

Answering Reviewers

Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Accept (General priority)

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.

Answer: Thank you very much. I have modified PRL, and I have also added the part of word abbreviations.

Reviewer #2:

Scientific Quality: Grade E (Do not publish)

Language Quality: Grade C (A great deal of language polishing)

Conclusion: Rejection

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 detailing the antitumor
antitumor effects of metformin in different setting

Answer:

First, Thank you very much. We've already added some of it, but the writing is
biased towards our further research plans, so it's more like a narrative, mini-review.

Second, Thank you very much. I have revised the problem of citing literature.

Third, The reviewer thinks that this article is not suitable for publication in WJCC
magazine. We have transfer it to another magazine "World Journal of Meta-Analysis"
following the advice.

Fourth, Thank you very much for your review. I have added some content as
requested. But because our initial idea was to do a mini-review, we didn't go very far.

Finally, We have added the abbreviations section.

"Metformin is a metformin drug" ?? it is not proper to cite 19
references in a row, without detailing the antitumor effects of
metformin in different setting

Thank you very much for your review. I have check and revised it.