

## ESPS PEER-REVIEW REPORT

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

**ESPS manuscript NO:** 26370

**Title:** Nitrate-nitrite-nitrosamines exposure and the risk of type 1 diabetes: A review of current data

**Reviewer's code:** 00037668

**Reviewer's country:** United States

**Science editor:** Jin-Xin Kong

**Date sent for review:** 2016-04-08 14:12

**Date reviewed:** 2016-05-11 23:26

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input checked="" type="checkbox"/> [ Y] Accept
<input checked="" type="checkbox"/> [ Y] Grade B: Very good	<input checked="" type="checkbox"/> [ Y] Grade B: Minor language polishing	<input type="checkbox"/> [ ] The same title	<input type="checkbox"/> [ ] High priority for publication
<input type="checkbox"/> [ ] Grade C: Good	<input type="checkbox"/> [ ] Grade C: A great deal of language polishing	<input type="checkbox"/> [ ] Duplicate publication	<input type="checkbox"/> [ ] Rejection
<input type="checkbox"/> [ ] Grade D: Fair	<input type="checkbox"/> [ ] Grade D: Rejected	<input checked="" type="checkbox"/> [ Y] No	<input type="checkbox"/> [ ] Minor revision
<input type="checkbox"/> [ ] Grade E: Poor		BPG Search:	<input type="checkbox"/> [ ] Major revision
		<input type="checkbox"/> [ ] The same title	
		<input type="checkbox"/> [ ] Duplicate publication	
		<input type="checkbox"/> [ ] Plagiarism	
		<input checked="" type="checkbox"/> [ Y] No	

## COMMENTS TO AUTHORS

This manuscript reviews the current literature relative to the potential protective or deleterious role of nitrate, nitrite, and nitrosamine on T1DM onset and progression. The conclusion of the authors is that currently there is no clear consensus and understanding of the relation between these nitrogen based compounds and diabetes. While some studies have provided potential support for a protective role, others have evidence no effect or actually a negative effect. Comments: Some minor English polishing is necessary. For example, page 3, last line of paragraph 1.1: It is unclear if the authors mean patients < 15 y.o. or patients that presented diabetes for less than 15 years. Also, there is some redundancy in adjectives that takes away from the message the authors want to convey (e.g. page 3, line 2 of paragraph 1.2: ...to be important etiologically (relevant?) to beta cells; or page 5, first three lines: rephrasing is needed).

## ESPS PEER-REVIEW REPORT

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

**ESPS manuscript NO:** 26370

**Title:** Nitrate-nitrite-nitrosamines exposure and the risk of type 1 diabetes: A review of current data

**Reviewer's code:** 02446589

**Reviewer's country:** Turkey

**Science editor:** Jin-Xin Kong

**Date sent for review:** 2016-04-08 14:12

**Date reviewed:** 2016-05-20 20:29

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ Y ] Grade A: Excellent	[ Y ] Grade A: Priority publishing	Google Search:	[ Y ] Accept
[ ] Grade B: Very good	[ ] Grade B: Minor language polishing	[ ] The same title	[ ] High priority for publication
[ ] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] Duplicate publication	[ ] Rejection
[ ] Grade D: Fair	[ ] Grade D: Rejected	[ Y ] No	[ ] Minor revision
[ ] Grade E: Poor		BPG Search:	[ ] Major revision
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[ Y ] No	

## COMMENTS TO AUTHORS

This review focuses on the potential effect of nitrate-nitrite-nitrosamines exposure on development of T1DM and examines the associations between nitrate-nitrite-nitrosamines exposure to ascertain whether higher nitrate-nitrite levels may contribute to the development of T1DM. Authors have performed a systematic search strategy of several databases using some relevant key words. Finally they concluded from ecologic surveys, case-control and cohort studies that the present results about relationship between nitrate-nitrite exposure from several sources and the risk of T1DM are conflicting or sometimes contradictory. As they suggested additional research is critical to clarify potential harmful effects of nitrate-nitrite-nitrosamine exposure on  $\beta$ -cell autoimmunity and the risk of T1DM which is particularly important for developing countries. This review provides a good collection of present data and emphasizes the importance of further studies to understand this issue.

## ESPS PEER-REVIEW REPORT

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

**ESPS manuscript NO:** 26370

**Title:** Nitrate-nitrite-nitrosamines exposure and the risk of type 1 diabetes: A review of current data

**Reviewer's code:** 00978063

**Reviewer's country:** Australia

**Science editor:** Jin-Xin Kong

**Date sent for review:** 2016-04-08 14:12

**Date reviewed:** 2016-04-21 15:42

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good		<input type="checkbox"/> Duplicate publication	
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input checked="" type="checkbox"/> Minor revision
	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

## COMMENTS TO AUTHORS

I enjoyed reading this review, which addresses the possible impact of dietary exposure to nitrite, nitrate and nitrosamines as regards risk of type I diabetes. Fundamentally, it looks as if nitrite and nitrate exposure is generally reasonably safe, except potentially with extreme doses, and indeed that dietary nitrate supplementation via green vegetables or beets may be cardioprotective. On the other hand, nitrosamines in particular (and also possibly nitrates and nitrites in high doses) may induce nitrosative/oxidative stress, and increase risk of beta-cell damage. I have only a few rather minor criticisms. 1. The conclusion in the abstract is too weak. Of course, there is some uncertainty, but the authors need not "sit on the fence". 2. There should be a brief section on toxicity in animal models, where it is possible to study these issues in a relatively "pure culture". 3. The authors do not discuss the potential impact of population incidence of glucose 6 phosphate dehydrogenase deficiency (favism) on the risk of adverse effects from nitrite-induced methaemoglobinaemia, and whether this might affect risk of type I diabetes. 4. The increase of type I diabetes is increasing (introduction). What are the other potential causes/