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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 47970

Title: Allyl isothiocyanate ameliorates lipid accumulation and inflammation in nonalcoholic fatty liver disease via the Sirt1/AMPK and NF-κB signaling pathways

Reviewer's code: 03465463

Reviewer's country: Taiwan

Science editor: Ruo-Yu Ma

Reviewer accepted review: 2019-04-04 07:36

Reviewer performed review: 2019-04-04 10:10

Review time: 2 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection	Peer-Review: [Y] Anonymous [ ] Onymous Peer-reviewer's expertise on the topic of the manuscript: [Y] Advanced [ ] General [ ] No expertise Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The present study investigated the effects of allyl isothiocyanate (AITC) on lipid accumulation and inflammation during nonalcoholic fatty liver disease (NAFLD) development using the mice fed a high fat diet (HFD) and the AML-12 cells treated with

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palmitate acid (PA). I like to give the following comments. 1. In the introduction, previous report(s) mentioned the mediation of signals such as Sirt1 and AMPK in NAFLD would be more helpful. 2. Link of AITC with NAFLD seems not enough. Please add more in the introduction section. Additionally, chemical structure of AITC was not indicated. 3. Daily intake of AITC at 100 mg/kg needs the reference(s) to support. Additionally, purity of AITC is also required. 4. Hepatic and cellular TG contents were unclear, particularly for TG. 5. In Figure 1, one group shown normal control is required. Figure 1B means AUC of body weight or what? Additionally, total cholesterol in blood not modified by AITC but is it higher than normal control? Similar concerns are extended to another indicator including AST, ALT and uremic acid. 6. Pro-fibrotic signals were not investigated in mice. Why? How to know the presence of NAFLD? 7. In the conclusion, it seems better to show as: therapeutic agent for "the progress of" NAFLD in the last sentence. 8. Effective dose of AITC for clinical practice seems helpful even it was perspective. Additionally, limitation(s) of this report could be included.

INITIAL REVIEW OF THE MANUSCRIPT

Google Search:

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 47970

Title: Allyl isothiocyanate ameliorates lipid accumulation and inflammation in nonalcoholic fatty liver disease via the Sirt1/AMPK and NF-κB signaling pathways

Reviewer's code: 03478516

Reviewer's country: Italy

Science editor: Ruo-Yu Ma

Reviewer accepted review: 2019-05-14 08:36

Reviewer performed review: 2019-05-14 14:01

Review time: 5 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection	Peer-Review: [Y] Anonymous [ ] Onymous Peer-reviewer's expertise on the topic of the manuscript: [Y] Advanced [ ] General [ ] No expertise Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Authors shpould comment on these specific points to give readers a more comprehensive view of the topic. Several isothiocyanates have been proposed as promising chemopreventive agents for human cancers. However, it has been reported

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that allyl isothiocyanate exhibit carcinogenic potential. Wauthors investigated whether these isothiocyanates could cause DNA damage, using (32)P-labeled DNA fragments obtained from the human p53 tumor suppressor gene and the c-Ha-ras-1 protooncogene. Allyl isothiocyanate caused Cu(II)-mediated DNA damage and formation of 8-oxo-7, 8-dihydro-2'-deoxyguanosine (8-oxodG) more strongly than benzyl and phenethyl isothiocyanates. Catalase and bathocuproine, a Cu(I)-specific chelator, inhibited Cu(II)-mediated DNA damage by these isothiocyanates, suggesting involvement of H(2)O(2) and Cu(I)....as evident in..Free Radic Biol Med. 2000 Mar 1;28(5):797-805. Mechanism of oxidative DNA damage induced by carcinogenic allyl isothiocyanat,e. This aspect is of main importance in the light of the impaired copper availability in obesity-related NAFLD and its comorbiditidy, .i.e., atherosclerosis as presented in...Prediction of carotid intima-media thickness in obese patients with low prevalence of comorbidities by serum copper bioavailability. J Gastroenterol Hepatol. 2018 Aug;33(8):1511-1517. What about the process of activating SIRT1 and subsequently inhibiting ER stress, as studied in...Send to Acta Pharmacol Sin. 2016 Mar;37(3):344-53. Sulforaphane prevents rat cardiomyocytes from hypoxia/reoxygenation injury in vitro via activating SIRT1 and subsequently inhibiting ER stress. Authors should clearly state that this animal model of NAFLD does not completely mirror the human one, although quite similar.

