Author's response to reviews

Title: Potential therapeutic role of Tridham in human hepatocellular carcinoma cell line through induction of p53 independent apoptosis

Authors:

Ravindran Jaganathan (jravimicro@gmail.com)
Vijaya Ravinayagam (vijiphd@gmail.com)
Sachdanandam Panchanadham (psachdanandam2000@yahoo.co.in)
Shanthi Palanivelu (pshanthi9@yahoo.co.in)

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Author's response to reviews: see over
From
Dr. P. Shanthi,
Professor and Head,
Dept. of Pathology,
Dr. A. L. M. P-G. Institute of Basic Medical Sciences,
University of Madras, Chennai-113.

To
The Editor,
BMC Complementary and Alternative Medicine

Sub: Resubmission of the revised research article entitled ‘Potential therapeutic role of Tridham in human hepatocellular carcinoma cell line through induction of p53 independent apoptosis’ (MS: 1278307699101581).

Dear Sir,

Please find herewith the revised research article entitled ‘Potential therapeutic role of Tridham in human hepatocellular carcinoma through induction of p53 independent apoptosis’ for consideration to be published in the original research paper category in your esteemed journal “BMC Complementary and Alternative Medicine”. We have modified the manuscript in accordance with the suggestions made by the editor and reviewers.

The manuscript has the written consent and approval from all authors and all authors accept complete responsibility for the contents of the manuscript. The manuscript is not currently under consideration elsewhere and the work reported will not be submitted for publication elsewhere until a final decision has been made. The authors declare that they have no conflict of interest. The manuscript is a truthful original work.

We look forward to a favorable decision.

With regards

Dr. P. Shanthi
RESPONSE TO EDITORIAL AND REVIEWER’S COMMENTS

We would like to thank the editorial committee and the reviewers for their valuable suggestions. We have revised the manuscript accordingly.

Editorial comments:

1. Please confirm whether a voucher specimen of the plant material used in your study has been deposited in a publicly available herbarium? Please include this information in the Methods section of your manuscript. A deposition number should also be included, if available

Response:

Voucher specimens of the plant materials used in our study have been deposited in the public herbarium of the Centre for advanced studies (CAS) in Botany, University of Madras, Guindy Campus, Chennai, India. The deposition numbers have been allotted. This data has been included in the Methods section of our revised manuscript.

2. Please include an Authors’ Contributions section in your manuscript.

Response:

Author’s contribution section has been included in the revised manuscript.
Reviewer comments:

Referee 1: (Aditi Roy)

The manuscript provides a relatively comprehensive study of the mechanism of action of TD in Huh 7 cells. The question posed by the authors is well defined. Methods are appropriate, well described and figures are clear and informative. However, my most major concern is the readability of the manuscript in its current form. The authors should pay closer attention to correct construction. There are also too many run on sentences to point out in this manuscript. These issues could be easily addressed with a careful editing and perhaps the input of a scientific writer.

Response

The major concerns regarding the readability of the manuscript and run on sentences have been addressed by careful editing and scrutiny. And the manuscript has been rewritten in a more readable form.

Minor Essential Revisions:

1. Abstract, Paragraph 1: “……antiproliferative and antiapoptotic” should be “……antiproliferative and pro-apoptotic”

Response

“……antiproliferative and antiapoptotic” is replaced by “……antiproliferative and pro-apoptotic”

2. Abstract, Paragraph 3: “Viability…” should be “Viability studies…..”

Response

“Viability…” has been replaced by “Viability studies…..”

3. Background, Paragraph 1: Although the study was performed for Bad there is no reference of it in this section or even as part of Discussion. The significance of Bad & the results with it needs to be mentioned to explain pro-apoptotic MOA of TD.

Response

We have included a brief mention of BAD, in the background section. A detailed note on the significance of BAD and the results have been incorporated into the discussion to explain the pro-apoptotic MOA of the TD.

