

Submission Confirmation

1 message

pharm.sci.tabriz@gmail.com <pharm.sci.tabriz@gmail.com>
To: mahardianr@ff.unair.ac.id

Tue, Oct 19, 2021 at 1:20 PM

Pharmaceutical Sciences

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Submission Confirmation

Dear Dr. Mahardian Rahmadi,

Your manuscript entitled Andrographolide and epigallocatechin gallate (EGCG) lower the risk of addiction induced by nicotine and cigarette smoke extract (CSE) in mice has been successfully submitted and is presently being given full consideration for publication in Pharmaceutical Sciences.

Best Regards

Editorial Office of Pharmaceutical Sciences (PS)

Manuscript Id: ps-34766



Your Submission

1 message

pharm.sci.tabriz@gmail.com <pharm.sci.tabriz@gmail.com>

Fri, Nov 5, 2021 at 5:28 PM

To: mahardianr@ff.unair.ac.id

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Your Submission

Dear Dr. Mahardian Rahmadi

With thanks for your submission entitled "Andrographolide and epigallocatechin gallate (EGCG) lower the risk of addiction induced by nicotine and cigarette smoke extract (CSE) in mice", please find out the reviewers' comments as follow. Reviewers have now commented on your paper. You will see that they are advising that you revise your manuscript. If you are prepared to undertake the work required, I would be pleased to reconsider my decision. If you decide to revise the work, please submit a list of changes or a rebuttal against each point which is being raised when you submit the revised manuscript.

The deadline for submission of revision is two months after receiving a decision on manuscript.

Thanks again for your cooperation.

Best Regards, Ali Shayanfar (Pharm.D and Ph.D.) Editor-in-Chief

Pharmaceutical Sciences-Indexed in ESCI (Web of Sciences) and Scopus https://ps.tbzmed.ac.ir/

Reviewer 1:

Manuscript: "Andrographolide and epigallocatechin gallate (EGCG) lower the risk of addiction induced by nicotine and cigarette smoke extract (CSE) in mice"

The authors wanted to investigate the role of andrographolide and EGCG on the addiction behavior induced by nicotine and cigarette smoke using the conditioned place preference method. The manuscript is well written, and the study provided a descriptive approach to the positive effect of andrographolide and EGCG on mice reward effects upon exposure to nicotine or cigarette smoke extract. However, some points should be addressed to persuade the reviewer.

Major comments:

The authors claim in the abstract that "Nicotine addiction occurs through increased reactive oxygen species production in nucleus accumbens, which

causes damage to the endogenous antioxidant defense system resulting in an increased need for nicotine intake, leads to addiction". This stamen was also reported in the introduction "The same thing happened to nicotine, where nicotine exposure resulted in ROS production that contributed to drug addiction." However, there are no references that support the fact that increased ROS is related to nicotine addiction. It is known that nicotine addiction is related to the activation of nicotine acetylcholine receptors that activate dopamine secretion. Additionally, the increase of oxidative stress associated with nicotine is reported to be dose-dependent. Therefore, the review suggests discussing this and presenting only as a hypothesis that ROS induced by cigarette smoke or nicotine could partially contribute to the addiction to nicotine.

Since the authors did not measure any marker related to oxidative stress in the different treatment groups, they should re considering if the positive effects related to andrographolide and epigallocatechin gallate (EGCG) supplementation are related to their antioxidative properties or with some influence of the antioxidants in the dopamine secretion levels, dopamine receptor activity or related signaling pathways. For example, it is reported that N-acetylcysteine enhances dopamine receptor binding [1]. The reviewer suggests discussing this topic and not limiting the positive effect to only the anti-oxidative properties of andrographolide and EGCG.

The authors have performed a one-way Anova turkey post hoc test, assuming a normal data distribution. Since the absolute number of mice in each study group was 5 and only one technical replicates was measure for each biological replicate, normal distribution could not be considered. The authors should perform a non-parametric test or demonstrate normal distribution of the data set.

The authors should report the nicotine concentration in CSE, to know if it is in the same range of nicotine concentration used in the study. The concentration of CSE is twice the dose of nicotine doesn't assure that the concentration of nicotine of the different groups (CSE or nicotine treatred mice) is comparable.

