Reviewer’s report

Title: Anti-hyperalgesic properties of a flavanone derivative Poncirin in acute and chronic inflammatory pain models in mice

Version: 2 Date: 29 Nov 2018

Reviewer: Aniella Abi-Gerges

Reviewer's report:

In this study, the authors explored the anti-hyperalgesic properties of a flavanone derivative Poncirin in acute and chronic inflammatory pain models in mice. The results showed that Poncirin at a dose of 30mg/kg significantly reduce the mice pain behaviors including mechanical hyperalgesia and allodynia, thermal hyperalgesia and cold allodynia. These effects were associated with a reduction in the pro-inflammatory cytokines expression and an increase in Nrf2, HO-1 and SDO2 expression.

1- Edit: Written English

The text needs to be slightly edited before being published. Please have your manuscript revised/edited.

Ex:

- Abstract: Pretreatment with Poncirin

- P:4, line 33

- P: 10, lines 4, 5, 6, etc are repetition

- P:12: line 14: doesn't instead of don't

- P:12: line 22, title should include NO in plasma instead of is

2- Methods:

- Formalin-induced tonic pain model:
o Please explain whether the mice were observed for first 5 or 10 min (early phase) [Page 5, lines 55 and 56]. You mention in your methods that the early phase corresponds to the first 10 min and then state in your results (P: 10-line 39, P14-line 14, P20-Figure2) and figure 2 that the early phase corresponds to the first 5 min. Please correct.

- Assessment of mechanical allodynia in Carrageenan-treated mice

o Why did you measure the baseline withdrawal threshold one day prior to the experiments? (P: 6, lines 32-33). It is not clear whether you did the same for the other experiments. If yes, please mention it. If not, why was it specific to this experiment?

- CFA-induced chronic inflammatory pain model and Assessment of mechanical hyperalgesia and allodynia as well as thermal hyperalgesia induced by CFA

o P:7, lines 24, 47, 49: the protocol you used regarding the 6 days while excluding the 5th day is not clear. Please edit.

- Please explain why are you using different methods of euthanasia? P: 8 (CO2 chamber) and 9 (chloroform). Why didn't use only one method?

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
**Declaration of competing interests**

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