Reviewer's report

Title: Potentiating and synergistic effect of grape fruit juice on the antioxidant and antiinflammatory activity of aripiprazole against hydrogen peroxide induced oxidative stress in mice

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Reviewer: Siwen Chen

Reviewer's report:
1. The text itself contains various grammatical errors, extensively long sentences, confusing statements and disorganisation. A native English speaker should review the document to ensure this is remedied. I only point out few of these mistakes below.

For example, "……having high concentration of polyphenols might potentiate and synergize to the therapeutic effect of ARI, by increasing its bioavailability and inherent antioxidant potential of grape fruit juice (GFJ) decreasing the dosage of the drug." in "Background" of "Abstract", the correct sentence maybe "……having high concentration of polyphenols might potentiate and synergize the therapeutic effect of ARI by increasing its bioavailability and inherent antioxidant potential of grape fruit juice (GFJ) could decrease the dosage of the drug."

For example, "To evaluate the protection against oxidative stress and inflammation by ARI and GFJ alone and in combination in H2O2 treated mice with respect to serum levels of certain biochemical markers (ALT, BUN, CK, creatinine and total protein) and pro-inflammatory cytokines (IL-1α, IL-2, IL-10 and TNF-α) were measured.", the correct sentence maybe "To evaluate the protection against oxidative stress and inflammation by ARI and GFJ alone and in combination in H2O2 treated mice, serum levels of certain biochemical markers (ALT, BUN, CK, creatinine and total protein) and pro-inflammatory cytokines (IL-1α, IL-2, IL-10 and TNF-α) were measured."

For example, what is the meaning of "BUN levels where significantly higher than H2O2 treated group compared to control group. " in the 4th paragraph of Results? Please correct it.
For example, what is the meaning of "……the difference between BUN levels of ARI+H2O2 treated group and GFJ+H2O2 treated group were significant compared to control group. " in the 4th paragraph of Results? Please correct it.

2. In the 4th paragraph of Background, they state that "The anti-inflammatory response is demonstrated by the increased production of the pro-inflammatory cytokines,……", which confuse me. Do they mean "The inflammatory response is demonstrated by the increased production of the pro-inflammatory cytokines,……"?

3. Are the "GF juice" in Experimental Protocol of Methods, "GF" in Table 2 and "GFJ" the same substance?

4. In the Biochemical Analysis of Methods, "Protein values are expressed as mg/gram fresh tissue. ", do they evaluate the protein values in fresh tissue? Please confirm.

5. In the results, they always compared the data in the treatment group with that in the control group (fed with normal saline), do they believe that ARI, GFJ, and ARI+GFJ can bring down the data to be lower than normal? The comparison between the treatment group and the model group (fed with H2O2) maybe more appropriate. They must rewrite them in the Results, Discussion and Figure legend.

6. If the phrase appears more than once, full names should be accompanied by abbreviations for the first time, then abbreviations should be used from the second time. So the "GFJ" should be instead of "grape fruit juices" in the last paragraph of Background, and the "ROS" should be instead of "Reactive Oxygen Species" in the last paragraph of Discussion.

7. They concluded that supplementing GFJ to ARI could decrease the potential side effects of ARI intake (in the Abstract). However in this manuscript, ARI had no influence on the liver function and kidney function. What was the potential side effects of ARI? How could they conclude that?

8. In this manuscript, results showed that supplementing GFJ to ARI treated mice could enhance the antioxidant and anti-inflammatory effects of ARI on hydrogen peroxide induced oxidative stress in mice. They conclude that "supplementing GFJ to psychotic patients treated with ARI might decrease the dosage of ARI" in the Abstract. I don't think this conclusion is rigorous, because that the model used in this study was not "psychotic patients", but "oxidative stress in mice". Please correct it.
9. In this study, H2O2 treated mice was used as oxidative stress animal model, and the damage of liver and kidney function were considered as the results of oxidative stress, why not use malondialdehyde (MDA), the direct production of oxidative stress? They concluded that "supplementing GFJ to psychotic patients treated with ARI might decrease the dosage of ARI", why not detect the oxidative stress in the brain? If they did, it will be helpful to draw this conclusion.

10. In this study, decreased serum total protein was considered as the results of oxidative stress, but I think it was also the results of impaired liver function. They have better state it in this manuscript.

11. The format of references must consolidate according to the guideline of the journal,

**Are the methods appropriate and well described?**

If not, please specify what is required in your comments to the authors.

No

**Does the work include the necessary controls?**

If not, please specify which controls are required in your comments to the authors.

Yes

**Are the conclusions drawn adequately supported by the data shown?**

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No

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If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I recommend additional statistical review

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