

Dear Editor,

We appreciate the editor and reviewers very much for their constructive comments suggestions. Thank you for arranging a timely review for our manuscript. We have carefully evaluated the reviewers' critical comments and thoughtful suggestions, responded to these suggestions point-by-point, and revised the manuscript accordingly. All changes made to the text are in red so that they may be easily identified. With to the reviewers' comments and suggestions, we wish to reply as follows:

Reviewer #1:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors: The study entitled "Protective effects of combined treatment with ciprofol and mild therapeutic hypothermia during cerebral ischemia-reperfusion injury" is a narrative review comparing the risk-benefits of using ciprofol as a sedative agent along with hypothermia instead of propofol in patients of Cardiac Arrest to prevent ischaemia-reperfusion injury. Overall, the authors have cited various studies wherein ciprofol has been used as a sedative and analgesic. The authors also present their hypothesis and a detailed plan to test their hypothesis. However, a detailed methodology is lacking regarding the collection and analysis of articles cited in the manuscript. The authors must consider using appropriate guidelines such as SANRA guidelines mentioned below: Baethge C, Goldbeck-Wood S, Mertens S. SANRA—a scale for the quality assessment of narrative review articles. *Research integrity and peer review*. 2019 Dec;4(1):1-7.

Reply: Thanks for your helpful recommendation. We have cited all the references and added corresponding descriptions in the manuscript. Since none of the references we cited were graded for evidence, we try to provide a table of evidence grading. A detailed methodology would be introduced according to recommendation.

Also the authors have merely mentioned the study results but added no interpretation regarding the same. The concept appears to be novel, but the authors need to rewrite the manuscript systematically.

Reply: Thanks for your kind recommendation. We have added the interpretations about study results in the manuscript, please review again.

Reviewer #2:

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Major revision

Specific Comments to Authors: In the manuscript: “Protective effects of combined treatment with HSK3486 and mild therapeutic hypothermia during cerebral ischemia-reperfusion injury”, the authors hypothesized that ciprofol post-treatment after CA, could provide brain protection undergo TH. The article is interesting and has useful observations, but needs some enhancements before publication. Please consider the following major remarks:

1. You should clearly highlight in the introduction, the novelty of the article.

Reply: Thanks for your kind recommendation. There are no studies on HSK3486 to improve survival rates of therapeutic hypothermia after cardiac arrest, we are the first to hypothesize about it. We have highlight the novelty of the article in the introduction , please review again.

2. You should mention some characteristics and the source/producer of the materials used.

Reply: Thanks for your helpful recommendation. We have cited the references about the source/producer of the materials used.

3. There is lack of appropriate representation through figures and tables. I think you should have at least 2-3 figures. E.g., you could add a figure with the chemical structure of Ciprofol and his mechanism of action, a schematic figure representing the

workflow of the study and so on.

Reply: Thanks for your helpful recommendation. We have added a figure with the chemical structure of Ciprofol.

4. Also, you can summarize and refine some data as a table, in order to make it more readable. E.g., you could reorganize the text regarding the four animal groups in a table.

Reply: Thanks for your helpful recommendation. A detailed table of this part of the experiment is available in the references we cited, so we will not repeat it in this article.

5. Can you provide a perspective and challenge section?

Reply: Thanks for your helpful recommendation. We have added a limitation before the conclusion, we have provided a perspective and challenge in this part.

6. I consider that a Conclusions section should be included.

Reply: Thanks for your helpful recommendation. We have added a conclusion in the manuscript , please review again.