



**Baishideng
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Answer to Editor's comments

Please provide an editable manuscript of word format.

Author response: A revised word file has been submitted containing all changes requested by the editors and reviewers (highlighted using track changes).

For manuscripts submitted by non-native speakers of English, please provided language certificate by professional English language editing companies.

Author response: I have discussed this issue previously with the editor Xiang Li in e-mails from April 29th and 30th. As I was not willing to submit such a certificate (as I find this highly discriminating); and the editor proceeded with the peer-review process without this certificate, I thought this matter was settled. Anyways, the manuscript was proof-read to eliminate some minor grammatical errors that were pointed out by one of the reviewers.

Please provide point to point answer to all reviewers.

Author response: All comments of the reviewers have been addressed (s.below)

Author contributions: The format of this section will be as follows: Author contributions: Wang CL, Liang L, Fu JF, Zou CC, Hong F and Wu XM designed the research; Wang CL, Zou CC, Hong F and Wu XM performed the research; Xue JZ and Lu JR contributed new reagents/analytic tools; Wang CL, Liang L and Fu JF analyzed the data; Wang CL, Liang L and Fu JF wrote the paper.

Author response: Such a section has been added after the Acknowledgement section at the end of the manuscript.

5~10 key words. Please don't include abbreviations in the key words

Author response: Abbreviations have been removed from the key words.

Audio core tip: Please offer the audio core tip, the requirement are as follows:

In order to attract readers to read your full-text article, we request that the first author make an audio file describing your final core tip. This audio file will be published online, along with your article. Please submit audio files according to the following specifications:

Acceptable file formats: .mp3, .wav, or .aiff

Maximum file size: 10 MB

To achieve the best quality, when saving audio files as an mp3, use a setting of 256 kbps or higher for stereo or 128 kbps or higher for mono. Sampling rate should be either 44.1 kHz or 48 kHz. Bit rate should be either 16 or 24 bit. To avoid audible clipping noise, please make sure that audio levels do not exceed 0 dBFS.

Author response: A core tip recording as mp3 has been submitted with the revised manuscript.



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Please distinguish between the title of the article series. Three levels of subtitles are allowed: (1) First subtitle: All in bold and capital; (2) Second subtitle: All in bold and italic; and (3) Third subtitle: All in bold.

Author response: The subtitles have been reformatted accordingly.

The author should number the references in Arabic numerals according to the citation order in the text. The reference numbers will be superscripted in square brackets at the end of the sentence with the citation content or after the cited author's name, with no spaces.

e.g. The reference numbers will be superscripted in square brackets at the end of the sentence with the citation content or after the cited author's name, with no spaces^[1].

Author response: The reference list has been corrected according to WJG style.

Regarding tables:

Please don't include abbreviations in the title of the figure/table.

Author response: Abbreviations have been removed from table/figure titles.

Please explain all the abbreviations in the figure/table legends: full name (abbreviation).

Please explain all the abbreviations of each figure/table under each piece of figure/table legends.

Author response: As the tables and figure are full of abbreviations (many repetitive), the lengths of the manuscript would increase too much if including all full names in each legend. Instead, we provide now a list of abbreviations before the introduction that is valid for the entire manuscript.

Regarding the figures:

Please provide the decomposable figure of figures, whose parts are all movable and editable, organize them into a PowerPoint file, and submit as "Manuscript No. -Figures.ppt" on the system, we need to edit the words in the figures. All submitted figures, including the text contained within the figures, must be editable. Please provide the text in your figure(s) in text boxes.

Author response: A ppt file has been submitted with the revised manuscript.

Please don't include abbreviations in the title of the figure/table.

Please explain all the abbreviations in the figure/table legends: full name (abbreviation).

Please explain all the abbreviations of each figure/table under each piece of figure/table legends.

Author response: See comment above regarding abbreviations.

Please check and confirm that there are no repeated references!

Author response: We double-checked the reference list and one repetitive reference has been removed.



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Please add PubMed citation numbers (PMID NOT PMCID) and DOI citation to the reference list and list all authors. Please revise throughout. The author should provide the first page of the paper without PMID and DOI.

PMID (<http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=PubMed>) (Please begin with PMID:)

DOI (<http://www.crossref.org/SimpleTextQuery/>) (Please begin with DOI: 10.**)

Author response: The reference list has been updated accordingly.

