Reviewer #1:

Scientific Quality: Grade D (Fair)

Language Quality: Grade B (Minor language polishing)

Conclusion: Major revision

Specific Comments to Authors: The comments are as follows, 1. The pathogenesis such as causes and mechanisms of hepatic cell death, repair and regeneration, and their relationships in the process of hepatic fibrogenesis should be summarized and illustrated in a figure. It is not only hepatic cell death, inflammation, immunity, ECM accumulation and HSCs activation, but also association with intrahepatic blood supply and angiogenesis and so on. Moreover, there still is an autophagy in the death subtypes of hepatic cells, which could be added in Figure 1. 2. Prevention and treatment guidelines, insufficiencies and countermeasures of liver fibrosis could be introduced. 3. The liver fibrosis is a histopathological concept, and histopathological/ imageological evaluations in the research progress of liver fibrosis treatments should also be introduced. 4. Biomarkers and their panel for the diagnosis and treatment of liver fibrosis screened by system biology, dig data and Artificial Intelligence (AI) analysis etc could also be introduced. 5. The natural products/herbal medicines including herbal medicines (e.g. Silybum marianum), herbal formulae (e.g. FuzhengHuayu) and their compounds (e.g. Tanshinone IIA) for the treatment of liver fibrosis in hepatitis or cirrhosis etc could be summarized and illustrated in Figure 2 and so on. e.g. 1) natural products/ Herbal medicines Ma X, et al. Eur J Pharmacol. 2020 Dec 5;888:173578; Li H. J Ethnopharmacol. 2020, 251:112442. 2) Silybum marianum: Abenavoli L, et al. Phytother Res. 2018, 32(11):2202-2213. 3) FuzhengHuayu Dong S, et al. Evid Based Complement Alternat Med. 2015; 2015:125659; Dong S, et al. Acta Pharmacol Sin. 2018, 39(6):930-941. 4) Tanshinone IIA：Shi MJ, et al. Biomed Pharmacother. 2019, 112:108676; Shi MJ, et al. Journal of Ethnopharmacology, 2020, 253:112689. 6. It is not only efficacy, but also safety in the intervention of liver fibrosis should be introduced and illustrated in Figure. 7. Studies on the compatibility combination between drugs and /or other interventions could also be added to this review. 8. Molecular targets for liver fibrosis treatments

could changed to Signaling pathways and molecular targets for liver fibrosis treatments. The signaling pathways is not only Wnt/β-catenin, but also PI3K/Akt signaling pathway (e.g. Cai FF, et al. Biomed Pharmacother. 2019, 114:108863; Zhou Y, et al. Pharm Biol. 2021, 59(1):1594-1606); TGF-β/Smad/ERK Signaling (e.g. Cai FF, et al. Scientific Reports, 2018, 8:15367); TGFβ/Smad and Akt/FoxO3 signaling pathways (e.g. Zhou Y, et al. Journal of Ethnopharmacology, 2021, 264:113021); and metabolic pathways (e.g. Hu XQ et al. Journal of Ethnopharmacology, 2019, 238:111888) are involved. In additional, Retinoid X receptor as a target of drugs could also be introduced. 9. The study for the prevention and treatment of hepatic cells death could be referenced (e.g. Cai FF, et al. Biomed Pharmacother. 2019, 114:108863). In additional, a report of clinical trial in the treatment of FuzhengHuayu on liver cirrhosis could also be introduced by citation (Song YN, et al. Evid Based Complement Alternat Med. 2013;2013:709305).

Response: Thanks for the reviewer's comments and suggestions. The suggested literature reports were reviewed and cited in the revised manuscript. Meanwhile, the comments were addressed point-by-point. All the changes in the manuscript were highlighted. Please see the following points.

1. The pathogenesis of hepatic cell death, repair, and regeneration in liver fibrosis was discussed, and autophagy as a subtype of cell death was discussed.
2. Prevention and treatment guidelines, insufficiencies, and countermeasures for liver fibrosis could be introduced.
3. The histopathological and imagological evaluations in the research progress of liver fibrosis treatments were introduced.
4. Biomarkers and their panel for the diagnosis and treatment of liver fibrosis screened by system biology and Artificial Intelligence (AI) analysis, etc could also be introduced.
5. The natural products/herbal medicines including herbal medicines (e.g. Silybum marianum), herbal formulae (e.g. FuzhengHuayu) and their compounds (e.g. Tanshinone IIA) for the treatment of liver fibrosis were summarized and illustrated in Figure 2. A separate paragraph was added to the revised manuscript.

