OPEN PEER REVIEW

Open Peer Review (OPR)

As a new feature for progressing towards transparency, we decided to open a new window for all of our editors as well as authors titled "**Open Peer Review**". We hope by this new facility, our reviewers will be more motivated and authors will be more satisfied with the review process. We believe that publishing our peer review reports could make a transparent and clear environment for all our efforts within a journal, but not all reviewers tend to publish their comments.

What is "Open Peer Review" process?

An "Open Peer Review" process is making the details of all review process (including reviewers, associate editors, and EICs comments) as "Public" as it is agreed by EIC, Authors, and reviewers.

Advantages of "Open Peer Review" process

- More transparency, constructiveness and tactful comments of the peer review process: leads to an increase in the quality of reviews
- More motivations for all involved roles in the review process
- Authors' satisfactions from the review process: Increases honesty between authors and reviewers
- Education of both authors and new students
- Prevents reviewers from following their individual agendas and leading to the detection of reviewers' conflicts of interests

You can find out more at:
https://sites.kowsarpub.com/kowsar/knowledgebase/category/tree.html#opr.html

Hepatitis Monthly
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Peer Review Report for "Effects of Silymarin and Baicalein on Glycogen Storage in the Hepatocytes of Rat Models of Hepatic Injury"

Author(s): Hongfei Yang, Didar Mehrabi Nasab, Seyyed Shamsadin Athari

Review Timeline:

Submit Date: 20 Jan 2021
Revised Date: 9 Mar 2021
Accepted Date: 16 Mar 2021

Revision (0)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: Reviewer | Revision (0)

5 Feb 2021

Dear editor,

After review, the manuscript entitled "Effects silymarin and Baicalein treatment on glycogen storage and hepatic injury" it was found that is an interesting manuscript. It can be accepted following minor revision and modification; however, the following issues must be properly addressed before it can be accepted.

Abstract
Part " There are several cases of hepatitis and glycogen saving in high amount is one of them and type I has G6PD deficiency" Is unclear. I recommend it's replaced with this "There are several cases of hepatitis and glycogen saving problems that one of glycogen storage disease is type I, which is induced by G6PD deficiency".

Introduction
In this section, G6PD with NOX4 have important effect in liver function", explain the important effect of these factors on liver.

Material and methods

What is the standard laboratory condition? Please explain.
How can you design Primer sequences?

Results
It's better that Table 1 will be separated in two tables includes liver enzymes and lipids.
I think the figs were missed in this manuscript.

Discussion
Part "ROS damages hepatocytes membranes to release ALT and silymarin is an effective radical scavenging, which attenuates reactive bioactivation products and prevents toxicity and ALT leakage. Mitochondria is principle generator of superoxide for initiating ROS cascades. Silymarin protects cells against oxidant attacks and mitochondrial actions in ROS production, prevents mtDNA damage, inhibits of membraneactive lipases, and protections the electron transport chain for ATP production", I recommend it's replaced with "The ROS damages membrane of the hepatocytes that leads to release ALT. Silymarin is an effective radical scavenging, which attenuates production of the bio-activate agents and prevents toxicity and ALT leakage. Mitochondria is principle generator of superoxide for initiating ROS cascades. Silymarin protects cells against oxidant attacks and mitochondrial actions in ROS production, prevents mtDNA damage, inhibits of membrane-active lipases, and protects the electron transport chain for ATP production".
Part "On the other hand, PI3K/Akt signaling pathway can inhibit ROS-induced oxidative damages by Nrf2 activation. Baicalein improves glands function via regulation of PI3K/Akt pathway", I recommend it's replaced with "On the other hand, PI3K/Akt signaling pathway can inhibit oxidative damages of the ROS by activation of the Nrf2. Baicalein improves glands function via regulation of the PI3K/Akt pathway".
Part "Chemical hepatotoxic agents such as CCL4 can elevates AST, ALT, ALP and LDH levels in serum. CCL4 hepatotoxicity involve two phases. The first, in hepatocytes, CCL4 is metabolized by cytochrome P450, giving rise reactive trichloromethyl radicals in the hepatocytes endoplasmic reticulium. Then these free radicals are unstable and lead to LPO", I recommend it's replaced with "Chemical hepatotoxic agents such as CCL4 can elevate levels of the AST, ALT, ALP and LDH in serum. CCL4 hepatotoxicity involves with two phases. The first, in hepatocytes, CCL4 is metabolized by cytochrome P450, giving rise reactive trichloromethyl radicals in the hepatocytes endoplasmic reticulium. Then these free radicals are unstable and can lead to LPO"
Please add limitation of this study at the end of discussion.

