



PEER-REVIEW REPORT

Name of journal: *World Journal of Diabetes*

Manuscript NO: 85269

Title: Potential role of microRNA-503 in Icariin-mediated prevention of high glucose-induced endoplasmic reticulum stress

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

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: 2023-04-20

Reviewer chosen by: Geng-Long Liu

Reviewer accepted review: 2023-05-07 18:50

Reviewer performed review: 2023-05-19 09:02

Review time: 11 Days and 14 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 Grade E: Do not publish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 checked="" type="checkbox"/> Grade A: Excellent <input 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



Scientific significance of the conclusion in 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 scientific significance
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 type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input type="checkbox"/> Anonymous <input checked="" type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

In this study, the authors have investigated the potential molecular mechanism by which Icaria (ICA) prevents high glucose (HG)-induced endoplasmic reticulum (ER) stress-dependent apoptosis by regulating miR-503/SIRT4 axis in primary rat kidney (PRK) cells. This study is potentially interesting and innovative, but the reviewer has several concerns that the authors should address before considering its publication in this journal. 1. The title should be changed since currently it is a conclusive; however, this study was only based on cultured cells, therefore, there was no evidence to support these findings in the cultured cells exposed to only high levels of glucose for 24 or 48 hr with and without ICA can be recaptured in diabetic rats, no evidence whether ICA treatment also regulate the miR-503 and ER stress as seen in the vitro study. Therefore, the authors should not conclude “miR-503 promotes the progression of diabetic nephropathy” 2. Abstract: (1) Lacking miR-503 and SIRT4 information in AIM, which two are very important component in this vitro study; (2) Lacking animal model and HG experimental information; (3) Conclusions need to be revised based on what the authors have done and seen. 3. Keywords should include one “Kidney damage” or



**Baishideng
Publishing
Group**

7041 Koll Center Parkway, Suite
160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

“Diabetic kidney injury” 4. Several comments regarding the Introduction, Methods, Results are directly provided in the manuscript. Generally these include (1) need clearly presenting how innovative of this study; (2) clearly presenting the model information for both in vitro and in vivo; lacking information for how many times of the vitro experiments were repeated and whether the cells for each experiments were come from different isolations from the rats (3) Since you do not have DN evidence (renal dysfunction and remodeled kidney pathology), DN should be removed from figures of results; 4) Discussion needs focusing on what you found, do not imply its directly to DN.



PEER-REVIEW REPORT

Name of journal: *World Journal of Diabetes*

Manuscript NO: 85269

Title: Potential role of microRNA-503 in Icariin-mediated prevention of high glucose-induced endoplasmic reticulum stress

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05754965

Position: Peer Reviewer

Academic degree: PhD

Professional title: Postdoc

Reviewer's Country/Territory: United States

Author's Country/Territory: China

Manuscript submission date: 2023-04-20

Reviewer chosen by: Geng-Long Liu

Reviewer accepted review: 2023-05-27 00:45

Reviewer performed review: 2023-06-01 00:54

Review time: 5 Days

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 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 type="checkbox"/> Grade B: Good <input checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation



Scientific significance of the conclusion in 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 scientific significance
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 type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	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

In this study, Su et al investigated the mechanism of Icariin to regulate apoptosis in high glucose (HG) -induced primary rat kidney cells (PRKs). Firstly, the authors identified miR-503 to be upregulated in diabetic nephropathy. Then they showed that Icariin treatment could repress miR-503. Next, they provided data to show that SIRT4 is a target of miR-503. In summary, they identified a Icariin/miR-503/SIRT4 in diabetic nephropathy. Here I have the following concerns about this study. 1. A major issue is that there were little data to demonstrate the role of miR-503 in the pathology of diabetic nephropathy. This should be a necessary part for this research. Authors only revealed the correlation between miR-503 level and diabetic nephropathy. The causative data between them is required. They need to prove that miR-503 contribute to diabetic nephropathy. 2. ERS could not be only determined by the expression of CHOP. Other markers are needed. 3. The role of miR-503 on the expression of SIRT4 should be demonstrated in different cell lines. 4. If the authors can validate their results in vivo, that will be better. 5. In fig 3E, the SIRT4 band seemed over-exposed. Please replace it with a less-exposed band. 6. In fig 4C, authors need to mark "SIRT4 WT" and "SIRT4



**Baishideng
Publishing
Group**

7041 Koll Center Parkway, Suite
160, Pleasanton, CA 94566, USA

Telephone: +1-925-399-1568

E-mail: bpgoffice@wjgnet.com

https://www.wjgnet.com

Mut". In the manuscript and figure legend, this luciferase assay should be depicted in detail. 7. The expression "HG induction" is confusing and not appropriate. Authors need to revise it.



PEER-REVIEW REPORT

Name of journal: *World Journal of Diabetes*

Manuscript NO: 85269

Title: Potential role of microRNA-503 in Icariin-mediated prevention of high glucose-induced endoplasmic reticulum stress

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05452652

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: India

Author's Country/Territory: China

Manuscript submission date: 2023-04-20

Reviewer chosen by: Geng-Long Liu

Reviewer accepted review: 2023-05-31 08:59

Reviewer performed review: 2023-06-01 01:42

Review time: 16 Hours

Scientific quality	<input checked="" type="checkbox"/> Grade A: Excellent <input 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 checked="" type="checkbox"/> Grade A: Excellent <input 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 checked="" type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation



Baishideng Publishing Group

7041 Koll Center Parkway, Suite
160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
<https://www.wjgnet.com>

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

SPECIFIC COMMENTS TO AUTHORS

This study can be accepted in the present format. It will be of interest to the clinicians and researchers and also help in developing newer drugs for prevention and treatment of diabetic nephropathy. Congratulations to these authors for an excellent study demonstrating the molecular mechanisms for development of nephropathy in diabetes and potential role of ICAnin the management of diabetic nephropathy.



RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: *World Journal of Diabetes*

Manuscript NO: 85269

Title: Potential role of microRNA-503 in Icariin-mediated prevention of high glucose-induced endoplasmic reticulum stress

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05754965

Position: Peer Reviewer

Academic degree: PhD

Professional title: Postdoc

Reviewer's Country/Territory: United States

Author's Country/Territory: China

Manuscript submission date: 2023-04-20

Reviewer chosen by: Jia-Ru Fan

Reviewer accepted review: 2023-06-13 13:54

Reviewer performed review: 2023-06-13 13:58

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
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input 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 checked="" type="checkbox"/> Accept (General priority) <input 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



**Baishideng
Publishing
Group**

7041 Koll Center Parkway, Suite
160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

statements

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

SPECIFIC COMMENTS TO AUTHORS

This version can be accepted now.