Name of journal: World Journal of Gastroenterology

Manuscript NO: 95345

Title: Calculus bovis inhibits M2 tumor-associated macrophage polarization via Wnt/β-catenin pathway modulation to suppress liver cancer

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer’s code: 02845080

Position: Peer Reviewer

Academic degree: DNB, FEBS, FICS, FRCS (Gen Surg), MA, MBBS, MMed, MNAMS, MS

Professional title: Associate Professor, Director, Surgical Oncologist

Reviewer’s Country/Territory: Singapore

Author’s Country/Territory: China

Manuscript submission date: 2024-04-09

Reviewer chosen by: AI Technique

Reviewer accepted review: 2024-04-11 10:24

Reviewer performed review: 2024-04-11 10:42

Review time: 1 Hour

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<th>[ ] Grade B: Very good</th>
<th>[ ] Grade C: Good</th>
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<td>Novelty of this manuscript</td>
<td>[ ] Grade A: Excellent</td>
<td>[ ] Grade B: Good</td>
<td>[ ] Grade C: Fair</td>
<td>[ ] Grade D: No novelty</td>
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The authors have performed robust experiments in animal models and proven the association of the herb for effectiveness in liver cancer patients with underlying molecular mechanisms that are reported in great details. I am a clinician, a liver surgeon and i find no gross issues in reporting the results and discussion section. I will recommend editor to also circulate this manuscript to another peer reviewer who is a basic scientist.
Name of journal: World Journal of Gastroenterology

Manuscript NO: 95345

Title: Calculus bovis inhibits M2 tumor-associated macrophage polarization via Wnt/β-catenin pathway modulation to suppress liver cancer

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer’s code: 03260178

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Associate Professor

Reviewer’s Country/Territory: Poland

Author’s Country/Territory: China

Manuscript submission date: 2024-04-09

Reviewer chosen by: Ming Fan

Reviewer accepted review: 2024-05-15 09:24

Reviewer performed review: 2024-05-15 09:50

Review time: 1 Hour

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<td>[ ] Grade A: Excellent</td>
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<td>Creativity or innovation of this manuscript</td>
<td>[ ] Grade A: Excellent</td>
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[ ] Grade D: Fair  [ ] Grade E: Do not publish

[ ] Grade D: No novelty

[ ] Grade D: No creativity or innovation
### SPECIFIC COMMENTS TO AUTHORS

The article is a well-executed in vitro in vivo model of the assessment of active pharmacological compound on the tumour biology. Nevertheless, in my opinion the major flaw is the study of extract that constitutes 22 compounds. In my opinion, such studies provide little progress. Such a good laboratory setup should be used to pursue effects of unique chemical entities. Regarding the manuscript itself, it is well written, with no outstanding issues.
Name of journal: World Journal of Gastroenterology

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Title: Calculus bovis inhibits M2 tumor-associated macrophage polarization via Wnt/β-catenin pathway modulation to suppress liver cancer

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer’s code: 05606615

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer’s Country/Territory: Italia

Author’s Country/Territory: China

Manuscript submission date: 2024-04-09

Reviewer chosen by: Ming Fan

Reviewer accepted review: 2024-05-16 16:02

Reviewer performed review: 2024-05-23 01:19

Review time: 6 Days and 9 Hours

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<td>[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair</td>
<td>[ ] Grade D: No creativity or innovation</td>
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</table>
SPECIFIC COMMENTS TO AUTHORS

The study addresses an important, timely topic in HCC. A linguistic revision is required. We suggest also the following modifications: Introduction section: although the authors correctly included important papers in this setting, we believe some recent papers regarding HCC should be cited within the introduction, only for a matter of consistency. The authors should also further discuss the limitations of the current study. We suggest a linguistic revision and the addition of some references for a matter of consistency. Moreover, the authors should better clarify some points. The discussion should also be expanded.
Name of journal: World Journal of Gastroenterology

Manuscript NO: 95345

Title: Calculus bovis inhibits M2 tumor-associated macrophage polarization via Wnt/β-catenin pathway modulation to suppress liver cancer

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer’s code: 05575380

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer’s Country/Territory: Italy

