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OPEN PEER REVIEW

Potential Antidepressant-Like Activity of *Rhus coriaria* L. (Sumac) Ethanolic Extract: The Mechanism of Action via the Monoaminergic System in a Mouse Model

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21 Jul 2023	16 Aug 2023	27 Aug 2023	10.5812/jjnpp-139330

About this report

This open peer review (OPR) report shows the public comments made on this article during peer review, by the reviewers, the associate editor and the editor-in-chief, for every revision round, together with the authors' replies. Comments appear only with the consent of the people who wrote them. Reviewers who chose to sign their report are named; the others are shown as "Referee". Comments are edited for language only, and confidential remarks to the editors are not included.

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1 Original submission

2 comments · 25 Jul 2023 – 28 Jul 2023

Referee 1 Reviewer

MAJOR REVISION 25 Jul 2023

The current manuscript "Potential Antidepressant-Like Activity of Rhus Coriaria L. (Sumac) Ethanolic Extract: The Mechanism of Action via The Monoaminergic System in an Animal Mode" is within the scope of the journal, and the work represents a substantial contribution to and advancement of the field. It can be accepted after MAJOR revision.

1. Please give more information about the conditions in which the animals were kept and the reason for the choice of male NMRI mice.
2. Why have you used intraperitoneal (i.p.) administration when Rhus Coriaria L. (Sumac), imipramine, haloperidol, and fluoxetine are all taken orally?
3. Why have you used Rhus Coriaria L. (Sumac) at this dosage?
4. In my opinion, using this number of animals is not ethical. You can determine the effective dose of the plant in a pilot study and carry out the study with a smaller number of animals.
5. The language needs to be more scientific and needs revision in its present form.
6. The discussion is just a report of other studies. I think a lot of what was said in the discussion is not relevant at all, and much of it should be deleted. It needs to be seriously revised.
7. The abbreviations were not defined in the figures' captions.
8. When referring to a PLANT, you should italicize the names in the text. After writing the complete name of a PLANT at the first mention, the genus name can be shortened to just the capital letter.

Referee 2 Reviewer

MINOR REVISION 28 Jul 2023

This is an interesting paper, and the content is very good, but I suggest the paper can be improved in the following ways:

Mice should be mentioned in the title of the article and in the abstract.

Abstract
The number of mice and the type of injection should be given in the abstract of the article.
In the results section, it is necessary to report the p-value.

Introduction
In the introduction of the article, more explanation should be given about the mechanism of action of the monoaminergic system.

Best regards

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Revision 1

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Journal: ***Jundishapur Journal of Natural Pharmaceutical Products***

Manuscript #: **139330**

Title of Paper: **Potential Antidepressant-Like Activity of Rhus Coriaria L. (Sumac) Ethanolic Extract: The Mechanism of Action via The Monoaminergic System in an Animal Model**

Date Sent: **August 15, 2023**

Editor-in-chief of Jundishapur Journal of Natural Pharmaceutical Products

Dear Professor Zahra Ramezani,

We highly appreciate the detailed valuable comments of the dear reviewers on our manuscript of '**139330**. The suggestions are quite helpful for us and we incorporate them in the revised paper. During the last weeks, we have referred to different literature and papers and reconstructed the manuscript to improve the quality of our paper. Please find attached a point-by-point response to dear reviewers' concerns. We hope that you find our response satisfactory and that the manuscript is now acceptable for publication.

* **Changes to the manuscript are shown in yellow and green highlights for dear reviewers 1 and 2, respectively.**

Response to comments from Dear Reviewer # 1

The current manuscript "Potential Antidepressant-Like Activity of Rhus Coriaria L. (Sumac) Ethanolic Extract: The Mechanism of Action via The Monoaminergic System in an Animal Mode" is inside the scope of the journal and work represents a substantial contribution to and advancement of the field. It can be accepted after MAJOR revision.

We highly appreciate the positive feedback from the dear reviewer to submit a revised draft of the manuscript. We have read your comments carefully and tried our best to address them one by one.

1. Please give more information about the conditions of keeping the animals and the reason for the choice of male NMRI mice

Apart from our recent study(Ref.no 7), previous studies have relieved that the most frequently used out strains, CD-1, **NMRI** and Swiss, respond positively to most of the antidepressants when subjected to the FST and TST[1-3] (Please see the below references):

1-Andreasen JT, Redrobe JP. Antidepressant-like effects of nicotine and mecamylamine in the mouse forced swim and tail suspension tests: role of strain, test and sex. Behav Pharmacol. 2009;20(3):286-95.

2- Qi CC, Ding YQ, Zhou JN. Biological Factors Influencing the Mice Forced Swim Test. J Neurol Neuromed .2016; 1(4): 21-4.

3-Petit-Demouliere B, Chenu F, Bourin M. Forced swimming test in mice: a review of antidepressant activity. Psychopharmacology (Berl). 2005;177(3):245-55.

2. Why have you used the intraperitoneally (i.p.) administration when all Rhus Coriaria L. (Sumac) and imipramine, haloperidol, and fluoxetine are taken orally?

