

## PEER-REVIEW REPORT

**Name of journal:** *World Journal of Diabetes*

**Manuscript NO:** 88354

**Title:** Empagliflozin ameliorates diabetic cardiomyopathy probably via activating AMPK/PGC-1a and inhibiting the RhoA/ROCK pathway

**Provenance and peer review:** Unsolicited Manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 06139840

**Position:** Peer Reviewer

**Academic degree:** PhD

**Professional title:** Professor

**Reviewer's Country/Territory:** Iraq

**Author's Country/Territory:** China

**Manuscript submission date:** 2023-09-21

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2023-09-21 19:50

**Reviewer performed review:** 2023-09-24 08:15

**Review time:** 2 Days and 12 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Novelty of this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
Creativity or innovation of this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation

<b>Scientific significance of the conclusion in this manuscript</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

## SPECIFIC COMMENTS TO AUTHORS

Thank you for asking my opinion about the manuscript entitled "Empagliflozin ameliorated high glucose-induced oxidative stress and apoptosis of cardiomyocytes via activating AMPK/PGC-1 $\alpha$  and inhibiting the RhoA/ROCK pathway". I believe that this manuscript should be major revision: Q1. It is very important to change and modify the title. the title is not appropriate. Q2. Are the objectives and the rationale of the study clearly stated? Q3. In the abstract, the research gap was not clearly stated. In addition, the authors need to rewrite the study objectives to be more academic writing Q4. In the introduction, include the study's significance and novelty. What makes the study different from the rest and what does it add to the current knowledge?. Q5. In the introduction, the authors should have explained the purpose of this study and the existing gaps in this field and explained why this study was conducted. Q6. Are the methods clear and replicable? Do all the results presented to match the methods described? Q7. If relevant are the results novel? Does the study provide an advance in the field? Is the data plausible? Q8. References are relevant, correct, and not recent. The number of references should be increased. please add some references. since this is a



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scientific review, all the sentences need to be supported with references. This study is very beautiful. I liked the sequence and enjoyed reading. Please add more references on similar studies. Q9. There are a lot of grammatical errors. This must be taken care of and addressed. Q10. What are the limitations of the study? A description of limitations is missing at the end of the discussion section. • If your manuscript is related to mine, you can cite it (ORCID: <https://orcid.org/0000-0002-5107-5550>).

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**Peer-review model:** Single blind

**Reviewer's code:** 02817134

**Position:** Editor-in-Chief

**Academic degree:** MD, PhD

**Professional title:** Professor

**Reviewer's Country/Territory:** United States

**Author's Country/Territory:** China

**Manuscript submission date:** 2023-09-21

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2023-09-28 08:44

**Reviewer performed review:** 2023-10-08 00:38

**Review time:** 9 Days and 15 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Novelty of this manuscript	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
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<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input checked="" type="checkbox"/> Rejection
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

## SPECIFIC COMMENTS TO AUTHORS

Li et al. explored the ameliorative effects of empagliflozin (EMP) on high glucose-induced oxidative stress and apoptosis of cardiomyocytes, and its potential underlying mechanisms of likely activating AMPK/PGC-1 $\alpha$  and inhibiting the RhoA/ROCK pathway. It seemed an interesting study, but did not reach out to the satisfied level and provide any really useful information. Majors 1. The study was superficial without a logical connection between in vivo and in vitro studies. Db/db mice are type 2 diabetes that should be hyperglycemia with hyperlipidemia, however, the in vitro study the authors used 30 mM glucose without any palmitate as most other in vitro studies used. 2. The authors stated “our study shows that beyond glycemic control, empagliflozin improved.....”. However, the authors might not see their results in the Table 1 where EMP significantly reduced the FBG and HbA1c. How to eliminate the glycemic control role at the in vivo level? The authors might try to use in vitro to explain whether hyperglycemic control is responsible for the cardiac dysfunction protection, but the model does not match, therefore these studies are two separately two unlinked studies, which can not explain each other now. 3. Results (page 13): The



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authors tried to state the cardiac apoptotic cell death is the key patho-mechanism responsible for cardiac dysfunction, and their improvement by EMP. However, the cardiac cell death was superficial, not quantitative evidence to indicate the mitochondrial apoptotic cell death existed in their mouse model. There was not solid evidence for the apoptotic cell death so far. Minors 4. There was control group of EMP.

5. In page 7: Animal models with  $n=7-11$ , why all results showed  $n=3$ . 6. Page 13: There was no description what kind of cardiac function change with these variables, diastolic and systolic function changes?

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**Reviewer's code:** 02991481

**Position:** Associate Editor

**Academic degree:** PhD

**Professional title:** Professor

**Reviewer's Country/Territory:** United States

**Author's Country/Territory:** China

**Manuscript submission date:** 2023-09-21

**Reviewer chosen by:** Yu-Lu Chen

**Reviewer accepted review:** 2023-10-09 14:34

**Reviewer performed review:** 2023-10-09 14:36

**Review time:** 1 Hour

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Novelty of this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
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<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

## SPECIFIC COMMENTS TO AUTHORS

Recommend accept.



## RE-REVIEW REPORT OF REVISED MANUSCRIPT

**Name of journal:** *World Journal of Diabetes*

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**Peer-review model:** Single blind

**Reviewer's code:** 02817134

**Position:** Editor-in-Chief

**Academic degree:** MD, PhD

**Professional title:** Professor

**Reviewer's Country/Territory:** United States

**Author's Country/Territory:** China

**Manuscript submission date:** 2023-09-21

**Reviewer chosen by:** Cong Lin

**Reviewer accepted review:** 2023-10-23 07:44

**Reviewer performed review:** 2023-10-23 08:12

**Review time:** 1 Hour

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Peer-reviewer	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous

statements

Conflicts-of-Interest: [ ] Yes [Y] No

## SPECIFIC COMMENTS TO AUTHORS

The authors were not well addressed the second reviewer's comments, instead of debating with the reviewer by providing a few published works to address these works used same models. In fact, different studies have different working focuses so that under certain conditions, their usage of the similar models might be acceptable. These facts do not mean that the authors can use what the previous works used to support the authors used a correct one. Therefore, these kinds of debates are not well addressing the second reviewer's concern. However, the authors have added the limitation of this study to explain their usage of this not well fit model, which is an acceptable way. Therefore, this work can be accepted as long as the authors can change their title "Empagliflozin ameliorated diabetic cardiomyopathy via activating AMPK/PGC-1 $\alpha$  and inhibiting the RhoA/ROCK pathway" to "Empagliflozin ameliorated diabetic cardiomyopathy probably via activating AMPK/PGC-1 $\alpha$  and inhibiting the RhoA/ROCK pathway" since their conclusion is too strong and was not support by the experimental evidence, but if it read like "..... probably via ....." is acceptable.