Name of journal: World Journal of Hepatology

Manuscript NO: 66490

Title: New progress in understanding roles of nitric oxide during hepatic ischemia-reperfusion injury

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer’s code: 05083839

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer’s Country/Territory: Egypt

Author’s Country/Territory: China

Manuscript submission date: 2021-03-29

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-04-15 14:13

Reviewer performed review: 2021-05-06 09:07

Review time: 20 Days and 18 Hours

<table>
<thead>
<tr>
<th>Scientific quality</th>
<th>[ ] Grade A: Excellent</th>
<th>[ ] Grade B: Very good</th>
<th>[ Y] Grade C: Good</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>[ ] Grade D: Fair</td>
<td>[ ] Grade E: Do not publish</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Language quality</th>
<th>[ ] Grade A: Priority publishing</th>
<th>[ ] Grade B: Minor language polishing</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>[ Y] Grade C: A great deal of language polishing</td>
<td>[ ] Grade D: Rejection</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Conclusion</th>
<th>[ ] Accept (High priority)</th>
<th>[ ] Accept (General priority)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>[ ] Minor revision</td>
<td>[ Y] Major revision</td>
</tr>
</tbody>
</table>

| Re-review | [ Y] Yes | [ ] No |
Dear Dr Shu-long Yang, your article is very important in the medical field however I’ve some comments for you & your team to consider. 1st of all is the language which needs precise revision by an expert as there are some spelling mistakes (for example in the abstract line 4 it is phase not phage as you wrote) also formulation of many sentences need to be adjusted. Regarding the scientific content I’ve some questions to raise so you can clarify or adjust in your manuscript 1st you just mentioned in the introduction that the ET/NO ratio is increased in early ischemia, however you didn’t mention any details as regarding the normal ratio or even the mechanism for this increase. Next, you mentioned in your manuscript that iNOS may decrease the HIRI however all mentioned data in your article showed only the bad aspect and deleterious effect of iNOS you just mentioned that its action depends on length & duration of ischemia without any clarification, moreover all data in your article revealed the deleterious effect of iNOS both early & prolonged ischemia without any evidence or even a mechanism for its role in improving the HIRI so I think this needs justification. Also the role of NO in apoptosis, you reported that it can induce or inhibits apoptosis, however you didn’t even write a single evidence for its role in stimulating apoptosis or even when this happens. Not only this, but you also reported that inhibiting NO can reduce HIRI by cell apoptosis which I think need to be revised. Finally I also would like to highlight 2 contradictory sentences in your conclusion, the 1st reporting that adding NO or increasing its bioavailability have both protective & deleterious effects then you reported that increasing NO bioavailability in hepatic tissue is a good way to prevent & treat HIRI. ] Thank you for in advance for having patience to my comments & considering them.
Name of journal: World Journal of Hepatology

Manuscript NO: 66490

Title: New progress in understanding roles of nitric oxide during hepatic ischemia-reperfusion injury

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer’s code: 03786725

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer’s Country/Territory: Italy

Author’s Country/Territory: China

Manuscript submission date: 2021-03-29

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-04-29 10:05

Reviewer performed review: 2021-05-11 11:21

Review time: 12 Days and 1 Hour

Scientific quality

[ ] Grade A: Excellent  [ ] Grade B: Very good  [ ] Grade C: Good

[ ] Grade D: Fair  [ ] Grade E: Do not publish

Language quality

[ ] Grade A: Priority publishing  [ ] Grade B: Minor language polishing

[ ] Grade C: A great deal of language polishing  [ ] Grade D: Rejection

Conclusion

[ ] Accept (High priority)  [ ] Accept (General priority)

[ ] Minor revision  [ ] Major revision  [ ] Rejection

Re-review

[ ] Yes  [ ] No
SPECIFIC COMMENTS TO AUTHORS
The manuscript of Yiping Zhang et al. deals with the role of nitric oxide during hepatic ischemia reperfusion injury. The authors conducted a systematic review analyzing a series of possible molecular interaction mechanisms. The topic would be interesting with important repercussions on clinical practice, especially in transplantology. However, The bibliographic research was not performed according to standardized methodologies (e.i PRISMA guidelines). Sometimes the results are listed in difficult to understand way. The discussion could be developed more extensively. Furthermore, the possible clinical implications of the research have not been reported and the study limits should be highlighted.