

Monday 15/07/2014



Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 11246-review.doc).

Title: Focus on emerging drugs for the treatment of patients with non-alcoholic fatty liver disease

Authors: Alessandro Federico, Claudio Zulli, Ilario de Sio, Anna Del Prete, Marcello Dallio, Mario Masarone, Carmela Loguercio

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 11246

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

The formatting has been updated. The changes are now incorporated in the text of the revised version and are marked in red. Below, you can find our point-by-point responses to the referee's comments.

We believe that the manuscript has been considerably improved by the reviewer's suggestions, and we hope that the Editorial Staff agrees on the worthiness of this publication for the Journal.

Reviewer 1 (01490291)

We thank the Reviewer for her/his comments.

(1) Section 3.1: add one or more examples of the unresolved issues about this approach

We agree with the reviewer's comment. We have added the example of the unresolved question of cholesterol ingestion and its implications on fatty liver disease. We also added bibliographic references.

(2) Section 3.2: the section regarding the vitamin E should be moved to homogeneity in section 6.2

We have moved this entire section to 6.2, and the relative bibliography was adjusted.

(3) Section 6 the sequence of cytoprotective agents must be reversed according to the sequence 6.1 6.2 (UDCA before and after antioxidants)

We have changed the sequence as suggested.

(4) Section 7.1 would add a statement on documented altered intestinal permeability as evidenced by Miele et al, Hepatology. 2009 Jun;49(6):1877-87. (add this bibliography)

We have added a statement on altered intestinal permeability and altered the relative bibliography.

(5) Section 7.3: add the bibliography citation of previous studies regarding the role of the renin angiotensin system

We have added this bibliography citation, as suggested.

(6) The title of Table 2 must be completed with the object of the meta-analysis and the reference number of the final bibliography

The title of Table 2 was corrected in accordance with the reviewer's suggestion, and references were

added.

Reviewer 2 (00006552)

We thank the Reviewer for her/his comments.

- (1) To help readers to have a solid message after each section, a brief summary or bullet points should be provided.**

We agree with the reviewer's comment. To help readers obtain a more rapidly delivered and solid take-home message, we added at the end of each section bullet points concerning the most important issues previously discussed.

- (2) Many anti-oxidants are included in 6.2 Anti-oxidants and Herbal Anti-Oxidants Products. A table should be given for comparison of property of agents, efficacy, side effects and study design, etc. 3.**

I chose to avoid inserting additional tables (which should be done for each of the properties mentioned here). Instead, I inserted bullet points at the end of each paragraph, and I hope that the reviewer approves of this choice.

- (3) Table 1 is less informative and a better design of the table with more information is needed for a comprehensive overview.**

Table 1 serves as a mere introduction for all of the paragraphs that follow. If the Reviewer believes that it can be eliminated, we respectfully disagree. Each intervention mentioned is explained in detail in the individual sections; adding more information on each intervention would make it too complex and distracting to read the table.

- (4) A number of linguistic defects are identified, including misspelling, tense, etc. A careful linguistic revision and polishing will guarantee the quality of this review article.**

This manuscript has been revised by a professional native English speaker.

- (5) For obeticholic acid, a late clinical trial published in Gastroenterology 2013 should be discussed.**

We agree with the reviewer's comment. We have considered this recent and late clinical trial published in Gastroenterology 2013, adding it to our discussion of new trials on this drug.

Reviewer 3 (02541391)

We thank the Reviewer for her/his comments.

- (1) Major point: The article is suitable for publication after deeply revising the language, grammar, some inconsistencies in the References section, as well as some assertions, inconsistent with the references.**

As previously indicated to Reviewer 2, the manuscript has been revised by a professional native English speaker. The references section and assertions referred have been verified, and inconsistencies, such as those indicated by Reviewer 1 and 2 and those regarding probiotics (reference 85), anti-hypertensive drugs (references 96-98), or Farnesoid X receptors (references 122, 125), have been removed or corrected.

- (2) Section 4.2 "Exenatide, when compared with metformin, is better to control blood glucose values, improves body weight and ameliorates hepatic enzymes and histological features of steatosis in patients with NAFLD concomitant to T2DM [54]". However, liver histology was not performed in the study conducted by Fan H et al (please see Fan H et al, ref. 54).**

We agree with the reviewer's comment and apologize for the sentence's mistake. We have deleted the liver histology from results of the study.

(3) Table 1 - the title should be reviewed because it does not fully reflect the table contents (...actually proposed" and "Emerging drugs and new horizons" - the safety and tolerability of these drugs are currently being evaluated).

The title of the table has been changed in accordance with this suggestion.

(4) In each section, small paragraphs can be dedicated to the conclusions.

To help readers to obtain a more rapidly delivered and solid take-home message and in accordance with Reviewer 2's suggestion, we have added bullet points to the end of each section.

Reviewer 4 (00058441)

We thank the Reviewer for her/his comment.

Sincerely,

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