Author's response to reviews

Title: Aqueous extract of post-fermented tea reverts the hepatic steatosis of hyperlipidemia rat by regulating the lipogenic genes expression and hepatic fatty acid composition

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Author's response to reviews: see over
Dear editor and all reviewers,

Thank you for reviewing our manuscript. You gave us many valuable suggestions, so that we can improve the quality of our paper. For each suggestion, we made a careful revision on the previous content of our manuscript. We double checked the grammar and other errors in the whole paper. The references were also re-edited as the guide for author. We invited an English specialist to check our paper from beginning to end. All the response to your comments are listed as below. Now, we believe this manuscript is improved than before, and hope it could meet the requirements of BMC complementary and alternative medicine.

Best regards.
Liang Zhang
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July 3, 2014
1. Page 2, line 19: Replace 'put' with 'putting'.
   “Aqueous extract of JWFT was prepared by putting them in boiling water…….”
2. Page 2, line 30: Replace 'increasing of' with 'increase in'.
   “The results showed that JWFT inhibited the increase in the body weight”
3. Page 4, Background, line 50: Replace 'converses' with 'converts'.
   “In the de novo synthesis, acetyl-CoA carboxylase (ACC) converts the acetyl-CoA to malonyl-CoA”
4. Page 4, line 64: Replace 'resistant' with 'resistance'.
   “insulin sensitivity and resistance to diet-induced obesity”
5. Page 5, line 70: Replace ‘in tea’ with ‘as tea’.
   “For a long time, epigallocatechin gallate (EGCG) was considered a critical compound of inhibiting lipids absorption and synthesis.”
   “observed in numerous above-mentioned human diseases.”
7. Page 5, line 75: Replace 'catechin-esters' with 'catechin-ester'.
   “But after post-fermentation, these compounds were highly decreased compared with unfermented tea.”
8. Page 5, line 76-77: Poor English. Try to correct it.
   “Therefore, it was suggested the catechins’ metabolite formed in post-fermentation may contribute to the health benefits of post-fermented tea.”
   “Its history could be dated back to the Ming Dynasty during 1500 A.D.”
   “Jing-weifu tea (JWFT) is made of the mature leaves of Camellia sinensis by undergoing an intensified fermentation of Eurotium cristatum [12].”
11. Page 5, line 87: Replace ‘relative expression of relative’ with ‘relative expression of’. Thank you for your suggestion. We deleted this sentence.
12. Page 6, line 91: Replace ‘anti-obesity’ with ‘anti-obesity activities’.
   “The aim of this paper is to elucidate JWFT’s function of regulating lipid metabolism and provide a novel understanding on lipid-lowering and anti-obesity activities of tea”
13. Page 6, line 104 & 105: degree Celsius (0C) should be appropriately written. This correction is required at many more places in the manuscript. This symbol may be not appropriately shown in different Office software. We checked this symbol whole paper.
14. Page 6, line 105-107: Rephrase the text to make it correct.
   “The procedures of sample preparation and HPLC analysis referenced published methods [13].”
15. Page 7, line 114: Delete the word ‘were’.
   “These rats were housed in an environmentally controlled room (22±2 °C, 60±5% relative humidity, and 12 hours light/dark cycle) and received food and water ad libitum.”
16. Page 14, line 267: Rectify the error ‘i a’. “Furthermore, the variations of gene expression suggested the regulation pathways of molecular
pathogenesis of hepatic steatosis.”


Thank you for your suggestion. We found these papers contained many valuable investigations about herbal materials and biological activities. We cited some articles which are directly related to our study.

18. Page 23, Table 2: Full form of abbreviations used in the first row should be given below in the foot notes. Similar corrections are required in other tables.

Thank you for your suggestion. We added the abbreviations information.

19. Journal references should be given as per Journal norms.

Thank you for your suggestion. We corrected these according to the requirements of BMC complementary and alternative medicine.

20. Only few English language corrections have been included in the comments. There are many more. Authors should go through the manuscript thoroughly and rectify the language errors.

