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PEER-REVIEW REPORT

Name of journal: *World Journal of Diabetes*

Manuscript NO: 90256

Title: Regulatory role of peroxynitrite in advanced glycation end products mediated diabetic cardiovascular complications

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 00504362
Position: Editorial Board
Academic degree: PhD
Professional title: Professor
Reviewer's Country/Territory: Chile
Author's Country/Territory: India

Manuscript submission date: 2023-11-28

Reviewer chosen by: Jia-Ru Fan

Reviewer accepted review: 2024-01-02 10:56

Reviewer performed review: 2024-01-03 14:08

Review time: 1 Day and 3 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Novelty of this manuscript	[ ] Grade A: Excellent [ ] Grade B: Good [Y] Grade C: Fair [ ] Grade D: No novelty
Creativity or innovation of this manuscript	[ ] Grade A: Excellent [ ] Grade B: Good [Y] Grade C: Fair [ ] Grade D: No creativity or innovation

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Scientific significance of the conclusion in this manuscript	[ ] Grade A: Excellent [ ] Grade B: Good [Y] Grade C: Fair [ ] Grade D: No scientific significance
Language quality	[Y] 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 [Y] Rejection
Re-review	[ ] Yes [Y] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous
	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

To this reviewer, the point raised by the author highlighting that the original article does not address the significant role of Nitric oxide Synthase (NOS) in regulating AGE formation is not proper, because the author did cover key well-documented processes by which AGEs can interfere with either nitric oxide synthesis and/or NO bioavailability, and thus contributing to vascular dysfunction. AGEs can quench inactive nitric oxide. Additionally, AGEs, through RAGE-dependent mechanisms can reduce nitric oxide synthesis by endothelium by reducing eNOS expression by either suppressing gene expression or increasing the rate of mRNA degradation

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Peer-review model: Single blind

Reviewer's code: 07303215
Position: Editorial Board
Academic degree: MD
Professional title: Assistant Professor
Reviewer's Country/Territory: United States
Author's Country/Territory: India

Manuscript submission date: 2023-11-28

Reviewer chosen by: Jia-Ru Fan

Reviewer accepted review: 2024-01-05 20:28

Reviewer performed review: 2024-01-05 20:35

Review time: 1 Hour

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Novelty of this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No novelty
Creativity or innovation of this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No creativity or innovation

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Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [Y] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No
Peer-reviewer statements	Peer-Review: [ ] Anonymous [Y] Onymous
	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

This is a letter to the editor describing the regulatory role of peroxynitrite (ONOO-) in advanced glycation end product mediated diabetic cardiovascular complications. The letter is succinct, concise, and raises key points in terms of the consideration of nitric oxide synthase and peroxynitrite. I would spell out NADPH with first use.

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Peer-review model: Single blind

Reviewer's code: 05111420
Position: Peer Reviewer
Academic degree: PhD

Professional title: Attending Doctor

Reviewer's Country/Territory: China

Author's Country/Territory: India

Manuscript submission date: 2023-11-28

Reviewer chosen by: Jia-Ru Fan

Reviewer accepted review: 2024-01-04 00:59

Reviewer performed review: 2024-01-11 03:51

Review time: 7 Days and 2 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Novelty of this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No novelty
Creativity or innovation of this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No creativity or innovation

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Language quality	[ ] Grade A: Priority publishing [Y] 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 [Y] Major revision [ ] Rejection
Re-review	[ ] Yes [Y] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous
	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Thanks for the invitation for reviewing the letter. 1.Damage and dysfunction of vascular endothelial cells (ECs) have been shown to be the initiating factors leading to the onset and development of diabetic vascular complications, and 25% of ECs in neovascularisation have been shown to be differentiated from endothelial progenitor cells (EPCs), making EPCs important biochemical factors for the treatment of various cardiovascular diseases and damaged blood vessels. Endothelial nitric oxide synthase (eNOS) is an important factor in the ability of EPCs to migrate. High levels of glucose in the body can induce oxidative stress, which in turn can lead to impaired EPC function and reduced nitric oxide (NO) production. The authors propose that nitric oxide (NO) has anti-inflammatory, anticoagulant and vasodilatory effects, but can be inactivated by reacting with O2-. This produces a powerful oxidant, peroxynitrite (ONOO-). Therefore, the authors argue that the regulatory role of peroxynitrite (ONOO-) in the late glycation end products of diabetic cardiovascular complications is considered a modulator of diabetic cardiovascular complications. This idea is innovative。 2.I noticed most citations were from review or book.Coud you prove some basic research articles or clinical

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research support from citations. 3.The author states that the beneficial or detrimental effects of O2- and O2-mediated ROS or RNS depend on their concentration and site of formation[3]. It has also been suggested that O2- can directly interact with nitric oxide (NO) to produce highly toxic peroxynitrite (ONOO-), which plays a key role in the vascular changes of cardiovascular complications of diabetes. The letter seems to lack the description of ONOO- the key role in diabetes cardiovascular, which can be supplemented or adjusted. It could be better that more explicit and detailed about the specific relationship between the beneficial or harmful effects of ROS or RNS and their concentrations and where they are formed, otherwise it is just a repetition of the previous article. 4.“Prostaglandin E2 (PGE2), a lipid signaling molecule involved in immune modulation for regulating pain and inflammation, might potentiate tissue regeneration and repair following injury in diverse organ systems.” I don't understand why this passage is included in the article. This doesn't seem to be related to the topic of the article. 5.At the end of the article you suggested that the anti-inflammatory, anti-clotting and vasodilating effects of NO can be abolished by reaction with O2-, resulting in the production of the potent oxidant peroxynitrite (ONOO-), I understand that diabetes complications are related to the inactivation of NO, but I do not understand how you arrived at your conclusion that peroxynitrite (ONOO-) has an important regulatory role in diabetes complications. 6.Based on the role of peroxynitrite (ONOO-) in AGE， which aspects should be followed for treatment or research on cardiovascular complications in the future?