

Department of Gastroenterology
Shengjing Hospital of China Medical University
No.36. Sanhao Street, Heping District
110004 Shenyang,
People's Republic of China
Tel:024-96615-27111
Fax: 024-96615-27112
Email: sanglixuan2008@163.com
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Dear Ma,

We would like to thank the editor and the reviewers for their conscientious reviews, and insightful comments and suggestions to improve the manuscript. In the response below, we have addressed all the concerns raised by the editor and the reviewers in the revised manuscript. We hope the editor and the reviewers will find that our revised manuscript has improved and is suitable for publication. If somewhere of the revised manuscript is not appropriate, we will spare no effort to revise it again to meet the requirements of editor and reviewers.

I hope my paper could achieve the academic standards of your magazine and be published finally. Thank you very much.

Response to Editor and Reviewers Comments

Manuscript NO: 88713

Title: "Application of curcumin and its nano-preparations in the treatment of inflammatory bowel disease (IBD)"

Author(s): Meng, Ziwen; Chang, Bing; Sang, Lixuan

Editorial office's comments:

(1) Science editor:

1 Scientific classification: Grade C and Grade B.

2 Language classification: Grade B and Grade B.

3 Specific comments: (1) Please provide the Language certificate. The English-language grammatical presentation needs to be improved to a certain extent. There are many errors in grammar and format, throughout the entire manuscript. Before final acceptance, the authors must provide the English Language Certificate issued by a professional English language editing company. Please visit the following website for the professional English language editing companies we recommend: <https://www.wjgnet.com/bpg/gerinfo/240>.

4 Recommendation: Conditional acceptance.

Language Quality: Grade B (Minor language polishing)

Scientific Quality: Grade C (Good)

Response: Thank you very much for your careful reading of the manuscript and thank you for your valuable comments for our manuscript. According to your comments, we made a point-to-point response. we have corrected the errors in grammar and format, throughout the entire manuscript. In addition, we have provided the English Language Certificate issued by a professional English language editing company.

(2) Company editor-in-chief:

I have reviewed the Peer-Review Report, the full text of the manuscript, the relevant ethics documents, and the English Language Certificate, 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. When revising the manuscript, it is recommended that the author supplement and improve the highlights of the latest cutting-edge research results, thereby further improving the content of the manuscript. To this end, authors are advised to apply PubMed, or a new tool, the RCA, of which data source is PubMed. RCA is a unique artificial intelligence system for citation index evaluation of medical science and life science literature. In it, upon obtaining search results from the keywords entered by the author, "Impact Index Per Article" under "Ranked by" should be selected to find the latest highlight articles, which can then be used to further improve an article under

preparation/peer-review/revision. Please visit our RCA database for more information at: <https://www.referencecitationanalysis.com/> or visit PubMed at: <https://pubmed.ncbi.nlm.nih.gov/>.

Response: Yes, thank you very much for your valuable and constructive comments. We have supplemented and improved the highlights of the latest cutting-edge research results, thereby further improving the content of the manuscript by application PubMed or the RCA.

Reviewer reports:

Reviewer #1

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Accept (General priority)

Comments:

This letter to the editor discusses the application of curcumin in patients with IBD. The authors showed the main anti-inflammatory activity of curcumin and cited some articles regarding the curcumin formulation to treat IBD patients. It is a new and interesting area of research that may be promising in the future for the treatment of patients with IBD, especially in patients with UC.

Response: Yes, thank you very much for your careful reading of the manuscript, and thank you for your valuable comments for our manuscript. Many basic and clinical studies have shown that curcumin has the effect of treating IBD and can maintain the remission of IBD. Nano formulations and the free form of cur have been investigated in human clinical trials for treatment of various of diseases such as cancer, inflammatory diseases, neurodegenerative diseases, metabolic diseases and more.

Reviewer #2

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Comments:

The authors comment on the effectiveness of curcumin nanoparticles.

1. Is this nanoparticle of curcumin available on a commercial basis on a ready-to-use basis?

Response: Yes, thank you very much for your valuable and constructive comments. There are several successful cur formulations which are reported in recent years with higher C_{max} and bioavailability. For example, Sasaki *et al.* have successfully developed a highly absorptive curcumin dispersed with colloidal nanoparticles and named it THERACURMIN^[1]. Theracurmin® is a proprietary form of curcumin using Japanese technology to show one of the highest bioavailability. In another research, its modest efficacy as a remission induction therapy may indicate that Theracurmin® would be a better maintenance therapy than induction therapy in patients with IBD, particularly given its safety profile^[2].

References:

- 1 **Sasaki H**, Sunagawa Y, Takahashi K, Imaizumi A, Fukuda H, Hashimoto T, Wada H, Katanasaka Y, Kakeya H, Fujita M, Hasegawa K, Morimoto T. Innovative preparation of curcumin for improved oral bioavailability. *BIOL PHARM BULL* 2011 2011-1-20; **34(5)**: 660-665. [PMID: 21532153 DOI: 10.1248/bpb.34.660]
- 2 **Sugimoto K**, Ikeya K, Bamba S, Andoh A, Yamasaki H, Mitsuyama K, Nasuno M, Tanaka H, Matsuura A, Kato M, Ishida N, Tamura S, Takano R, Tani S, Osawa S, Nishihira J, Hanai H. Highly Bioavailable Curcumin Derivative Ameliorates Crohn's Disease Symptoms: A Randomized, Double-Blind, Multicenter Study. *J CROHNS COLITIS* 2020 2020-12-2; **14(12)**: 1693-1701. [PMID: 32412598 DOI: 10.1093/ecco-jcc/jjaa097]