



**Baishideng  
Publishing  
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**30<sup>th</sup> November, 2020**

Editor  
World Journal of Gastroenterology

**Subject: Manuscript ID: 60352**

Dear Editor,

We have considered carefully the criticism by the reviewers, and hope to have been able to answer it in a satisfactory way, as you will see from the response to reviewer's reports. **(Manuscript ID: 60352; Manuscript Title "Sinapic acid ameliorates D-GalN/LPS-induced fulminant hepatitis in rats: Role of Nrf2/HO-1 pathways").**

The changes indicated have been incorporated into the revised manuscript and have been highlighted in red text.

Yours truly,  
**Mushtaq A. Ansari, PhD**  
Associate Professor,  
College of Pharmacy  
King Saud University  
Riyadh 11451, Saudi Arabia  
Email: muansari@ksu.edu.sa

## PEER-REVIEW REPORT

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

**Manuscript NO:** 60352

**Title:** Sinapic acid ameliorates D-GalN/LPS-induced fulminant hepatitis in rats: Role of Nrf2/HO-1 pathways

**Reviewer's code:** 03536031

**Position:** Peer Reviewer

**Academic degree:**

**Professional title:**

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

**Author's Country/Territory:** Saudi Arabia

**Manuscript submission date:** 2020-10-26

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2020-10-27 06:38

**Reviewer performed review:** 2020-11-11 12:57

**Review time:** 15 Days and 6 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 Grade E: Do not publish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 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 checked="" type="checkbox"/> Accept (High priority) <input 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

### SPECIFIC COMMENTS TO AUTHORS

The manuscript is interesting. The methodology used is adequate and consistent with the objective of the study. The results support the discussion. However, I have the following comments.

Major Comments: 1. The expression and activity of the transcription factor Nrf2 depend on oxidative stress. Changes that modify the antioxidant and anti-inflammatory response. Discuss this point. Suggested reference: Docosahexaenoic acid and hydroxytyrosol co-

administration fully prevents liver steatosis and related parameters in mice subjected to high-fat diet: A molecular approach. *Biofactors*. 2019; 45: 930-943. PMID: 31454114

**Response:** The expression and activity of the transcription factor Nrf2 depend on oxidative stress. Changes that modify the antioxidant and anti-inflammatory response has been discussed and incorporated the suggested reference along with others (*Biofactors*. 2019; 45: 930-943. PMID: 31454114)

2. Inflammation and subsequent cellular damage is determined by oxidative stress. In this regard, the modulation of Nrf2 directly influences the changes in the activity of NF- $\kappa$ B. This interaction is essential to understand the benefits generated by the intervention. Discuss this point. Molecular adaptations underlying the beneficial effects of hydroxytyrosol in the pathogenic alterations induced by a high-fat diet in mouse liver: PPAR- $\alpha$  and Nrf2 activation, and NF- $\kappa$ B down-regulation. *Food Funct*. 2017; 8: 1526-1537. PMID: 28386616

**Response:** The suggested reference has been incorporated. The role of Inflammation and subsequent cellular damage is determined by oxidative stress. In this regard, the modulation of Nrf2 directly influences the changes in the activity of NF- $\kappa$ B has been discussed and incorporated (PMID: 28386616)

3. A relevant aspect to understand the hepatoprotective effects and the mechanisms involved is to link the molecular changes described with the prevention of mitochondrial dysfunction. The prevention of cellular damage is mainly explained by the conservation of mitochondrial activity. In this regard, the modulation of oxidative stress and inflammation influence the activity of other transcription factors and pathways involved in the function of the mitochondria. Suggested references: Impact of the Co-Administration of N-3 Fatty Acids and Olive Oil Components in Preclinical Nonalcoholic Fatty Liver Disease Models: A Mechanistic View. *Nutrients*. 2020 Feb; 12: 499. PMID: 32075238 Suppression of high-fat diet-induced obesity-associated liver mitochondrial dysfunction by docosahexaenoic acid and hydroxytyrosol co-administration. *Dig Liver Dis*. 2020; 52: 895-904. PMID: 32620521

**Response:** Understanding of the hepatoprotective effects and the mechanisms involved is to link the molecular changes described with the prevention of mitochondrial dysfunction has been discussed in detail in the revised manuscript. The suggested references have been incorporated in the revised manuscript along with other references.

## **II. Minor comments:**

1. Include the weight of animals and livers. Were significant differences observed?



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**Response:** We did not measure the weight of livers and weight of rats as we didn't perform the organ weight ratio experiment though the initial weight of rats were 212–226 g with average weight of  $219.08 \pm 4.26$ .