INITIAL REVIEW OF THE MANUSCRIPT

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 47970

Title: Allyl isothiocyanate ameliorates lipid accumulation and inflammation in nonalcoholic fatty liver disease via the Sirt1/AMPK and NF-κB signaling pathways

Reviewer's code: 00199807

Reviewer's country: Turkey

Science editor: Ruo-Yu Ma

Reviewer accepted review: 2019-05-14 12:16

Reviewer performed review: 2019-05-20 09:00

Review time: 5 Days and 20 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection	Peer-Review: [Y] Anonymous [ ] Onymous Peer-reviewer's expertise on the topic of the manuscript: [ ] Advanced [Y] General [ ] No expertise Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Dear Editor, I reviewed the manuscript titled "Allyl isothiocyanate ameliorates lipid accumulation and inflammation in nonalcoholic fatty liver disease via the Sirt1/AMPK and NF-κB signaling pathways". This si very interesting manuscript. I think it can be

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accepted after these revisions. My comments are listed below: 1. How did The Authors choose the daily dosage of AITC (100 mg/kg)? 2. Some general informations about the methods and results of the manuscript should be moved from results to methods or discussion sections: such as: "Chronic inflammation characterized by increased proinflammatory cytokine levels and the activation of principal inflammatory pathways is closely associated with the development of NAFLD[28]. The IKK/NF-κB pathway can be activated by HFD challenge in vivo and by palmitate treatment in vitro, thus playing a crucial role in the development of metabolic disorders, including NAFLD[8, 9]. In response to numerous inflammatory stimuli, IKK complex activation induces IκB phosphorylation and subsequent degradation, which releases NF-κB and allows it to translocate into the nucleus[29]."

INITIAL REVIEW OF THE MANUSCRIPT

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 47970

Title: Allyl isothiocyanate ameliorates lipid accumulation and inflammation in nonalcoholic fatty liver disease via the Sirt1/AMPK and NF-κB signaling pathways

Reviewer's code: 00053493

Reviewer's country: Mexico

Science editor: Ruo-Yu Ma

Reviewer accepted review: 2019-05-14 12:51

Reviewer performed review: 2019-05-20 13:00

Review time: 6 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
[ ] Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good [Y] Grade D: Fair [ ] Grade E: Do not publish	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection	[ ] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [Y] Major revision [ ] Rejection	Peer-Review: [Y] Anonymous [ ] Onymous Peer-reviewer's expertise on the topic of the manuscript: [ ] Advanced [Y] General [ ] No expertise Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Title: Allyl isothiocyanate ameliorates lipid accumulation and inflammation in nonalcoholic fatty liver disease via the Sirt1/AMPK and NF-κB signaling pathways Authors aimed to investigate the effect allyl isothiocyanate in a nonalcoholic fatty liver

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disease mouse model and in vitro. The concluded that allyl isothiocyanate decreased liver inflammation and steatosis by activating the Sirt1/AMPK and inhibiting the NF-κB pathways and propose allyl isothiocyanate as a potential therapeutic agent for NAFLD. This study is very interestingly with a degree of novelty and it seems that the results support their conclusions and that the methodology is robust. Unfortunately, they present only two groups in their results (diet and diet plus allyl isothiocyanate) and performed a student's two-tailed t-test. Authors need to show all the groups (including a vehicle, normal control and control of the allyl isothiocyanate) and then to perform an ANOVA with Turkey's test to see if the difference reach a significant value, otherwise their results lack relevance. I will be willing to re-review a new version.

INITIAL REVIEW OF THE MANUSCRIPT

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