

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastrointestinal Oncology*

Manuscript NO: 88815

Title: Chinese herbal medicine decreases incidence of hepatocellular carcinoma in diabetes mellitus patients with regular insulin management

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05231286

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Associate Chief Physician

Reviewer's Country/Territory: China

Author's Country/Territory: Taiwan

Manuscript submission date: 2023-10-10

Reviewer chosen by: AI Technique

Reviewer accepted review: 2023-10-11 11:38

Reviewer performed review: 2023-10-11 13:45

Review time: 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 Grade E: Do not publish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 type="checkbox"/> Major revision <input checked="" type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input checked="" 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

SPECIFIC COMMENTS TO AUTHORS

The authors conducted an interesting report. My main concerns are as follows. 1. Since the insulin treatment was considered as a risk factor for HCC incidence. It would be better if the dosages of insulin treatment in DM patients were provided and analyzed. 2. In the Introduction section, the authors declared that “While these medications generally provide satisfactory control of blood sugar levels, they fail to significantly reduce the risk of HCC occurrence”. This conclusion is inadequate. Evidences have been emerged that metformin could decrease hepatocellular carcinoma risk (pmid: 22773548, 26013675). 3. The references of “studies have demonstrated an elevated risk of HCC incidence in diabetic patients treated with insulin” (line 14-15, page 11) should be added. 4. Some baseline variables were not similar between the two groups, please provide the statistic p values in table 1. 5. In the results of table 2, the authors stated that “After adjustment for the variables noted in Table 1, the adjusted HR of HCC was 0.88 (95%CI=0.80, 0.97) for herb users compared to the control group”. All the variables in table 1 were adjusted or the different distributed variables were adjusted? 6. In the “Chinese herbal medicine decreased HCC risk among DM patients with insulin management” part of the Results

section, please provide the p value and the results reference in the text. 7. In table 3, some bias existed. Patients had longer survival time had more chance to receive herbal treatment. 8. The results in this report indicated that HBV and HCV infections as major risk factors of developing HCC. Confusingly, the results also demonstrated that the HBV treatment and HCV treatment were risk factors for HCC incidence.

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Manuscript NO: 88815

Title: Chinese herbal medicine decreases incidence of hepatocellular carcinoma in diabetes mellitus patients with regular insulin management

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05771243

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: China

Author's Country/Territory: Taiwan

Manuscript submission date: 2023-10-10

Reviewer chosen by: AI Technique

Reviewer accepted review: 2023-10-12 23:20

Reviewer performed review: 2023-11-18 04:06

Review time: 36 Days and 4 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 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 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 type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input checked="" 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 checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

The manuscript describe herbal medicine may decrease HCC risk in DM patients with insulin use. But Taiwan is not a nation and it is not a nationwide study. 1 Hepatocellular carcinoma (HCC) is the fifth[a1] most common cancer where is the fifth from? There is no citation. 2 Treatments for DM fail to significantly reduce the risk of HCC occurrence, and insulin increasing HCC risk. But the literature also indicated that in the last decade, increasing evidence has suggested that metformin may reduce the risk of HCC. The evidence was insufficient in the manuscript. 3 The index date for herb-use group and non-exposure was not inconsistent which may induce a significant bias and influence the results of HCC occurrence and survival: The prior was set at the first day of herb use after insulin prescription; The latter was assigned a random date[a2] after insulin prescription for non-exposure patients 4 GLP[a3] -1 is an insulin secretagogue which reduced HCC risk, while insulin increases the risk of HCC. The conclusion of GLP-1 should be cautious.

RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: *World Journal of Gastrointestinal Oncology*

Manuscript NO: 88815

Title: Chinese herbal medicine decreases incidence of hepatocellular carcinoma in diabetes mellitus patients with regular insulin management

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03195661

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Professor

Reviewer's Country/Territory: China

Author's Country/Territory: Taiwan

Manuscript submission date: 2023-10-10

Reviewer chosen by: Li Li

Reviewer accepted review: 2024-01-13 02:34

Reviewer performed review: 2024-01-15 00:10

Review time: 1 Day and 21 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 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 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

I have no further requirement and comment.