We appreciate the reviewer's insightful comment. Apart from our recent study(Ref.no 7), the intraperitoneal (i.p.) route of drug administration in laboratory animals is a common practice in many in vivo studies of disease models. This route is easy to master, quick, suitable for chronic treatments, and with low impact of stress on laboratory rodents. (Please see the blow reference):

1.Al Shoyaib A, Archie SR, Karamyan VT. Intraperitoneal Route of Drug Administration: Should it Be Used in Experimental Animal Studies? Pharm Res. 2019;37(1):12. doi: 10.1007/s11095-019-2745-x

Moreover, a study demonstrated that the calculated absolute bioavailability (F% = AUC IP/AUC IV × 100%) of IP-administered docetaxel is 69% (69), which is much higher compared to the absolute bioavailability of docetaxel after oral administration (~2.8%). Notably, the documented maximum plasma concentration (Cmax) of docetaxel was also similar after IP and IV administration in this study(Please see below reference):

2.Hu K, Cao S, Hu F, Feng J. Enhanced oral bioavailability of docetaxel by lecithin nanoparticles: preparation, in vitro, and in vivo evaluation. Int J Nanomedicine. 2012;7:3537–45.

Among these, the IP route stands out because the rate and extent of drug absorption are faster in IP followed by intramuscular> SC > oral routes(In this study, we evaluate the acute administration of Sumac). (Please see the below reference).

3.Wolfensohn SE, Lloyd MH. Aleutian disease in laboratory ferrets. Vet Rec. 1994;134(4):100.

3. Why have you used Rhus Coriaria L. (Sumac) at this dosage?

Thank you for the comment. The doses of Sumac were chosen basis of a pilot study in our laboratory and a review of the literature (Please see Ref. no. 19). So, we use low. intermediate and high doses of Sumac.

4. In my opinion, using this number of animals is not ethical. You can reach the effective dose of the plant in a pilot study and carry out the study with a smaller number of animals.

Thank you for pointing this out. But, our experimental design is exactly based on previous studies:

-Ishola IO, Agbaje EO, Akinleye MO, Ibeh CO, Adeyemi O. Antidepressant-like effect of the hydroethanolic leaf extract of Alchorneacordifolia (Schumach. &Thonn.) Mull. Arg.(Euphorbiaceae) in mice: Involvement of monoaminergic system. J Ethnopharmacol. 2014; 158:364-372.

-Ostadhadi, S., Norouzi-Javidan, A., Nikoui, V., Zolfaghari, S., Moradi, A., & Dehpour, A. R. (2018). Nitric oxide involvement in additive antidepressant-like effect of agmatine and lithium in mice forced swim test. Psychiatry research, 266, 262–268.

-etc.

In addition, the monoaminergic system consists of different receptors that are involved in different drug mechanisms of action. However, after the behavioral testing, we don't euthanize the animals, and based on the ethical committee recommendations we used them only for breeding.

5. The language need to be more scientific and need revision in the present form.

We greatly appreciate the reviewer's efforts to carefully review the paper and the valuable suggestions offered. The manuscript was completely amended grammatically and typographically.

6. The discussion is just a report of other studies. I think a lot of what was said in the discussion is not relevant at all and many of them should be deleted. It needs to be seriously revised.

We appreciate the reviewer's insightful comment. The discussion is completely revised and we used related papers to our results.

7. The abbreviations did not define in the figures' captions.

Thank you for the comment. As suggested by the dear reviewer, the abbreviations are deleted from the figure's captions.

8. When referring to a PLANT, you should italicize the names in the text. After writing the complete name of a PLANT in the first mention, the genus name can be shortened to just the capital letter

We appreciate the reviewer's insightful comments. As suggested by the reviewer, we corrected the expression of the plant's scientific name in the text and use the extract instead of RC in the figures.

Response to comments from Dear reviewer # 2

This is an interesting paper and the content is very good but I suggest the paper can be improved in the following ways:

We thank the reviewer for their time and effort and the positive critique.

1.Mice should be mentioned in the title of the article and abstract.

As suggested by the dear reviewer, the mice are added to the title and abstract.

2. Abstract

- The number of mice and the type of injection should be given in the abstract of the article.

Thank you for the comment, the correction has been made.

- The number of mice and the type of injection should be given in the abstract of the article.

Thank you for the comment, the correction has been made.

-In the result part: it is necessary to write P-value.

As suggested by the dear reviewer, the P-value is added to the abstract.

3. Introduction

In the introduction of the article, more explanations should be given about the mechanism of action of the monoaminergic system.

Thank you for the comment. As suggested by a dear reviewer we briefly describe the monoaminergic system.

But, I should be mentioned that the main limitation in this journal(JJNPP) is word limitation (3500 words for original research). So, in most parts of the manuscript, we have deleted extra explanations. Dear referees, thank you very much for understanding our conditions.

Sincerely yours,

Corresponding author

2 Revision 1

2 comments · 22 Aug 2023 – 27 Aug 2023

Referee 1 Reviewer

ACCEPT 22 Aug 2023

The current manuscript "Potential Antidepressant-Like Activity of Rhus Coriaria L. (Sumac) Ethanolic Extract: The
Mechanism of Action via The Monoaminergic System in an Animal Mode" is within the scope of the journal, and the work represents a substantial contribution to and advancement of the field. It can be accepted.

Editor-in-Chief

ACCEPT 27 Aug 2023

Dear Authors,

I am glad to inform you that your manuscript has been accepted for publication in JJNPP. I will send it to the publisher for further processing.

Kind Regards,
JJNPP EIC