Reviewer’s report

Title: Radix Scrophulariae Extracts (Harpagoside) Suppresses Hypoxia-induced Microglial Activation and Neurotoxicity

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Reviewer: María Luisa Soto-Montenegro

Reviewer’s report:

The manuscript by Sheu et al describes the anti-inflammatory mechanism of harpagoside and the protection against hypoxia-induced toxicity on microglial cells. Despite of the originality of the manuscript, methods are not well described and discussion is somewhat bundled. The category for this manuscript is: Major Compulsory Revision.

1. Is the question posed by the authors well defined?
   Yes

2. Are the methods appropriate and well described?
   Not exactly. Although they describe in detail the different techniques, they do not include a design of the study and it is difficult to understand what exactly they have studied. Also, it is not clear if the experiments were repeated 4 times (page 8) or 3 times (page 10).

3. Are the data sound?
   Data sound well. However, they must include the statistical significance in the result section and in the figures. It is COX-2, not COX II as it appeared in the abstract and in the discussion sections.

4. Do the figures appear to be genuine, i.e. without evidence of manipulation?
   Yes

5. Does the manuscript adhere to the relevant standards for reporting and data deposition?
   Yes. Despite the results are very interesting, they have failed to capture it in the manuscript. Discussion would be rewritten. First, the problem in AD; second, the use of poliphenols and so on; and third, the findings

6. Are the discussion and conclusions well balanced and adequately supported by the data?
   Discussion is long. It must be shorter.

7. Are limitations of the work clearly stated?
   No

8. Do the authors clearly acknowledge any work upon which they are building, both published and unpublished?
   No, 33 references from 37 were written before 2008. Only 3 references are from
2012 and 1 from 2010. Authors must update the state of the art; and compare harpagoside with other compounds.

9. Do the title and abstract accurately convey what has been found?
   Yes

10. Is the writing acceptable?
    The manuscript requires revision of English

**Level of interest:** An article of importance in its field

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**
I declare that I have no competing interests' below