Author’s Country/Territory: China

Manuscript submission date: 2024-04-09

Reviewer chosen by: Ming Fan

Reviewer accepted review: 2024-05-10 11:24

Reviewer performed review: 2024-05-23 01:21

Review time: 12 Days and 13 Hours

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| Novelty of this manuscript | [ ] Grade A: Excellent | [Y] Grade B: Good | [ ] Grade C: Fair |
|                            | [ ] Grade D: No novelty |

| Creativity or innovation of this manuscript | [ ] Grade A: Excellent | [Y] Grade B: Good | [ ] Grade C: Fair |
|                                             | [ ] Grade D: No creativity or innovation |
SPECIFIC COMMENTS TO AUTHORS
Dear Editor, thank you so much for inviting me to revise this manuscript about HCC. This paper addresses a current topic. The manuscript is quite well written and organized. English could be improved. Figures and tables are comprehensive and clear. The introduction explains in a clear and coherent manner the background of this study. We suggest the following modifications: • Introduction section: although the authors correctly included important papers in this setting, we believe the evolving systemic treatment scenario for liver cancer should be further discussed and some recent papers added within the introduction, only for a matter of consistency. We think it might be useful to introduce the topic of this interesting study. • Methods and Statistical Analysis: nothing to add. • Discussion section: Very interesting and timely discussion. Of note, the authors should expand the Discussion section, including a more personal perspective to reflect on. For example, they could answer the following questions – in order to facilitate the understanding of this complex topic to readers: what potential does this study hold? What are the knowledge gaps and how do researchers tackle them? How do you see this area unfolding in the next 5 years? We think it would be extremely interesting for the
readers. However, we think the authors should be acknowledged for their work. In fact, they correctly addressed an important topic in liver cancer, the methods sound good and their discussion is well balanced. One additional little flaw: the authors could better explain the limitations of their work, in the last part of the Discussion. In particular, the small sample size should preclude from making strong statements regarding the use of this combinatorial treatment. We believe this article is suitable for publication in the journal although major revisions are needed. The main strengths of this paper are that it addresses an interesting and very timely question and provides a clear answer, with some limitations. We suggest a linguistic revision and the addition of some references for a matter of consistency. Moreover, the authors should better clarify some points.
RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: World Journal of Gastroenterology
Manuscript NO: 95345
Title: Calculus bovis inhibits M2 tumor-associated macrophage polarization via Wnt/β-catenin pathway modulation to suppress liver cancer
Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed
Peer-review model: Single blind
Reviewer’s code: 05575380
Position: Peer Reviewer
Academic degree: MD
Professional title: Doctor
Reviewer’s Country/Territory: Italy
Author’s Country/Territory: China
Manuscript submission date: 2024-04-09
Reviewer chosen by: Xin-Liang Qu
Reviewer accepted review: 2024-06-13 04:44
Reviewer performed review: 2024-06-13 04:46
Review time: 1 Hour

Scientific quality
[ ] Grade A: Excellent  [ Y ] Grade B: Very good  [ ] Grade C: Good
[ ] Grade D: Fair  [ ] Grade E: Do not publish

Language quality
[ Y ] Grade A: Priority publishing  [ ] Grade B: Minor language polishing
[ ] Grade C: A great deal of language polishing  [ ] Grade D: Rejection

Conclusion
[ Y ] Accept (High priority)  [ ] Accept (General priority)
[ ] Minor revision  [ ] Major revision  [ ] Rejection

Peer-reviewer
Peer-Review: [ Y ] Anonymous  [ ] Onymous
SPECIFIC COMMENTS TO AUTHORS

acceptance.

Conflicts-of-Interest: [ ] Yes [ Y ] No
RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 95345

Title: Calculus bovis inhibits M2 tumor-associated macrophage polarization via Wnt/β-catenin pathway modulation to suppress liver cancer

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer’s code: 05606615

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer’s Country/Territory: Italia

Author’s Country/Territory: China

Manuscript submission date: 2024-04-09

Reviewer chosen by: Xin-Liang Qu

Reviewer accepted review: 2024-06-13 04:47

Reviewer performed review: 2024-06-13 04:50

Review time: 1 Hour

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SPECIFIC COMMENTS TO AUTHORS

Introduction section: although the authors correctly included important papers in this setting, we believe the references should be updated and some recent papers should be added within the introduction (PMID: 36695827; PMID: 33225800; PMID: 32772560; PMID: 33508960), only for a matter of consistency. Minor rev