Reviewer’s report

Title: Absence of herb-drug interactions of Mistletoe with the Tamoxifen metabolite (E/Z)- Endoxifen and Cytochrome P450 3A4/5 and 2D6 in vitro

Version: 1 Date: 14 Sep 2018

Reviewer: Yogendra Nayak

Reviewer's report:

Dear Sir,

The manuscript entitled "Interaction of standardized mistletoe (Viscum album) preparations with antitumor effects of the Tamoxifen metabolite (E/Z)-Endoxifen and with Cytochrome P450 isotypes CYP3A4/5 and CYP2D6 in vitro" (manuscript number BCAM-D-18-00525R1) can be accepted for publication after major modifications. The work explains the importance of drug herb interaction due to enzyme induction in cancer therapy. Though, there are clinical studies which confidently says that there is no drug-herb interaction, the basic experimental support is given by this article. In the context of high use of alternative medicine along with modern medicine, this study plays important role. But, there are many lacuna to accept in current state of the article. Following clarifications/ questions answer to be made before accepting this manuscript.

1. It is better if the conclusion of the study reflect in the title, such as 'absence of herb drug interaction'. This would catch many audience/ readers. Usually people read titles at first then they read abstract.

2. The manuscript has lot of grammatical errors especially punctuation. For example, the the abstract results, the sentence 'All VAE preparations showed no statistically significant inhibition of CYP3A4/5 and CYP2D6 catalyzed tamoxifen metabolism' can be improved. It can be made short like 'VAE preparations did not show inhibition of CYP3A4/5 and CYP2D6 (p>0.001).

The uniformity in the written article is important, especially when writing units 'ml' and 'mL'.

Sentences starting with numbers can be written in words to begin the paragraph/ sentence. (Page 10 line 222)

3. References such as 6, 7, 25, 29, 32 etc required to be rewritten as per the author instructions.

4. Fig 1 and Fig 2, The authors should explain how they will get units more than 100% on Y- axis when % proliferation / inhibition is considered. Author need to explain the procedure or it has to
be recheked and explained how they have arrived at such values.

5. Number of figures/photos can be reduced by clubbing some of them.

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

Yes

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Yes

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

Yes

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

**Quality of written English**
Please indicate the quality of language in the manuscript:

Needs some language corrections before being published

**Declaration of competing interests**
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?
4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

'I declare that I have no competing interests'

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal.