

PEER-REVIEW REPORT

Name of journal: *World Journal of Meta-Analysis*

Manuscript NO: 84084

Title: Advances in the mechanism of action of metformin in pituitary tumors--a review

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 06130220

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Adjunct Professor

Reviewer's Country/Territory: Italy

Author's Country/Territory: China

Manuscript submission date: 2023-02-24

Reviewer chosen by: AI Technique

Reviewer accepted review: 2023-02-24 12:22

Reviewer performed review: 2023-02-27 12:05

Review time: 2 Days and 23 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input checked="" type="checkbox"/> Grade E: Do not publish
Novelty of 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 novelty
Creativity or innovation of 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 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 checked="" 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 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 article by Zhang et al. entitled “Advances in the mechanism of action of metformin in pituitary tumors--a review” is a review article attempting to describe the potential anti-cancer effects of metformin in different types of pituitary adenomas. As far as I am concerned, the article has different drawbacks that prevent the suitability for publication in WJCC in its present form. First, there is no mention on methodology through which the literature review was conducted: it seems more a narrative, mini-review. Second, several references are misquoted, particularly in the first part of the manuscript, where Authors cite papers on anti-cancer effects of metformin to support statements regarding the epidemiology of pituitary adenomas. Third, the review is essentially focused on research studies conducted in vitro. Although this is reasonable due to the lack of clinical trials investigating the efficacy of metformin in pituitary adenomas, the present manuscript may be out of scope for a Clinical Journal like WJCC. Fourth, the different molecular pathways on which metformin has been shown to act in studies conducted in vitro are poorly described and poorly understandable (particularly to clinical readers). Authors should first describe in brief a given molecular pathway

(and its main function in pituitary physiology) and then the possible metformin actions on that specific pathway. Furthermore, Authors should insert a figure illustrating the potential metformin actions on different pathways in different pituitary cell lines. In addition, authors discuss data obtained from a heterogeneous range of pituitary tumors (GH-secreting adenomas, ACTH-secreting adenomas, PRL-secreting adenomas, etc.) without a proper and accurate paragraph organization in the text (each tumor type should be discussed separately, including non-functioning pituitary adenomas). Authors may also consider a brief discussion on pituitary carcinomas (although these tumors represent a rare entity in the context of pituitary tumors). Finally, the discussion is too long based on the paucity of the existing data. Moreover, it provides strong statements that cannot be made based on the scarcity of studies conducted in clinical settings. Other comments are as follows: - There is need for major English editing, aimed to improve punctuation and grammar - Abbreviations: abbreviated terms should be written in full the first time they appear in the manuscript; afterwards, abbreviations can be used; e.g. "growth hormone (GH)" and then "GH"..... - "Pituitary adenoma is a common intracranial tumor, accounting for approximately 10% to 15% of neurological tumors (literature cited), and its incidence is second only to glioma and meningioma, ranking third among intracranial tumors[1-5]": authors improperly cite references about metformin effects on pituitary tumors here; references supporting the aforementioned epidemiologic statement are missing - The same concept applies to the subsequent statements quoting inappropriately references nr. 6 and 7 - ---- references 8, 9 and 10 - Authors forgot to mention LH- and FSH-secreting pituitary adenomas - - "Metformin is a metformin drug" ?? - Metformin does not promote insulin production; this can be an indirect consequence of reduced glucotoxicity and improved insulin sensitivity after metformin therapy - Metformin is mainly used in type 2 diabetes mellitus - "neuroendocrine tumors[1-19]" it is not proper to cite 19 references in a row, without



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detailing the antitumor effects of metformin in different setting

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Reviewer's code: 03604107

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Academic degree: MD, PhD

Professional title: Professor

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Author's Country/Territory: China

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Review time: 6 Days

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
Novelty of this manuscript	<input checked="" type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
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Re-review	<input type="checkbox"/> Yes <input checked="" 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

Thank you for exposing a well-written review on a drug of particular interest. Metformin has seen a rebirth in pharmacology, generally speaking, with different off-label usages and some of them proven to be safe and effective. Maybe you might want to mention its potential role against atherosclerosis, overweight etc. apart from being a good oral antidiabetic preparation. Therefore, the new perspective as an anti-tumoral drug is interesting and worth of publishing. Take care of some minor grammatical issues: Metformin is a metformin drug widely..... PRLoma: please write prolactinoma. I would also strongly suggest to add an abbreviation section: there are too many acronyms. Some sentences are excessively long: please use a more simple syntax.