6. The safety in the intervention of liver fibrosis should be introduced and illustrated in Figure.
7. Studies on the compatibility combination between drugs and /or other interventions could also be added to this review.
8. 'Molecular targets for liver fibrosis treatments' was changed to 'Signaling pathways and molecular targets for liver fibrosis treatments'. The suggested signaling pathways were also discussed in the revised manuscript.
9. The study for the prevention and treatment of hepatic cell death was referenced, including the clinical trial in the treatment of FuzhengHuayu on liver cirrhosis. References such as Biomed Pharmacother 2019; 112: 108676 [PMID: 30797157 DOI: 10.1016/j.biopha.2019.108676] & Evid Based Complement Alternat Med 2013: 709305 [PMID: 23533516 DOI: 10.1155/2013/709305] were referenced.

Reviewer #2:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: I have read with great interest the manuscript entitled "Treatment of liver fibrosis: past, current, and future" submitted to the World Journal of Gastroenterology. The manuscript is well-written, and the topic is of clinical interest. All the basic cellular and molecular mechanisms related to liver fibrosis were comprehensively covered, making the path for the targets for their potential treatment. In addition, current and future treatment options were presented, including clinical trials on the subject. MAJOR COMMENTS - The tables from the article, specifically Table 2, are too long, making it difficult for the reader to get a clear message. Therefore, I would suggest the authors present a summary of the most promising drugs in clinical trials and refer the readers to the full table for completeness. - In the Summary section, it would be great to summarise briefly what is currently clinically done for treating liver fibrosis and how the authors envisage the next steps for implementing the new treatment options.

Response: Thanks for the reviewer's interest in the manuscript and we appreciate the comments. All the changes in the revised manuscript were highlighted.

Table 2 was shorted as the comments to clearly describe the most promising drugs in clinical trials. Meanwhile, in the Future treatment section, the preventive and therapeutic treatments such as treatments of hepatitis viral infection (e.g., Peginterferon Alfa 2a), transplantation of mesenchymal stem cells, bariatric surgery for patients with obesity and NAFLD, dietary modification (e.g., Mediterranean diet or Calorie-restricted diet).' were highlighted.

In the Summary section, 'Currently, promising treatments for liver fibrosis are still the preventive strategies, such as treatment of hepatitis viral infection (e.g., Peginterferon Alfa 2a), inhibition of the progression of MAFLD and obesity (e.g., bariatric surgery), dietary modification (e.g., Mediterranean diet or Calorie-restricted diet)' was summarized.

4 LANGUAGE POLISHING REQUIREMENTS FOR REVISED MANUSCRIPTS SUBMITTED BY AUTHORS WHO ARE NON-NATIVE SPEAKERS OF ENGLISH

Response: Academic English was polished by native speakers.

6 EDITORIAL OFFICE'S COMMENTS

Authors must revise the manuscript according to the Editorial Office's comments and suggestions, which are listed below:

(1) Science editor:

The manuscript has been peer-reviewed, and it' s ready for the first decision.

Language Quality: Grade B (Minor language polishing)

Scientific Quality: Grade C (Good)

Response: All the comments from reviewers have been solved and changes are highlighted in the revised manuscript.

(2) Company editor-in-chief:

I recommend the manuscript to be published in the World Journal of Hepatology. Before final acceptance, when revising the manuscript, the author must supplement and improve the highlights of the latest cutting-edge research results, thereby further improving the content of the manuscript. To this end, authors are advised to apply a new tool, the Reference Citation Analysis (RCA). RCA is an artificial intelligence technology-based open multidisciplinary citation analysis database. In it, upon obtaining search results from the keywords entered by the author, "Impact Index Per Article" under "Ranked by" should be selected to find the latest highlight articles, which can then be used to further improve an article under preparation/peer-review/revision. Please visit our RCA database for more information at: https://www.referencecitationanalysis.com/.

Response: Thank you for the suggestion. RCA database has been references when the manuscript was revised. All the changes in the revised manuscript were highlighted.