Author’s response to reviews

Title: Phytochemical profiling and in vitro screening for anticholinesterase, antioxidant, antiglucosidase and neuroprotective effect of three traditional medicinal plants for Alzheimer's Disease and Diabetes Mellitus dual therapy

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Answers to the comments of Reviewers

Greetings for today. We thank the reviewers for their valuable suggestions and comments which helped to strengthen our manuscript. According to their suggestions, changes have been incorporated in the revised manuscript. All the modifications are highlighted in ‘yellow’ colour. The point by point changes and explanation to the reviewer’s comments are given below.

Answer to the queries raised by Reviewer 1

1. Title was revised as per the suggestion of reviewer and the abbreviations were expanded in the title. As same terms need to be repeated several times in abstract, abbreviations become inevitable. Hence, as per reviewer’s suggestion, abbreviations were explained on first use in the abstract.

2. According to reviewer, language errors were corrected in page 3. Introduction was shortened as per reviewer’s suggestion. The present work aimed at evaluating biological
potentials of three titled plants as multifunctional agents to use in the AD and T2D dual therapy. Hence, they were screened against many targets using several methods. Finally, with all the data obtained, we proved that the chloroform fractions of methanol extract of titled plants as multifunctional therapeutic remedy for the treatment of diabetes and Alzheimer’s disease simultaneously.

3. While revising the introduction, line 60 in page 3 was omitted.

4. According to reviewer, page 5, line 90-92 (at present 81-82) was corrected. As part of our project, we screened large number of plant extracts and the most active plants were selected for publication in the present manuscript.

5. As per reviewer’s suggestion, table 2 was deleted and information in table 2 was included in extraction section. However, Table 1 was retained and information regarding reported biological activities of titled plants was also included in Table 1 to avoid too lengthy introduction.

6. According to reviewer, the results and discussion section was modified. Results were described first followed by discussion of findings.

7. In all in vitro assays, positive controls were used. Statistical comparison of test samples and controls were included in the revised manuscript.

8. Yes we do agree with reviewer’s statement regarding alpha-glucosidase and alpha-amylase targets for management of diabetes. However, our group has proposed and carried out a project on alpha- and beta-glucosidase inhibitors for management of diabetes based on review reports in literature and the obtained results were discussed in the manuscript. One main review was mentioned hereunder for reviewer’s perusal “E. Borges de Melo et al. Tetrahedron, 62 (2006) 10277–10302”.

9. According to the “cholinergic hypothesis”, AChE acts primarily as a regulatory enzyme at cholinergic synapses, while BuChE functions as an enzyme closely related to AChE and serves as a co-regulator of cholinergic neurotransmission by hydrolysing ACh. It was also reported that during the development of AD, BuChE activity increases by 40–90% in the most affected brain areas such as the temporal cortex and hippocampus while at the same
time AChE activity declines. Moreover, high levels of BuChE are found to have a role in amyloid beta-peptide aggregation during the early stages of senile plaque formation as well as in other pathological characteristics of AD. Therefore, inhibition of BuChE, not only AChE, may have clinical benefits in treating symptoms and alleviating the manifestation of AD.

References


10. The cell survival was increased with escalating cell proliferation even in the presence of high concentrations and thus considered as nontoxic to SK N SH cells. This observation suggests that certain compounds present in fractions were likely to promote cell survival or delay the natural death of neurons in culture medium.

11. As per Reviewer’s advice, Correlation analysis between phytochemical profile and biological activity was carried out and discussion in this regard was included in the revised manuscript.

Answer to the queries raised by Reviewer 2

1. Neuroblastoma cell line SK N SH is one of the most extensively used cell lines to study diabetic neuropathy in the literature (Hattangady et al. In vitro models of diabetic neuropathy, Int J Diab Dev Ctries, 2009, 29 (4), 143-149). Similarly, neuroblastoma cell line was also used to assess neuroprotectivity in previous reports on AD. Ref: 1). Rizzo et al. European Journal of Medicinal Chemistry, 58 (2012) 519-532. 2). Ykwon et al.
2. Corresponding controls were included for each in vitro study.

3. Present study is mainly focused on in vitro screening of plant extracts and fractions. As per reviewer’s suggestion, in vivo studies will be carried out in due course.

4. The figure legends were rearranged and related details were included in the text.

Answer to the queries raised by Reviewer 3

1. The abbreviations were expanded in the title. As per reviewer’s suggestion, abbreviations were explained on first use in the abstract as well in the manuscript.

2. T2D abbreviation is included in the list.

3. Formatting inconsistencies were rectified in the revised manuscript.

4. As per reviewer’s suggestion all in vitro assays were mentioned in line 253-254.