

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 88715

Title: Potential therapeutic targets for nonalcoholic fatty liver disease: Glucagon-like peptide 1

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05238521

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Assistant Professor

Reviewer's Country/Territory: Croatia

Author's Country/Territory: China

Manuscript submission date: 2023-10-07

Reviewer chosen by: AI Technique

Reviewer accepted review: 2023-10-07 06:54

Reviewer performed review: 2023-10-07 14:17

Review time: 7 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 Grade E: Do not publish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 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 checked="" 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 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 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 title of the manuscript is intriguing, yet not very precise. The abstract summarizes well the content of the manuscript, and the key words are selected appropriately. The manuscript is concise. However, while briefly describing the current knowledge regarding the treatment options for NASH, the authors offer not much novelty nor different view of the problem. So, the Letter to the Editor does not add much to the field.

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Title: Potential therapeutic targets for nonalcoholic fatty liver disease: Glucagon-like peptide 1

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 00000663

Position: Peer Reviewer

Academic degree: PhD

Professional title: Professor

Reviewer's Country/Territory: Italy

Author's Country/Territory: China

Manuscript submission date: 2023-10-07

Reviewer chosen by: AI Technique

Reviewer accepted review: 2023-10-11 21:52

Reviewer performed review: 2023-10-12 15:37

Review time: 17 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 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 checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input 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 checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input 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 discuss the potential advantage of combination therapy in NAFLD/NASH, following the recent paper in WJG discussing the role of semaglutide. Considerations are not new. It remains to determine whether combination therapy with sema + colofexor, firsocostat and an abundance of new drugs is really able to improve the results. I have a lot of concern regarding the positive expectations reported in the letter; as far as I know, cilofexor and firsocostat had been aborted by pipeline of respective companies, and for most combination treatments the results are not much better than with semaglutide alone (except for liver enzymes). I would greatly suggest to down-tune the enthusiasm. If sema works via weight loss, then we'll expect results in the long term, given the impressive results of new antiobesity drugs.

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Title: Potential therapeutic targets for nonalcoholic fatty liver disease: Glucagon-like peptide 1

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 02860814

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Assistant Professor

Reviewer's Country/Territory: Greece

Author's Country/Territory: China

Manuscript submission date: 2023-10-07

Reviewer chosen by: Yu-Lu Chen

Reviewer accepted review: 2023-10-16 05:22

Reviewer performed review: 2023-10-22 12:23

Review time: 6 Days and 7 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 checked="" type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
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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

I read with great interest the letter by Yin et al entitled “Popular potential treatments for non-alcoholic fatty liver disease”. This letter will be improved by the addition of more details regarding the results of the trials and mechanism of action of drugs mentioned by the authors. Here are my comments: 1. Results from the combination treatments of semaglutide + cilofexor and semaglutide + firsocostat should be provided in more details. 2. Similarly, cotadutide and tirzepatide efficacy should be given in more details.

3. Which is the mechanism of action of cotadutide, tirzepatide, lanifibranor and aramchol?