

Response to reviewer's comments

We thank the reviewers for the careful assessment of the manuscript and their considered comments. Relevant changes have been highlighted in the text and are mentioned in a point to point answer below.

Reviewer 1

1. The manuscript should be rearranged regarding adding comma (,) where is needed, and deleting the parenthesis where is not needed as for example on page 5, second paragraph, line 8.

This has now been corrected.

2. Related to the first paragraph on page 8, I propose to add a brief discussion why alcohol, if it is so, increases gut permeability of large molecules more than small molecules.

As mentioned in the manuscript, several studies report increased permeability for smaller molecules (MW 340-400Da) while others do not, suggesting that there may be methodological issues. We felt, however, that it may be beyond the scope of this review to discuss this possibility, the main argument being the increased permeability to large molecules such as LPS. The statement that “permeability seems to be electively increased for molecules of high molecular weight...” has been toned down and the adverb “electively” removed.

3. Page 9, first paragraph: after the word "dogs" some relevant references should be added.

Two additional references (45 and 46) have been added.

4. Page 9, the first and the small second paragraph should be combined.

This has been done as requested.

5. Page 14, first paragraph, line 11: immediately after "pancreatic stellate cells", the abbreviation (PSCs) should be present.

The abbreviation has been added.

6. Page 15, first paragraph, line 5: after the word "increased" the phrase "in the systemic circulation" should be added.

This has been added in the text.

7. Page 17: the third and fourth paragraphs should be combined.

Done.

8. Page 18, second paragraph, lines 8 and 9: the abbreviation TEN should be preceded by the phrase "total enteral nutrition", the TPN should be written fully without the abbreviation, and on line 9, total enteral nutrition should be replaced by TEN.

This has now been corrected and highlighted in the manuscript.

9. Page 6, line 5: "thatmediates" should be "that mediates".

Done as requested.

Reviewer 2

1. The author should provide a figure to cover the effect of alcohol on the gut flora and permeability.

*We thank the reviewer for this comment. We were somewhat surprised, since the sole figure of the manuscript actually aims at depicting the effect of alcohol on bacterial flora, junctional proteins and Kupffer cells. In order to increase the clarity of the figure, we have added the following headings in the figure and its legend: (A) **Alcohol abstinence** and (B) **Chronic ethanol consumption**.*