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 48672

Title: Beneficial effects of nutritional supplements on intestinal epithelial barrier functions in experimental colitis models in vivo

Reviewer's code: 02441062

Reviewer's country: Italy

Science editor: Jia-Ping Yan

Reviewer accepted review: 2019-04-30 10:02

Reviewer performed review: 2019-05-09 12:44

Review time: 9 Days and 2 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
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<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept (High priority)	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> Accept (General priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input checked="" type="checkbox"/> Minor revision	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	Peer-reviewer's expertise on the topic of the manuscript:
<input type="checkbox"/> Grade E: Do not publish		<input type="checkbox"/> Rejection	<input type="checkbox"/> Advanced
			<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

This is an interesting topic, but in my opinion, it would be useful to change the setting of the review. In particular, the authors describe the two types of experimental colitis, namely the DSS model and the TNBS model, but the two parts are very unbalanced. I would suggest to improve the part concerning the TNBS model, and to group the two models of experimental colitis into a single chapter. Subsequently the various nutritional supplements used can be discussed without dividing them according to the experimental model.

Author response: We extended the paragraph of the TNBS model to have it more balanced with the DSS model paragraph. Another reason why the DSS section is more extensive, is, that it has simply been used in more studies than the TNBS model. This is the main reason why the two chapters seem unbalanced.

We would prefer to keep the order of the text, as we think it is critical to separate the two models because they actually represent the two different manifestations of human IBD: while DSS is more commonly used to resemble signs of human ulcerative colitis, TNBS is rather used to resemble signs of CD. As the other reviewers did not ask for such a change, we would feel more comfortable leaving the order of the text as is.



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Furthermore, it would be necessary to add a more in-depth discussion part, in which to draw some conclusions and highlighting the key points, also discussing the possible use of some of these substances in humans.

Author response: We added some statements and summarized the key points in the “Conclusions” section, which has been renamed “Discussion and Conclusions” (compare also comment of reviewer 2). We now highlight a recent review article describing the outcome of clinical studies in which some supplements have been proven to be beneficial in humans.

INITIAL REVIEW OF THE MANUSCRIPT

Google Search:

- The same title
- Duplicate publication
- Plagiarism
- No

BPG Search:

- The same title
- Duplicate publication
- Plagiarism
- No



PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 48672

Title: Beneficial effects of nutritional supplements on intestinal epithelial barrier functions in experimental colitis models in vivo

Reviewer’s code: 03538272

Reviewer’s country: Australia

Science editor: Jia-Ping Yan

Reviewer accepted review: 2019-05-04 09:45

Reviewer performed review: 2019-05-11 11:53

Review time: 7 Days and 2 Hours

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 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 checked="" 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 checked="" type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input 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 authors provide a comprehensive review of nutritional supplements with anti-inflammatory and anti-oxidative and how they may contribute to the intestinal barrier function based on mouse models. There are a number of minor grammatical, but



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the content is very interesting.

Author response: The manuscript has been proof-read to eliminate some minor grammatical and typographical errors.

There are just a couple of points relating to the structure: - A methods section detailing the scope of the study should be added and how relevant studies were identified (even briefly) -

Author response: A statement has been added at the end of the introduction explaining the search criteria.

A discussion section should be added which addresses the potential issues with the findings or limitations of the study and how this will impact on the interpretations.

Author response: We extended the discussion of study limitations and use of supplements in humans (compare comment of reviewer 1) in the "Conclusions" section, which has been renamed "Discussion and Conclusions".

Minor points: - Abstract Line 2 - remove "the" from before diet -

Author response: Agreed. This has been changed accordingly.

Introduction: Line 2: consider changing the sentence "Most of these cases do not require treatment, with changes in life-style resolving the problems" to "Most cases are self-limited and resolve without specific treatment".

Author response: Agreed. This has been changed accordingly.

The next sentence should then discuss that some forms of colitis require long term therapy (like IBD)



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Author response: This has been added in the following sentence. Changed as: “These forms of colitis are as of today incurable and require life-long treatment to manage the symptoms”

Line 12 - consider removing word “strongly”

Author response: Done.

Line 15 - consider changing chemodrugs to immunosuppressive therapy or immunomodulators -

Author response: Agreed. Chemodrugs has been changed to immunomodulators.

DSS colitis model Paragraph 2 line 2: add “an” between “as important”

Author response: Agreed. This has been changed accordingly.

Page 7 second last line - colon should be colonic -

Author response: Agreed. This has been changed accordingly.

Section 3.4 Paragraph 2 Line 4 - change gavage to lavage -

Author response: No, we actually mean gavage here (the feeding process).

3.6 Line 1 - change fibers to fiber

Author response: Agreed. This has been changed accordingly.

