**Reviewer's report**

**Title:** In vitro antioxidant and cholinesterase inhibitory activities of Elatostema papillosum leaves and correlation with their phytochemical profiles: a study relevant to the treatment of Alzheimer's disease

**Version:** 1  **Date:** 13 Sep 2017

**Reviewer:** Jason Eriksen

**Reviewer's report:**

In this revised manuscript, the authors have made a number of changes that have moderated the discussion and improved the overall quality. I appreciate the general degree of responsiveness displayed by the authors. I do however have a few suggestions that I feel will improve the overall quality of the final manuscript:

page 3, line 56: there is substantial loss of both cholinergic and cortical neurons, not just cholinergic neurons. Furthermore, the term "associated cognitive deficits" is not entirely clear; this should be revised to reflect specific cognitive deficits.

Pg 3, ln 64: "The aberrant accumulation of ROS is the causative agent for a range of chronic diseases, including AD, by inducing oxidative stress [8, 9]." This statement that ROS is the triggering agent does not reflect current scientific consensus in the field of Alzheimer's disease. A variety of studies have looked at ROS and therapeutic interventions in this area exhibit no clinical impact on the progression of disease. While I think it's fine to stay to that ROS scavenging may positively impact the disease, the authors should revise their statements to reflect current scientific consensus.

Pg 11: in addition to a set of cholinesterase inhibitors, memantine (an NMDA blocker) is also used as a pharmacological agent. The authors should revise the wording in the discussion to reflect the pharmacological treatments that are currently available.
Pg 12: The authors repeatedly imply that a benefit of EPL - M80 is potentially reduced toxicity compared to that reported with synthetic agents like Aricept. Typically the toxicity of current cholinesterase inhibitors is primarily due to the inhibition of acetylcholinesterase. Consequently, it is not clear why the Authors expect that EPL - M80 will have an improved toxicity profile over synthetic agents when given at therapeutic concentrations, particularly since this is not been assessed in animal studies. The IC50 of EPL-M80 appears substantially greater than that of synthetic compounds. While the current traditional use of EPL may not have toxicity, the extract is a highly concentrated form and if given in doses that are sufficient to inhibit acetylcholinesterase, there is likely to be a similar degree of toxicity. The authors should word their discussion carefully so as to not oversell EPL-M80.

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

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