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PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 119800

Title: Berberine as a Dual-Target Therapeutic for Ulcerative Colitis

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 06529223
Position: Peer Reviewer
Academic degree and professional title: Assistant Professor, PhD
Reviewer's Country/Territory: China
Author's Country/Territory: India

Manuscript submission date: 2026-02-06

Reviewer chosen by: AI Editor

Reviewer accepted review: 2026-02-09 11:55

Reviewer performed review: 2026-02-12 12:48

Review time: 3 Days

Content to be reviewed	Does the manuscript's content fall within the scope of the journal? **Yes** Is there any Key Word that is not included in the manuscript title? **No** Do authors' affiliations correspond to the content of the manuscript? **Yes** Does the Abstract contain the contents of each part of the manuscript (IMRaD)? **Yes** Are the Key Words complete? **Yes** Is the content of the Introduction adequate? **Yes**

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	Is the content of the Materials and Methods complete? **Yes** Is the description of the experiments clear and complete? **Yes** Are the experimental data presented in the manuscript's biostatistics content reliable? **Yes** Are the experimental data of the Results true and reliable? **Yes** Are the quality and resolution of the images up to standard? **Yes** Do the selection and design of the figures and tables follow the principles of necessity and clarity? **Yes** Is there any duplication between various parts of the manuscript and between the main text and the content presented in the figures and tables? **No** Are the figures and tables numbered consecutively in the order in which they appear in the manuscript? **Yes** Is the content of the Discussion reasonable? **Yes** Is the Conclusion reasonable? **Yes** Are all references necessary and reasonable? **Yes** Do authors omit important references? **No** Do authors only cite their own earlier publications? **No** Is the manuscript's text correct, concise, and clear? **Yes** Will the manuscript's content be of interest to readers? **Yes** Are additional experiments needed for the study? **No** Are all references related to the topic of the manuscript? **Yes** Does the research scope comply with ethics? **No**
Scientific quality	Grade B (Very good)

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Novelty of this manuscript	Grade B (Very Good)
Creativity or innovation of this manuscript	Grade C (Good)
Scientific significance of the conclusion in this manuscript	Grade B (Very Good)
Language quality	Grade C (Good)
Does this manuscript describe a study of the existing knowledge system?	Yes
Does this manuscript report a revolutionary innovation?	No
Does this manuscript report an unconventional innovation?	Yes
Conclusion	Minor revision
Re-review	Yes
Peer-reviewer statements	Peer-Review: Anonymous
	Conflicts-of-Interest: No
Reviewer's AI contribution statement	

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.

1.The paper only provides a general description of the synergistic effect between gut

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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.

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.

3.Carefully check the formatting of all cited literature.

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".

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".

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.

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PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 119800

Title: Berberine as a Dual-Target Therapeutic for Ulcerative Colitis

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 08549003
Position: Peer Reviewer
Academic degree and professional title: Assistant Professor, DM, MD
Reviewer's Country/Territory: India
Author's Country/Territory: India

Manuscript submission date: 2026-02-06

Reviewer chosen by: Hong-Xin Jiang

Reviewer accepted review: 2026-02-13 04:29

Reviewer performed review: 2026-02-22 05:04

Review time: 9 Days

Content to be reviewed	Is there any Key Word that is not included in the manuscript title? **No** Do the selection and design of the figures and tables follow the principles of necessity and clarity? **Yes** Is the description of the experiments clear and complete? **Not Applicable** Do authors' affiliations correspond to the content of the manuscript? **Yes** Is there any duplication between various parts of the manuscript and between the main text and the content

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	presented in the figures and tables? **No** Is the content of the Discussion reasonable? **Yes** Are the figures and tables numbered consecutively in the order in which they appear in the manuscript? **Yes** Are all references necessary and reasonable? **Yes** Do authors omit important references? **No** Are the quality and resolution of the images up to standard? **Not Applicable** Is the Conclusion reasonable? **Yes** Are the experimental data of the Results true and reliable? **Not Applicable** Are the experimental data presented in the manuscript's biostatistics content reliable? **Not Applicable** Are all references related to the topic of the manuscript? **Yes** Do authors only cite their own earlier publications? **No** Is the manuscript's text correct, concise, and clear? **Yes** Will the manuscript's content be of interest to readers? **Yes** Are additional experiments needed for the study? **No** Does the research scope comply with ethics? **Yes**
Scientific quality	Grade B (Very good)
Novelty of this manuscript	Grade B (Very Good)
Creativity or innovation of this manuscript	Grade B (Very Good)
Scientific significance of the conclusion in this manuscript	Grade C (Good)
Language quality	Grade C (Good)

