



PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 71686

Title: Qingyi decoction attenuates intestinal epithelial cell injury via the calcineurin/nuclear factor of activated T-cells pathway

Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03866293

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: China

Author's Country/Territory: China

Manuscript submission date: 2021-09-18

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-09-18 02:14

Reviewer performed review: 2021-09-27 08:09

Review time: 9 Days and 5 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" 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 type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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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
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SPECIFIC COMMENTS TO AUTHORS

Major concerns: 1. More experiments are needed to make the findings more solid.

Minor concerns: 1. What is the source of QingYi decoction used in this study? An HPLC-based chemoprofile has to be provided. 2. Some figures could be combined into one figure, such as Fig.2 and Fig.3, as well as Fig.5 and Fig.6. 3. Some typos are needed to be corrected, such as NFATc3Expression in page 11.



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Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03976790

Position: Editor-in-Chief

Academic degree: DSc, PhD

Professional title: Emeritus Professor

Reviewer's Country/Territory: France

Author's Country/Territory: China

Manuscript submission date: 2021-09-18

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-10-19 07:41

Reviewer performed review: 2021-10-23 18:55

Review time: 4 Days and 11 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
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" 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
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SPECIFIC COMMENTS TO AUTHORS

Comments on the manuscript: “Qingyi decoction attenuates intestinal epithelial cell injury caused by severe acute pancreatitis via the calcineurin/NFATc3 pathway”
Dysfunction of the intestinal barrier contributes to the development of severe acute pancreatitis. A stable intestinal mucosal barrier balances the proliferation and apoptosis of intestinal cells. Calcium overload can trigger apoptosis and calcineurin / NFAT signaling may play a role in this process. On the other hand, QingYi decoction, a Chinese herbal medicine composed of several species of plants, is known to decrease the production of endotoxins, the activation of neutrophils, the release of inflammatory cytokines and to inhibit apoptosis. The aim of this study was to investigate the potential mechanisms for the therapeutic effect of QingYi decoction (QYD) in severe acute pancreatitis. This work, which is an in-depth study of the activity of a traditional substance, is interesting and useful. However, the manuscript requires several improvements before considering publication. Here are several remarks. Pages 5, 6: In the paragraph “QingYi decoction (QYD), a Chinese herbal medicine composed of Radix Bupleuri (Chaihu, *Bupleurum scorzonerifolium* Willd.), Scutellariae Radix (Huangqin, *Scutellaria baicalensis* Georgi), Aucklandia lappa *Aucklandiae* Radix (Muxiang, *Aucklandia lappa* Decne.), Corydalis Rhizoma (Yanhusuo, *Cordalis ambigua* Cham.et Schlecht.), Coptidis Rhizoma (Huanglian, *Coptis chinensis* Franch.), Paeoniae Radix Alba (Baishao, *Paeonia lactiflora* Pall.), Rhei Radix Et Rhizoma (Dahuang, *Rheum palmatum*, L.) and Natrii Sulfas (Mangxiao, Mirabilite) has been used in China for many years.”, Write the names of the genus and species, respecting the rules of nomenclature: names of the genus and species in italics, a capital letter at the beginning of the name of

the genus and a lower case at the beginning of the name of the species. Page 6: in the sentence “impact on AP through multiple pathways”, what is AP? Acute pancreatitis? Write in full. Page 7, “Measurement of serum amylase, IL-6, TNF- α , D-lactic acid, and DAO”: Provide minimal explanations for each detection method used. To refer to the kit supplier's instructions does not seem sufficient to me for a scientific article. Page 7, Histological Examination: Specify which fixative was used. What was the method of dehydration of the fixed tissues? Page 8, Apoptosis Detection: What was the fixative used? The same than for histological study? Please, specify. Page 8, “according to the manufacturer’s protocol”: quickly specify the method. Page 8, immunofluorescence analysis: “according to the manufacturer’s protocol”: idem, quickly specify the method. How were the negative controls carried out in order to verify if the reaction is indeed due to the application of the specific antibody and not an artefact? (Removal of the first antibody, or replacement, etc.) Page 8, western blot analysis: “Western blotting was performed as previously described”: idem, quickly specify the method. Figure 1: The explanation of the figure is very brief. Explain what the pictures represent. Add a scale bar on each image. What is shown in Figures B and C? Thanks to explain. Figures 2, 3, 4, 6, 8, 10: Add “CON: Control; QYD: decoction of Qingyi; SAP: Severe acute pancreatitis” Figures 5: Give some explanations of these three figures. Add a scale bar on each image. An insert with a control without first antibody (or other, see materials and methods) would be useful. Figure 7: Give some explanations of these three figures. Add a scale bar on each image. An insert with a control without first antibody (or other, see materials and methods) would be useful. Figure 9: Explain figure 9A.



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Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03034197

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: Serbia

Author's Country/Territory: China

Manuscript submission date: 2021-09-18

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-10-19 19:52

Reviewer performed review: 2021-10-26 07:21

Review time: 6 Days and 11 Hours

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
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 checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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Peer-reviewer statements	Peer-Review: [<input checked="" type="checkbox"/>] Anonymous [] Onymous Conflicts-of-Interest: [] Yes [<input checked="" type="checkbox"/>] No
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SPECIFIC COMMENTS TO AUTHORS

This is correctly conducted, well-designed, interesting animal study regarding the role of the calcineurin/NFATc3 pathway in the apoptosis of intestinal epithelial cells (IECs) in SAP and the potential mechanisms underlying the therapeutic effect of QingYi decoction (QYD). Manuscript should be published.



RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Title: Qingyi decoction attenuates intestinal epithelial cell injury via the calcineurin/nuclear factor of activated T-cells pathway

Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03866293

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: China

Author's Country/Territory: China

Manuscript submission date: 2021-09-18

Reviewer chosen by: Jing-Jie Wang

Reviewer accepted review: 2022-01-06 04:44

Reviewer performed review: 2022-01-07 03:34

Review time: 22 Hours

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
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 checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Peer-reviewer	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous



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statements

Conflicts-of-Interest: [] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

All the questions were well addressed.