:

We thank the reviewer for carefully reading the manuscript (MS) and providing constructive criticisms that significantly improved the MS. As suggested, we revised the MS to specifically clarify the experimental design, rationalize the selected PN doses and better interpret the gathered data. Below, we provided our point-by-point responses to the remaining critiques (written by italic fonts) and marked the changes made in the MS accordingly by highlighting the relevant lines with yellow color.

1- *I feel that it requires extensive re-writing if it is to be published.*

Thank you, we received help from a native-English speaker with scientific expertise at Edanz (www.edanzediting.com/bmc1), as recommended by the editor for proofing the English grammar and style of the revised MS.

2- *Introduction: The objective of the study and the justification for the originality of the study should be explained more clearly. Information related to introduction has been written incomprehensible and mixed. The scientific language used in the manuscript has to be improved. English usage can be checked.*

Thank you. We have overhauled the whole section in the revision. The section is now more explained, clarified and compacted, but to the point.

3- *Materials & Methods: Experimental procedure is not understood exactly such as analysis method. This part should be written more clearly. Author mentioned of using 40 rats but only 3 groups of 8 animals each are stated. Justification is not given for the dose selection of PN extract. Why only single dose has been tested. A low dose, moderate dose and high dose was appropriate. An acute toxicity study according to OECD guidelines has to be conducted to determine the safety of the extract. Author has not mentioned about it. Since the solvents used in the extract may have its own physiological effects it was better to include one more group treated with PN extract (200mg/kg) alone to see the PN extract effects per se.*

Good point. The experimental protocol is more clarified now and the typing mistake of the number of animals was corrected. Regarding the effects of the solvent used (10% Tween 20), we tested the effects of it and referred to it as the vehicle control group as mentioned in Page 6 line 9. Moreover, we agree that before examining any plant extract for a biological activity the acute toxicity test should be tested to prove the safety of it; and in order to test the hepatoprotective activity at least two doses should be chosen. That’s exactly what our group had done and published in our previous publication:


A detailed section explaining this statement was added.
4- Results & discussion: In fig 2. Significance is indicated in the figure legend but its not seen in the graph given. Figure caption may be revised.

Thank you, the significance is indicated now in the figure legend and the given graph. Figure captions were revised.

Discussion part should be rewritten in more detail and scientific way. The results of the study should be discussed in light of the available information and taking into consideration the causal link. The conclusion part should be rewritten to also highlight the contributions of the study results to science and should be revised to include the suggestions of the researchers.

As suggested, the discussion section was reorganized and separated from the results section. The data was interpreted within its own merits and compared with the findings from the previous research. Also the conclusion part was rewritten and went through.
Responses to comments of Reviewer Vijaya Kumar:

We were pleased with this reviewer’s positive comments on our manuscript and providing constructive criticisms that significantly improved the MS. Below, we provided our point-by-point responses to the remaining critiques (written by italic fonts) and marked the changes made in the MS accordingly by highlighting the relevant lines with yellow color.

1- *Co relate the phytochemistry with mechanisms*

Thank you. In the revision, we included the possible mechanisms of the isolated chemicals.

2- *Name the figure with Numbers*

All figures were named with numbers.

Responses to the Editorial comments:

1 - *Please include a Conclusions section in your manuscript.*

Thank you, a Conclusion section is included now in the MS.

2 - *We recommend that you ask a native English speaking colleague to help you copyedit the paper. If this is not possible, you may need to use a professional language editing service.*

Thank you, we received help from a native-English speaker with scientific expertise at Edanz (www.edanzediting.com/bmc1), as recommended by the editor for proofing the English grammar and style of the revised MS.

Responses to comments of the associate editor:

1- *Who identified the specimen or experimental plant (name)? What is the voucher specimen number of the deposited plant?*

Good point. Fresh plants were purchased from (Ethno Resources Sdn Bhd, Selangor Malaysia) and identified by comparison with the voucher specimen deposited at the Herbarium of Rimba Ilmu, Institute of Science Biology, University of Malaya, Kuala Lumpur (voucher number KLU46618). This statement has been included in the MS.

2- *40 animals used, but says only 3 groups with 8 animals, what happened to the rest of the 16 animals?*

That was a typing mistake and corrected accordingly in the MS.
We believe that we have satisfactorily dealt with all the comments to the best of our ability. Several of the constructive comments and suggestions made by the reviewers indeed made the manuscript reads better and more informative. We thank the reviewers for their careful reading of the manuscripts. We look forward to hearing from you soon.

Thank you for your kind help

Sincerely yours,

Prof. Mahmood Ameen Abdulla