Name of journal: World Journal of Gastroenterology

Manuscript NO: 95779

Title: Fanlian Huazhuo Formula alleviates high-fat diet-induced non-alcoholic fatty liver disease by modulating autophagy and lipid synthesis signaling pathway

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer’s code: 00607640

Position: Editor-in-Chief

Academic degree: PhD

Professional title: Professor

Reviewer’s Country/Territory: Taiwan

Author’s Country/Territory: China

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Reviewer chosen by: AI Technique

Reviewer accepted review: 2024-05-16 04:46

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<th>[ Y] Grade B: Very good</th>
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SPECIFIC COMMENTS TO AUTHORS

The study demonstrates several strengths, including a well-structured experimental design, clear methodology, and comprehensive analysis of Fanlian Huazhuo Formula (FLHZF)'s therapeutic effects on nonalcoholic fatty liver disease (NAFLD). The authors effectively justify their research focus in the introduction, highlighting the need for alternative therapies for NAFLD. Detailed descriptions of experimental protocols, including animal handling, cell culture, and molecular assays, enhance reproducibility and reliability. Furthermore, the inclusion of diverse endpoints, such as serum markers, histological analyses, and molecular assays, provides a thorough assessment of FLHZF's effects. The discussion integrates the study's findings with existing literature, offering insights into the potential mechanisms underlying FLHZF's action. Overall, the study's rigorous approach and comprehensive analysis contribute to its scientific validity and potential clinical relevance. However, some recommendations are for your consideration:

1. Consider providing a rationale for the selection of specific dosages of FLHZF and the duration of treatment. This would enhance the transparency of the study's methodology and provide valuable insights into the optimal therapeutic regimen for FLHZF in...
NAFLD management. 2. It is recommended to incorporate blinding procedures into future studies to minimize potential bias during data collection and analysis. Implementing blinding methods, such as blinded assessment of outcomes or data analysis by blinded researchers, would enhance the methodological rigor of the study. 3. Expand the discussion to include a thorough assessment of FLHZF's safety profile and potential side effects. Addressing safety considerations and discussing any observed adverse events associated with FLHZF treatment would provide a more comprehensive evaluation of its therapeutic potential and support informed decision-making in clinical practice. 4. In the conclusion, consider outlining specific directions for future research, such as clinical trials or mechanistic studies, to further investigate FLHZF's efficacy and underlying mechanisms of action. Providing clear guidance on future research directions would help advance the understanding of FLHZF's therapeutic benefits and its potential applications in clinical settings. 5. Strengthen the study's conclusions by including additional control groups or comparisons, such as positive control groups or comparisons with existing treatments for NAFLD. This would provide a more robust context for interpreting FLHZF's therapeutic effects and enhance the study's overall scientific validity.
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Reviewer’s code: 07687754

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer’s Country/Territory: Spain

Author’s Country/Territory: China

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Reviewer chosen by: Yu Bai

Reviewer accepted review: 2024-06-17 07:42

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SPECIFIC COMMENTS TO AUTHORS
The manuscript By Niu et al. describes the use of new plant-based treatment for NAFLD. The results shown are very promising, although there are some changes to be addressed before manuscript acceptance. First of all, it is necessary to improve figure quality and increase dimensions of the figures which are hardly readable. In all microscope images there is no indication about the scale bar. Both in cell and animal studies, there is no quantification of OilRedO or hematoxylin eosin. Also, there is no indication in methods about what is liver/fat index which are shown in fig.3. Also, a quantification of TUNEL assay in fig 8 is missing. Also, it could be necessary a quantification of phosphorilated forms of AMPKa and ACC; to evaluate if there is some change in their level of activation and not only expression. I suggest to add a paragraph of limitations: there is no evaluation of effect of sex in these studies. Also, justification about the dose used in cell and mice may be needed: are they based on previous studies? I suggest to incorporate these references to the manuscript: Kostapanos M. S.; Kei A.; Elisaf M. S. Current role of fenofibrate in the prevention and management of non-alcoholic fatty liver disease. World. J. Hepatol. 2013, 5 (9), 470–478. 10.4254/wjh.v5.i9.470. - DOI - PMC - PubMed Han D.;