Iranian Journal of Pharmaceutical Research
Volume 23 · Issue 1 · e156838

OPEN PEER REVIEW

Bupropion Showed Neuroprotective Impacts Against Cerebral Ischemia/Reperfusion Injury by Reducing Oxidative Stress and Inflammation

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SUBMITTED	REVISED	ACCEPTED	DOI
5 Oct 2024	30 Nov 2024	17 Dec 2024	10.5812/ijpr-156838

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1 Original submission

2 comments · 23 Oct 2024 – 2 Nov 2024

Referee 1 Reviewer

MINOR REVISION 23 Oct 2024

Overall, while the study presents promising findings regarding the neuroprotective effects of bupropion, it lacks critical details in methodology and analysis that are essential for robust scientific reporting. Addressing these gaps will enhance the credibility and reproducibility of the research:

1. Study Design: The study appears to be an experimental study using a rat model to assess the neuroprotective effects of bupropion, which is appropriate.

2. Participants:
- The study involved 40 male rats divided into four groups, which is a reasonable sample size. However, details about the randomization process and inclusion/exclusion criteria are not provided.
- Kindly clarify the randomization process and the use of blinding techniques during outcome assessment.

3. Interventions: The interventions (doses of bupropion) are clearly described, but the method of administration (e.g., oral, injection) is not specified.

4. Methods:
- For histopathological evaluations, was an expert pathologist involved in reporting the data? Please provide this information.

5. Results:
- The results indicate improvements in sensorimotor function and reductions in inflammatory markers, but specific statistical results (e.g., p-values, confidence intervals) are not provided.
- Present the results with appropriate statistical measures (e.g., means, standard deviations, p-values) to support the conclusions.
- Please provide descriptions for the symbols (*), (&), ($), etc. used in the graph in the figure caption.

6. Discussion:
- The conclusions drawn are consistent with the results presented, but there is no discussion of potential limitations or biases in the study.
- Acknowledge any limitations of the study, such as sample size, potential biases, or generalizability of the findings.

Associate Editor

MAJOR REVISION 2 Nov 2024

Review for Manuscript ID: 156838
Reviewer 1:
This paper on the neuroprotective effects of bupropion against cerebral ischemia/reperfusion (I/R) injury in rats is comprehensive and well-structured. Here are some suggestions and observations to improve your research.
Begin with a brief sentence framing the significance of cerebral I/R injury. Include the main findings more concisely, focusing on the key results of the behavioral and biochemical tests in the abstract section.
In the Induction of Cerebral I/R Injury section, specifying details about the surgical procedure, like the duration of anesthesia and methods to monitor recovery, would be helpful.
Include more about the proposed mechanism by which bupropion might reduce inflammation and oxidative

stress based on previous studies.
Provide more clarity on the rationale behind the selected bupropion doses (60 mg/kg and 100 mg/kg). Explain why these doses were chosen.
If there are dose-dependent effects (e.g., with 60 mg/kg vs. 100 mg/kg bupropion), emphasizing these in the text would give a clearer understanding of bupropion's efficacy.
Adding exact p-values (e.g., $p < 0.01$) or confidence intervals for key findings would improve scientific rigor.
Expand on how the study's findings compare to those of similar neuroprotective agents. This can include discussion of the potential for combination therapies with bupropion in treating ischemic stroke.
The limitations of the research are not addressed in this paper.
Please add a Dose-Response Table. A table showing each dose's effect on various parameters (inflammation, oxidative stress, behavior) could provide a clear comparison of outcomes.
Please refine the language and readability, use consistent terminology, and simplify complex sentences.
Briefly outline how these findings could inform clinical treatments or how bupropion might complement current stroke therapies.
Reviewer 2:
Overall, while the study presents promising findings regarding the neuroprotective effects of bupropion, it lacks critical details in methodology and analysis that are essential for robust scientific reporting. Addressing these gaps will enhance the credibility and reproducibility of the research:
1. Study Design: The study appears to be an experimental study using a rat model to assess the neuroprotective effects of bupropion, which is appropriate.
2. Participants:
- The study involved 40 male rats divided into four groups, which is a reasonable sample size. However, details about the randomization process and inclusion/exclusion criteria are not provided.
- Kindly clarify the randomization process and the use of blinding techniques during outcome assessment.
3. Interventions: The interventions (doses of bupropion) are clearly described, but the method of administration (e.g., oral, injection) is not specified.
4. Methods:
- For histopathological evaluations, was an expert pathologist involved in reporting the data? Please provide this information.
5. Results:
- The results indicate improvements in sensorimotor function and reductions in inflammatory markers, but specific statistical results (e.g., p-values, confidence intervals) are not provided.
- Present the results with appropriate statistical measures (e.g., means, standard deviations, p-values) to support the conclusions.
- Please provide descriptions for the symbols (*), (&), ($), etc. used in the graph in the figure caption.
6. Discussion:
- The conclusions drawn are consistent with the results presented, but there is no discussion of potential limitations or biases in the study.
- Acknowledge any limitations of the study, such as sample size, potential biases, or generalization of the findings.

