Peer-Review Report(s). Authors must resolve all issues in the manuscript that are raised in the peer-review report(s) and provide point-by-point responses to each of the issues raised in the peer-review report(s):

Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade C (Good)

Conclusion: Minor revision

Specific Comments to Authors:

I would like to congratulate the authors on this well-written editorial. The manuscript provides a timely overview of the proposed mechanisms of action and recent evidence supporting the potential role of berberine in ulcerative colitis (UC). The overall structure and flow are clear. I offer the following suggestions to further enhance readability and scientific precision.

Response

We sincerely thank the reviewer for the careful evaluation of our manuscript and for the constructive suggestions that have helped improve the clarity and scientific rigor of the editorial. We have revised the manuscript accordingly. Our detailed responses are provided below.

Comment 1

Introduction: Please give a reference to the in-press article for which this editorial is addressing.

Response:

We thank the reviewer for this suggestion. However, it is not feasible from our side because the Auto-Analyser tools do not allow us to add references. This can be incorporated manually during the journal's production process.

Comment 2

This line needs to be modified: "Ulcerative colitis (UC) affects millions globally and is characterised by relapsing mucosal inflammation confined to the colon. Even though the

disease is intestinal, it has varied extra-intestinal manifestations, such as peripheral arthritis, and the terminal ileum is also involved as backwash ileitis."

Also modify: "Th2 cytokine dominance (e.g., IL-13, TNF-α)" since UC is not purely Th2-dominant. The H_2O_2 hypothesis is controversial.

Response:

We appreciate this important clarification. The sentence describing the pathophysiology of UC has been revised to better reflect the current understanding of immune mechanisms. Specifically, we have modified the description of cytokine signaling to indicate that UC involves Th2-like responses, Th17 pathways, innate immune activation, and epithelial stress responses, rather than a purely Th2-dominant process. Additionally, the discussion of the hydrogen peroxide hypothesis has been toned down to acknowledge the ongoing debate and limited consensus in the field.

Comment 3

This study speaks about adjunctive therapy in UC. They can also quote/add the role of coconut water in UC (RCT published in Clinical Gastroenterology and Hepatology).

Response:

Thank you for highlighting this recent study. We have now included a brief discussion of the recent randomized controlled trial evaluating coconut water as adjunctive therapy in UC, published in Clinical Gastroenterology and Hepatology. This has been incorporated in the section discussing adjunctive and complementary therapeutic strategies.

Comment 4

The findings of the Yang et al. study can be summarised to avoid repetition from the original study.

Response:

We agree with this suggestion. We have done necessory changes in the main text.

Comment 5

The details of how berberine modulates microbiota can be given.

Response:

We thank the reviewer for this suggestion. Additional details have now been included describing the potential mechanisms through which berberine modulates the gut microbiota, including its reported effects on microbial diversity, short-chain fatty acid-producing bacteria, and intestinal barrier function.

Comment 6

The conclusion should include the limitations of availability (FDA, EMA, DGCI approval), lack of studies outside China, and avoid repeating microbiota. Also mention limitations of the DSS model and explain meta-analysis details (sample sizes, endpoints, heterogeneity).

Response:

We appreciate these valuable suggestions and have revised the conclusion accordingly. Specifically:

1) We now discuss the limited regulatory approval of berberine formulations by major agencies such as the FDA, EMA, and DGCI.
2) The geographical limitation of current clinical studies (predominantly conducted in China) has been acknowledged.
3) Repetitive discussion of microbiota-related mechanisms has been reduced to improve clarity and avoid redundancy.
4) We have included a brief discussion of the limitations of the DSS colitis model, noting that it primarily reflects innate immune responses, whereas UC involves both innate and adaptive immune pathways.

The section referencing the meta-analysis comparing berberine with 5-ASA has been expanded to include more information regarding sample sizes, clinical endpoints, and heterogeneity among studies.

Reviewer #2:

Scientific Quality: Grade B (Very good)

Language Quality: Grade C (Good)

Conclusion: Minor revision

Specific Comments to Authors:

This paper focuses on the dual-target mechanism of action of berberine in the treatment of ulcerative colitis (UC), i.e., gut microbiota remodeling and Gasdermin D (GSDMD)-mediated inhibition of pyroptosis. It systematically reviews the research progress of bioactive components of traditional Chinese medicine (TCM) in UC treatment and clarifies the potential of berberine as an adjunctive therapeutic agent for UC. However, the manuscript still requires improvement in terms of the depth of mechanism elaboration, the support of experimental data, the standardization of literature citations, and the expression of detailed content.

Response:

We sincerely thank the reviewer for the careful evaluation of our manuscript and for the constructive suggestions that have helped improve the clarity and scientific rigor of the editorial.

Comment 1

The paper only provides a general description of the synergistic effect between gut microbiota remodeling and GSDMD inhibition, yet fails to identify the specific molecular nodes through which gut microbiota remodeling (e.g., short-chain fatty acid (SCFA) production) modulates the GSDMD pathway.

Response:

We agree with the reviewer. As this is an editorial article, providing such detailed explanations is beyond its scope. The original authors may be conducting research in this area. In the limitation section, we have included the various limitations of the main research work on which this editorial is based.

Comment 2

The schematic diagram of the mechanism is merely given simple annotations in the paper, and the text does not explain step-by-step the DSS-induced pathological pathways of UC, the regulatory nodes of berberine on the gut microbiota, and the key steps of GSDMD inhibition in combination with the schematic diagram.

Response:

We agree that the schematic diagram and accompanying text should more clearly delineate the mechanistic sequence underlying DSS-induced ulcerative colitis, the regulatory actions of berberine on the gut microbiota, and the key steps through which GSDMD inhibition confers protection. In the revised manuscript, we have substantially refined the mechanistic description in both the main text and the schematic legends to enhance clarity and coherence.

