Author’s response to reviews

Title: A botanical from the antiproliferative Cameroonian spice, Imperata cylindrica is safe at lower doses, as demonstrated by oral acute and sub-chronic toxicity screenings.

Authors:

Paul Nayim (nayimpaul@yahoo.fr)
Armelle T. Mbaveng (armbatsa@yahoo.fr)
Arsene M. Ntyam (arsenemsc@gmail.com)
Victor Kuete (kuetevictor@yahoo.fr)

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DETAILED ANSWERS TO REVIEWER 3

1) It is not clearly given for which treatment the root extract is considered. Several activities were described and one main target is the antiproliferative activity. For a cancer treatment 30 days seems to be too short to find conclusion.

-ANSWER: In the background, we highlighted the proven pharmacological properties of Imperata cylindrica, based on which, this plant can be a potential drug source. We have insisted on the anti-proliferative aspect because our team has carried out research on the anti-proliferative properties of this plant against several malignant cell lines, but to carry the study further it was necessary to get information about the toxicity of this plant. So, the current study was designed not to assess the in vivo antiproliferative activity of the plant, but to assess it acute and sub-chronical oral toxicity. We used healthy rats and the plant extract was administered to them daily during 30 days for sub-chronical study as. (OECD. Guidelines for the testing of chemicals, Test № 407, repeated dose oral toxicity study in rodents. 2008b; 1-14)

2) An explanation why to use roots extract when leaves apparently have the same or similar effect and why methanol root extract when aqueous root extract has same or similar effect is missing at all. Leaves are much easier to collect without destroying the plant (sustainable) and water extract is more useful and greener than methanol (its self is toxic and not common in pharmacy). This should be clearly explained and proven e.g. different metabolites in the different tissues and extractions etc.

-ANSWER: In this study, designed to evaluate the acute and subchronical toxicity of Imperata cylindrica, we used the roots instead of leaf because all our preliminary studies regarding the

In this study, we used methanol for metabolite extraction, but after the extraction process, the methanol was removed using a rotary evaporator (BÜCHI R - 200) at 65°C and the crude extract was recovered in a sterile vial and dried in oven at 40°C until the trace of extraction solvent completely evaporated, afterward the resulting product was dried to make sure our metabolites are totally methanol free. The extract used to perform all our experiments was methanol free.

3) The whole manuscript need to be revised very carefully for typos, unnecessary spaces, redundancies, commas

-ANSWER: The whole manuscript has been revised carefully as recommended by the reviewer, and the points he raised has been corrected.

4) whole manuscript: there is a lot of redundancy, e.g. mentioning the plant the extract is not needed in every third line; readers know after introduction which plant is used and in what concentration; smooth this to make the reading more attractive! Use abbreviations after they were introduced first time; correct in whole manuscript!

-ANSWER: The whole manuscript has been revised carefully as recommended by the reviewer, and the points he raised has been corrected.

5) It is not necessary to mention "below" for tables and figures; delete!

-ANSWER : This point has been corrected in the manuscript as recommended by the reviewer.

6) In the discussion many sentence are separated by "semicolon". Avoid and make clear full sentence instead.

-ANSWER: This point has been corrected in the manuscript as recommended by the reviewer.

7) whole manuscript: use always "b.w."

ANSWER: This point has been corrected in the whole manuscript as recommended by the reviewer.
8) page 5, line 32: write the first time in the text *Imperata cylindrica* as full name and in the following *I. cylindrica* - correct in the whole manuscript including figuer and table legends!

page 5, line 40: delete "activity" and twice "properties"

page 5, line 59: delete "of this plant"

page 6, lines 6 to 21: to gibe here all the IC50 values is not relevant and should be deleted!

page 6 line 36 to 41: rephrase the sentence "In addition, some chemicals ...."

page 9 line 21: instead of "04" write "four"

page 9, line 26: instead of "03" write "remaining three"

page 9, line 33: specify the test periode; how long it is? 30 days?

page 10, lines 30 to 35: dont use capitals; write "Haemo..." not "Hemo...">

page 10 line 45: insert "(TC)" for total cholesterol

page 11: line 41: rephrase; is not the pplant which kills!!

page 11, line 56: write "higher" instead of "greater"

page 12/13: each paragraph starts with the exact same sentence; rephrase!!!

Page 15, line 36: is the first hypothesis is rejected provide another

Page 15, lines 21 to page 16, line 9: rephrase the whole paragraph; is not in logical order

Page 16, line 29: abbreviations "SDH" and "GLGH" are not necessary as not used again!

Page 16, line 48 to 54: rephrase "so one can think" and "is not far from" - that is not scientifically correct language!

Page 17, line 16: explain the "many factors" in more detail

-**ANSWER :** All these points above have been carefully corrected in the manuscript as recommended by the reviewer.

9) page 16, line 6: if the effect of the plant is toxic why it should be used?????

-**ANSWER :** The toxicity of a plant mainly depends on used doses. In our study we have used 3 doses, and from the obtained results, the methanol extract of *I. cylindrica* is safe, but till a certain doses. However we encourage the use at lower doses (250, 500mg/kg) and we discourage the use of highest doses around 1000 mg/Kg b.w.

10) how decreased LDL in the present study can confirm the cited works of others?