Page 14 section on magnolol - it should be “the anti-inflammatory mechanism of magnolol was shown to relate to the”

Author response: Agreed. This has been changed accordingly.



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INITIAL REVIEW OF THE MANUSCRIPT

Google Search:

- The same title
- Duplicate publication
- Plagiarism
- No

BPG Search:

- The same title
- Duplicate publication
- Plagiarism
- No



PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 48672

Title: Beneficial effects of nutritional supplements on intestinal epithelial barrier functions in experimental colitis models in vivo

Reviewer's code: 00502973

Reviewer's country: China

Science editor: Jia-Ping Yan

Reviewer accepted review: 2019-05-02 11:32

Reviewer performed review: 2019-05-13 12:33

Review time: 11 Days and 1 Hour

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input checked="" type="checkbox"/> Grade B: Very good	<input 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 checked="" type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

In this manuscript, the authors reviewed the pathogenesis mechanisms of DSS and TNBS induced colitis in rodents and the effects of some bioactive molecules. These two animal models are the most common used animal models in the study of IBD. The



effects of these bioactive molecules would shed light on the development of new therapeutic drugs for IBD. Thus this review is within the scope of WJG. The English used in this manuscript is good for publication. I would have 2 suggestions for this submission.

1. As most of the molecules mentioned in this manuscript are from alternative medicine, and not from conventional nutritional supplements, I would suggest to change the title "Beneficial effects of nutritional supplements on intestinal epithelial barrier functions in experimental colitis models in vivo" to "Beneficial effects of some bioactive molecules from alternative medicine on intestinal epithelial barrier functions in experimental colitis models in vivo"

Author response: As not all described supplements come from alternative medicine, we prefer not to replace "supplements", but rather add "bioactive molecules from alternative medicine" to the title: "Beneficial effects of nutritional supplements and bioactive molecules from alternative medicine on intestinal epithelial barrier functions in experimental colitis models in vivo"

2. In Conclusion, I think that "Thus, preservation of epithelial barrier functions is the most important goal of all colitis treatments" changing to "Thus, preservation of epithelial barrier functions is an important goal of all colitis treatments" would be more safe and reasonable. The reason is that it is not widely accepted that preservation of epithelial barrier functions is the top one target of all colitis treatment.

Author response: Agreed. We changed the sentence to "Thus, preservation of epithelial barrier functions is an important goal of colitis treatments".



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Google Search:

- The same title
- Duplicate publication
- Plagiarism
- No

BPG Search:

- The same title
- Duplicate publication
- Plagiarism
- No



JOURNAL EDITOR-IN-CHIEF'S REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 48672

Title: Beneficial effects of nutritional supplements on intestinal epithelial barrier functions in experimental colitis models in vivo

Journal Editor-in-Chief (Associate Editor): Andrzej S. Tarnawski

Country: United States

Editorial Director: Ze-Mao Gong

Date accepted review: 2019-06-28 04:45

Date reviewed: 2019-06-28 19:32

Review time: 14 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	<input checked="" type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	language polishing	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Major revision

JOURNAL EDITOR-IN-CHIEF (ASSOCIATE EDITOR) COMMENTS TO AUTHORS

In this minireview the authors discussed in detail the potential beneficial effects of nutritional supplements on intestinal epithelial barrier functions in experimental colitis models in vivo. The article is well designed and contains a lot of information, including the mechanisms involved. Importantly, in the discussion the authors addressed the limitation of the described animal studies, and posed a major question whether findings from experimental colitis models are applicable to human disease. Clearly, humans are very different from rodents, thus limiting the usefulness of these data so that data from experimental colitis models have to be interpreted with caution. The article was reviewed by 3 reviewers who rated it positively - "minor revisions". The authors responded in my opinion positively to reviewers' comments .

Author response: We thank you for your kind comments on our manuscript.



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If possible I would suggest the authors to include a paragraph on the important role of not only epithelial but also endothelial barrier in the mechanisms of colitis.

Author response: We have reviewed the literature on endothelial (vascular effects) during experimental colitis. In general, this field is also very vast and would require writing an additional manuscript. However, when focusing on endothelial junctions and permeability regulation, not so much is known. Direct effects of TNBS and DSS on endothelial junction molecules have not been described in detail, which is not surprising given that that they rather happenize epithelial proteins to gain access to the body. It has been shown for example that DSS does not affect endothelial JAM-A, which is an important TJ protein in endothelial regulating vascular permeability and leukocyte recruitment. We have briefly discussed this issue in the Conclusion/Discussion section and referred the interested reader to another review addressing this topic.