Comment 3

Carefully check the formatting of all cited literature.

Response

In the revised version of manuscript we have cerefully checked the formatting of the cited literature.

Comment 4

There are several grammatical and formatting errors in the paper, such as the misplaced space before the period in the sentence "exhibits potent anti-inflammatory effects relevant to UC management".

Response

In the revised version of manuscript we have taken-care of grammatical issues.

Comment 5

The gut microbiota analysis only employed 16S rRNA sequencing, with no shotgun metagenomic sequencing or quantitative detection of SCFAs performed. This makes it impossible to clarify the causal relationship between changes in microbiota functions and berberine intervention. It is recommended to supplement the necessity of SCFA quantitative detection in the "LIMITATIONS OF THE STUDY" section.

Response

I fully agree with the reviwer and in the revised manuscript we have included the suggested limitation of the study.

Editorial Office's comments. Authors must revise the manuscript according to the

Editorial Office's comments and suggestions, which are provided below:

(1) Science Editor:

1 Scientific quality: The authors submitted an editorial of Berberine in ulcerative colitis.

(1) **Classification:** Grade B and Grade B;

(2) **Summary of the Peer-Review Report:** The language of the manuscript should be improved to enhance clarity. The manuscript lacks in-depth discussion of mechanisms. The authors should carefully check the formatting specifications of all citations.

(3) **Manuscript Type:** After verification, the manuscript type is "Editorial".

2 Specific comments

(1) **Country/Territory of origin:** India.

(2) The language classification are Grade C and Grade C. Please provide the latest language certificate after Return the Manuscript to Author for Revision. Please visit the following website for the professional English language editing companies that we recommend: https://www.wjgnet.com/bpg/gerinfo/240.

(3) **Manuscript Title:**

Except for capitalization of the first word, all other words are represented in lowercase (excluding specific words such as Crohn's disease).

(4) **Author contributions:** The 'Author contributions' passage describes the specific contribution(s) made by each author. The author's names will be listed in the following format: full family (sur)name, followed by abbreviated first and middle names. For example, Bryan L Copple should be revised as Copple BL. A full multi-author example is: Wang CL, Liang L, Fu JF, Zou CC, Hong F and Wu XM designed the research study; Wang CL, Zou CC, Hong F and Wu XM performed the research.

(5) **Core Tip.** Abbreviations must be defined upon first appearance in the Core Tip. Do not use non-standard abbreviations, unless they appear at least two times in the text preceding the first usage/definition.

(6) **Audio Core Tip.** In order to attract readers to read the full-text article, we request that the first author make an audio file describing the final core tip. This audio file will be published online, along with the article. **The author can invite English language editing company to assist in resolving the language issues of Audio Core Tip.**

(7) **Reference numbers in the main text.**

If there are only 2, use ",". For example, mitigating the risk of disease progression[10,11]. The name of the author(s) of a reference is listed in the sentence, the reference number should be placed immediately after the author(s) of the reference. **Example:** Mandal *et al*[8] proposed that retractor aponeurosis disinsertion is the most likely cause of congenital low lid entropion.

(8) **There are issues with the references:**

To ensure the accuracy of the references, please use "**Edit References by Auto-Analyser**" (https://www.f6publishing.com/Forms/main/ArticleReferenceTool.aspx) to edit the references of the manuscript.

(9) **Figures.** Figures must be presented in the order that they appear in the main text of the manuscript (numbered as 1, 2, 3, *etc*.).

Original figure documents. *In the meantime, authors should provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor, and upload it to the file destination of "**Image File**" in the F6Pubishing system.*

(10) Please verify if all pictures (s) are original? If an author of a submission is re-using a figure or figures published elsewhere, or that is copyrighted, the author must provide documentation that the previous publisher or copyright holder has given permission for the figure to be re-published, and correctly indicate the reference source and copyrights. For example, "**Figure 1 Histopathological examination by hematoxylin-eosin staining (200 ×).** A: Control group; B: Model group; C: Pioglitazone hydrochloride group; D: Chinese herbal medicine group. **Citation:** Yang JM, Sun Y, Wang M, Zhang XL, Zhang SJ, Gao YS, Chen L, Wu MY, Zhou L, Zhou YM, Wang Y, Zheng FJ, Li YH. Regulatory effect of a Chinese herbal medicine formula on non-alcoholic fatty liver disease. *World J Gastroenterol* 2019; 25(34): 5105-5119. Copyright ©The Author(s) 2019. Published by Baishideng Publishing Group Inc[6]". And please cite the reference source in the references list. If the author fails to properly cite the published or copyrighted picture(s) or table(s) as described above, he/she will be subject to withdrawal of the article from BPG publications and may even be held liable.

(11) The *WJG* article which this editorial discussed has not been listed in the references list. Please add the *WJG* article which this editorial discussed into the main text and

references list < Yang P, Wang R, Zhou YP, Wen JF, Yang DX. Berberine alleviates experimental colitis by enhancing gut-microbiota-dependent intestinal barrier function and suppressing gasdermin D activation. *World J Gastroenterol* 2026; In press>.

(12) Regarding abbreviations, please do not list them separately. Abbreviations must be defined at the first occurrence. For example, when CT first appears in the manuscript, please use the format "computed tomography (CT)".

(13) **Abstract.** Abbreviations should be avoided, but if used should be spelled out at first mention.

3 Recommendation: Conditional acceptance.

Language Quality: Grade C (Good)

Scientific Quality: Grade B (Very good)

(2) Executive Editor-in-Chief:

I have reviewed the Peer-Review Report, full text of the manuscript, 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.