Author's response to reviews

Title: Red ginseng abrogates oxidative stress as mediated with mitochondria protection via LKB1-AMPK pathway

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Author's response to reviews:

The authors express sincere thanks to the referee for the valuable comments. We revised the manuscript according to the referee’s helpful comments.

EDITORIAL REQUIREMENT

Please make the following formatting changes during revision of your manuscript. Ensuring that the manuscript meets the journal? Manuscript structure will help to speed the production process if your manuscript is accepted for publication.

Comment #1: After reading through your manuscript, we feel that the quality of written English needs to be improved before the manuscript can be considered further.

Answer: As editors recommended, we improved the quality of written English by Editing Program.

Comment #2: Kindly tone down the background section of abstract.

Answer: We changed the background section of abstract

Reviewer #1

Kim et al. described the preventive effect of red ginseng extract (RGE) on Iron plus AA-induced hepatocyte death and oxidative stress. RGE treatment effectively increased cell viability against iron plus AA, which was also supported by TUNEL staining and apoptosis marker gene expression. Moreover, RGE attenuated ROS generation and recovered intracellular GSH contents. They found that RGE inhibits mitochondria damage through LKB1-AMPk pathway. In general, the experiments are well designed and appear to be carefully carried out. However, many questions have to be addressed before publication, as can be seen from the following content

Comment #1: The authors used just 1 mg/ml of RGE except MTT analysis. The authors need to show dose dependency in some critical data and describe dose
used is physiologically relevant.

Answer: In Fig. 3, we showed that RGE protected mitochondria in a dose dependent manner, and discussed the dose used.

Comment #2: In Figure 5C, authors should show total LKB1 protein level for the control of LKB1 knockdown.

Answer: In Fig. 5C, we showed a LKB1 protein level for the control of LKB1 knockdown.

Comment #3: The authors should use antibody detected total form of AMPK and ACC, not but beta-actin, for the p-AMPK and p-ACC throughout the paper.

Answer: We assessed total form of AMPK and ACC in Fig. 4A, 4C, 5D and 6A.

Comment #4: The authors had better show the negative effect of CAMKK, which is another AMPK upstream kinase, to emphasize RGE-induced LKB-AMPK pathway.

Answer: STO609 is an inhibitor of calcium/calmodulin-dependent kinase kinase (CaMKK) # that is another upstream kinase of AMPK#. The treatment of STO609 had no effect in reversing the RGE-induced AMPK# phosphorylation in Fig. 5D.

Comment #5: The authors can add schematic diagram for the better understanding.

Answer: We added the schematic diagram in Fig. 6C.

Minor Comments:
1. p8, important intercellular antioxidant --> important intracellular antioxidant.
2. p8, compared with control cells --> comparable to control cells.
3. p9, AML12 hepatoma cell lines --> AML12 immortalized hepatocytes.
4. p9, RGE protection of hepatoytes --> RGE protection of hepatocytes
5. There are many grammar and type error. The authors should edit manuscript carefully.
6. The authors should check reference carefully.

Answer: We changed and edited the MS as reviewer recommended. We also checked references.

Reviewer #2
This is well designed and written article. There are only minor essential revisions authors should carry out before it is published. Listed as below:

Comment #1. Background should be shortened, it is not necessary to give that much information especially in first two paragraphs

Answer: We changed the MS as reviewer recommended

Comment #2. Page 5: First paragraph:...... 2',7'-dichlorofluorescein diacetate 2',7'
' should be added from symbols. There is an error in the word.... anti- -actin
Answer: We corrected the error.

Comment #3. Page 8: Last paragraph, Next,............ sentence should change to
Next, whether AA4................. mitochondria was determined
Answer: We changed the sentence.

Comment #4. Page 9: Last paragraph, last sentence ...............RGE actives
AMPK.... should be corrected as RGE activates........
Answer: We changed the sentence.

Comment #5. Page 10-11: Too much details were given on examples in
discussion (about resveratrol, sauchinone etc). Authors could name the
examples but generalize and shortened the explanation.
Answer: We changed the discussion section, as a reviewer recommended.