The authors said that "Based on the results of previous studies, administration of CSE provides a more significant reward effect than administration of nicotine alone because CSE contains ingredients other than nicotine which function to inhibit monoamine oxidase (MAO), which increases dopaminergic and serotonergic neurotransmitters that contribute to self-administration or addiction". However, the more significant reward effect could also be related to increased nicotine concentration levels in the CSE group compared to the nicotine exposure group. Measure cotinine levels in the study groups would be highly recommended to know the level of exposure to nicotine in all study groups. The reviewer also suggests discussing the limitations of the study regarding the lack of knowledge of the nicotine concentration on the CSE extract and the study groups.

The dose of CSE and nicotine used in the study has been optimized to produce a reward effect, however, correlate these doses with the nicotine levels of smokers? Please discuss about it.

Additionally, "Both nicotine and CSE were administered to mice by the subcutaneous route because, based on previous studies, the use of this route provided a stronger and more consistent addictive effect than the intravenous route. Furthermore, the dose of andrographolide and EGCG used was 50 mg/kg BW. The route of administration used for andrographolide and EGCG is intraperitoneal because of the faster onset of action before exposure to nicotine or CSE." The subcutaneous administration of nicotine and CSE and the intraperitoneal administration of antioxidants is far from the way in smokers and not feasible as preventive therapy. Therefore, the review suggests discussing this limitation of the study.

Additionally, the authors conclude that "andrographolide and EGCG lower the risk of addiction and potential to be developed as preventive therapy for smoking cessation", however, it could be interesting to discuss if the

concentrations of antioxidants used in this study could be archived by oral intake if this wants to use as supplementation to enhance the successful to quick smoking.

The authors claim that there was loss of smoke during the CSE extraction and mention that this could explain the not significant differences observed on the average CPP score between nicotine and CSE groups. Could it not be due to lower nicotine exposure in the CSE treated group?

Minor comments:

Foreign words should always be in italic (e.g., in vivo)

temperature (25 ± 2) should be changed to temperature (25 ± 2 °C)

Several references are missing e.g.: "Increased ROS, if not balanced with endogenous antioxidants, such as SOD, causes desensitization of nAChRs implicated in the risk of nicotine addiction increases

Reviewer 2:

The authors investigated the Andrographolide and epigallocatechin gallate (EGCG) lower the risk of addiction induced by nicotine and cigarette smoke extract (CSE) in mice. There are several concerns. Below I have listed my specific concerns.

- 1-Evidence should be presented for "Lots of in-vivo models have been developed to investigate possible pharmacological solutions" in introduction.
- 2-Authors should mention the physiological/reproductive status of the mice.
- 3-There are many typographical and English language usage errors in the manuscript. The paper should be proofread carefully for proper English language usage. It is advised that the authors should turn to linguistic editing in English.

Reviewer 3:

- 1. The English of manuscript carefully should be checked and improved.
- 2. Please expand abbreviations such as EGCG and CSE when you use them for the first time.
- 3. The results in abstract should be improved and compared between groups. In addition, P values should be mention.
- 4. Introduction has been not started properly. Please improve it.
- 5. Please mention the name of the city and country where the project was completed in Experimental Animals section.
- 6. Please mention groups in material and methods based on grouping presented in figures.
- 7. How did you select doses of drugs and injection time?
- 8. Please omit the first paragraph in Data Analysis section.
- 9. Please mention P values in results part.
- 10. In this study, the authors declared that andrographolide and epigallocatechin gallate exerted their effects on the risk of addiction induced

by nicotine and CSE via improving oxidative status. It strongly is suggested to measure oxidant and antioxidant parameters to further verify this effect.

11. Discussion is very long. Please modify it.



Revised Manuscript

pharm.sci.tabriz@gmail.com <pharm.sci.tabriz@gmail.com>
To: mahardianr@ff.unair.ac.id

Tue, Jan 4, 2022 at 3:10 PM

Pharmaceutical Sciences

Pharmaceutical Sciences



Revised Manuscript

Dear Dr. Mahardian Rahmadi,

Your revised manuscript entitled "Andrographolide and epigallocatechin gallate (EGCG) lower the risk of addiction induced by nicotine and cigarette smoke extract (CSE) in mice" has been successfully submitted and is presently being given full consideration for publication in Pharmaceutical

Sciences.

