

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 71742

Title: The Jianpi Qingchang Bushen Decoction Improves the Inflammatory Response and Metabolic Bone Disorder in Inflammatory Bowel Disease-induced Bone Loss

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05045708

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Assistant Professor, Doctor

Reviewer's Country/Territory: Turkey

Author's Country/Territory: China

Manuscript submission date: 2021-09-20

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-10-04 06:04

Reviewer performed review: 2021-10-04 06:19

Review time: 1 Hour

Scientific quality	☐ Grade A: Excellent ☒ Grade B: Very good ☐ Grade C: Good ☐ Grade D: Fair ☐ Grade E: Do not publish
Language quality	☐ Grade A: Priority publishing ☒ Grade B: Minor language polishing ☐ Grade C: A great deal of language polishing ☐ Grade D: Rejection
Conclusion	☒ Accept (High priority) ☐ Accept (General priority) ☐ Minor revision ☐ Major revision ☐ Rejection
Re-review	☒ Yes ☐ No



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Peer-reviewer statements	Peer-Review: [☐] Anonymous [☒] Onymous Conflicts-of-Interest: [☐] Yes [☒] No
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SPECIFIC COMMENTS TO AUTHORS

Thank you for highly interesting and well design study..The topic is important in IBD and bone loss disease, however authors should cite possible effect mechanisms of JQBD on intestinal mucosa, JQBD has two major effects on intestinal mucosa , here of summarized and references 1- Falvanol contains of JQBD have major substance on gut microbiome (possible mechanism that inducer of gut microbiome Bifidobacteria) 2- Inducer of Bifidobacteria provides increasing Il-10 levels and decreasing IL-6,Tnf a levels (1-<https://journals.sagepub.com/doi/full/10.1177/2058739220942626> 2-<https://pubmed.ncbi.nlm.nih.gov/33103512/>) Best Regards,

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Peer-review model: Single blind

Reviewer's code: 02440884

Position: Editorial Board

Academic degree: MD

Professional title: Chief Doctor, Full Professor, Professor, Senior Lecturer

Reviewer's Country/Territory: Germany

Author's Country/Territory: China

Manuscript submission date: 2021-09-20

Reviewer chosen by: Xin Liu (Online Science Editor)

Reviewer accepted review: 2021-12-17 18:41

Reviewer performed review: 2021-12-17 19:50

Review time: 1 Hour

Scientific quality	☐ Grade A: Excellent ☒ Grade B: Very good ☐ Grade C: Good ☐ Grade D: Fair ☐ Grade E: Do not publish
Language quality	☐ Grade A: Priority publishing ☒ Grade B: Minor language polishing ☐ Grade C: A great deal of language polishing ☐ Grade D: Rejection
Conclusion	☐ Accept (High priority) ☐ Accept (General priority) ☒ Minor revision ☐ Major revision ☐ Rejection
Re-review	☒ Yes ☐ No

Peer-reviewer statements	Peer-Review: [☒] Anonymous [☐] Onymous Conflicts-of-Interest: [☐] Yes [☒] No
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SPECIFIC COMMENTS TO AUTHORS

In the experimental study the effect of JQBD on the bone loss IBD model in IL-10-knockout mice by peroral administration of piroxicam was investigated. The authors demonstrate data argue for a JQBD protective effect against IBD-induced bone loss and identify the inhibition of the RANK/RANKL/OPG signaling pathway as important molecular target . The manuscript is well-written and in the scope of the Journal. Comments 1. The Ca-P metabolism should be addressed, in particular the cholecalciferol levels. Is there any chance to do so? 2. The histology of trabecular structures should be shown in order to demonstrate the osseous cell types and the morphology of matrix composition. 3. Is there any chance in the content of Ca and P in stool probes of index-mice and controls?

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Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 02536349

Position: Editorial Board

Academic degree: MD

Professional title: Doctor, Professor

Reviewer's Country/Territory: Turkey

Author's Country/Territory: China

Manuscript submission date: 2021-09-20

Reviewer chosen by: Xin Liu (Online Science Editor)

Reviewer accepted review: 2021-12-16 20:30

Reviewer performed review: 2021-12-20 19:46

Review time: 3 Days and 23 Hours

Scientific quality	☐ Grade A: Excellent ☐ Grade B: Very good ☒ Grade C: Good ☐ Grade D: Fair ☐ Grade E: Do not publish
Language quality	☒ Grade A: Priority publishing ☐ Grade B: Minor language polishing ☐ Grade C: A great deal of language polishing ☐ Grade D: Rejection
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Peer-reviewer statements	Peer-Review: [☒] Anonymous [☐] Onymous Conflicts-of-Interest: [☐] Yes [☒] No
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SPECIFIC COMMENTS TO AUTHORS

This is a nice experimental work and deserves to be published But I comment this mixture of tens of substances may be a problem and work to be supported by other studies and published in an experimental journal rather than wide evidence based clinic ones. (very few typographic errors.. eg Institutiongal)

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Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 01552044

Position: Editorial Board

Academic degree: MD

Professional title: Associate Professor, Professor

Reviewer's Country/Territory: Italy

Author's Country/Territory: China

Manuscript submission date: 2021-09-20

Reviewer chosen by: Xin Liu (Online Science Editor)

