



## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 62561

**Title:** Hepatitis Delta Virus: from infection to new therapeutic strategies

**Reviewer's code:** 00863327

**Position:** Peer Reviewer

**Academic degree:** MD, PhD

**Professional title:** Full Professor

**Reviewer's Country/Territory:** Taiwan

**Author's Country/Territory:** Italy

**Manuscript submission date:** 2021-02-07

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2021-02-08 04:04

**Reviewer performed review:** 2021-02-09 07:14

**Review time:** 1 Day and 3 Hours

<b>Scientific quality</b>	<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 Grade E: Do not publish
<b>Language quality</b>	<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
<b>Conclusion</b>	<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
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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## **SPECIFIC COMMENTS TO AUTHORS**

It is an interesting review article explores hepatitis delta virus (HDV), a RNA virus requiring the hepatitis B virus (HBV)-encoded hepatitis B surface antigen (HBsAg) for its assembly and transmission, either in co-infection or super-infection status. The main option of conventional treatment is interferon administered as mono-therapy, while only a minority of patients achieve a sustained response. Nevertheless, this article puts an emphasis on new therapeutic strategies that target specific steps in the HDV life cycle. The most promising drugs are myrcludex B and lonafarnib, which inhibit virus entry into hepatocytes and farnesylation of the viral-encoded large hepatitis D antigen, respectively.

The manuscript is well written in English and directly relevant to clinical application. There are some suggestions as follows. 1. Since this article emphasizes the novel therapies of HDV infection, the authors should summary the current knowledge including both established and undergoing treatments into a Table. 2. Some typographical errors needed to be corrected as follows. In page 3 Key words, the authors should remove "Hepatitis D". In page 11, there were no references for "Delta-4 fibrosis score" and "Delta Fibrosis Score". In page 15 New therapeutic targets in HDV, --- these represent inhibitors of the NTCP receptor and farnesyltransferase and "to" the group of nucleic acid polymers. The authors should remove "to". In page 31 Figure 1, L-HDAg - "HBsAG". The author should use HBsAg.



## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 62561

**Title:** Hepatitis Delta Virus: from infection to new therapeutic strategies

**Reviewer's code:** 00070897

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Doctor

**Reviewer's Country/Territory:** China

**Author's Country/Territory:** Italy

**Manuscript submission date:** 2021-02-07

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2021-02-19 00:56

**Reviewer performed review:** 2021-02-19 09:17

**Review time:** 8 Hours

<b>Scientific quality</b>	<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
<b>Language quality</b>	<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
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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#### **SPECIFIC COMMENTS TO AUTHORS**

This review focuses on new advances in HDV infection and treatment. The knowledge is helpful for further understanding of life cycle and new therapeutic strategies of hepatitis delta virus.



## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 62561

**Title:** Hepatitis Delta Virus: from infection to new therapeutic strategies

**Reviewer's code:** 03664122

**Position:** Peer Reviewer

**Academic degree:** PhD

**Professional title:** Research Scientist

**Reviewer's Country/Territory:** Latvia

**Author's Country/Territory:** Italy

**Manuscript submission date:** 2021-02-07

**Reviewer chosen by:** Jia-Ping Yan

**Reviewer accepted review:** 2021-02-15 08:57

**Reviewer performed review:** 2021-02-25 16:13

**Review time:** 10 Days and 7 Hours

<b>Scientific quality</b>	<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
<b>Language quality</b>	<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
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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#### **SPECIFIC COMMENTS TO AUTHORS**

Since the discovery of HDV, it has remained an important pathogen influencing the course of hepatitis B virus disease. The continuing need for increased attention to routine HDV screening and the search for new treatments is a prerequisite for the publication of such a review. I do not have any specific comments on the review, it is well written and includes an analysis of interesting treatment options, even though there were no alternative points of view or hypotheses. Just, the mentioned role of integrated HBV DNA in maintaining high HBsAg levels even after Myrcludex treatment seems rather questionable, but not impossible.



## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 62561

**Title:** Hepatitis Delta Virus: from infection to new therapeutic strategies

**Reviewer's code:** 05848252

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Associate Chief Physician

**Reviewer's Country/Territory:** China

**Author's Country/Territory:** Italy

**Manuscript submission date:** 2021-02-07

**Reviewer chosen by:** Jia-Ping Yan

**Reviewer accepted review:** 2021-02-15 12:25

**Reviewer performed review:** 2021-03-04 15:06

**Review time:** 17 Days and 2 Hours

<b>Scientific quality</b>	<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
<b>Language quality</b>	<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
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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#### **SPECIFIC COMMENTS TO AUTHORS**

In this paper, the author made a detailed review of HDV, introduced the virology, epidemiology and clinical diagnosis and treatment of HDV. From more attention to HBV infection, we have turned our attention to HDV infection and realize the severity of HDV-related infections. Overall, the article is well organized and its presentation is good. However, on one point, i suggest that CHD should be commented to avoid ambiguity when it first appears in the text.



## RE-REVIEW REPORT OF REVISED MANUSCRIPT

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**Manuscript NO:** 62561

**Title:** Hepatitis Delta Virus: from infection to new therapeutic strategies

**Reviewer's code:** 00863327

**Position:** Peer Reviewer

**Academic degree:** MD, PhD

**Professional title:** Full Professor

**Reviewer's Country/Territory:** Taiwan

**Author's Country/Territory:** Italy

**Manuscript submission date:** 2021-02-07

**Reviewer chosen by:** Man Liu

**Reviewer accepted review:** 2021-04-09 07:18

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**Review time:** 1 Hour

<b>Scientific quality</b>	<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
<b>Language quality</b>	<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
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Peer-reviewer statements</b>	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 have revised their manuscript according to the reviewer's suggestions, and



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all of the raised issues have been clarified. There is no further comments on the revised manuscript.