Author’s response to reviews

Title: Identification of cryptolepine metabolites in rat and human hepatocytes and metabolism and pharmacokinetics of cryptolepine in Sprague Dawley rats

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RESPONSE TO REVIEWER COMMENTS

COMMENT 1: We note the addition of a new author since original submission of the manuscript, Colin Wright. In line with COPE guidelines, BioMed Central requires written confirmation from all authors that they agree with any proposed changes in authorship of submitted manuscripts or published articles.

RESPONSE: Professor Colin W. Wright’s (University of Bradford) name was mistakenly omitted in the original submission of the manuscript. He synthesized cryptolepine for some of the metabolism assays, contributed to the study design as well as manuscript drafting and reviewing. The initial omission was corrected during the first review months ago with the involvement of all co-authors. The recommended changes went through the Open Access Knowledge (OAK) system of Novartis AG, Basel, Switzerland. This was aimed at getting institutional and author confirmation for the changes made.
As at June 2017, Werner, Amanda, Adam and Caroline (Principal Investigator) were no longer at Novartis making it very difficult to contact them for any written confirmation. I will humbly request for more time to get the written confirmation or possibly resubmit the manuscript to your highly esteemed firm.

Thank you.

COMMENT 2: In line with our submission guidelines, please change the heading "Objectives" in the abstract to "Background" and rephrase it as a full sentence.

- Please also change the heading "Key Findings" to "Results."

RESPONSE: Changes effected as recommended.

COMMENT 3: If human cell lines are used, please include the source of the cell line in your Methods, along with the catalogue number.

RESPONSE: Hepatocytes were obtained from Bioreclamation IVT (catalogue numbers M00005 for rat and X008001 for human).

The source and catalogue number of the human cell line has been included on page 4 line 14-16 of the manuscript.

COMMENT 4: As your study includes the use of animals, please include an ethics statement in the Ethics approval section of your Declarations. A statement detailing compliance with relevant guidelines and ethical approval (including the name of the ethics committee and the reference number where appropriate) should be included.

RESPONSE: A statement detailing compliance to the Institutional Animal Care and Use is included in the manuscript (Page 5 line 33-35).

COMMENT 5: Please add a Funding section to your Declarations. All sources of funding for the research reported should be declared in this section. Please also state the role of the funding body
in the design of the study and collection, analysis, and interpretation of data and in writing the manuscript.

- Please note that any sections that are not applicable to your manuscript should still be included with the statement “Not applicable.”

RESPONSE: No external funding was obtained for this study (Not applicable).

COMMENT 6: Please upload your figures as separate figure files and remove them from the main manuscript. Please remove the figure titles and captions from these files and include them separately at the end of the main manuscript after References.

RESPONSE: Effected as suggested.

COMMENT 7: Upon uploading your revisions, please remove any tracked changes or highlighting and include only a single clean copy of the manuscript.

RESPONSE: All tracked changes and highlights have been removed.