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COMMENTS	REPLY
SPECIFIC COMMENTS TO AUTHORS	
REVIEWER 1	
Scientific Quality: Grade C (Good) **Language Quality:** Grade B (Minor language polishing) **Conclusion:** Major revision	I appreciate the valuable comments. And thanks for giving me opportunity to improve the letter.
Thanks for the invitation to review the letter.	Thanks for your valuable comments.
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	Thanks for kind appreciation to my letter. I have incorporated the necessary information in the revised manuscript.

innovative。	
2. I noticed most citations were from review or book.Coud you prove some basic research articles or clinical research support from citations.	I have increased the number of references and cited them properly according to the journal's format.
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.	Thanks for the valuable comments. The relevant information was incorporated in the revised Letter. New paragraph was incorporated describing the same with appropriate citations.
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.	I appreciate the Reviewer’s concern. The context was removed and rewritten as per the respected reviewer’s suggestion and fact.
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	The scientific aspect of the role of ONOO- is explained broadly in the revised letter. Highlighted as yellow ink.

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 future treatment or research on cardiovascular complications?	The role of peroxynitrite (ONOO-) in diabetic cardiovascular complications and advanced glycation end products requires further investigation from a scientific perspective.
REVIEWER 2	
Scientific Quality: Grade B (Very good) **Language Quality:** Grade B (Minor language polishing) **Conclusion:** Accept (General priority)	"Thank you for your encouragement & Appreciation for my Letter"
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.	"Thank you for your encouragement & Appreciation for my Letter" Proper abbreviation is included in the revised letter.
REVIEWER 3	
Scientific Quality: Grade C (Good) **Language Quality:** Grade A (Priority publishing) **Conclusion:** Rejection	Many Thanks for the Scientific criticism.
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.	Many Thanks for the Scientific criticism. I have revised the letter as per all the respected reviewer's comments to make it suitable for consideration for publication.
Additionally, AGEs, through RAGE-dependent	The letter is now improved with more

mechanisms can reduce nitric oxide synthesis by endothelium by reducing eNOS expression by either suppressing gene expression or increasing the rate of mRNA degradation.	references and scientifically explains the role of peroxynitrite (ONOO-) in relation to site/ tissue /cells specific regulation of endothelial damage to cardiovascular complications.
EDITORIAL OFFICE'S COMMENTS	
(1) Science editor:	
Conflict of interest statement: Academic Editor has no conflict of interest.	Declaration Given.
2 Scientific quality: The author submitted a study of the regulatory role of peroxynitrite in cardiovascularcomplications of diabetes mediated by advanced glycation end products. The manuscript is overall qualified. (1) Advantages and disadvantages: The reviewer have given positive peer-review reports for themanuscript. Classification: Grade B, Grade C, and Grade C; Language Quality: Grade B, Grade A, and GradeB. This is a letter to the editor describing the regulatory role of peroxynitrite (ONOO-) in advanced glycationend product mediated diabetic cardiovascular complications. The letter is succinct, concise, and raises keypoints in terms of the consideration of nitric oxide synthase and peroxynitrite. The letter seems to lack thedescription of ONOO- the key role in diabetes cardiovascular, which can be supplemented or adjusted. (2) Main manuscript content: The author clearly stated the purpose of the study and the research structureis complete. However, the manuscript is still required a further revision according to the detailed commentslisted below. (3) Table(s) and figure(s): There are no Figures and no Tables should be improved. (4) References: A total of 8 references are cited, including 5 published in the last 3 years. The reviewerdidn't request the authors to cite improper references published by him/herself. 3 Language evaluation: The English-language grammatical presentation needs to be improved to a certainextent. There are many errors in grammar and format, throughout the entire manuscript. Before finalacceptance, the authors must provide the English Language Certificate issued by a professional Englishlanguage editing company. Please visit the following website for the professional English language	Thanks for giving me the opportunity to improve the letter. All changes are Highlighted as yellow ink. Moreover, I have increased the number of references and cited them properly according to the journal's format. Major grammatical mistakes were corrected by "Grammarly" AI assisted software I have made all the necessary corrections based on the reviewers' comments and provided a reply to their queries. DOI and PUBID provided in all

editingcompanies we recommend: https://www.wjgnet.com/bpg/gerinfo/240 . 4 Specific comments: (1) Please provide the filled conflict-of-interest disclosure form. (2) Please provide the PubMed numbers (https://pubmed.ncbi.nlm.nih.gov/) and DOI citation numbers(https://doi.crossref.org/simpleTextQuery) to the reference list and list all authors of the references. If areference has no PMID and DOI, please provide the source website address of this reference. 5 Recommendation: Conditional acceptance. Language Quality: Grade B (Minor language polishing) Scientific Quality: Grade C (Good)	references.
(2) Company editor-in-chief:	
I have reviewed the Peer-Review Report, and full text of the manuscript, all of which have met thebasic publishing requirements of the World Journal of Diabetes , and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-ReviewReport, Editorial Office's comments and the Criteria for Manuscript Revision by Authors. When revising the manuscript, it is recommended that the author supplement and improve thehighlights of the latest cutting-edge research results, thereby further improving the content of themanuscript. To this end, authors are advised to apply PubMed, or a new tool, theRCA, of which datasource is PubMed.RCA is a unique artificial intelligence system for citation index evaluation ofmedical science and life science literature. In it, upon obtaining search results from the keywordsentered by the author, "Impact Index Per Article" under "Ranked by" should be selected to find thelatest highlight articles, which can then be used to further improve an article under preparation/peer-review/revision. Please visit our RCAdatabase for more information at:https://www.referencecitationanalysis.com/, or visit PubMed at: https://pubmed.ncbi.nlm.nih.gov/.	I appreciate your consideration. I appreciate the Editor-in-Chief's continuous effort to maintain the journal's quality. I have made all the necessary corrections based on the reviewers' comments and provided a reply to their queries. The changes I made are highlighted in yellow ink for easy identification. Moreover, I have increased the number of references and cited them properly according to the journal's format. DOI and PUBID provided in all references.