Reviewer’s report

Title: Chronic oral safety study of the aqueous extract of Combre tum molle twigs on biochemical, haematological and antioxidant parameters of Wistar rats

Version: 0 Date: 05 Aug 2019

Reviewer: Almir Gonçalves Wanderley

Reviewer's report:

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Please overwrite this text when adding your comments to the authors.

Questions

1. How were the doses chosen? Include in the text.

2. What is the reason for recording water consumption, animal weight every 2 months. Does the OECD 408 protocol recommend weekly registration?

3. The distilled water administered to the control group and as a vehicle of the treated groups did not produce diarrhea?

4. Check the Hb value (2.77 ± 0.09) of the control group?

5. Results needs to be reviewed. Only the dose 62.5 mg/kg produced a significant increase (p < 0.05) of the number of lymphocytes? table 5

6. The discussion needs to be reviewed. Some statements need proof.

eg "The change in internal organ weight is an indicator of atrophy and hypertrophy [24]. In this study, the relative weight of the internal organs did not undergo any significant change. This is explained by the lack of toxic effect of the extract on these organs ".

Was histology performed on these tissues?

"In this study, the concentration of these two enzymes (ALT and ASAT) decreased significantly in animals treated with doses of 125 and/or 250 mg/kg. These results show that CMAE may have a hepatoprotective effect ".

Is the reduction in ALT and AST sufficient to state that the extract has a hepatoprotective action?
7. Detailed revision of the manuscript

**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**
Please indicate the quality of language in the manuscript:

Needs some language corrections before being published

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