

**World Journal of Gastroenterology**

**Manuscript NO: 74622**

**PPAR-alpha activation and DPP-4 inhibition target gut dysbiosis and inflammation to treat NAFLD in diet-induced obese mice**

Dear Editor,

I am glad to resubmit the manuscript mentioned above after some amendments suggested by the Editor and the referees. 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:** Minor revision

**Specific Comments to Authors:** The manuscript of "PPAR-alpha activation and DPP-4 inhibition target gut dysbiosis and inflammation to treat MAFLD in diet-induced obesity" cover up to date, very important topic. However, I would add in the title ... in diet induced obesity mice, as the work has been done on mice not on humans.

**Response:** We agree with the reviewer and modified the title.

Abstract and key words summarize and focus on the work described in the manuscript. In the background authors add sentence about COVID-19 pandemic - in my opinion it is useless. Was this only for the reference 3? Other sentences in the introduction are well prepared and describe the most important things I need to know about the manuscript.

**Response:** We agree and removed this sentence.

Methods. In the methods authors describe the oral glucose tolerance test - but the WHO recommend to measure the glucose in the plasma of the blood and the manual glucometer (which was used by the authors) is for the glucose level in the whole blood. So the methods should be also described in the end of the discussion as the part of limitation of the study. Moreover, the authors describe the Trayenta - the linagliptin drug which is DPP-4 inhibitor, I would delete the name of the "Trayenta" as a name of Boehringer Ingelheim International drug.

**Response:** We added this limitation to the end of the discussion and the group treated with linagliptin is now referred as HFL group.

Results the results are properly described and are repeatable. The discussion is clear and in logical manner interpret the results and adequately highlight the novelty of the experiments. The figures are well prepared and described, however the same as in the methods, and results I would delete the Trayenta name.

**Response:** We are grateful for your comments. Trayenta (T) was deleted and replaced by linagliptin (L) in the figures and results.

Minor points. Grammar and spelling should be checked (eg. increased insulin sensitiveness - increased insulin sensitivity). I recommend to publish the manuscript after minor revision.

**Response:** English grammar and spelling were checked.

Reviewer #2:

**Scientific Quality:** Grade B (Very good)

**Language Quality:** Grade B (Minor language polishing)

**Conclusion:** Accept (General priority)

**Specific Comments to Authors:** This submission was to address the effects of PPAR-alpha activation and DPP-4 inhibition upon the gut-liver axis,

emphasizing inflammatory pathways in MAFLD management in high-fat-fed C57BL/6J mice.

Response: We are grateful for your positive comments and for the time spent to read and improve the quality of our work.

Editorial Office's comments and suggestions:

**(1) *Science editor:***

The manuscript describes a basic study of PPAR-alpha activation and DPP-4 inhibition target gut dysbiosis and inflammation to treat MAFLD in diet-induced obesity. The topic is within the scope of World Journal of Gastrointestinal. The manuscript covers up to date, very important topic, addressing the effects of PPAR-alpha activation and DPP-4 inhibition upon the gut-liver axis, emphasizing inflammatory pathways in MAFLD management in high-fat-fed male C57BL/6J mice. And the design of this paper is scientific, the conclusion is reliable and valuable for clinic. So it could be acceptable for publication after a minor revision. The questions raised by the reviewers should be answered. Recommendation : Minor revision.

Language Quality: Grade B (Minor language polishing)

Scientific Quality: Grade B (Very good)

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

**(2) *Company editor-in-chief:***

I have reviewed the Peer-Review Report, the full text of the manuscript, and the relevant ethics documents, 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.

Before final acceptance, uniform presentation should be used for figures showing the same or similar contents; for example, "Figure 1 Pathological

changes of atrophic gastritis after treatment. A: ...; B: ...; C: ...; D: ...; E: ...; F: ...; G: ...".

**Response: We changed the figure legends accordingly.**

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.**

Please authors are required to provide standard three-line tables, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden. The contents of each cell in the table should conform to the editing specifications, and the lines of each row or column of the table should be aligned. Do not use carriage returns or spaces to replace lines or vertical lines and do not segment cell content.

**Response: The tables were reformulated.**

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**Response: All figures are original. We added this information in PowerPoint as requested.**