OPEN PEER REVIEW

Open Peer Review (OPR)

As a new feature for progressing towards transparency, we decided to open a new window for all of our editors as well as authors titled "**Open Peer Review**". We hope by this new facility, our reviewers will be more motivated and authors will be more satisfied with the review process. We believe that publishing our peer review reports could make a transparent and clear environment for all our efforts within a journal, but not all reviewers tend to publish their comments.

What is "Open Peer Review" process?

An "Open Peer Review" process is making the details of all review process (including reviewers, associate editors, and EICs comments) as "Public" as it is agreed by EIC, Authors, and reviewers.

Advantages of "Open Peer Review" process

- More transparency, constructiveness and tactful comments of the peer review process: leads to an increase in the quality of reviews
- More motivations for all involved roles in the review process
- Authors' satisfactions from the review process: Increases honesty between authors and reviewers
- Education of both authors and new students
- Prevents reviewers from following their individual agendas and leading to the detection of reviewers' conflicts of interests

You can find out more at:
https://sites.kowsarpub.com/kowsar/knowledgebase/category/tree.html#opr.html

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Peer Review Report for "Protection Against Blood-Brain Barrier Permeability as a Possible Mechanism for Protective Effects of Thymoquinone Against Sickness Behaviors Induced by Lipopolysaccharide in Rats"

Author(s): Rahimeh Bargi, Mahmoud Hosseini, Fereshteh Asgharzadeh, Majid Khazaei, Mohammad Naser Shafei, Farimah Beheshti

Review Timeline:

Submit Date: 9 Jun 2018
Revised Date: 1 May 2019
Accepted Date: 11 May 2019

Revision (0)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: Reviewer | **Revision** (0) 17 Sep 2018

Dear author;
Thank you for choosing JJNPP for publishing your work. Here are some comments for making it much more better:

Abstract:
1- In the abstract, the exact timing of thymquinone injection prior to LPS should be mentioned.
2- Enter the EB abbreviation in front of Evans Blue in parentheses.

Introduction:
3-in line 13 “Lipopolysaccharide (LPS), a is a piece of gram negative bacteria……” Letter "a" should be deleted.

Material and methods:

4- The dose of anesthetic (Urethane) must be mentioned.

Results

5-In the results section, the mean ± standard deviation of each test should be written in each group.

6- In the discussion section, it is better to follow the order of the results

Results: the order is OF, EPM and FST., while in discussion section order becomes FTS , EPM, and then OF.

7- Do Thymoquinone groups have a significant change in comparison with control in Figures 1A and 1B? Group TQ5 seems to have a significant increase compared to the control group. However, if all of the beneficial effects of thymoquinone are attributed to LPS permeability, the results of thymoquinone would be at most equal to the control group. Perhaps thyoquinone alone and independent to the effect on the LPS permeability had played a role in reducing anxiety. But the researcher did not mention it in the discussion.

8- According to the figure 7A and 7B, the effect of thymoquinone in decreasing permeability in the cortex is greater than the brain stem. How does the researcher discuss this?

9- In all figures, move the grouping box to the bottom right corner.

10- In figure 7, write the full name of Evans blue (EV) in the vertical axis or legend of the figure.

11- Check the references 1, 9, 15, and 33: Year, page, and journal .

Good Luck!

REFEREE: Reviewer | **Revision (0)** 17 Mar 2019

Dear author;

Thank you for choosing JJNPP for publishing your manuscript. I reviewed this manuscript. The experimental design is direct and the results are clear. Here there are some comments for you for making it more suitable for publication:

• The manuscript should be carefully checked for writing errors.

In the result part:

• Authors stated that: "The animals of LPS group also spent a lower time in the central segment than the control group. Administration of 2 and 10 mg/ kg TQ was not effective to change the time spent in the central zone compared to LPS group (Figure 1C) however, 5 mg/ kg TQ increased the time spent in the central zone($p<0.05$; Figure 1C)." However, it can be corrected as follow:

As shown in Fig.1C, The animals of LPS group also spent a significant (($p<0.05$) lower time in the central segment than the control group. However, treatment with TQ reversed this LPS-induced change and there was no significant difference between LPS-TG (2, 5, 10) and LPS groups.