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Your Submission

1 message

pharm.sci.tabriz@gmail.com <pharm.sci.tabriz@gmail.com>

Tue, Jan 25, 2022 at 7:49 PM

To: mahardianr@ff.unair.ac.id

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Your Submission

Dear Dr. Mahardian Rahmadi

We are pleased to inform you that your manuscript entitled "Andrographolide and epigallocatechin gallate (EGCG) lower the risk of addiction induced by nicotine and cigarette smoke extract (CSE) in mice" has been accepted for publication in Pharmaceutical Sciences. Please note that you will be able to make any necessary corrections to your paper when you receive the production proofs. The production proofs will be emailed to you within the next few months. Many thanks for submitting your fine paper to Pharmaceutical Sciences. We look forward to receiving additional papers from you in the future.

Best Regards, Ali Shayanfar (Pharm.D and Ph.D.) Editor-in-Chief

Pharmaceutical Sciences-Indexed in ESCI (Web of Sciences) and Scopus https://ps.tbzmed.ac.ir/



Proof-Pharmaceutical Sciences

5 messages

Pharmaceutical Sciences <pharm.sci.tabriz@gmail.com>

To: mahardianr@ff.unair.ac.id

Fri, Sep 16, 2022 at 10:06 PM

Dear Author

We are pleased to inform you that your paper is nearing publication. Enclosed please find a PDF file corresponding to the galley proof of the article to be published in Pharmaceutical Sciences.

Proof corrections should be returned to the editor within 72h after reception.

Please consider that only minor corrections will be accepted.

It will be considered to be published without any proof reading if you do not return until 3 days.

Sincerely yours

Editorial Office of Pharmaceutical Sciences (PS)

Editor Comments:

- -Please check and confirm/correct the highlights.
- -Please confirm the layout and values for all Tables are correct.



28(4)4-Andrographolide and epigallocatechin gallate (EGCG).pdf

1226K

mahardian rahmadi <mahardianr@ff.unair.ac.id>

To: Pharmaceutical Sciences <pharm.sci.tabriz@gmail.com>

Mon, Sep 19, 2022 at 9:27 AM

Dear

Editor of Pharmaceutical Sciences (PS) Journal

Thank you for your kind correction.

Herewith we confirmed the highlights, the layout and values of all Tables are correct.

We thank you for giving us the opportunity to publish our article in the Pharmaceutical Sciences (PS) journal.

Sincerely,

Mahardian Rahmadi

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Faculty of Pharmacy
Airlangga University
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[Quoted text hidden]

mahardian rahmadi <mahardianr@ff.unair.ac.id>

To: Pharmaceutical Sciences <pharm.sci.tabriz@gmail.com>

Thu, Sep 29, 2022 at 11:38 AM

Dear

Editor of Pharmaceutical Sciences (PS) Journal

Hope you are doing well,

Would you please to tell us about the progress of our accepted manuscript entitled "Andrographolide and Epigallocatechin Gallate (EGCG) Lower the Risk of Addiction Induced by Nicotine and Cigarette Smoke Extract (CSE) in Mice" because we can't find our manuscript anymore both in "In Press section" or in "Current Issue section" on your Journal website.

Sincerely,

Mahardian Rahmadi

Department of Clinical Pharmacy Faculty of Pharmacy Airlangga University

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[Quoted text hidden]

Pharmaceutical Sciences <pharm.sci.tabriz@gmail.com>

To: mahardian rahmadi <mahardianr@ff.unair.ac.id>

Dear Dr. Rahmadi

New issue will be published by 4 October 2022. Regards A. Shayanfar Editor

[Quoted text hidden]

mahardian rahmadi <mahardianr@ff.unair.ac.id>

To: Pharmaceutical Sciences <pharm.sci.tabriz@gmail.com>

Thank you for your information.

Mahardian Rahmadi

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Thu, Sep 29, 2022 at 12:33 PM

Tue, Oct 4, 2022 at 7:44 AM

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