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PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 78408

Title: Liver-specific drug delivery platforms: Applications for the treatment of alcohol-associated liver disease

Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03252330
Position: Editorial Board
Academic degree: MD, MSc
Professional title: Associate Professor
Reviewer's Country/Territory: Italy
Author's Country/Territory: United States

Manuscript submission date: 2022-06-24
Reviewer chosen by: AI Technique
Reviewer accepted review: 2022-06-27 08:28
Reviewer performed review: 2022-07-06 15:32
Review time: 9 Days and 7 Hours

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No

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Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The review by Warner et al. tackles an important issue, i.e. the possible use of new liver-specific delivery method for molecules aiming to treat ALD. Although these methods/materials (mostly nanoparticles) represent a great opportunity for site-specific delivery, it is quite appropriate to provide an up-to-date summary of the data obtained in animal models. The authors subdivide the possible delivery systems according to their specific characteristics, i.e liposomes, exosomes, nanoparticles or bacteria/viruses. For each one of these sub-categories they summarize the available data, also considering the different kind of molecules vehiculated by the various carriers. This analysis is quite detailed, however there are some points that should be further discussed by the authors: - Most of the data have been obtained using intraperitoneal injections or, in the best case, via intravenous administration. This raises possible problems for the future use of these approaches for patients' treatment, and this aspect should be discussed in the paper, also possibly considering future developments for oral delivery. - The authors rightly point out that the different characteristics of the nanoparticles can affect their ability to reach a specific target, focusing in particular on hepatocytes. Even if fibrosis is not the first manifestation of ALD, it may be worth mentioning that some delivery systems could deliver their cargo to macrophages and/or stellate cells.

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Reviewer's code: 06128243
Position: Peer Reviewer
Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: China

Author's Country/Territory: United States

Manuscript submission date: 2022-06-24

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-07-07 00:49

Reviewer performed review: 2022-07-22 00:13

Review time: 14 Days and 23 Hours

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Re-review	[ ] Yes [Y] No

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Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The topic of this article is novel ,currently few articles have such a detailed overview of liver-targeting drug delivery platforms for ALD. However,on the whole,there is still some small problems in your work. 1. There is a lack of discussion on targeted drug delivery for advanced and end-stage ALD. 2.In section"Liposome-Mediated Drug Delivery in ALD", what is emphasized is the effect of using liposomes to transport different drugs,and it does not explain the application of different liposomes. 3.Figure 3 only depicts the structure and distribution of liver cell,it would be more effective if you add depiction of the pathophysiological mechanism of ALD. 4.This paper only searched the literature of Pubmed,publication bias need to be examined. 5..It will be better to increase the effect comparision of different liver-targeting drug delivery routes. 6.The high-level literatures in the past five years in the references are insufficient.

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Reviewer's code: 03270609
Position: Editorial Board
Academic degree: PhD
Professional title: Professor
Reviewer's Country/Territory: Russia
Author's Country/Territory: United States

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Reviewer performed review: 2022-07-26 15:45

Review time: 5 Days and 2 Hours

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [Y] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
Re-review	[ ] Yes [Y] No

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Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Alcoholic liver disease is a medical, social and economic problem. The authors of the manuscript presented interesting material regarding modern approaches to the treatment of this pathology using platforms allow drugs to target the liver. The manuscript discusses in detail not only modern drug delivery platforms, their advantages and disadvantages, but also substantiates the pathogenetic mechanisms of their use. Of particular interest is the discussion of studies in which the therapeutic effect is achieved not only through a targeted effect on liver cells, but is mediated through the impact on the integrity of the intestinal barrier. For example, this applies to exosomes derived from bacteria or engineered bacteria that help restore the integrity of the intestinal barrier, the violation of which exacerbates liver damage. The manuscript is beautifully illustrated with drawings that make it easier to understand complex material. The manuscript is written in an accessible, understandable language and may be of interest to both developers of new drugs and practitioners. There are a few technical notes. Introduction. ….but importantly, these drugs only improve short-term mortality and can cause immunosuppression [4, 5]. - Probably better - drugs reduce short-term mortality? Page 7 LIVER-SPECIFIC DRUG DELIVERY: IMPLICATIONS FOR ALD - avoid abbreviations in names. Page 10 … Indeed, in an acute-on-chronic mouse model of ALD, rolipram-loaded liposomes improved liver injury … - it is better used to reduce liver damage. And further in the text, the authors should pay attention to similar aspects. References Reference 13 on page 6 does not match the text given.