Reviewer’s report

Title: Effects of ChondroT on Potassium Oxonate-Induced Hyperuricemic Mice: Downregulation of Xanthine Oxidase and Urate Transporter 1

Version: 0 Date: 25 May 2018

Reviewer: Vikneswaran Murugaiyah

Reviewer's report:

I recommend the manuscript for publication after some revisions on the issues raised below:

1. Abstract
   - The results should include some data.
   - Indicate the level of significance when describing the results.

2. Introduction
   - Hyperuricemia itself is not a disease but rather a condition whereby blood uric acid level is elevated. Suggest correcting the first sentence of this section.

3. Methods
   - It was mentioned that the extraction was carried out at 100°C for 3 hrs. The temperature seems high for extraction and may cause degradation of thermolabile compounds.
   - The three concentrations mentioned in XOD inhibition in vitro (100, 300 and 500µg/ml) are the initial concentrations. What are the final concentrations measured in the final reaction mixtures.
   - The number of mice used was 5 per group. Is that sample size sufficient for meaningful statistical analysis? Usually for studies using mice, a sample size of at least 8-10 will be employed.
   - In the animal study, potassium oxonate was administered intraperitoneally once daily for seven days. Will that cause stress and pain to the animals? What measures were taken to minimise the stress and pain in the animals.

4. Results
The IC50 for in vitro inhibition was 414µg/ml. How does one categorise the extract potency. Is it considered potent, moderate or weak inhibitor?

Authors did measure the XOD activity in serum and liver. However, in animals and human there are two kind of enzymes, namely xanthine oxidase (XOD) and xanthine dehydrogenase (XDH). Both are capable to breakdown hypoxanthine to xanthine and further to uric acid. Hence the measurement reported here could be a net activity of both XOD and XDH.

The concentrations shown in table 3 are the initial concentrations. Authors should mention the final concentrations in the reaction mixture and not the initial concentrations.

5. Discussion

In general, there is not much discussion in this manuscript. Authors should include more papers/literature data to support their findings and enrich the discussion.

ChondroT comprises of five plants. Is there any literature/papers describing the uric acid lowering effect of any of these plants? Likewise, is there any literature/papers describing the uric acid lowering effect of any of the compounds identified in chondroT (chlorogenic acid, berberine Cl, nodakenin, isoferulic acid, oxypeucedanin hydrate, decursin, and decursinol angelate).

In this study, ChondroT was found to reduce uric acid in hyperuricemic animals (hence having antihyperuricemia effect). Has ChondroT been evaluated in normouricemic animals to rule out any possible hypouricemic effect?

The present study suggests that ChondroT also works as uricosuric agent besides inhibiting XOD. It is well known that currently available uricosuric agents have very limited clinical use. Perhaps authors should highlight this limitation maybe applicable to ChondroT as well.

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
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