4. Please provide reference information on the therapeutic potential of Prosopis cineraria component of TD/address this aspect which is missing in the manuscript.
Response:

We have included additional information on the therapeutic potential of *P. cineraria*, component of TD and also included two additional references.

5. Please be consistent on how you would like to cite *Terminalia chebula* – either as “*Terminalia chebula*” or “*T. chebula*”; also cytochrome c as either “cytochrome c” or “cytochrome C” all through.

Response:

We have restored the consistency on citation of *Terminalia chebula* (*T. chebula*) and cytochrome c throughout our revised manuscript.

6. Background, Paragraph 5: The presentation of literature review of the therapeutic properties of TD could be more organized, discussing each component in sequence followed by presentation of information that is common to more than one component in TD.

Response:

The presentation of literature review of the therapeutic properties of TD has been changed as per suggestions of the reviewer and each component has been discussed in sequence followed by information that is common to more than one component in TD.

7. Results, Induction of apoptosis by activation of caspase-3: “Expression of Caspase 3 gene was found to be up regulated in both Western blot (Figure 6) and colorimetric assay (Figure 7)”’. The figure represents data obtained by flow cytometry. Please correct the construction of the legend too. “Effect of TD on cell cycle analysis.” is not an accurate representation.

Response:

We regret the error. We have corrected the error and included the figure representing colorimetric assay of caspase 3 as figure 6g. The construction of the legend of figure 7 has also been corrected as “Cell cycle phase analysis by flow cytometry in Huh7 cells treated with TD”.

8. Discussion, Paragraph 1: “However, instead of using individual herbal drugs, for treating multiple diseases, a combinational therapy is currently gaining higher importance [44] elicit.” Please replace “treating multiple diseases” by “treating diseases with multiple indications.”
Response:

“Treating multiple diseases” has been replaced by “treating diseases with multiple indications” as per the suggestions of referee.

9. Discussion, Paragraph 2: Please discuss the implications of vacuolation of the cytoplasm with relevant supporting reference(s)

Response:

Implication of vacuolation of cytoplasm has been discussed with the supporting reference.

10. Discussion, Paragraph 5: Please cite reference in support of the text “…DNA ladder formation, characteristic of apoptosis ….”

Response:

Reference has been cited in support of the text “…DNA ladder formation, characteristic of apoptosis ….”

11. Discussion, Paragraph 6: “The mitochondrial membrane translocation of Bax from cytosol has been reported in response to various death stimuli [51-54]”. Is not an accurate representation.

Response:

The inaccuracy in representation of this sentence has been corrected as “The translocation of Bax from cytosol to the mitochondrial membrane has been reported in response to various death stimuli”.

12. Discussion, Paragraph 7: “…..cytochrome C thus, forming a pore in the outer membrane of mitochondria…” Please replace “thus” with “by”

Response:

“thus” has been replaced by “by” as suggested by the reviewer.

13. Please be consistent with font style. Certain segments of the text are in italics.

Response:

Consistency has been restored to font style as suggested by the reviewer.
Referee 2: (Piyali Bhattacharyya)

Minor Essential Revisions:

Spelling errors have been corrected as per suggestions of the reviewer.

1) subdiploid, should be sub diploid; - corrected
2) downregulation, should be down regulation; - corrected
3) upregulation, should be up regulation; - corrected
4) hyperproliferative, should be hyper proliferative; - corrected
5) tumour, should be tumor (According to US English); - corrected
6) antidiabetic should be anti - diabetic; - corrected
7) subconfluent should be sub confluent; - corrected
8) transilluminator should be trans illuminator; - corrected
9) analysed should be analyzed; - corrected
10) timedependent should be time dependent; - corrected
11) colour should be color (According to US English); - corrected
12) subdiploid should be sub diploid; - corrected
13) signalling should be signaling; - corrected
14) flavanoids should be flavonoids; - corrected
15) synergestic should be synergistic. - corrected