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Does this manuscript describe a study of the existing knowledge system?	Yes
Does this manuscript report a revolutionary innovation?	No
Does this manuscript report an unconventional innovation?	No
Conclusion	Minor revision
Re-review	Yes
Peer-reviewer statements	Peer-Review: Onymous
	Conflicts-of-Interest: No
Reviewer's AI contribution statement	

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.1. Introduction: Please give a reference to the in-press article, for which this editorial is addressing. All references have been quoted as per journal policy. 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 backwater ileitis. This statement also needs to be modified: Th2 cytokine dominance (e.g., IL-13, TNF-α), as UC is not purely Th2-dominant; the modern understanding includes Th2-like, Th17, innate immune, and epithelial stress pathways. The H2O2 hypothesis is controversial, can tone regarding that. 3. This study speaks about adjunctive therapy in UC. They can also quote/add the role

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of coconut water in UC. A recently published RCT in Clinical Gastroenterology and Hepatology demonstrated a beneficial effect of this treatment in UC. 4. The findings of the Yang et al. study can be summarised to avoid repetition from the original study 5. The details of how berberine modulates microbiota can be given. 6. The conclusion should include the limitations of the availability (Regulatory body approval, like the FDA, the European agency and the DGCI) of this particle and the lack of studies outside China. Avoid repeating microbiota across sections and shorten it to reduce redundancy. Overall manuscript needs language policies to avoid grammatical errors. Limitations of the DSS model must be noted, as it affects only the innate immune mechanism, whereas UC involves both innate and adaptive immunity. Since high-quality studies are not available on berberine, you can explain in detail (ex, sample sizes, endpoints, heterogeneity) about the findings of the meta-analysis you quoted on the superiority of Berberine and ASA.

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RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 119800

Title: Berberine as a Dual-Target Therapeutic for Ulcerative Colitis

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 08549003
Position: Peer Reviewer
Academic degree and professional title: Assistant Professor, DM, MD
Reviewer's Country/Territory: India
Author's Country/Territory: India

Manuscript submission date: 2026-02-06

Reviewer chosen by: Ming Fan

Reviewer accepted review: 2026-03-13 04:06

Reviewer performed review: 2026-03-13 12:22

Review time: 8 Hours

Content to be reviewed	Does the manuscript's content fall within the scope of the journal? **Yes** Is there any Key Word that is not included in the manuscript title? **Yes** Do authors' affiliations correspond to the content of the manuscript? **No** Does the Abstract contain the contents of each part of the manuscript (IMRaD)? **No** Are the Key Words complete? **Yes** Is the content of the Introduction adequate? **Not**

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	Applicable Is the content of the Materials and Methods complete? **Not Applicable** Is the description of the experiments clear and complete? **Not Applicable** Are the experimental data presented in the manuscript's biostatistics content reliable? **Not Applicable** Are the experimental data of the Results true and reliable? **Not Applicable** Are the quality and resolution of the images up to standard? **Not Applicable** Do the selection and design of the figures and tables follow the principles of necessity and clarity? **Not Applicable** Is there any duplication between various parts of the manuscript and between the main text and the content presented in the figures and tables? **Not Applicable** Are the figures and tables numbered consecutively in the order in which they appear in the manuscript? **Yes** Is the content of the Discussion reasonable? **Yes** Is the Conclusion reasonable? **Yes** Are all references necessary and reasonable? **Yes** Do authors omit important references? **No** Are all references related to the topic of the manuscript? **Yes** Do authors only cite their own earlier publications? **No** Is the manuscript's text correct, concise, and clear? **Yes** Will the manuscript's content be of interest to readers? **Yes**

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	Are additional experiments needed for the study? **No** Does the research scope comply with ethics? **Yes**
Scientific quality	Grade B (Very good)
Novelty of this manuscript	Grade C (Good)
Creativity or innovation of this manuscript	Grade C (Good)
Scientific significance of the conclusion in this manuscript	Grade B (Very Good)
Language quality	Grade B (Very good)
Does this manuscript describe a study of the existing knowledge system?	Yes
Does this manuscript report a revolutionary innovation?	No
Does this manuscript report an unconventional innovation?	No
Conclusion	Accept
Peer-reviewer statements	Peer-Review: Anonymous
	Conflicts-of-Interest: No
Are your review comments generated by AI tools?	

SPECIFIC COMMENTS TO AUTHORS

I thank the authors for making the changes in response to the reviewers' comments. The In-Press article could have been cited manually as per the science editor's comments. I have no further comments, and the authors have addressed all comments and provided satisfactory responses.