Thank you. We revised the whole paper again and again. We also invited a English editor to check our manuscript. We hope the paper could be improved.
Abstract section:
Line 15, can be used metabolic syndromes or metabolic syndrome
Thank you for indicating this mistake. We unified this term in whole paper.
Line 21-23, should delete sentence Rats given high fat diet showed significant hyperlipidemia compared to the no-intervention control group. or add into the “Results”
Thank you for your suggestion. We also though these sentences should not be placed in introduction. We deleted these sentences.
Line 22-23, should change control group.. to control group.
This error was corrected.
Line 25, should change ELISA to enzyme-linked immunosorbent assay (ELISA)
We rewrote this term according to your suggestion.
Line 36-37, should check grammar and re-written
“For furthermore, the results also showed that JWFT inhibited the absorption of lipids.”
Line 39-40, should check grammar and re-written
“JWFT could mitigate the obesity-induced hepatic steatosis by regulating hepatic lipogenesis and lipolysis.”

Background section:
Line 45, should change a balance disrupts to a balance disruption
“Obesity is a balance disruption of energy intake and expenditure [1].”
Line 45-47, should check grammar and re-written of the sentence “For most of metabolic syndromes, hepatic steatosis is a kind of liver fat pathological change caused by high-fat or high carbohydrate diet”
“As a typical symptom of metabolic syndromes, hepatic steatosis is usually induced by high-fat and high carbohydrate diet [2].”
Line 46, can be used metabolic syndromes or metabolic syndrome
Thank you for indicating this mistake. We unified this term in whole paper.
Line 50, ACC or ACC (authors use “Italic” in Abstract section)
This abbreviation was corrected to be Italic.
Line 52, FAS or FAS (authors use “Italic” in Abstract section)
This abbreviation was corrected to be Italic.
Line 53 and 62, SCD1 or SCD1 (authors use “Italic” in Abstract section)
This abbreviation was corrected to be Italic.
Line 55 and 58, CPT1 or CPT1 (authors use “Italic” in Abstract section)
This abbreviation was corrected to be Italic.
Line 74, can be used metabolic syndromes or metabolic syndrome
Thank you for indicating this mistake. We unified this term in whole paper.
Line 86-89, should delete the sentences “In the present study, the influence of JWFT treatment on blood and hepatic lipids, were determined. Hepatic fatty acid composition and relative expression of relative genes in liver were investigated by the GCMS based lipidomics and RT-PCR analysis.” or add into the “Methods section”
Thank you for your suggestion. We also thought these sentences were not appropriate in this place. We deleted these sentences.

- Methods section:
After 1-week acclimatization, rats were randomly divided into five groups of 10 animals each.

The supernatant containing FAME was decanted and diluted with hexane, and then added 2 g sodium sulfate anhydrous for overnight.

Thank you for your suggestion. We unified this unit whole paper according to your suggestion.


β-oxidation

- Conclusion section, line 314, should add full stop (.) after “the expression of lipogenesis genes”
- Reference section, journal title of references No. 13 and 21 should change to journal title abbreviation
- Figure name e.g. A, B, C, should change the position from center to left side of the figure

We moved these capital letters to the left side.
1. Line 54: “The carnitine palmitoyltransferase 1 (CPT1) is essential in the β-oxidation of long chain….” This statement as written fosters confusion. Evidence in the literature suggests that the role of CPT1 in hepatic steatosis. The original statement therefore, needs to be revised to include additional published evidence that is specific for the role of CPT1 in hepatic steatosis or hepatic disease.

Thank you for your suggestion. We revised this reference. As you suggested, this reference was not so closely related to the content and results. A published article about the CPT1 and hepatic triglycerides was cited in the Introduction of this paper.

2. The result of this research shows the phenomenon. The authors declare that JWFT regulates up regulation of β-oxidation and down-regulation of de novo synthesis. Yes, I understand that promotion of this effect is the most clear-cut result from JWFT treatment, but why does it have anything to do with CPT1 and another genes? And also, What is the mechanism between that genes? I want the definite result about this question.

Many studies already reported the biochemical mechanism of lipids-lowering effects of teas. In the present study, it was supposed that JWFT attenuated the gene expression of sterol regulatory element binding protein-1c, and then regulated its target lipogenic genes, such as FAS, ACC and SCD1. Furthermore, Fu tea also regulated the activation of liver FXR and PPARδ, and unregulated the expression of lipogenesis and SREBP-1c.

ACC, acetyl-CoA carboxylase catalyzes the synthesis of malonyl-CoA, while malonyl-CoA inhibits the mitochondrial oxidation of fatty acids by binding to and blocking carnitine palmitoyltransferase (CPT1).