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)

Version: 3 Date: 10 Jun 2020

Author’s response to reviews:

DETAILED ANSWERS TO REVIEWER 3

a)Comment 2) The answer is not really convincing; just because previous studies were done with roots - apparently solid studies with leaves are available - and most people use roots is a fact but lacks scientific novelty and improvement; for sustainable production is much easier to use leaves as a source of the drug without destroying the plant if is has - as stated - the same activity. For a good experimental design it would have been useful to include leaf extracts too. Regarding extraction, a water extract is much easier and environmentally friendly, so again why was a methanol extract used although authors ensure a methanol-free extract. Is much greener, easier and cheaper extraction and at least it should have been used as a control!!

ANSWER: (Additional answers)

-Why choosing roots?
This is a continuation of the previous studies performed by our research team on the roots. In fact, the roots are the parts traditionally used in Cameroon to treat cancers; We have previously demonstrated the cytotoxic effects of the root’s methanol extract on a panel of human cancer cell lines, such as CCRF-CEM, CEM/ADR5000, HL60 and HL60AR leukemia cell lines, MDA-MB231 and MDA-MB231/BCRP breast adenocarcinoma cell line, HCT116 p53+/+ and HCT116 p53-/- colon carcinoma cell line, U87MG, and U87MG.ΔEGFR gliobastoma cell line, HepG2 hepatocarcinoma cell line and Mia Paca2 pancreatic cancer cell line [Kuete V, Sandjo LP, Wiench B, Efferth T, et al. Cytotoxicity and modes of action of four Cameroonian dietary spices ethnomedically used to treat Cancers: Echinops giganteus, Xylopia aethiopica, Imperata cylindrica and Piper capense. J. Ethnopharmacol. 2013; 149: 245–253].
Hence, our aim is to use the roots as potential anticancer drug for two main reasons: They are commercially available, and extract from the roots had established cytotoxicity in vitro. The investigation of the toxicity profile of the leaf have now been added at the end of the discussion system, as their cytotoxicity, though not well investigated as that of the roots, have been reported.
-Why choosing methanol instead of water?
Thank you for this question; In fact, our previous study were based on methanol extract that displayed impressive cytotoxic effects in vitro [Kuete V, Sandjo LP, Wiench B, Efferth T, et al. Cytotoxicity and modes of action of four Cameroonian dietary spices ethno-medically used to treat Cancers: Echinops giganteus, Xylopia aethiopica, Imperata cylindrica and Piper capense. J. Ethnopharmacol. 2013; 149: 245–253]. The objective, is to assess the toxicity of that active extract instead of the water extract that was not previously studied in vitro.

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

ANSWER : (Additional answer)
Acute and sub-chronic oral toxicity assay of the roots methanol extract of I. cylindrica was to determine the short-term adverse effects of this plant when administered in a single dose an to determine the likely adverse effects to arise from repeated exposures of several months. From this toxicity we got information about a safe doses (around 250 and 500 mg/Kg) for future studies.

c)Comment 10: how decreased LDL in the present study can confirm the cited works of others? 
ANSWER : Additional correction on the manuscript (Discussion section).