



SDI Review Form 1.6

Journal Name:	<u>International Journal of Biochemistry Research & Review</u>
Manuscript Number:	Ms_IJBCRR_31435
Title of the Manuscript:	Mechanistic Insight of Transient Receptor Potential Melastatin 8 Role in Streptozotocin Induced Diabetic Nephropathy
Type of the Article	Original Research Article

General guideline for Peer Review process:

This journal's peer review policy states that **NO** manuscript should be rejected only on the basis of '**lack of Novelty**', provided the manuscript is scientifically robust and technically sound.

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PART 1: Review Comments

	Reviewer's comment	Author's comment (if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)
Compulsory REVISION comments	This submission aims to know the functional role of TRPM8 via the use of its agonist in an animal model of diabetic nephropathy (DN). Please take the concerns below. 1. Association of TRPM8 with DN was not introduced in clear. 2. Purity of geraniol (GE) was not indicated. Also, preparation of GE in vegetable oil was unclear. 3. Main mechanism(s) for GE remained obscure. 4. Direct inhibition of TRPM8 is helpful to know the action of GE. 5. Linkage of VEGF with TRPM8 did not introduce in a good way. 6. Antioxidant-like action and reduction of hyperglycemia by GE shall be connected to TRPM8 in the discussion section. 7. Basic action of GE for decrease of hyperglycemia was not concerned in discussion section. 8. It has been established that DN can be improved by reduction of hyperglycemia. Similarly, GE produced both effects. Is this related to TRPM8 activation?	Dear reviewer thank you so much for your valuable comments that had greatly improved our manuscript. Here are responses point by point 1. Association of TRPM8 with DN was not introduced in clear. -We agree with the reviewer, but since this association is novel and has been searched before so no previous works state this association. We included sentences in this regard in the introduction section (highlighted in yellow). 2. Purity of geraniol (GE) was not indicated. Also, preparation of GE in vegetable oil was unclear. We apologize for not including this part and we added it to the methods section. 3. Main mechanism(s) for GE remained obscure. The GE underlying mechanisms are multifaceted in this work we have focused on TRPM8 activation and expression and we re-explained it in discussion section. 4. Direct inhibition of TRPM8 is helpful to know the action of GE. -We totally agree with reviewer in this regard, however the knock out experiments are out of the scope of this paper and we are currently performing this experiments for next papers.



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		5. Linkage of VEGF with TRPM8 did not introduce in a good way. -We totally agree with the reviewer and we added this part in the introduction, Table (2) for correlation and discussion sections. 6. Antioxidant-like action and reduction of hyperglycaemia by GE shall be connected to TRPM8 in the discussion section. -We thank the reviewer for this note and we introduced a correlation table to TRPM8 expression and explained it in the discussion section.
<u>Minor</u> REVISION comments	As the above.	7. Basic action of GE for decrease of hyperglycemias was not concerned in discussion section. We agree with the reviewer comment and we added it to the discussion section 8. It has been established that DN can be improved by reduction of hyperglycaemia. Similarly, GE produced both effects. Is this related to TRPM8 activation? We thank the reviewer for this comment, although this was the scope of next paper, however we added figure (4, D), about the expression of TRPM8 mRNA in pancreatic tissues of diabetic and control rats, that reveals a role of TRPM8 in reduction of hyperglycemia and insulin action.
<u>Optional/General</u> comments	This submission shows interesting and helpful data.	