• Please check all Figures regarding possible significant differences between groups (LPS-TQs with LPS and LPS-TQs with control group). Is there any significant difference between LPS-TQ5 and LPS groups in Fig. 1C? Please indicate this difference with "+" symbol.

Good Luck!

REFEREE: Reviewer | **Revision (0)** 18 Mar 2019

Dear author;
I reviewed the manuscript entitled "Protection against blood-brain barrier permeability as a possible mechanism for protective effects of thymoquinone against sickness behaviors induced by lipopolysaccharide in rats". This is an interesting and mostly well-written manuscript. My comments and suggestion for the authors regarding this paper have been listed as follows:
Minor comments:
1. The manuscript should be carefully checked for typographical errors, punctuation, and style.
2. Regarding abbreviations, please spell out full names when any abbreviation is mentioned in the text for the first time (like abstract).
E.g. please replace this sentence in the method part "One week after the injection, the activity of the animals was evaluated in open-field" with this " One week after the injection, the activity of the animals was evaluated in open-field (OF)"
Also for
"Elevated plus maze (EPM)"
3. Please delete illustrating box located in the border of all graphs (this box is shown below).
4. Please check and rewrite this part in the first paragraph of the result section
"Administration of 2 and 10 mg/ kg TQ was not effective to change the time spent in the central zone compared to LPS group (Figure 1C) however, 5 mg/ kg TQ increased the time spent in the central zone."
5. Please check any possible significant difference between LPS-TQ groups and control groups in Fig. 4A and B (Please check this item in all Figs).

Thanks.

REFEREE: Associate Editor | **Revision (0)** 27 Mar 2019

Dear EIC
The reviewer(s) have recommended publication, but also suggest some minor revisions to the manuscript. Therefore, I invite the author to respond to the reviewer(s)' comments and revise his manuscript.
Kind regards,

REFEREE: EIC | **Revision (0)** 27 Mar 2019

Dear Author,
Your article is reviewed by the reviewers carefully. According to their comments, this document needs minor revision. Please follow their comments as requested.
Thanks.

OPEN PEER REVIEW

Revision (1)

Reply to Reviewers

Ideally, the reviewing process can significantly improve the submitted manuscripts by allowing the authors to take into account the advice of reviewers. Author(s) must reply to all reviewers' comments in a separate Word file, point by point. A "**Reply to Reviewers**" document is submitted along with revised manuscript during submission of revised files, summarizing the changes that the authors made in response to the reviewers' comments. The responses to reviewers' comments specifies how the authors addressed each comment the reviewers made.

You can read the authors' responses to the reviewers' comments in the next page.

Reviewer 1:

1- In the abstract, the exact timing of thymquinone injection prior to LPS should be mentioned.

Answer: The exact timing of thymquinone injection prior to LPS was mentioned in the abstract.

2- Enter the EB abbreviation in the front of Evans Blue in parentheses.

Answer: The EB abbreviation in the front of Evans Blue in parentheses was added in the abstract

3-in line 13 “Lipopolysaccharide (LPS), a is a piece of gram negative bacteria……” Letter a be deleted

Answer: Letter a in line 13 be deleted. Thank you.

4- The dose of anesthetic (Urethane) must be mentioned.

Answer: The dose was added. A reference was also provided.

5-In the results section, the mean ± standard deviation of each test should be written in all groups.

Answer: Thank you for your suggestion but I think providing the data in the text makes the results segment too long. Additionally, they will be a repeat of what that has been provided in the figures.

6- In the discussion section, it is better to follow the order of the results
Results: OF, EPM and FST respectively while in discussion section FTS, EPM then OF is discussed.

Answer: The mentioned item was corrected

7- Do Thymoquinone groups have a significant change in comparison with control in Figure 1A and 1B? Group TQ5 seems to have a significant increase compared to control group. However, if all of the beneficial effects of thymoquinone are attributed to LPS permeability, the results of thymoquinone would be at most equal to the control group. Perhaps thyoquinone alone and independently of the effect on the LPS permeability, had played a role in reducing anxiety. But the researcher did not mention it in the discussion.

Answer: Yes, in the figure s 1A and 1B, the difference between the effect of thymoquinone and the control group was provided.

