Author's response to reviews

Title: L-Citrulline increases hepatic sensitivity to insulin by reducing the phosphorylation of serine 1101 in insulin receptor substrate-1

Authors:

Hisae Yoshitomi (hisa4403@mukogawa-u.ac.jp)
Maki Momoo (peachmomo6@hotmail.com)
Xiao Ma (ma.xiao.edu@gmail.com)
Yewe Huang (huangyeweiyi2011@gmail.com)
Shiori Suguro (suguro@prochemi.ne.jp)
Yoshie Yamagishi (yamagishi@prochemi.ne.jp)
Ming Gao (gaoming@mukogawa-u.ac.jp)

Version: 4 Date: 27 April 2015

Author's response to reviews: see over
L-Citrulline increases hepatic sensitivity to insulin by reducing the phosphorylation of serine 1101 in insulin receptor substrate-1

Hisae Yoshitomi, Maki Momoo, Xiao Ma, Yewei Huang, Shiori Suguro, Yoshie Yamagishi and Ming Gao

Dear Editor,

Thank you very much for your letter dated April 16, 2015 together with the reviewers’ comments.

The following are our responses to the reviewer’s comments regarding the above manuscript, and the text has been revised to accommodate these comments.

Responses to Reviewer Dr. Elisa Keating:

2) L-Cit is a naturally occurring amino acid and widely may exist for different tissue. Few studies have demonstrated on the toxicology of supplemental L-Cit, it is generally recognized as safe for oral administration [Romero MJ, et.al.]. Regarding the animal experiments, we referred to a previous study using L-arginine supplemental doses rate from human to rat. L-arginine is one of the amino acid which is closely-linked to L-Cit. J.R. McKnight proposed that L-arginine doses for animals are equivalent to approximately 10-20 times amount of it for humans. In fact, we conducted preliminary experiment using low dosage (1g/kg/day) L-Cit, but it has no effect. Then we selected 20 times dose rate for L-Cit consumption to rats based on the fact that Waugh WH et.al administered L-Cit orally at doses of 0.1g/kg/day for human. We added the information in the methods on page 7, line 126-127.


3) We performed by one-way analysis of variance followed by Tukey's test to determine the significance of differences. We state in the “Statistical Analysis” section, page 10, line 201-202.

6a) n=3 corresponds to 3 independent experiments cells. So, based on this comment, we specified this information in the figure captions, page 23. Also we added information on the interval of passage numbers used in the cell culture, page 6, line 95-96.

6b) Based on this comment, we detailed about sample size in the method section, page 7 line 132-133. We added sample size information to table 1.

9) We add expression, comment and changed sentence based on the reviewer’s comment, page 14, line 296-299.

We would like to thank the editor and reviewer for the valuable comments to our present study and for having allowed us to revise and improve our manuscript. We hope that our revised manuscript is now acceptable for publication in *BMC Complementary and Alternative medicine.*

With kindest regards,

Sincerely yours,

Hisae Yoshitomi and Ming Gao

School of Pharmaceutical Sciences, Mukogawa Women’s University, 11-68 Koshien Kyuban-cho, Nishinomiya, Hyogo 663-8179, Japan.

Email: hisa4403@mukogawa-u.ac.jp, gaoming@mukogawa-u.ac.jp