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March 8, 2017

Dr. Yuan Qi

Scientific Editor

World Journal of Gastroenterology

RE: Manuscript No.: 32796

We thank you for your email dated on 6th of March 2017, regarding our manuscript, entitled "Optimal management for alcoholic liver disease: conventional medications, natural therapy or combination?"

I appreciate both the Editor and the Reviewers for their scholarly and thoughtful comments. My response and modification to the reviewers' comments are in a point by point manner as below and inserted in the revised manuscript with yellow colour. We believe that these revisions have improved the quality of the manuscript substantially.

We have completed the copyright assignment, audio core-tip and google scholar check as required. We thank you for considering our revised manuscript for publication in World Journal of Gastroenterology**.**

Yours Sincerely,

Xianqin Qu

List of Changes and Rebuttal

Correction and modification for the editor's comments

Comment 1: Scientific report has been signed and attached in PDF file 1.

Comment 2: Please provided language certificate by professional English language editing: We have authors who are native English speakers. We have thoroughly checked the manuscript and made necessary corrections.

Comment 3 : the Animal Care and Ethics Committee (ACEC # 2009-325A) of the University of Technology Sydney is attached as PDF file 2.

Comment 4-8: PDF file 3 includes statements below:

- **Animal care and use statement**
- Institutional review board statement
- Conflict-of-interest statement
- Data sharing statement : Technical appendix, statistical code, and dataset available from the corresponding author at Xianqin.qu@uts.edu.au. No additional data are available.
- Biostatistics statement
- Open-Access statement

Comment 9: COEMNTS has been created on page 18-19 as below:

Background

Non-alcoholic fatty liver disease (NAFLD) has a dramatically rising incidence and is emerging as a potential health burden in society because hepatic lipid accumulation can trigger hepatocyte damage, inflammation and fibrogenesis leading to more serious liver disorders. There is an urgent need to discover agents for NAFLD treatment and prevention.

Green tea polyphenols (GTP) has received considerable attention for its metabolic effects against metabolic syndrome and type 2 diabetes. Our previous studies have

demonstrated that GTP has direct effects on glucose and lipid metabolism *in vitro* study. Thus, we hypothesise that GTP can reduce hepatic lipid accumulation against fatty liver *in vivo*. We tested this hypothesis in high fat diet (HFD) fed genetically Zucker obese rat.

Research frontiers

Currently, no pharmacological therapy is approved for NAFLD and there is also a recent surge in interest in naturally derived products for the treatment of metabolic disorders. There have been no previous studies into GTP on animal models of NAFLD from both dietary and genetic factors

Innovations and breakthroughs

We provide the first evidence that consistent administration of green tea polyphenols protect genetically obese rodent against HFD induced hepatic steatosis. This protection was associated with increased activation of AMPK pathway to control hepatic *de novo* lipogenesis and hepatic TG secretion.

Applications

Our results encourage further study into the effects and safety for GTP conferring protection against NAFLD in human.

Terminology

AMPK: AMP-activated protein kinase (AMPK) activity plays a vital role in mediating hepatic lipogenesis and a therapeutic target for NAFLD.

Peer-review

In this article, the authors showed beneficially effects of GTP on NAFLD, including improved lipid profiles and drastically reduced visceral fat, improved liver function and reduced TG accumulation in the liver. The overall study is solid and well designed. The results are consistent with the proposed hypothesis.

Comment 10: the decomposable figure of Figures, whose parts are movable and can be edited has been submitted in ppt version

Correction and modification for the reviewers' comments

Reviewer 1:

Comments To Authors	In this article, the authors showed beneficially effects of GTP on NAFLD, including improved lipid profiles and drastically reduced visceral fat, improved liver function and reduced TG accumulation in the liver. The overall study is solid and well designed. The results are consistent with the proposed hypothesis. One minor suggestion with the current study is that it would be more convincing if at least three or 4 samples from each groups are analyzed in Western blot analysis, and a detailed explanation how the quantification analysis were performed. Likewise, in the IHC analysis, please provides the number of animals and the number of images from each animal being analyzed, and how the quantification analysis being performed.

Response: Thanks for the comments.

1) Regarding to "at least three or 4 samples from each groups are analyzed in Western blot analysis**"**, we have described that data are expressed as mean ± SEM (n=8) in figure legends. We added the following sentence in the method section of Western blot analysis, line 7 of page 11

The density of bands was quantified with Quality One 4.6.1 software (Bio-Rad, CA) and the quantified results from 8 rats of each group were calculated as percentage of control lean rats for statistical analysis.

2) We are confused regarding to IHC (Immunohistochemistry?) analysis because we did not perform IHC experiment. However, in the section of ***Liver histological analysis (line xxx-xx on page xx)*** we have described that "*liver samples from 6-8 rats, and six fragments from each liver were further analysed. Lipid droplets were quantified at least 5 different high-power fields in a blinded way*". We did not make any modification because of no IHC image analysis in our study.

Reviewer 2:

Comments To Authors	Minor point -page 12, section "Effects of GTP on de novo lipogenesis pathway in the liver of ZF rats", line 2: "Figure 5" should be corrected by "Figure 4".

Response: Thanks for this comment, "Figure 5" has been corrected as Figure 4 , on line 9 of page 13.