

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 45203

**Title:** Procyanidin B2 protects against diet-induced obesity and non-alcoholic fatty liver disease via the modulation of the gut microbiota in rabbits

**Reviewer's code:** 02885976

**Reviewer's country:** Argentina

**Science editor:** Ruo-Yu Ma

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**Review time:** 23 Hours, 5 Days

| SCIENTIFIC QUALITY                                     | LANGUAGE QUALITY  | CONCLUSION   | PEER-REVIEWER STATEMENTS                      |
|--|---|--|---|
| <input type="checkbox"/> Grade A: Excellent            | <input type="checkbox"/> Grade A: Priority publishing       | <input type="checkbox"/> Accept                    | Peer-Review:                                  |
| <input checked="" type="checkbox"/> Grade B: Very good | <input checked="" type="checkbox"/> Grade B: Minor language | (High priority)                                    | <input checked="" type="checkbox"/> Anonymous |
| <input type="checkbox"/> Grade C: Good                 | polishing   | <input type="checkbox"/> Accept                    | <input type="checkbox"/> Onymous              |
| <input type="checkbox"/> Grade D: Fair                 | <input type="checkbox"/> Grade C: A great deal of           | (General priority)                                 | Peer-reviewer's expertise on the              |
| <input type="checkbox"/> Grade E: Do not               | language polishing  | <input type="checkbox"/> Minor revision            | topic of the manuscript:                      |
| publish  | <input type="checkbox"/> Grade D: Rejection                 | <input checked="" type="checkbox"/> Major revision | <input type="checkbox"/> Advanced             |
|  |   | <input type="checkbox"/> Rejection                 | <input checked="" type="checkbox"/> General   |
|  |   |  | <input type="checkbox"/> No expertise         |
|  |   |  | Conflicts-of-Interest:                        |
|  |   |  | <input type="checkbox"/> Yes                  |
|  |   |  | <input checked="" type="checkbox"/> No        |

## SPECIFIC COMMENTS TO AUTHORS

The present manuscript studied the effects of procyanidins B2 (PB2) on non-alcoholic fatty liver disease (NAFLD) and the role of gut microbiota as a possible mechanism involved. After a carefully reading, these are my concerns: 1) Language: the

manuscript needs to be revised, there are some grammatical mistakes, misspellings and typos. 2) Methods: the authors mentioned in page 7, line 4: "Thirty New Zealand White rabbits" .....and after in lines 8 and 9: "The rabbits were randomly divided into three groups of 8 animals". Why the authors use three groups of 8 animals? What happen with the rest of the rabbits? 3) The authors mentioned in the introduction section that PB2 is a natural plant compound with low bioavailability in humans. Can the author provide the corresponding percentage of bioavailability? Is this low bioavailability also observed in rabbits? 4) Rabbits received a daily dose of PB2 of 150 mg/kg. Please indicate how PB2 was administrated (route of administration). 5) Is PB2 dose equivalent to the average consumption of this compound in a human regular diet? This issue should be considered in the discussion section. 6) Taking into consideration that PB2 has low bioavailability and its possible benefits through modification of gut microbiota, a Control plus PB2 group must be included in order to determine the effect of PB2 on control healthy gut microbiota and metabolic parameters. 7) Please provide the composition of the high fat cholesterol diet in materials and methods section (Supplementary 1 file is missed or not available for the reviewer). 8) The author should explain in the manuscript the concept of "liver index" 9) Introduction section should be shortened. 10) Is it plasma lipid or serum lipid? Please check and correct it. 11) Given that PB2 was administered at the beginning of the experiments, all the effects regarding PB2 group must be referred as preventive. In this way, authors must replace terms like "increased" "decreased" "downregulated" "upregulated" to describe the PB2 effects along the entire manuscript. 12) Figure 2H: there are not significant differences between the groups?? 13) Figure 2I: page 11, lines 11 to 14: "....which was fully prevented by PB2....." According to figure 2I, the effect elicited by PB2 partially prevented the increase in circulating LPS of HCD group. 14) Figure 3A: please add arrows or head arrows in the images to point out the histological findings. Also, bar line

measure is missing. 15) Figure 4E and 4D is unreadable. 16) Page 12, lines 5 to 11: Results about the effects of PB2 on the expression of genes that regulate lipid metabolism are repeated. These sentences should be re-written. 17) Figure legend 3: (F) correspond to FASN and (G) to CPT. 18) Figure 3F and page 12, line 9 of the manuscript: "...CPT was significantly increased compared to the HCD group...." According to the figure 3F, PB2 treatment was not able to prevent the upregulation of CPT expression by HCD. Please correct as well as in discussion section. 19) Figure 3G and page 12, line 10 of the manuscript: "The expression of FASN was also downregulated but the difference was not significant...." According to the figure 3G, PB2 treatment partially prevent the downregulation of FASN expression by HCD and it was significant compared to HCD and Chow groups. Please correct it as well as in discussion section. 20) Discussion section: please revised, some sentences and phrases are repeating the same concept. 21) Page 15, lines 5 to 7: "Thus, SREBP1 may be emerges as a PB2 target gene.....triggered by PB2 in hepatic cells". This sentence should be revised. What do the authors want to explain? Are the authors suggesting that this is a direct effect of PB2 on SREBP1 gene? Given the low bioavailability of PB2, how could it be a direct effect of PB2 at gene level? 22) Along the manuscript, "a" and "b" are used to refer p value, however in Figure legends appears as # and \*.

## INITIAL REVIEW OF THE MANUSCRIPT

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