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October 23, 2015.

Lian-Sheng Ma
Editors-in-Chief
World Journal of Diabetes.

Dear Editor:

On behalf of my colleagues, I am sending the new version of the review by invitation entitled: "Novel nutraceutic therapies for the treatment of metabolic syndrome" (22334), for the consideration of your editorial authority.

We appreciate the Reviewers' comments, which we believe have helped to strengthen our manuscript. We have provided our responses to the Reviewers' comments below and with the above-mentioned changes; we hope that the manuscript is now acceptable for publication.

Sincerely,

A handwritten signature in black ink, appearing to be 'M. González-Ortiz', with a stylized, overlapping structure.

Manuel González-Ortiz, MD, MSc, PhD.

COMMENTS TO THE REVIEWERS:

COMMENTS TO AUTHORS

In this review article, authors focused on berberine, bitter melon, *Gymnema sylvestre*, *Irvingia gabonensis*, resveratrol and ursolic acid as nutraceutical therapies for metabolic syndrome.

I like to give the following comments.

1. Rationale for you to pick up these nutrients only shall be explained in the introduction in detail.

- Rationale to pick up specifically these nutrients was added to the introduction section.

2. Effective dose of each nutrient was not mentioned either in animals or human subjects.

- When they were available, effective doses were described in the paper.

3. Effect of each nutrient on body weight and/or feeding behavior was not conducted.

- Available information of each nutrient on body weight and/or feeding behavior was given in the correspondent section.

4. Curcumin is more popular than *Gymnema sylvestre* or *Irvingia gabonensis*. But it was involved in this article. Why?

- Curcumin was not involved in the present paper because we are not studying it at this moment in our Research Institute as was described in the introduction section.

5. Conclusion is too simple and without novelty. Additionally, perspectives of nutraceutical therapies were not included.

- The conclusion was changed.

COMMENTS TO AUTHORS

General Comments:

1. The review has a very interesting and relevant topic, especially with the immergence and prevalence of the MetS. The manuscript is very well written and there are only a few issues that should be addressed to strengthen this review.

Abstract:

1. The abstract is very short. A longer, more informational abstract may be warranted (if allowed due to word counts).

- The abstract was improved with more information.

Berberine:

1. Page 6; Para 1: The authors state "...patients had a remission of 36% ($p = 0.037$) in the presence of MetS and a significant decrease in waist circumference in females (106 ± 4 vs. 103 ± 3 cm, $p < 0.05$), systolic blood pressure (123 ± 7 vs. 115 ± 9 mmHg, $p < 0.01$), and triglycerides (2.4 ± 0.7 vs. 1.4 ± 0.5 mmol/L, $p < 0.01$)[12]." Are the changes in SBP and Triglycerides also in females only? The wording is a bit confusing and may suggest that these changes are all in females only. Suggest clarifying.

- Redaction of the paragraph was improved, clarifying the results.

2. Page 7; Para 1: The authors state "Male db/db mice were given sterile....." Please clarify what db/db mice are and why these types may be significant.

- Redaction of the paragraph was improved, clarifying the results.

3. Page 9; Para 1: The authors state "Except for waist circumference...." How much did the waist circumference decrease?

- Results of waist circumference were added.

COMMENTS TO AUTHORS

At least one time Authors should refer to NAFLD, universally recognized as strictly linked to Metabolic Syndrome, quoting one of the most recent and comprehensive reviews on this hot topic, completely overlooked. What about non-alcoholic fatty liver disease as a new criterion to define metabolic syndrome? World J Gastroenterol. 2013 Jun 14;19(22):3375-84.

- This information was added to the introduction section with the correspondent reference.