References
Please check ref.15 and if it is possible, please replace with accessible references.

REFEREE: Reviewer | **Revision** (0) 7 Feb 2021

Dear AE

1. Unfortunately, I found many spelling and grammatical errors in the text. I recommend that the text be seriously evaluated and rewritten. Many sentences are vague.

2. Keywords should start with capital letters. There is even a misspelling in the title. In addition, the title is ambiguous.

3. In the method section, the working method should be explained in more detail. It was not enough at all.

4. The legends of tables and figures are not scientific and should be rewritten.

5. Ethical considerations?

6. Unfortunately, I did not see figures one and two.

7. In the discussion section, irrelevant items are mentioned that should be removed and give a more appropriate view to the audience.

8. Some of the mentioned sources are not in the format of the journal.

Regards

Abdol Majid Cheraghali: Associate Editor | **Revision** (0) 14 Feb 2021

Dear chief editor,

Please ask authors to review and respond to the comments of referees for further decision.

Regards,
AE

Seyed Moayed Alavian: EIC | **Revision** (0) 14 Feb 2021

Dear Authors,

Thank you for your submission. Following the peer-review process, your manuscript needs major revision before considering for publication in Hepatitis Monthly.

Regards,
EIC

OPEN PEER REVIEW

Revision (1)

Reply to Reviewers

Ideally, the reviewing process can significantly improve the submitted manuscripts by allowing the authors to take into account the advice of reviewers. Author(s) must reply to all reviewers' comments in a separate Word file, point by point. A "**Reply to Reviewers**" document is submitted along with revised manuscript during submission of revised files, summarizing the changes that the authors made in response to the reviewers' comments. The responses to reviewers' comments specifies how the authors addressed each comment the reviewers made.

You can read the authors' responses to the reviewers' comments in the next page.

Dear Dr. Editor-in-Chief and Dear Dr. Reviewers,

Thank you for review and your valuable comments for the manuscript submitted "**Effects silymarin and Baicalein treatment on glycogen storage and hepatic injury**" for consideration for publication in the **Hepatitis Monthly,** Ref.: Manuscript ID: 113114.

I confirm that all comments of reviewers and editor have been done point-by-point in response to the reviewer's comments, and revised manuscript was resubmitted the journal. Also, all comments are listed here with responses and that were highlighted in manuscript main file with yellow color.

Reviewer 1:

Unfortunately, I found many spelling and grammatical errors in the text. I recommend that the text be seriously evaluated and rewritten. Many sentences are vague. This was done in all context of manuscript.
Keywords should start with capital letters. There is even a misspelling in the title. In addition, the title is ambiguous. This was done in "keyword" section.
In the method section, the working method should be explained in more detail. It was not enough at all.
The legends of tables and figures are not scientific and should be rewritten. This was done in line 2-3 "Animals and treatment" and line 2-4 "Induction of hepatotoxicity" and line 3-6 "Gene expression" sections.
Ethical considerations? This was inserted in separated section "Ethics approval and consent to participate"
Unfortunately, I did not see figures one and two. These were inserted in manuscript file.
In the discussion section, irrelevant items are mentioned that should be removed and give a more appropriate view to the audience. These were revised and corrected in line 2-9 and line 30-32 and last part od discussion.
Some of the mentioned sources are not in the format of the journal. The references 1, 3, 4, 6, 15 were edited

Reviewer 2:

After review, the manuscript entitled "Effects silymarin and Baicalein treatment on glycogen storage and hepatic injury" it was found that is an interesting manuscript. It can be accepted following minor revision and modification; however, the following issues must be properly addressed before it can be accepted.
Abstract
Part " There are several cases of hepatitis and glycogen saving in high amount is one of them and type I has G6PD deficiency" Is unclear. I recommend it's replaced with this "There are several cases of hepatitis and glycogen saving problems that one of glycogen storage disease is type I, which is induced by G6PD deficiency". This was edited and corrected in line 1-4 abstract.
Introduction
In this section, G6PD with NOX4 have important effect in liver function", explain the important effect of these factors on liver. This part was added in Line 22-26 of the introduction.
Material and methods
What is the standard laboratory condition? Please explain. These conditions were added in line 1-4 Materials and methods; Animals and treatments section.

How can you design Primer sequences? Primer sequences were designed according to references 6, 18, 19 and 20 that were added in table 1.

Results

It's better that Table 1 will be separated in two tables includes liver enzymes and lipids. This was Done

I think the figs were missed in this manuscript. These were added in manuscript text.

Discussion

Part "ROS damages hepatocytes membranes to release ALT and silymarin is an effective radical scavenging, which attenuates reactive bioactivation products and prevents toxicity and ALT leakage. Mitochondria is principle generator of superoxide for initiating ROS cascades. Silymarin protects cells against oxidant attacks and mitochondrial actions in ROS production, prevents mtDNA damage, inhibits of membraneactive lipases, and protections the electron transport chain for ATP production", I recommend it's replaced with "The ROS damages membrane of the hepatocytes that leads to release ALT. Silymarin is an effective radical scavenging, which attenuates production of the bio-activate agents and prevents toxicity and ALT leakage. Mitochondria is principle generator of superoxide for initiating ROS cascades. Silymarin protects cells against oxidant attacks and mitochondrial actions in ROS production, prevents mtDNA damage, inhibits of membrane-active lipases, and protects the electron transport chain for ATP production". This was done in line 1-10 discussion section.

Part "On the other hand, PI3K/Akt signaling pathway can inhibit ROS-induced oxidative damages by Nrf2 activation. Baicalein improves glands function via regulation of PI3K/Akt pathway", I recommend it's replaced with "On the other hand, PI3K/Akt signaling pathway can inhibit oxidative damages of the ROS by activation of the Nrf2. Baicalein improves glands function via regulation of the PI3K/Akt pathway". This was done in line 39-42 discussion section.

Part "Chemical hepatotoxic agents such as CCL4 can elevates AST, ALT, ALP and LDH levels in serum. CCL4 hepatotoxicity involve two phases. The first, in hepatocytes, CCL4 is metabolized by cytochrome P450, giving rise reactive trichloromethyl radicals in the hepatocytes endoplasmic reticulium. Then these free radicals are unstable and lead to LPO", I recommend it's replaced with "Chemical hepatotoxic agents such as CCL4 can elevate levels of the AST, ALT, ALP and LDH in serum. CCL4 hepatotoxicity involves with two phases. The first, in hepatocytes, CCL4 is metabolized by cytochrome P450, giving rise reactive trichloromethyl radicals in the hepatocytes endoplasmic reticulium. Then these free radicals are unstable and can lead to LPO" this was done in line 54-59 discussion section.

Please add limitation of this study at the end of discussion. This was added in last part od discussion.

References

Please check ref.15 and if it is possible, please replace with accessible references. This reference was checked and edited.

Thank you very much with best regards for your kindly comments and noted points.
Corresponding author

OPEN PEER REVIEW

Revision (1)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: Reviewer | **Revision** (1) 16 Mar 2021

Hello,

This manuscript was revised correctly.

Yours

REFEREE: Associate Editor | **Revision** (1) 16 Mar 2021

Dear EIC,

accept the revised manuscript.

Regards

Seyed Moayed Alavian: EIC | **Revision** (1) 16 Mar 2021

Dear Authors,

Thank you for submitting the revised manuscript. I am delighted to inform you that your manuscript is accepted for publication in Hepatitis Monthly journal.

Regards,
EIC