

World Journal of Gastroenterology

Manuscript NO: 85307

Peroxisome proliferator-activated receptors as targets to treat metabolic diseases: focus on the adipose tissue, liver, and pancreas

Dear Editor,

I am glad to resubmit the manuscript mentioned above after some amendments suggested by the referees and editors. I believe that the suggestions made by them improved the message that we want to give to the readers of the *World Journal of Gastroenterology*. We hope that the modifications in the text, which are highlighted to facilitate the identification, fulfill their request. Furthermore, some points which were raised by the referees could not be inserted into the text, and therefore they are listed below.

I am looking forward to hearing from you soon.

Yours sincerely,

Vanessa Souza-Mello (corresponding author)

Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: This manuscript should be accepted in this style.

Response: We are grateful for your attention and interest in our manuscript.

Reviewer #2:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: Dear authors! I read with pleasure and interest your manuscript "Peroxisome proliferator-activated receptors as targets to treat metabolic diseases: focus on the adipose tissue, liver, and pancreas", which is a well-written and informative narrative review that covers mechanisms of action and therapeutic potential of the named biological targets. I do not see major flaws. However, it would be nice if at least some preclinical and clinical data on the efficacy/negative effects were summarized, for example, in a table, with certain digital support. Otherwise, conclusion that "PPARs are intriguing therapeutic targets" for metabolic disorders looks vague. No discussion is provided. The paper would benefit if the controversies, unmet need, possible future research directions were listed there.

Response: We are grateful for your enthusiasm and the suggestions to improve the quality of our manuscript. In this revised version, we summarized the main effects of PPAR activation on the studied organs in Table 1. As a narrative review, we discussed the mechanisms of the beneficial effects and the drawbacks in each section (separated according to the target organs: adipose tissue, pancreas, and liver). Therefore, we rewrote the conclusion to fit the format of our review.

It seems that there is a need for re-organization of the text according to standard requirements. Some of the abbreviations are not disclosed even in a list of abbreviations provided at the end of the manuscript.

Response: The abbreviation list was updated as requested.

Figure 1 - please, add an arrow at way "B" and disclose abbreviations shown on the right side of the figure in the footnote (including physiological effects related to certain gene expression).

Response: It was corrected accordingly.

Figure 2 - the font size is too small and hardly visible. The fonts' color is not optimal (pale green and pale brown is difficult to read, it is not contrast against white background).

Response: We agree with the reviewer, changed the font colors, and augmented the font size.

Figure 3 - Is it really necessary? As this is not a book chapter, this may be excessive.

Response: We agree and withdraw Figure 3.

Figure 5 - the text within a "cell" is hardly visible, please, consider to make the font size bigger. Supposedly, these minor flaws could be easily amended. I hope that my comments help the authors to make their manuscript better.

Response: We corrected Figure 5 (now Figure 4) and are grateful for all the comments that improved our manuscript.

Editorial Office's comments and suggestions:

(1) Science editor:

The manuscript has been peer-reviewed, and it's ready for the first decision.

Response: We are grateful for your interest in our study. We made all the modifications and amendments suggested by the reviewer and company editor-in-chief. We hope this revised manuscript improved the message we want to give to the World Journal of Gastroenterology's readers.

(2) Company editor-in-chief:

I have reviewed the Peer-Review Report, the full text of the manuscript, the relevant ethics documents, and the English Language Certificate, all of which have met the basic publishing requirements of the World Journal of Gastroenterology, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors.

Response: We appreciate all the comments and suggestions that improved our manuscript.

Please provide decomposable Figures (in which all components are movable and editable), organize them into a single PowerPoint file.

Response: The PowerPoint with all the figures is attached to the revised version of the manuscript. Many of them were designed using biorender.com. Therefore, it is not possible to offer a decomposable format.

Please check and confirm whether the figures are original (i.e. generated de novo by the author(s) for this paper). If the picture is 'original', the author needs to add the following copyright information to the bottom right-hand side of the picture in PowerPoint (PPT): Copyright ©The Author(s) 2022. If an author of a submission is re-using a figure or figures published elsewhere, or that is copyrighted, the author must provide documentation that the previous publisher or copyright holder has given permission for the figure to be re-published; and correctly indicating the reference source and copyrights. For example, "Figure 1 Histopathological examination by hematoxylin-eosin staining (200 ×). A: Control group; B: Model group; C: Pioglitazone hydrochloride group; D: Chinese herbal medicine group. Citation: Yang JM, Sun Y, Wang M, Zhang XL, Zhang SJ, Gao YS, Chen L, Wu MY, Zhou L, Zhou YM, Wang Y, Zheng FJ, Li YH. Regulatory effect of a Chinese herbal medicine formula on non-alcoholic fatty liver disease. World J Gastroenterol 2019; 25(34): 5105-5119. Copyright ©The Author(s) 2019. Published by Baishideng Publishing Group Inc[6]". And please cite the reference source in the references list. If the author fails to properly cite the published or copyrighted picture(s) or table(s) as described above, he/she will be subject to withdrawal of the article from BPG publications and may even be held liable.

Response: We confirm that all the figures are original and added Copyright ©The Author(s) 2023 to the powerpoint file as requested.

Before final acceptance, when revising the manuscript, the author must supplement and improve the highlights of the latest cutting-edge research results, thereby further improving the content of the manuscript. To this end, authors are advised to apply a new tool, the Reference Citation Analysis (RCA). RCA is an artificial intelligence technology-based open multidisciplinary citation analysis database. In it, upon obtaining search results from the keywords entered by the author, "Impact Index Per Article" under "Ranked by" should be selected to find the latest highlight articles, which can then be used to further improve an article under preparation/peer-review/revision. Please visit our RCA database for more information at: <https://www.referencecitationanalysis.com/>.

Response: Thank you. We used RCA tool in this revised version.