2. In the figure legends include the number (n) of animals

**Response:** The number of animals used is already mentioned in the figure legends

3. Figure 6, is it possible to include a damage score? Also, arrows with different colors are difficult to understand. I suggest changing.

**Response:** The liver damage score has been incorporated in Figure 7 and arrows has been removed as suggested.

## PEER-REVIEW REPORT

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

**Manuscript NO:** 60352

**Title:** Sinapic acid ameliorates D-GalN/LPS-induced fulminant hepatitis in rats: Role of Nrf2/HO-1 pathways

**Reviewer's code:** 02887546

**Position:** Editorial Board

**Academic degree:** MAMS, MBBS, PhD

**Professional title:** Dean, Doctor, Professor

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

**Author's Country/Territory:** Saudi Arabia

**Manuscript submission date:** 2020-10-26

**Reviewer chosen by:** Xi-Fang Chen (Part-Time Editor)

**Reviewer accepted review:** 2020-11-11 11:55

**Reviewer performed review:** 2020-11-20 06:53

**Review time:** 8 Days and 18 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 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 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 type="checkbox"/> Anonymous <input checked="" type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

## SPECIFIC COMMENTS TO AUTHORS

60352 check list Sinapic acid ameliorates D-GalN/LPS-induced fulminant hepatitis in rats:  
Role of Nrf2/HO-1 pathways

Title. Does the title reflect the main subject/hypothesis of the manuscript? **YES**

2 Abstract. Does the abstract summarize and reflect the work described in the manuscript?

**YES**

3 Key words. Do the key words reflect the focus of the manuscript? **YES**

4 Background. Does the manuscript adequately describe the background, present status and significance of the study? **YES**

5 Methods. Does the manuscript describe methods (e.g., experiments, data analysis, surveys, and clinical trials, etc.) in adequate detail? **YES**

6 Results. Are the research objectives achieved by the experiments used in this study? **YES**  
What are the contributions that the study has made for research progress in this field?

**The authors have reiterated the usefulness of sinapic acid in protecting the liver from the toxic effects of LPS/D-GalN-induced acute liver failure.**

7 Discussion. Does the manuscript interpret the findings adequately and appropriately, highlighting the key points concisely, clearly and logically? **YES**

Are the findings and their applicability/relevance to the literature stated in a clear and definite manner? **YES**

Is the discussion accurate and does it discuss the paper's scientific significance and/or relevance to clinical practice sufficiently? **YES**

8 Illustrations and tables. Are the figures, diagrams and tables sufficient, good quality and appropriately illustrative of the paper contents? Do figures require labeling with arrows, asterisks etc., better legends? **YES**

9 Biostatistics. Does the manuscript meet the requirements of biostatistics? **YES**

10 Units. Does the manuscript meet the requirements of use of SI units? **YES**

11 References. Does the manuscript cite appropriately the latest, important and authoritative references in the introduction and discussion sections? Does the author self-cite, omit, incorrectly cite and/or over-cite references? **YES**

12 Quality of manuscript organization and presentation. Is the manuscript well, concisely and coherently organized and presented? **YES**

Is the style, language and grammar accurate and appropriate? No GRAMMATICAL CORRECTIONS SUGGESTED IN RETURNED MANUSCRIPT.

13 Research methods and reporting. Authors should have prepared their manuscripts according to manuscript type and the appropriate categories, as follows: (1) CARE Checklist (2013) - Case report; (2) CONSORT 2010 Statement - Clinical Trials study, Prospective study, Randomized Controlled trial, Randomized Clinical trial; (3) PRISMA 2009 Checklist - Evidence-Based Medicine, Systematic review, Meta-Analysis; (4) STROBE Statement - Case Control study, Observational study, Retrospective Cohort study; and (5) The ARRIVE Guidelines - Basic study.

Did the author prepare the manuscript according to the appropriate research methods and reporting? **YES**

14 Ethics statements. For all manuscripts involving human studies and/or animal experiments, author(s) must submit the related formal ethics documents that were



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reviewed and approved by their local ethical review committee. Did the manuscript meet the requirements of ethics? **YES**

AUTHORS MAY MAKE THE SUGGESTED CORRECTIONS IN THE MANUSCRIPT RETURNED. 1. Grammatical corrections to be made. 2. p value should be uniformly either small p or Capital P.

**Response:** The authors are thankful to the reviewer for his constructive remark on our manuscript. All suggested changes have been incorporated in the revised manuscript.