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Chemical Profiles and In Vitro Cholinesterase Inhibitory Activities of the Flower Extracts of *Cassia spectabilis*: A Comparative study

SUBMITTED

Suciati - [SA](#) [CA](#) ¹ - [Hide Affiliations](#)
Airlangga University¹

Article Type
Research Article

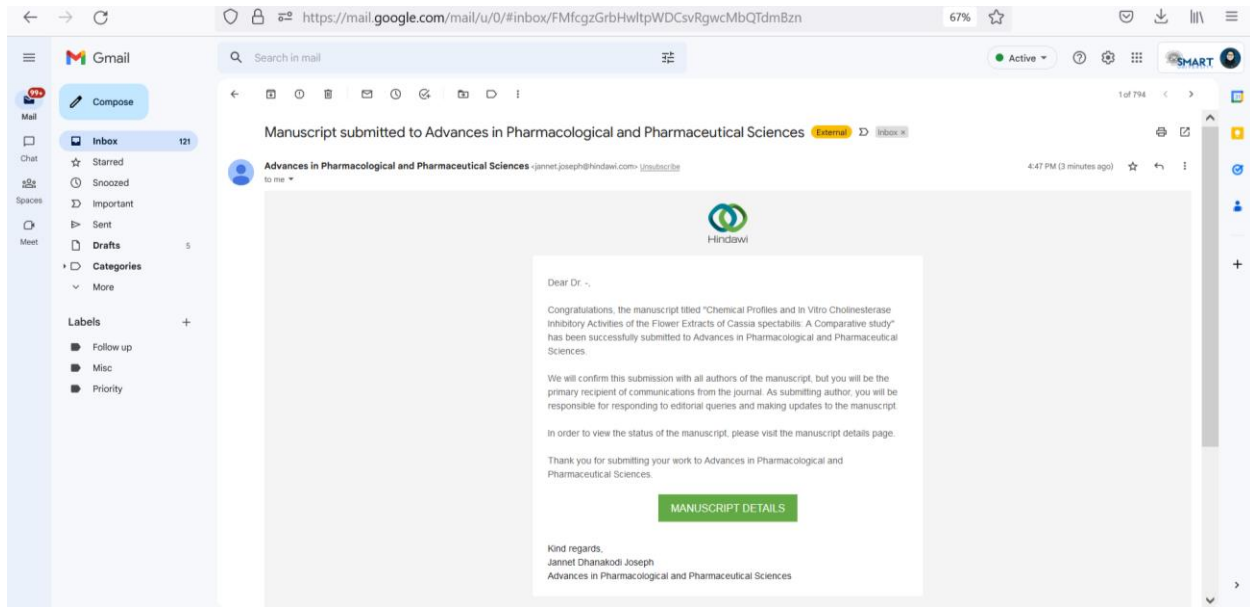
Journal
Advances in Pharmacological and Pharmaceutical Sciences

Academic Editor Unassigned Submitted on 2022-11-28 (3 hours ago)

▼ **Abstract**

Background. *Cassia spectabilis* is a flowering plant containing various metabolites that provide potencies for pharmacological activities. The objectives of the current study were to investigate the ethanolic and water extracts of *Cassia spectabilis* as cholinesterase inhibitor as one of the target treatments for Alzheimer's disease and to investigate the chemical composition in the extracts. Methods. The cholinesterase inhibitory activity assay was carried out by the modified Ellman's method against acetylcholinesterase (AChE) and butyrylcholinesterase (BChE). LC-MS/MS analysis was carried out to investigate the chemical profiles of the extracts followed by a molecular networking study by GNPS. Results. Both extracts showed inhibition against AChE and BChE in a dose-dependent manner, with the higher potency exhibited by the ethanolic extract with IC50 values of 7.9 and 3.8 µg/mL. The chemical analysis and molecular networking study of the flower extracts revealed similarity between the

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— Editorial Comments

Recommendation Kuldeep Singh 28.12.2022
 Major Revision Requested

Message for Author
 Please revise manuscript as suggested by reviewers.

— Reviewer Reports 1 submitted

Report Reviewer 3 26.12.2022

After extensive revision, the current study of *C. spectabilis* on cholinesterase inhibitory effect can be approved. Here are a few of the comments:

1. At the conclusion of the Introduction section, the hypothesis and novelty of the study can be stated clearly.
2. The results can be made contemporaneous (by providing references) with other studies of *C. spectabilis* in brain conditions other than Alzheimer's in the Discussion section.
3. The Conclusion section can provide limitations and look ahead viewpoints.
4. Was it possible to determine *C. spectabilis*'s ability to inhibit cholinesterase in an animal model of Alzheimer's disease?
5. Plant names need to be italic

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Revisi 1

Response to Reviewers' Comments 1

Manuscript Title: Chemical Profiles and *In Vitro* Cholinesterase Inhibitory Activities of the Flower Extracts of *Cassia spectabilis*: A Comparative study

