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PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 79802

Title: In vivo recognition of bioactive substances of Polygonum multiflorum for regulating mitochondria against metabolic dysfunction-associated fatty liver disease

Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 06373083
Position: Peer Reviewer
Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: China

Author's Country/Territory: China

Manuscript submission date: 2022-09-07

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-09-21 09:40

Reviewer performed review: 2022-10-04 04:03

Review time: 12 Days and 18 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Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish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

In this manuscript, Li and colleages assessed the role of Polygonum multiflorum(PM) in regulating HFD-induced MAFLD . The authors report that PM improves the mitochondrial ultrastructure and prevented oxidative stress and energy metabolism disorder in liver mitochondria to mitigate fat emulsion-induced cellular steatosis and HFD-induced MAFLD. This manuscript writing still needs to be strengthened. The presented data are clear and most conclusions are solid and sound. The used methods are largely adequate. But there remains some criticism. 1.Mitochondria undergo constant mitochondrial fission and fusion, mitochondrial biogenesis, and mitophagy, which coordinately control mitochondrial morphology, quantity, quality, turnover, and inheritance. Do the authors know whether PM regulates which process in mitochondria and thus protects the mitochondrial ultrastructure. 2.All figure does not use Western Blot and qPCR to strengthen the reliability of the data, it is recommended to detect markers of MAFLD in vivo and in vitro at least. 3.The clarity of electron microscopy results is difficult to distinguish whether it is mitochondria, lysosomes or other organelles. It is recommended to count mitochondrial parameters(Mitochondrial length, diameter and area) from electron microscopy images.

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Reviewer's code: 06197162
Position: Peer Reviewer
Academic degree: MD, PhD
Professional title: Director
Reviewer's Country/Territory: Japan
Author's Country/Territory: China

Manuscript submission date: 2022-09-07

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-10-05 02:29

Reviewer performed review: 2022-10-08 05:40

Review time: 3 Days and 3 Hours

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[Y] Grade A: Priority publishing [ ] 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

This study demonstrated that Polygonum multiflorum (PM), a traditional herbal medicine in China, might have the beneficial effects on patients with metabolic dysfunction-associated fatty liver disease, probably through restoring mitochondrial dysfunction. The authors also identified 8 PM-derived monomers which could be the candidates to have such effects, by UHPLC/MS. Their methods of both in vitro and in vivo studies were well designed and scientific. However, there might be several issues to be addressed for strengthening the impact of this manuscript. Major points: 1) The reviewer is concerned about less or absence of dose-dependency, especially in vitro study using L02 cells,as compared with in vivo study. For example, Fig. 1-K, Complex-II; Fig. 5-F, Na+-K+ ATPase; Fig. 5-G, Ca2+-Ma2+ ATPase; Fig. 7-I, Ca2+-Ma2+ ATPase. Please add some comments on these data. 2) As the authors described that even MME (live mitochondrial extract of MOD group) had remarkable lowering effects on the cell levels of TC with dose-dependency (Fig. 5-B). If the authors have any UHPLC/MS data of MME, those informations would be useful to understand its mechanism. Please add some comments on this interesting finding. 3) According to Table 3, the authors' description of "spleen index showed a downward trend" in line 549, seemed to be wrong. The SD value of HMG was too big, as compared with that of other groups. Minor points: 1) The authors should add some comments on Limitations of this study, at the end of Discussion section.