Reviewer's report

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

Version: 3  Date: 13 April 2015

Reviewer: Elisa Keating

Reviewer's report:

The authors did not clearly highlight the changes in the manuscript, which made the revision more complicated.

In addition, there are some issues that were not clarified in sufficient detail which are listed below. Please note that the numbering used here is the same as the numbering in the authors responses.

2) I understand that the dose of 2 g/Kg/day in the rat would be similar to the human dose of 0.1 g/Kg/day. However, my calculation, based on Reagan-Shaw S, et al. 2007 [1], retrieves an animal dose of 0.62 g/Kg/day for the human dose of 0.1 g/Kg/day, which is 3 times lower than the dose used in the study: 2 g/Kg/day.

b) please rectify and explain the calculation that underlies the choice of 2 g/Kg/day

c) add a comment to the manuscript regarding the dose translation from human to rat.

5) I understand that Tukey’s test was employed whenever there were multiple comparisons. This is usually preceded by an analyses of variance (ANOVA). If this was the case, please state in the “Statistical analyses” section that analyses of variance was performed. If it was not the case the authors should consider doing analyses of variance with multiple comparison by tukey’s test.

6) This question addressed the sample size used in cell culture experiments and in animal experiments:

a) regarding cell culture experiments: please specify in the “statistical analyses” section if n=3 corresponds to 3 replicates from the same cell clone (all the 3 performed in the same day of experiment corresponding to 3 different wells) or whether n= 3 corresponds to 3 different cell clones (at least 3 different days of experiments). Please add also information on the interval of passage numbers used in the cell culture.

b) regarding animal experiments: please detail the answer “The rat two were selected at random and used for formalin perfusion”. Please add sample size information to table 1.

9) Please add the expression “and devoid of statistical significance” after the word “slight” in the end of the sentence in page 14, line 292: “…by the stimulation
of insulin was slight”. Please add a comment on this apparent contradiction to the manuscript. In page 14, line 286, the word “phosphorylation” is missing after the word “stimulates”.

Reference

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Needs some language corrections before being published

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:
I declare that I have no competing interests