

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 80210

Title: Gaseous metabolites as therapeutic targets in ulcerative colitis

Provenance and peer review: Invited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 04010086

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: China

Author's Country/Territory: Australia

Manuscript submission date: 2022-09-20

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-09-24 08:41

Reviewer performed review: 2022-10-04 10:12

Review time: 10 Days and 1 Hour

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Novelty of this manuscript	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
Creativity or innovation of this manuscript	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation

Scientific significance of the conclusion in this manuscript	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

Thank you for the opportunity to review manuscript WJG- 80210 which is well-designed and well-written. This review summarizes the possible relationship between microbial production of gaseous metabolites and the development and progression of ulcerative colitis, with emphasis on the evidence of excessive exposure to H₂S and NO as the etiology of ulcerative colitis. In addition, this study reviews studies related to dietary regimens aimed at reducing these gas metabolites as a treatment strategy for UC and summarizes the results of these studies. Even after thoroughly reviewing this article I was not able to find any major flaws. However some minor points could be rectified: 1. The relationship between gas metabolites and the pathogenesis of UC needs to be explored in more detail, and it is better to summarize the possible mechanisms in the form of pictures. 2. It is better to list the results of clinical studies on targeted reduction of gas metabolites through dietary regimen as a treatment strategy for UC in the form of tables, and put forward constructive suggestions for subsequent clinical studies combined with the existing research conclusions. After these minor modifications, I think the manuscript can be accepted for publication.

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Title: Gaseous metabolites as therapeutic targets in ulcerative colitis

Provenance and peer review: Invited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 06404369

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: Turkey

Author's Country/Territory: Australia

Manuscript submission date: 2022-09-20

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-10-19 06:47

Reviewer performed review: 2022-10-19 08:01

Review time: 1 Hour

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Novelty of this manuscript	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
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Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

Dear Author, Your paper "Gaseous metabolites as therapeutic targets in ulcerative colitis" interestingly reviews the dietary approaches in H₂S and NO as causative agents in UC. However, there are some minor concerns with the paper as outlined below; - Throughout the manuscript there is lack of bibliographic references. - Core tip doesn't include in the Word document. - Under DIET AS PRIMARY STRATEGY FOR COLONIC H₂S & NITRIC OXIDE MANIPULATION I would add some literature notes to better contextualize the impact of probiotics and prebiotics. Additionally, BIOMARKERS FOR ASSESSING RESPONSE OF DIETARY THERAPY other self-reported questionnaires (abdominal pain frequency with visual analog scale, food frequency questionnaire, Food-related quality of life (FRQoL), health-related quality of life (HRQoL)) could be mentioned under this topic to evaluate adherence/response of diet interventions. Otherwise, the review is interesting and well-written.

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Title: Gaseous metabolites as therapeutic targets in ulcerative colitis

Provenance and peer review: Invited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 04025443

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Doctor, Senior Researcher

Reviewer's Country/Territory: Russia

Author's Country/Territory: Australia

Manuscript submission date: 2022-09-20

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-10-19 05:17

Reviewer performed review: 2022-10-25 13:19

Review time: 6 Days and 8 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Novelty of this manuscript	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
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	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

Dear authors! I read with pleasure and interest your manuscript "Gaseous metabolites as therapeutic targets in ulcerative colitis", which is a narrative review. In the manuscript under review several problems were raised, including association of diet, intestinal microbiome, it's metabolites and flow of an inflammatory bowel disease (namely, ulcerative colitis). The paper is well-organized, clearly written, contains novelty and, in my opinion, worth publishing. The principal drawback of the main topic discussed in the paper, is that it can be hardly supported directly at the current stage of technology. However, this point is partially mentioned by the authors in the Biomarkers for assessing response of dietary therapy section. there are some minor comments that requires authors' attention. 1. In the abstract, the role of H₂S (only is discussed). I would suggest to revise the abstract in accordance to what is discussed in the paper. Please, pay attention to the keywords as well. 2. The role of dysbiosis in pathogenesis of ulcerative colitis is not commonly accepted. Please, revise the statement of the paragraph 1 on page 6, accordingly. 3. In table 1, please use the other markers to refer the footnotes, as superscripted 1-3 seems weird (ml² or kg³). Here, references [32] and [34] seem

inappropriate. Please, provide the table's title before the table. 4. Figure 1 is not clear. Could you explain what is shown in the main part of the picture (not in the text boxes)? The text labels don't match the figure itself. 5. Minor language polishing is required.