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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 Chief Editor of

Thank you very much for your e-mail having the referee's comments about our article entitled " Bupropion showed neuroprotective impacts against cerebral ischemia/reperfusion injury by reducing oxidative stress and inflammation ". In response to the comments and suggestions in your letter, I would like to thank you and the referees for your valuable point of views and suggestions. Our changes in the text in response to respected referee are highlighted. Q is the question or suggestion raised by each of the respected referee and *Answer* is our explanation in response to the respected referee's suggestion.

Response to respected reviewer #1:

Q1. This paper on the neuroprotective effects of bupropion against cerebral ischemia/reperfusion (I/R) injury in rats is comprehensive and well-structured. Here are some suggestions and observations to improve your research.

Answer: The opinion of the respected referee is appreciated..

Q2. Begin with a brief sentence framing the significance of cerebral I/R injury. Include the main findings more concisely, focusing on the key results of the behavioral and biochemical tests in abstract section.

Answer: The result section of abstract was rewritten completely.

Q3. In the Induction of Cerebral I/R Injury section, specifying details about the surgical procedure, like the duration of anesthesia and methods to monitor recovery, would be helpful.

Answer: More details were added for induction of disease in MS and highlighted by red color.

Q4. Include more about the proposed mechanism by which bupropion might reduce inflammation and oxidative stress based on previous studies.

Answer: More details were added in discussion section of MS and highlighted by red color.

Q- Provide more clarity on the rationale behind the selected bupropion doses (60 mg/kg and 100 mg/kg). Explaining why these doses were chosen.

Answer: We selected the drug doses based on the pre-test experiment and this was stated and highlighted in MS.

Q- If there are dose-dependent effects (e.g., with 60 mg/kg vs. 100 mg/kg bupropion), emphasizing these in the text would give a clearer understanding of bupropion's efficacy..

Answer: The significant effects were demonstrated in Figure 2 and 3. Also, there were mentioned in the text of results.

Q- Adding exact p-values (e.g., $p < 0.01$) or confidence intervals for key findings would improve scientific rigor.

Answer: All P-values were mentioned in Figures.

Q- Expand on how the study's findings compare to those of similar neuroprotective agents. This can include discussion of the potential for combination therapies with bupropion in treating ischemic stroke.

Answer: this was added in Last paragraph of discussion.

Q- Limitations of research Not Addressed in this paper.

Answer: In discussion section we added the limitation of research.

Q- Please add a Dose-Response Table. A table showing each dose's effect on various parameters (inflammation, oxidative stress, behavior) could provide a clear comparison of outcomes. Please refine Language and Readability and use Consistent Terminology and Simplify Complex Sentences.

Answer: All of these effects are provided in the figures presented in the article and it is not appropriate to repeat them in table, again. The MS edited grammatically.

Q- Briefly outline how these findings could inform clinical treatments or how bupropion might complement current stroke therapies.

Answer: This was stated in Last paragraph of Discussion.

Response to respected reviewer #2

Q: Overall, while the study presents promising findings regarding the neuroprotective effects of bupropion, it lacks critical details in methodology and analysis that are essential for robust scientific reporting. Addressing these gaps will enhance the credibility and reproducibility of the research:

Answer: We would like to thank the respected referee for his/her encouraging point of view and.

Study Design: The study appears to be an experimental study using a rat model to assess the neuroprotective effects of bupropion, which is appropriate.

Answer: Thanks.

2. Participants:

- The study involved 40 male rats divided into four groups, which is a reasonable sample size. However, details about the randomization process and inclusion/exclusion criteria are not provided.

Answer: Rats were randomly divided into groups. The all used rats were suitable for current study.

- Kindly clarify the randomization process and the use of blinding techniques during outcome assessment.

Answer: All the behavioral test were done by conducted by operators blinded for grouping of animals.

3. ***Interventions: The interventions (doses of bupropion) are clearly described, but the method of administration (e.g., oral, injection) is not specified.***

Answer: The drug administration was done Intraperitoneally, as stated in Animals and grouping section of artile.

4. **Methods:**

- For histopathological evaluations, was a pathologist expert involved in reporting the data? Please provide this information.

Answer: We provided this information in Material and methods section and highlighted by red color.

5. ***Results:***

- The results indicate improvements in sensorimotor function and reductions in inflammatory markers, but specific statistical results (e.g., p-values, confidence intervals) are not provided.

- Present the results with appropriate statistical measures (e.g., means, standard deviations, p-values) to support the conclusions.

- Please provide descriptions for the symbols (*) , (&), ($), etc. used in the graph in the figure caption.

Answer: ***All the aforementioned Parameters were provided in MS.***

6. ***Discussion:***

- The conclusions drawn are consistent with the results presented, but there is no discussion of potential limitations or biases in the study.

Answer: The limitation of current study was in added in Last paragraph of MS.

- Acknowledge any limitations of the study, such as sample size, potential biases, or generalizability of the findings.

Answer: The limitation of current study was in added in Last paragraph of MS.

Best regards,

Dr. Mousavi

2 Revision 1

1 comment · 16 Dec 2024

Associate Editor

ACCEPT 16 Dec 2024

The authors provided acceptable answers to the final reviewer's comments. So, in my opinion, the manuscript is now satisfactory for publication in IJPR.