Reviewer accepted review: 2021-12-16 14:06

Reviewer performed review: 2021-12-21 07:13

Review time: 4 Days and 17 Hours

Scientific quality	☐ Grade A: Excellent ☐ Grade B: Very good ☒ Grade C: Good ☐ Grade D: Fair ☐ Grade E: Do not publish
Language quality	☐ Grade A: Priority publishing ☒ Grade B: Minor language polishing ☐ Grade C: A great deal of language polishing ☐ Grade D: Rejection
Conclusion	☐ Accept (High priority) ☒ Accept (General priority) ☐ Minor revision ☐ Major revision ☐ Rejection
Re-review	☒ Yes ☐ No

Peer-reviewer statements	Peer-Review: ☒ Anonymous ☐ Onymous
	Conflicts-of-Interest: ☐ Yes ☒ No

SPECIFIC COMMENTS TO AUTHORS

This is an interesting article exploring the therapeutic role of a natural compound on IBD-associated bone mass alteration. The issue of bone mass alteration in patients with IBD is novel and clinically relevant as is the increasing importance of nutraceuticals in therapy of many GI disorders including IBD. The manuscript is well written, methodologically sound, results are presented clearly and conclusions are largely supported by results. I only have a few suggestions. **COMMENTS** The Authors may want to quote in the text and also in the reference list the article written by Sgambato D et al Bone alterations in inflammatory bowel diseases *World J Clin Cases* 2019; 6:1908-1925, which is an interesting review on prevalence and mechanisms of bone mass loss in this clinical setting. Also, the review on the role of nutraceuticals in GI disorder written by Romano M et al, Nutraceuticals for protection and healing of gastrointestinal mucosa *Curr Med Chem* 19: 109-117, 2012, might be worth of mentioning.

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Peer-review model: Single blind

Reviewer's code: 00503545

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Director, Doctor

Reviewer's Country/Territory: Japan

Author's Country/Territory: China

Manuscript submission date: 2021-09-20

Reviewer chosen by: Xin Liu (Online Science Editor)

Reviewer accepted review: 2021-12-17 09:47

Reviewer performed review: 2021-12-24 10:30

Review time: 7 Days

Scientific quality	☐ Grade A: Excellent ☐ Grade B: Very good ☒ Grade C: Good ☐ Grade D: Fair ☐ Grade E: Do not publish
Language quality	☐ Grade A: Priority publishing ☒ Grade B: Minor language polishing ☐ Grade C: A great deal of language polishing ☐ Grade D: Rejection
Conclusion	☐ Accept (High priority) ☐ Accept (General priority) ☒ Minor revision ☐ Major revision ☐ Rejection
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Peer-reviewer statements	Peer-Review: [☒] Anonymous [☐] Onymous Conflicts-of-Interest: [☐] Yes [☒] No
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SPECIFIC COMMENTS TO AUTHORS

In this study, the authors showed that JQBD can reduce colonic mucosa inflammation and inhibit the RANK/RANKL/OPG signaling pathway activation and they concluded that JQBD played a role in treating IBD-related bone metabolic abnormalities by inhibiting colonic mucosal inflammation, promoting mucosal healing, and inhibiting the activation of the RANK/RANKL/OPG signaling pathway, osteoclast formation, and bone resorption. This paper has been well written and the contents are novel and interesting. However, I suggest that the authors should address the following points.

Major 1) I think that it is unclear whether the only JQBD specifically inhibit RANK/RANKL/OPG signaling pathway activation or other drugs for inflammatory bowel disease (such as 5-ASA) also have the similar function. Therefore, like the previous research of the authors, if possible, I suggest that the authors should examine the effects of 5-ASA as well as JQBD on the RANK/RANKL/OPG signaling pathway. 2)

JQBD has generally been little known to date. Thus, I suggest that the authors should explain JQBD in more detail. Minor 1) I suggest that Fig. 4 and Fig. 5 should be explained using arrows. 2) The results of DAI in each group (Fig. 3A) has not been explained in the text. 3) Table S1 has not been found in the manuscript.

RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Reviewer's code: 02536349

Position: Editorial Board

Academic degree: MD

Professional title: Doctor, Professor

Reviewer's Country/Territory: Turkey

Author's Country/Territory: China

Manuscript submission date: 2021-09-20

Reviewer chosen by: Jia-Ru Fan

Reviewer accepted review: 2022-01-21 09:46

Reviewer performed review: 2022-01-24 21:38

Review time: 3 Days and 11 Hours

Scientific quality	☐ Grade A: Excellent ☐ Grade B: Very good ☒ Grade C: Good ☐ Grade D: Fair ☐ Grade E: Do not publish
Language quality	☒ Grade A: Priority publishing ☐ Grade B: Minor language polishing ☐ Grade C: A great deal of language polishing ☐ Grade D: Rejection
Conclusion	☐ Accept (High priority) ☐ Accept (General priority) ☐ Minor revision ☐ Major revision ☒ Rejection
Peer-reviewer	Peer-Review: ☒ Anonymous ☐ Onymous

statementsConflicts-of-Interest: [] Yes [**Y**] No**SPECIFIC COMMENTS TO AUTHORS**

Design and Methodology is acceptable and successful. Congratulations. A nice work with details reported. Unfortunately my final comment is : The beneficial effect of the composition has to be addressed to main effective ingredient or combination of ingredients. . The study does not indicate which herbal or a dual, triple or more combination of herbals was effective. Thus stepwise of different combination of eight content have to be tried. 4 + 4 > then dividing the effective four to 2+2 etc.. Otherwise if there is an unnecessary substitution, the additive possibility of its toxicity will be a problem. Certainly this manuscript has to be published in an experimental journal but not in a clinical reference journal.