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OPEN PEER REVIEW

The Protective Effects of *Pistacia Atlantica* Gum in a Rat Model of Aluminum Chloride-Induced Alzheimer's Disease via Affecting BDNF and NF-kB

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About this report

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1 Original submission

1 comment · 19 Dec 2023

Referee 1 Reviewer

MINOR REVISION 19 Dec 2023

The manuscript titled “The Protective Effects of Pistacia atlantica Gum in a Rat Model of Aluminum Chloride-Induced Alzheimer’s Disease via Affecting BDNF and NF-kB” shows a beneficial effect of Pistacia atlantica gum on the memory impairment induced by aluminum chloride, in addition to its potential anti-inflammatory and neuroprotective effects. The final data showed that P. atlantica was effective in behavioral and molecular evaluations.

However, some points in this manuscript should be considered:

In the text, P. atlantica gum should be replaced by P. atlantica when it is related to the results.

Reference 47 has Arabic font.

Why was the dose of 200 mg/kg omitted from this study, given that, according to the reference article, it was the best dose with anti-inflammatory activity?

In the discussion, it has been mentioned that P. atlantica has anti-Alzheimer effects based on articles, but the associated references are traditional books.

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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.

Dear Editor of Iranian Journal of Pharmaceutical Research

We sincerely thank the reviewers for constructive criticisms and valuable comments, which were of great help in revising the manuscript. Accordingly, the revised manuscript has been systematically improved with new information and additional interpretations. Our responses to the referee's comments are given below and also, highlighted in yellow font in the text of manuscript.

Reviewer 1:

The manuscript titled "The Protective Effects of Pistacia atlantica Gum in a Rat Model of Aluminum Chloride-Induced Alzheimer's Disease via Affecting BDNF and NF-kB" shows beneficial effect of Pistacia atlantica Gum on the memory impairment induced by aluminum chloride, besides of its potential anti-inflammatory and neuroprotective effects. Final data showed that P.atlantica was effective in behavioral and molecular evaluations.

However, some points in this manuscript should be considered:

In the text, P. atlantica gum should be replaced by P. atlantica, when it is related to the results.

The reference 47 has Arabic font.

Why the dose of 200 mg/kg is missed in this study, since based on the reference article, it was the best dose with anti-inflammatory activity?

In discussion, it has been mentioned that P. atlantica has anti-Alzheimer effects based on articles, but associated references are traditional books.

Response: We thank the reviewer for this comment. P. *atlantica* gum has been corrected. Because of the anti-inflammatory and neuroprotective effects of low doses (50 and 100) we thought its was needless to use the high dose (200). As we know, a higher dose does not necessarily mean a better effect. So, in some tests of this research, a dose of 50 worked better than 100. Some new references were added.

Reviewer 2:

Dear editor in chief

Although the paper presents useful information, the following changes must be generated:

1) There is no graphical abstract in your manuscript.

Response: Added.

2) Please make the introduction section a little shorter.

Response: Corrected.

3) Why have only two dosages of Pistacia Atlantica Gum been utilized in the treatment groups?

Response: Because of the anti-inflammatory and neuroprotective effects of low doses (50 and 100) we thought it was needless to use the high dose (200). As we know, a higher dose does not necessarily mean a better effect. So, in some tests of this research, a dose of 50 worked better than 100. Therefore, to reduce the number of animals only two doses were used.

4) Please add a reference for the open field test's square size.

Response: Done.

5) There is no reference for the passive test.

Response: Added.

6) Why was only the passive avoidance test utilized to determine the degree of memory destruction?

Response: The passive avoidance test is used to evaluate learning and memory in animal models of CNS disorders. In this test, animals learn to avoid an environment in which an undesirable stimulus was previously delivered.

7) The method's and results' order need to be followed.

Response: corrected.

8) The day when the electric shock was administered to the animal is mentioned on the seventh day of the passive avoidance test, and the day of the test is mentioned on the eighth and fourteenth days. Is there any reason to do this?

The day 7 was a training day. So, the animal got familiar to the chambers and for the first time it received the electric shock. The days 8 and 14 were testing days which showed the memory ability of animal to memorize the electric shock which received on day 7.

9) How to create memory destruction is missed in the method part.

Response: in part of “Animals and experimental procedure” and in the grouping of animals, the use of aluminum chloride to induce Alzheimer's is mentioned with reference.

10) The plant subspecies used is unclear.

Response: *P. atlantica* was used, which was purchased from the Department of Pharmacognosy at the Faculty of Pharmacy at the Kermanshah University of Medical Sciences in Iran.

11) On which day was ITL performed during the EPM test?

Response: ITL was done only for passive avoidance tests due to training on day 7 which animal received electric shock for the first time.

12) In the histopathology assessment, the scale bar is frequently ignored.

Response: added.

13) In the BDNF Immunostaining, the 50 mg/kg dose of Pistacia Atlantica Gum exceeded the 100 mg/kg dose. What is the explanation and reason for this?

Response: Based on previous studies, different species of pistachio have shown neuroprotective effect with several mechanisms, as following reference. The fact that the dose of 50 has a better effect in increasing bdnf can be related to various mechanisms such as reducing oxidative stress, improving mitochondrial function, etc., which requires investigating more mechanisms in future studies.

- Moeini R, Memariani Z, Asadi F, Bozorgi M, Gorji N. Pistacia genus as a potential source of neuroprotective natural products. Planta medica. 2019 Nov;85(17):1326-50.

2 Revision 1

0 comments

No public comments in this round.