

Cordoba, Argentina
March 1, 2017

Executive Editor
World Journal of Gastroenterology
Dr. Jing Yu

Dear Dr. Jing Yu,

Please find enclosed the edited manuscript in Word format (file name: **32421 revised**).

Name of journal: World Journal of Gastroenterology

Manuscript NO.: 32421

Column: Minireviews

Title: Oxidative stress, antioxidants and intestinal calcium absorption

Authors: Gabriela Diaz de Barboza, Solange Guizzardi, Luciana Moine and Nori Tolosa de Talamoni

Correspondence to: Nori Tolosa de Talamoni, Professor, Cátedra de Bioquímica y Biología Molecular, Facultad de Ciencias Médicas, Universidad Nacional de Córdoba, Av. Haya de la Torre s/n, Córdoba 5000, Argentina. ntolosa@biomed.fcm.unc.edu.ar

Reviewer code: 03335792 and 03476668

First decision: 2017-02-09 13:45

Scientific editor: Jing Yu

The manuscript has been improved according to the suggestions of reviewers:

- 1) Format has been updated
- 2) Revision has been made according to the suggestions of the reviewers.

Reviewer 3335792. As the Reviewer said “whether "ROS/RNS" implies "ROS or RNS", "ROS and RNS" or "ROS and/or RNS", this was clarified in each instance according to the context along the entire ms.

Reviewer 3335792. The reviewer said: “A sentence in the middle paragraph on page 7 reads incomplete and would need correction - "if the redox environment ...promotes

apoptosis or necrosis". The sentence was changed to this one: "If the redox environment is highly oxidized, it promotes apoptosis or necrosis" (Page 9, line 239).

Reviewer 3335792. On page 7 (lines 182-194), a paragraph related to xanthine oxidase, xanthine dehydrogenase and Mo was added, as suggested by the reviewer. New references were added (Ref. 26-30)

Reviewer 3335792. Does excess Calcium dampens the activities of SODs and other important endogenous antioxidant enzymes? (Reviewer's question).

Answer: At the intestinal level, it is not clear whether excess calcium dampens the activities of SOD's and other important endogenous antioxidant enzymes. The sensitivity of SOD and catalase activity to calcium was determined in both smooth muscle and mucosa of the rabbit bladder, and it has been shown that both enzymes have different sensitivity to the cation. In muscle, 1 to 5 mM calcium decreased the SOD activity. With regard to catalase, 1 mM calcium decreased its activity in muscle, but did not produce change in the enzyme activity in mucosa. At 5 mM calcium increased catalase activity from mucosa and produced no change in the activity from the muscle (Fitzpatrick B. ·Schuler C. ·Leggett R.E. ·Levin R.M., Urol Int. 2012;88(1):107-11. doi: 10.1159/000333144.).

Reviewer 3476668. The reviewer said: "Title looks incomplete. Please modify it accordingly". We consider that this title covers all the topics of the revision. **Oxidative stress** covers the generation of ROS and RNS and the action of pro-oxidants, **antioxidants** covers endogenous antioxidant defense system in the gut, and **the intestinal calcium absorption** covers mechanisms of intestinal calcium absorption, actions of pro-oxidants on intestinal calcium absorption and antioxidants and their molecular mechanisms for the preservation of intestinal calcium absorption. The title was not considered incomplete by the Reviewer 3335792.

Reviewer 3476668. Are there any FDA approved or synthetic agents available other than Quercetin, melatonin, lithocholic and ursodeoxycholic acids, which can block the effect of GSH depleting drugs?

There are some other drugs that can block the effect of GSH depleting drugs (acetylcysteine, OTC, etc), but there is no information whether they can restore or not the intestinal calcium absorption altered by oxidative stress, the aim of this review. An interesting review entitled "Glutathione and glutathione analogues; Therapeutic potentials" (Jian Hui Wu, Gerald Batist, BBActa general Subjects, 2013) describes different synthetic drugs and their applications, but apparently most of them are being investigated or are in early phase clinical studies in humans.

Reviewer 3476668.

Minor language polishing has been made:

INTRODUCTION

Lines 124-125: “high fat high carbohydrate” was replaced by **high-fat and high-carbohydrate**

Line 130: “exacerbate” was replaced by “**exacerbating**”

Line 140: “by” was replaced by “**they**”

Line 157: “develop” was replaced by “**developing**”

ENDOGENOUS ANTIOXIDANT DEFENSE SYSTEM IN GUT

Line 210: “which” was replaced by “**and**”

Line 252: “**the**” was added

Line 270: “is descomposed to” was replaced by “**is descomposed into**”

Line 272: “GPx not only reduces H₂O₂, but” was replaced by “**GPx reduces not only H₂O₂, but**”

Line 280: “reduce” was replaced by “**reducing**”

Line 288: “**the**” was added

MECHANISMS OF INTESTINAL CALCIUM ABSORPTION

Line 304: “**the**” was added

Line 315: “which apparently are” was replaced by “**which are apparently**”

Line 317: “**the**” was added

Line 318: “which apparently is” was replaced by “**which is apparently**”

ACTIONS OF PRO-OXIDANTS ON INTESTINAL CALCIUM ABSORPTION

Line 358: “decreases” was replaced by “**decreased**”

Line 393: “mitochondria” was replaced by “**mitochondrial**”

Line 395: “**it**” was added

Line 433: “**the**” was added

ANTIOXIDANTS AND THEIR MOLECULAR MECHANISMS FOR THE PRESERVATION OF INTESTINAL CALCIUM ABSORPTION

Line 488: “**a**” was added

Line 532: the sentence was reordered

Line 541: “work” was replaced by “**study**”

Note: I guarantee that after these changes, the quality of the language in this ms is Grade A.

We hope that after these changes, the manuscript could be considered suitable for publication in WJG.

Thank you very much.

Sincerely yours,

A handwritten signature in black ink, appearing to read 'Nori Tolosa de Talamoni', with a horizontal line underneath.

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