Reviewers Comments	Response
<p>At the conclusion of the Introduction section, the hypothesis and novelty of the study can be stated clearly.</p>	<p>The introduction section has been revised to state the hypothesis and novelty of the study as follows:</p> <p>In the development of herbal medicine product for the treatment of Alzheimer's disease from <i>C. spectabilis</i>, information on the extraction solvent that gives the optimum potency as a cholinesterase inhibitor is needed. Traditional use of the plant as an infusion and decoction has been documented [12]. Meanwhile, studies on the methanolic extract of <i>C. spectabilis</i> flower as cholinesterase inhibitor has been reported [23]. Therefore, it is interesting to know which extraction solvents that will give the best cholinesterase inhibitory activity. The current study evaluated the cholinesterase inhibitory activities and the phytochemical profile of the water and ethanolic extracts of <i>C. spectabilis</i> flowers. We hypothesize that different extraction solvents will have effect on the chemical profiles and the</p>

	<p>cholinesterase inhibitory activities. To the best of our knowledge, there is no report on the effect of different extraction solvents to the cholinesterase inhibitory activity and the chemical profile of <i>C. spectabilis</i> flower.</p>
<p>The results can be made contemporaneous (by providing references) with other studies of <i>C. spectabilis</i> in brain conditions other than Alzheimer's in the Discussion section.</p>	<p>Other studies of <i>C. spectabilis</i> related to brain diseases other than Alzheimer's have been added to the discussion section as follows:</p> <p>Studies on the effect of <i>C. spectabilis</i> on central nervous system disorders have been documented. The ethanolic extract of <i>C. spectabilis</i> leaves showed anticonvulsant and sedative activity in mice [12]. Further study by Nkantchoua et al (2018) investigated the anticonvulsant activity of <i>C. spectabilis</i> leaves decoction. The oral administration of the decoction can completely inhibit seizure in mice induced by maximal electroshock, antagonizes completely seizures induced by pentylenetetrazole, and partially inhibit seizure induced by bicuculline [29]. Silva et al (2011) reported that iso-6-cassine and iso-6-spectraline isolated from <i>C. spectabilis</i> possess anticonvulsant and depressant effects on mice [19, 30]. Oral administration of iso-6-cassine and iso-6-spectraline at a dose of 1.5 mg/kg BW and 1.0 mg/kg BW, respectively, can significantly decrease motor activity of the animal on rota-rod apparatus. Both compounds were capable of promoting an increase in latency for the development of convulsion triggered by picrotoxin.</p>
<p>The Conclusion section can provide limitations and look ahead viewpoints.</p>	<p>The limitation of the study and look ahead viewpoints have been added in the conclusion section as follows:</p> <p>The ethanolic extract of <i>C. spectabilis</i> flowers displayed higher potency as cholinesterase inhibitors compared to the water extract. Despite the qualitative analysis of the component in the extract, the presence of piperidine alkaloids in the extract may be responsible for the bioactivity. Future works could focus on the quantitative analysis of the alkaloid in the extract and the <i>in vivo</i> study using using Alzheimer's disease animal model in the behavioural assays.</p>
<p>Was it possible to determine <i>C. spectabilis</i> ability to inhibit cholinesterase in an animal model of Alzheimer's disease?</p>	<p>The animal model study is currently being carried out in our lab. Suggestion for animal study has been added in the conclusion section</p>

Plant names need to be italic

Thank you, all plant names have been revised written in italic.

Please note

1. Correction as requested by reviewers are written in green highlighted texts
2. Additional correction made by authors included in yellow highlighted texts: addition of references, information, and revision of grammar

The screenshot shows a web browser window with the URL <https://review.hindawi.com/details/d83ab4df-a832-4a18-a8ae-863a181033d6/cc5e194a-1560-47c6-b1e>. The page is titled "Response to Revision Request" and displays two reviewer reports. The first report, from Reviewer 3 dated 02.02.2023, contains the following text: "page 2 line 67 'medicine' should be 'medicinal'. page 3 line 98 'vacuo' should be 'vacuum'. The 'results and discussion' section can be enriched with the following references. -Determination of Cholinesterase Inhibition Potential of Rose Extract. Anadolu Tarim Bilim. Derg./Anadolu J Agr Sci. 2018, 33, 237-240. -Inhibitory Effects and Kinetic-Docking Studies of Xanthohumol from Humulus lupulus Cones against Carbonic Anhydrase, Acetylcholinesterase and Butyrylcholinesterase. Natural Product Communications. 2019. 14 (10), doi.org/10.1177/1934578X19881503. -Biological activity and molecular docking studies of some N-phenylsulfonamides against cholinesterases and carbonic anhydrase isoenzymes. Journal of molecular recognition. 2022, doi: 10.1002/jmr.2982." The second report, from Reviewer 2 dated 18.01.2023, says: "I have a few more comments to the authors and hope that the authors can rectify the comments ASAP so the publication process will be smooth. Best wishes. The comments are included in the attached file." Below the second report, a file named "manuscript Cassia spectabilis-submitted-rev2.docx" (405 kB) is listed with a download icon.