Yes, it seems that the effects of TQ may in part be due to its effects on BBB permeability. It was discussed.

8- According to the figure 7A and 7B, the effect of thymoquinone in decreasing permeability in the cortex in greater than the brain stem. How does the researcher discuss this?

Answer: It was discussed in the discussion segment.

9- In the all figures, move the grouping box to the bottom right corner

Answer: Considering the comment of another reviewer, the grouping box was deleted form the corner of the figures. It is below the commons.

10- In the figure 7, write the full name of Evans blue (EV) in the vertical axis or legend on the figure

Answer: *In the figure 7, the full* name of Evans blue (EV) added in the vertical axis

11- Check the references 1, 9, 15 and 33: Year, page and journal

Answer: The references 1, 9, 15 and 33: Year, page and journal was Checked and corrected.

Reviewer 2:

1- The manuscript should be carefully checked for writing errors.

Answer: The manuscript checked for writing errors.

2- Authors stated that: “The animals of LPS group also spent a lower time in the central segment than the control group. Administration of 2 and 10 mg/ kg TQ was not effective to change the time spent in the central zone compared to LPS group (Figure 1C) however, 5 mg/ kg TQ increased the time spent in the central zone($p<0.05$; Figure 1C)." However, it can be corrected as follow:
As shown in Fig.1C, The animals of LPS group also spent a significant (($p<0.05$) lower time in the central segment than the control group. However, treatment with TQ reversed this LPS-induced change and there was no significant difference between LPS-TG (2, 5, 10) and LPS groups.

Answer: This item was corrected based on the comment

3- Please check all Figures regarding possible significant differences between groups (LPS-TQs with LPS and LPS-TQs with control group). Is there any significant difference between LPS-TQ5 and LPS groups in Fig. 1C? Please indicate this difference with + symbol.

Answer*:* All the results were checked again and the differences were added.

Reviewer 3:

1. The manuscript should be carefully checked for typographical errors, punctuation and style.

Answer: The manuscript checked and corrected for typographical errors, punctuation and style.

2. Regarding abbreviations, please spell out full names when any term abbreviation is mentioned in text for the first time (like abstract).
E.g. please replace this sentence in method part "One week after the injection, activity of the animals was evaluated in open-field" with this " One week after the injection, activity of the animals was evaluated in open-field (OF)"Also"Elevated plus maze was a device that designed with two" with"Elevated plus maze (EPM) was a device that designed with two" and …

Answer: It was corrected

3. Please delete illustrating box located in the border of all graphs (this box is shown below):

Answer: The illustrating box located in the border of all graphs was deleted. It is below the columns

4. Please check and rewrite this part in the first paragraph of the result section "Administration of 2 and 10 mg/ kg TQ was not effective to change the time spent in the central zone compared to LPS group (Figure 1C) however, 5 mg/ kg TQ increased the time spent in the central zone."

Answer: It was checked and corrected.

5. Please check any possible significant difference between LPS-TQ groups and control group in Fig. 4A and B (Please check this item in all Figs).

Answer: All the results were checked again and the mentioned differences were added.

6. Since your manuscript contains a single nuclear factor kappa B, please delete its abbreviation (NF-KB) from this sentence: "…accompanying with a reduced level in nuclear factor kappa B (NF-KB) activity…" (Please check this item in throughout the text)

Answer: Item checked in throughout the text and corrected

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Revision (1)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: Reviewer | **Revision** (1) — 4 May 2019

Dear authors,
All needed corrections have been done. It is now accepted for publishing.

Thanks!

REFEREE: Reviewer | **Revision** (1) — 8 May 2019

Dear AE,
The study is reviewed carefully. According to comments and revisions by the author, this manuscript is accepted.
Thanks

REFEREE: Associate Editor | **Revision** (1) — 11 May 2019

Dear EIC
Based on the authors' answers to the reviewers' comments, the reviewer(s) have recommended publication.
Kind regards.

REFEREE: EIC | **Revision** (1) — 11 May 2019

Dear Author,
Your article is reviewed by the reviewers carefully. According to their comments, this document needs minor revision. Please follow their comments as requested.
Thanks.