Author’s response to reviews

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

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Author’s response to reviews:

Dear Editor and Reviewers

Thank you for your positive comments and providing me the revision opportunity for our manuscript entitled “In vitro antioxidant and cholinesterase inhibitory activities of Elatostema papilloseum leaves and correlation with their phytochemical profiles: a study relevant to the treatment of Alzheimer's disease”. We have made necessary changes (red colored) in the revised manuscript as the reviewer suggested. In the following I have written a point-to-point response to address the reviewer’s concern.

We believe the manuscript has been improved substantially after necessary revisions. Therefore, it would be highly appreciated if you kindly consider our manuscript for publication in your journal.
Sincerely

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A response to reviewer’s comments

Sarada Subramanian (Reviewer 1):

Minor comments:

Comments-1: Since no pharmacological effects of Elatostema papillosum have been reported till date, the authors may explain as to what prompted them to choose this plant for their studies.

Response: In the background section in page no. 4, line 79-85, we have mentioned in details regarding the reasons of choosing this plant for study.

It has been mentioned clearly in the text- “In our traditional medicine, the plant, Elatostema papillosum, has widely been used by local practitioner against various diseases, including hysteria [1], which is characterized by psychological disorder whose symptoms (include conversion of psychological stress into physical symptoms (somatization), selective amnesia, shallow volatile emotions, and overdramatic or attention-seeking behavior) are closely related with Alzheimer’s disease [2]. The use of this plant as traditional medicine against hysteria was the basis to carry out the pharmacological activity of this plant in this study”.

It may be mentioned here that this plant has not been documented in the Ayurvedic or Unani types of traditional medicine.
Comments-2: Since no information is available regarding the safety/ toxicity of this plant species, the authors need to add a comment on these in their 'Discussion'.

Response: We have mentioned in the discussion section in page no. 13, line no 292-293 regarding the safety of the plant- “The widespread traditional uses of EPL (leaves of Elatostema papillosum) suggest there are no toxic effects on the human body as a result from therapeutic doses and it is primarily assumed that EPL is free from toxic hazards”[1].

We have further added in discussion section in page no. 14, line no. 305-306 – “Further studies are necessary to evaluate the neuroprotective effects and the safety/toxicity profile of the plant in animal model”.

References


Jason Eriksen (Reviewer 2):

Comments-1: Evidence is provided that supports the idea that EPL - M80 has anti-cholinesterase activity in vitro, but there is no evidence in this manuscript to support claims that this extract has relevance in vivo; there are no experiments show in vivo activity and or that this agent can successfully cross the blood brain barrier.

Response: This study was carried out in vitro in cell free assay, which is relevant in vivo, to investigate the acetylcholinesterase and butyrylcholinesterase inhibitory and antioxidant activities of the crude methanol extract of Elatostema papillosum and to characterize the type of compounds responsible for the activities. The finding of the study is interesting and significant. The data presented here has demonstrated the potential of this plant in the inhibition of
cholinesterases and the multiple components of oxidative stress. It has been further shown that the polyphenolic compounds are possibly responsible for the activities.

These studies warrant testing of this plant in an animal model and to identify the active compound that crosses the blood-brain barrier, which is our next plan of research.

Comments-2: There are numerous, generally small, errors in word choice and grammar. The authors need to carefully review and revise their work to eliminate these errors.

Response: According to the reviewer’s suggestions, we have extensively revised our manuscript and tried our level best to eliminate all grammatical errors that we marked in red color throughout the manuscript.

Comments-3: Antioxidant agents have a very limited impact on in vivo degradation of acetylcholine.

Response: Antioxidant agents from plant sources are mostly phenolic and flavonoid type of compounds. They are found to be effective not only in neutralizing the oxidants, but also in the inhibition of the cholinesterases. Examples of these compound are gallic acid, catechin, (−)-epigallocatechin-3-gallate, quercetin, etc. I have mentioned here two references of review articles in this regard [1. Ana Paula Murraya, María Belén Faraonia, María Julia Castroa, Natalia Paola Alzaa and Valeria Cavallaro. Natural AChE Inhibitors from Plants and their Contribution to Alzheimer’s Disease Therapy. Current Neuropharmacology, 2013, 11, 388-413; 2. Yara Hassaan, Heba Handoussa, Ahmed H. El-Khatib, MichaelW. Linscheid, Nesrine El Sayed, and Nahla Ayoub. Evaluation of Plant Phenolic Metabolites as a Source of Alzheimer’s Drug Leads. BioMed Research International, volume 2014, Article ID 843263, 10 pages.]

Comments-4: Antioxidants have not shown any degree of effectiveness in slowing signs or progression of Alzheimer's disease in clinical trials.
Response: It is still true that antioxidant itself has not shown effectiveness in slowing signs or progression of Alzheimer's disease in clinical trials. Oppositely, it is now established that oxidative stress is an important feature of AD. Excessive lipid peroxidation, protein oxidation, DNA and RNA oxidation, glycooxidation have all been documented in AD brains. Since AD is a multifactorial disease, it is thus suggested that a drug candidate that will target the cholinesterases and multiple components of the oxidative stress would be considered as effective lead drug candidates for the treatment of AD.

Comments-5: Statistical differences are not indicated on the graphs. A Dunnet's test is used but differences between groups are not shown.

Response: Thank you for your comment. According to your suggestion, statistical differences between groups have shown in the revised graphs.