Reviewer’s report

Title: Antinociceptive activity of petroleum ether fraction obtained from methanolic extract of Clinacanthus nutans leaves involves the activation of opioid receptors and NO-mediated/cGMP-independent pathway

Version: 0 Date: 26 Dec 2018

Reviewer: Mona F Mahmoud

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Manuscript Number: BCAM-D-18-01581
Full Title: Antinociceptive activity of petroleum ether fraction obtained from methanolic extract of Clinacanthus nutans leaves involves the activation of opioid receptors and NO-mediated/cGMP-independent pathway.

The authors investigated the antinociceptive potential of orally administered petroleum ether extract of C. nutans, PECN (100, 250, 500 mg/kg) and determining the role of opioid receptors and L-arginine/nitric oxide/cyclic-guanosine monophosphate (L-arg/NO/cGMP) pathway in the observed antinociceptive activity. They found that PECN exerted antinociceptive activity at peripheral and central levels possibly via the activation of non-selective opioid receptors and modulation of the NO-mediated/cGMP independent pathway partly via the synergistic action of phenolic compounds.

The study is well designed but there are some points:

1- Please write the full words of any abbreviation in the text when you mentioned it for the first time like ICR, UPM........etc.
2- Please write the source of animals, housing conditions and number of animals/cage and food and water access type.
3- Why opioid antagonists are injected at different time intervals before the administration of the extract.
4- Why did not measure any biochemical parameter in blood like LOX or COX activities.
5- Statistical analysis. Why 2-way ANOVA was used. Something is missing in line 53:

5-Why the mechanism of action of the extract was investigated only in one model, acetic acid model only.
6- Why the highest dose level was only investigated?
7- In table legends, please write the doses, route of administration, duration in the title and write the full words of abbreviations in the footnote under the table.
8- In figure 5 A you mentioned L-NAME but there is nothing mentioned about it in the manuscript.
9- Please make a table containing the active constituents of the extract and their percentag
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 recommend additional statistical review

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

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