Revisi 2

Response to Reviewers' Comments 2

Manuscript Title: Chemical Profiles and *In Vitro* Cholinesterase Inhibitory Activities of the Flower Extracts of *Cassia spectabilis*

Reviewers Comments	Response
Line 21-22: for what the extract, I would suggest to split the objective to 3 obj and reword	The objectives of the study have been revised as follows: The current study aimed to investigate the ethanolic and water extracts of <i>C. spectabilis</i> as cholinesterase inhibitor as one of the target treatments for Alzheimer's disease. The chemical composition of the extracts was also studied to find out which components that may responsible for the bioactivity.
Line 67: "medicine" should be "medicinal"	Has been revised as suggested
Line 98: "vacuo" should be "vacuum"	Has been revised as suggested

Line 157-158: Where can I see this outcome in the figure 1. Cause your figure only end at log concentration 3.	Figure 1 is the plot of Log concentration and %inhibition of samples. The IC ₅₀ values of the ethanolic extract were of 7.88 µg/mL and 3.78 µg/mL. These values are in the graph which are equivalent to 0.987 and 0.577 (Log 10)
Figure 2: Please include an arrow in the figure from 19-33 min indicating not the same	The arrow showing region at 19-31 minutes has been added to Figure 2.
Tables 2 and 3: Maybe you should add ## or * at the same compounds found in the water and ethanol extracts in table.	Thank you for the suggestion. We have added "*" to the compounds that were identified in the water and ethanol extracts
Line 246-248: Include at least 2 references	References have been added
The "results and discussion" section can be enriched with the following references. - Determination of Cholinesterase Inhibition Potential of Rose Extract. Anadolu Tarım Bilim. Derg./ Anadolu J Agr Sci. 2018, 33, 237-240. -Inhibitory Effects and Kinetic-Docking Studies of Xanthohumol from Humulus lupulus Cones against Carbonic Anhydrase, Acetylcholinesterase and Butyrylcholinesterase. Natural Product Communications. 2019. 14 (10), doi.org/10.1177/1934578X19881503. - Biological activity and molecular docking studies of some N-phenylsulfonamides against cholinesterases and carbonic anhydrase isoenzymes. Journal of molecular recognition. 2022, doi: 10.1002/jmr.2982.	Thank you for the suggestion. The discussion section focusses on the potency of the <i>C. spectabilis</i> and other species from the genus <i>Cassia</i> , as well as piperidine alkaloids as cholinesterase inhibitor. Therefore, we did not include the references suggested by reviewers

Please note: correction in the manuscript is yellow highlighted

3. Acceptance Letter

The screenshot shows a Gmail interface with a sidebar on the left containing navigation options like Mail, Compose, Inbox (178), Starred, Snoozed, Important, Sent, Drafts (6), Categories, and Labels. The main content area displays an email from 'Advances in Pharmacological and Pharmaceutical Sciences' received on Fri, Feb 17, 5:05 PM. The subject is 'Your manuscript has been accepted for publication'. The email body features the Hindawi logo and a message to 'Dear Dr. Suciati', stating that the review of her research article (6066601) is complete and it has been accepted for publication. It also provides instructions on how to access the manuscript details page and update the preprint server.

This screenshot shows the continuation of the email content. It includes the following text:

publication in *Advances in Pharmacological and Pharmaceutical Sciences*.

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- > Author Declaration
- > Files 2

— Editorial Comments

Recommendation Publish Kuldeep Singh  17.02.2023

+ Response to Revision Request

+ Reviewer Reports 1 submitted

+ Submit Quality Check Updates

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4. Galley Proof

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Feb 24, 2023, 4:49 PM ☆ ↶ ⋮

Dear Dr. Suciati,

I am pleased to let you know that the first set of galley proofs of your Research Article 6066601 titled "Chemical Profiles and In Vitro Cholinesterase Inhibitory Activities of the Flower Extracts of *Cassia spectabilis*," is ready. You can apply your corrections directly to the manuscript with the Online Proofing System (OPS).

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Best regards,

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Dear Dr. Suciati,

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Jannet Dhanakodi Joseph <jannet.joseph@hindawi.com>
to me ▾

Wed, Mar 1, 5:16 PM ☆ ↶ ⋮

Dear Dr. Suciati,

I am pleased to let you know that your article has been published in its final form in "Advances in Pharmacological and Pharmaceutical Sciences."

Suciati, "Chemical Profiles and In Vitro Cholinesterase Inhibitory Activities of the Flower Extracts of *Cassia spectabilis*," *Advances in Pharmacological and Pharmaceutical Sciences*, vol. 2023, Article ID 6066601, 9 pages, 2023. <https://doi.org/10.1155/2023/6066601>.

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