Reviewer’s report

Title: Anti-viral activity of culinary and medicinal mushroom extracts against dengue virus serotype 2 : an in-vitro study

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Reviewer: Gayathri Chadalapaka

Reviewer's report:

The manuscript, 'Anti-viral activity of culinary and medicinal mushroom extracts against dengue virus serotype 2 : an in-vitro study' by Ellan et. al., demonstrated the likelihood of mushroom extract as an anti-dengue remedial agent along with exhibiting least toxic effect. The antiviral components were supposed to be glucan and protein complex present plentifully in the extracts.

This report is well written, clearly presented and experiments are designed well. The data presented clearly supports the hypothesis that antiviral activity of the extracts and is evidenced by reduction of ENV and NS5 genes in dengue-infected versus mushroom treated infected cells.

However, below are some comments to improve the quality of this report:

1. Mushrooms are edible as well as used by many populations as medicine. But is the dose used in this study biologically relevant? What is the rationale for choosing this dose? Because the authors use the extracts to prove antiviral activity, its applicability and relevance would be significant if the availability of the dose/active compound is biologically feasible considering oral bioavailability and metabolism.

2. Do the authors intend to suggest the human use of these mushroom extracts as a preventive measure or as a therapeutic measure? Are there any indications of these extracts altering the reproductive or physiological parameters in Aedes mosquito, upon feeding on human blood?

3. Generally most of the naturally derived agents carry a risk of nonspecific toxicity and off target effects. Did the authors evaluate the toxicity of the medicinal mushroom extract? Some medicinal/therapeutic mushrooms at high doses are shown to cause psycho-memetic effects in humans. Are there any toxic effects of these mushrooms reported in the literature?

4. The authors use only two dengue genes in this study (ENV and NS5). They looked at very limited markers to demonstrate that the mushroom extracts exhibit anti-dengue properties? NS1 is another dengue specific marker; did the authors look at that marker?

5. Viral markers specific for Dengue are Interleukins such as IL4, 10, 13, 1beta, 6, 8 and IP10 to name a few. Since the data looks promising, inclusion of dengue specific markers other than just ENV and NS5 will add support to the hypothesis.
6. Did the authors evaluate the effects of mushroom extracts on TNF-alpha, IL17 or other specific marker genes?

7. It is suggested that the authors include figures of few plaque reduction assays to show inhibition in in vitro setting.

8. Did the authors perform any in vivo studies? Since the results look promising (Fig 1) SchASE, LrASE and HeASE as compared to Ribavirin, it would be interesting to see how the antiviral activity translates into in vivo setting.

**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.

No

**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

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