Author’s response to reviews

Title: Curcumin and Inflammation in Non-alcoholic Fatty Liver Disease: a Randomized, Placebo Controlled Clinical Trial

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Curcumin and Inflammation in Non-alcoholic Fatty Liver Disease: a Randomized, Placebo Controlled Clinical Trial
BMC Gastroenterology

Dear Dr Conrado M Fernandez Rodriguez
BMC Gastroenterology

Thank you very much for your email regarding the evaluation of our manuscript and the opportunity to revise and resubmit the paper. We have taken each comment very seriously, and now submit a revised version in response to the reviewers’ comments.

Once again, thank you for inviting us to respond to the reviewers' comments and revise our manuscript.
Fernando Bril (Reviewer 1):

In this proof-of-concept study, Saadati et al assessed the role of curcumin to reduce subclinical inflammation in patients with NAFLD. The authors should be congratulated for a well-designed study. However, the presentation and interpretation of their results must be revised before this manuscript is ready for publication.

- Briefly, this is a negative study, where all comparisons between curcumin vs. placebo were negative. Therefore, the study should be presented as such. Within group comparisons (i.e., before vs. after) have only minimal importance in this scenario, and conclusions should not be driven by these.
  Response: Thanks for your comment. It was corrected in the text as follow:
  The conclusion in abstract and text was corrected as follow:
  Our results indicated that curcumin supplementation plus lifestyle modification is not superior to lifestyle modification alone in amelioration of inflammation and hepatic steatosis and fibrosis.

- Please re-write the manuscript (results and discussion) based on the main comparison of curcumin vs. placebo. Avoid statements claiming a significant action of curcumin based on within group comparisons.
  Response: Thanks for your comments. We emphasized that there was no significant difference between two groups.

- Sample size calculation: please provide more details. What do the authors mean by 2 units? 2 pg/ml? What was the expected SD? Is this clinically relevant? Please justify.
  Response: Thanks for your comment. The unit as pg/mL is added to the manuscript. The SD was predicted as 2 pg/mL.

- In addition to IRB approval, was this clinical trial included in any RCT registry (e.g., www.clinicaltrials.gov, etc.)? Please mention this under Methods.
  Response: Thanks for your suggestion. It is added as follow:
  The study protocol was registered at clinicaltrial.gov with registration number of NCT02908152.

- Table 1: % of smokers should be reported per column, not % per row.
  Response: Thanks for your notification. It is corrected.

- "3 capsules containing either 500mg curcumin or matched placebo per day after each meal for 12 weeks" is unclear. Please clarify dose. 500mg TID or 1500mg QD or 1500mg TID?
  Response: It is revised as follow:
  500mg curcumin or matched placebo TID (three times a day)

- There are several grammatical mistakes throughout the manuscript. I would suggest having it revised by a native English speaker.
  Response: It is revised by a native English speaker.

- No information is provided regarding physical activity and caloric intake between the groups during the 12 weeks of the trial.
  Response: It is added as follow:
Within both groups, daily energy intake decreased significantly while there was no significant difference between changes in two groups. In curcumin group, physical activity increased significantly more than placebo group.

Masahide Hamaguchi (Reviewer 2): Please include all comments for the authors in this box rather than uploading your report as an attachment. Please only upload as attachments annotated versions of manuscripts, graphs, supporting materials or other aspects of your report which cannot be included in a text format.

Please overwrite this text when adding your comments to the authors.
Response: There is no comment to respond.