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# PEER-REVIEW REPORT

**Name of journal:** World Journal of Hepatology

**Manuscript NO:** 60049

**Title:** Papaya Improves Nonalcoholic Fatty Liver Disease in Obese Rats by Attenuating Oxidative Stress, Inflammation and Lipogenic Gene Expression

**Reviewer's code:** 02541859

**Position:** Editor-in-Chief

**Academic degree:** FACG, FACP, FASGE, FRCP, MD, MRCP

**Professional title:** Associate Professor, Doctor

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

**Author's Country/Territory:** Thailand

**Manuscript submission date:** 2020-10-23

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2020-10-25 19:57

**Reviewer performed review:** 2020-10-25 20:30

**Review time:** 1 Hour

| | |
|---|---|
| **Scientific quality** | [ ] Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good<br>[Y] Grade D: Fair [ ] Grade E: Do not publish |
| **Language quality** | [Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing<br>[ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection |
| **Conclusion** | [ ] Accept (High priority) [Y] Accept (General priority)<br>[ ] Minor revision [ ] Major revision [ ] Rejection |
| **Re-review** | [ ] Yes [Y] No |
| **Peer-reviewer statements** | Peer-Review: [Y] Anonymous [ ] Onymous<br>Conflicts-of-Interest: [ ] Yes [Y] No |

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**SPECIFIC COMMENTS TO AUTHORS**

I think it is a good study showing the beneficial effects of papaya.

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# PEER-REVIEW REPORT

**Name of journal:** World Journal of Hepatology

**Manuscript NO:** 60049

**Title:** Papaya Improves Nonalcoholic Fatty Liver Disease in Obese Rats by Attenuating Oxidative Stress, Inflammation and Lipogenic Gene Expression

**Reviewer's code:** 02451447
**Position:** Editorial Board
**Academic degree:** MD, PhD
**Professional title:** Associate Professor
**Reviewer's Country/Territory:** United States
**Author's Country/Territory:** Thailand

**Manuscript submission date:** 2020-10-23
**Reviewer chosen by:** AI Technique
**Reviewer accepted review:** 2020-10-23 20:02
**Reviewer performed review:** 2020-11-01 14:21
**Review time:** 8 Days and 18 Hours

| | |
|---|---|
| **Scientific quality** | [ ] Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good<br>[ Y] Grade D: Fair [ ] Grade E: Do not publish |
| **Language quality** | [ ] Grade A: Priority publishing [ Y] Grade B: Minor language polishing<br>[ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection |
| **Conclusion** | [ ] Accept (High priority) [ ] Accept (General priority)<br>[ ] Minor revision [ Y] Major revision [ ] Rejection |
| **Re-review** | [ Y] Yes [ ] No |
| **Peer-reviewer statements** | Peer-Review: [ Y] Anonymous [ ] Onymous<br>Conflicts-of-Interest: [ ] Yes [ Y] No |

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**SPECIFIC COMMENTS TO AUTHORS**

The authors tried evaluate the anti-NAFLD effect of papaya in high fat diet induced obesity in rats, and concluded that papaya can suppress the lipogenic pathway, improve the balance of antioxidant status and lower systemic inflammation. The study is well designed. Comments: 1. The authors need to review the literature and discuss any health benefits in general population and individuals with obese and other health issues. Any clinical and human population data to support your study. E.g. Is there any difference in papaya-producing countries/regions compared to people in countries/regions without papaya? 2. In the result section "Effects of papaya on lipid accumulation". There are many repeated sentences from the method section. Result is only used to report result. 3. Figure 1, row 2. The oil-red O stain is not convincing, even normal liver, the oil-red-O can show few lipid droplets. I would recommend to add one more role of higher power picture to show the red lipid droplets clearly. 4. Still Figure 1, row 3. The H&E stained histology is not convincing. In this power, I do not see clear fat droplets, even in the HFD group. Please add a row of higher power picture. Also I want to make sure you need to show the ballooning degeneration of hepatocytes and lobular inflammation in a higher power picture. Since the HFD group mean NAS score is 6, that means the liver shows NASH. But the histology picture do not show features of NASH. The authors also mentioned that the fibrosis stage (0-4) was evaluated separately from NAS. How did the authors evaluated? any special stains used? The authors also said "The experiment groups were blinded and evaluated by the pathologist designated from the Faculty of Medicine, Naresuan University." Who is that pathologist? I do not see any pathologist author from the author list? Who took the pictures for this paper? The authors should be clear that the pathology evaluation is very important and critical for this current study. If there are no pathologic changes among these groups, other

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experimental data will not be convincing.

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# RE-REVIEW REPORT OF REVISED MANUSCRIPT

**Name of journal:** World Journal of Hepatology

**Manuscript NO:** 60049

**Title:** Papaya Improves Nonalcoholic Fatty Liver Disease in Obese Rats by Attenuating Oxidative Stress, Inflammation and Lipogenic Gene Expression

**Reviewer's code:** 02451447
**Position:** Editorial Board
**Academic degree:** MD, PhD
**Professional title:** Associate Professor
**Reviewer's Country/Territory:** United States
**Author's Country/Territory:** Thailand

**Manuscript submission date:** 2020-10-23
**Reviewer chosen by:** Jia-Ru Fan
**Reviewer accepted review:** 2021-01-08 23:27
**Reviewer performed review:** 2021-01-09 00:25
**Review time:** 1 Hour

| | |
|---|---|
| **Scientific quality** | [ ] Grade A: Excellent [ ] Grade B: Very good [ Y] Grade C: Good<br>[ ] Grade D: Fair [ ] Grade E: Do not publish |
| **Language quality** | [ Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing<br>[ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection |
| **Conclusion** | [ ] Accept (High priority) [ ] Accept (General priority)<br>[ Y] Minor revision [ ] Major revision [ ] Rejection |
| **Peer-reviewer statements** | Peer-Review: [ Y] Anonymous [ ] Onymous<br>Conflicts-of-Interest: [ ] Yes [ Y] No |

## SPECIFIC COMMENTS TO AUTHORS

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The authors made significant improvement and answered my questions/concerns. As a liver pathologist with expertise in liver pathology, I still have one concern regarding the one of the histology picture of the HFD H&E histology picture. The magnification may not be the same as other H&E histology in the same row. You can see the nuclei are much smaller and even the ballooning hepatocytes are smaller than the macrovesicular steatosis in the same row. Furthermore, The HFD H&E histology almost does not show macrovesicular steatosis, even though you have a arrow to point to it. Please replace with another better quality picture showing both hepatocytes with macrovesicular steatosis and ballooning in same magnification as other pictures.