

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 81096

Title: Cryptotanshinone induces apoptosis of activated hepatic stellate cells via modulating endoplasmic reticulum stress

Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03764379

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Director, Professor

Reviewer's Country/Territory: Argentina

Author's Country/Territory: China

Manuscript submission date: 2022-11-04

Reviewer chosen by: Dong-Mei Wang

Reviewer accepted review: 2023-01-27 14:38

Reviewer performed review: 2023-02-03 16:39

Review time: 7 Days and 2 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 Grade E: Do not publish
Novelty of this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
Creativity or innovation of this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation

Scientific significance of the conclusion in this manuscript	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
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 checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input type="checkbox"/> Anonymous <input checked="" type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

Cryptotanshinone induces apoptosis of activated hepatic stellate cells through endoplasmic reticulum stress. Authors: Xiaoxue Hou, Yuwen Li, Jiali Song, Wen Zhang, Rui Liu, Hui Yuan, Tiantong Feng, Zhengyi Jiang, Wenting Li, Chuanlong Zhu. The manuscript shows a new possibility of using TCP that inhibits hepatic fibrotic development. Although it is a very interesting proposal, and with hard work behind it, it must be studied in the context in which the experiment takes place. As an example, CCL4 also induces experimental hepatocarcinoma and there are many players who share both conditions (fibrosis and hepatocarcinoma), matricellular proteins such as SPARC (BM-40, osteonectin). It can be said that in 8 weeks of treatment hepatocellular carcinoma is not diagnosed, but the shared mechanisms are already working. In addition, the tumor microenvironment with ECM activation is already at work, including SPARC inducing ER regulation. Salubrinal directly exhibits antitumor activity and also reduces the resistance of tumor cells to other chemotherapeutic agents. In addition, Salubrinal reduces the intensity of protein synthesis processes, thus facilitating the release of a cell from a state of stress and literally saving its life (inhibition of the GADD34:PP1



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holoenzyme complex) (Madden et al, 2020, Zadorozhnii et al., 2022). So please, review your discussion and the basics of experimental design. The study by Xuiaoxue Hou et al. is of interest, but you have to clarify the methods, some of them very confusing, like ETM, "Fig.3 (G) Projection of electron fiberscope", !!!!!!! ?? ??, and electron micrographs show that CTP induces mitochondrial damage. Were only two of all groups observed? and with this result? With this result, your work could be under reasonable doubt. The authors should add a basic graph of the experimental design, since it is very confusing, some doses are missing, some run times too, others are explained in the results. Minor problem, check the English, in many paragraphs it's fine, but in others it should be rewritten, spellings too, like Annexin in Fig. 2.

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Reviewer's code: 05040484

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Assistant Professor, Doctor, Professor, Research Scientist

Reviewer's Country/Territory: Russia

Author's Country/Territory: China

Manuscript submission date: 2022-11-04

Reviewer chosen by: Dong-Mei Wang

Reviewer accepted review: 2023-02-07 08:23

Reviewer performed review: 2023-02-15 20:43

Review time: 8 Days and 12 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
Novelty of this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
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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

SPECIFIC COMMENTS TO AUTHORS

This is an interesting study, but I have a number of comments: 1) the authors write "Group 1 mice were not treated with CCl₄ or CPT. Group 2 were treated with CCl₄. Group 3 mice received intraperitoneal injection of salubrinal. Group 4 mice received intraperitoneal injection of CPT. Group 5 mice were intraperitoneally injected with CPT and salubrinal at the same time.", but further describes animals that received both CCl₄ and CPT, but this group is not in the group description. 2) the list of references is not designed in accordance with the requirements of the journal.

RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Manuscript submission date: 2022-11-04

Reviewer chosen by: Chen-Chen Gao

Reviewer accepted review: 2023-03-06 15:02

Reviewer performed review: 2023-03-06 16:22

Review time: 1 Hour

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
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statements

Conflicts-of-Interest: [☐] Yes [☒] No

SPECIFIC COMMENTS TO AUTHORS

Authors: Didn't you realize that SPARC is also known as BM-40 and osteonectin? It is the same matricellular protein, although it was referenced in that paragraph with 3 references. The same with the word "Annexin", (fig.2.D and 4.H) and ccl4 (?), and also with the electron micrographs. Avoid explaining to the reviewer the reviewer's own comments.

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Reviewer performed review: 2023-03-07 16:15

Review time: 1 Hour

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

SPECIFIC COMMENTS TO AUTHORS

No comments.