Reviewer’s report

Title: Effect of long-term feeding of the Obudu natural honey and table sugar-sweetened diets on obesity and pro-inflammatory biomarkers in rats.

Version: 2 Date: 29 Jul 2019

Reviewer: Marta Alegret

Reviewer's report:

The authors explore the effects of honey and table sugar on several zoometric and plasma parameters in male and female Wistar rats. The study is descriptive, and the conclusions would be reinforced if the authors could perform some new experiments. Specifically, the authors could assess whether insulin signaling is impaired, as they suggest in the discussion. Moreover, it would be interesting to assess whether sugar and honey supplementation cause an increase in liver lipids.

Specific points:
- **Methods:**
  o Ln 160: please explain how were the sugars incorporated to the diet
  o Ln 162: please, change this cite of a webpage for a reference
  o Ln 201-215, please remove, it is not necessary to give the details

- **Results:**
  o Figure 1 and 2: Graphs are not clear enough, could you try to express the results as the area under the curve?
  o Regarding the diet intake, it would be nice to calculate the caloric intake in the different treatment groups, based on the amount of food consumed and the energy supplied
  o High consumption of sugars, in particular fructose, can cause fatty liver, but this effect may depend also on the length of treatment. It would be interesting to assess whether under the conditions of the present study sugar and/or honey cause an increase in hepatic lipid levels

- **Discussion**
  o It is intriguing why H20% causes an increase in female weight gain but a decrease in the case of males. Do the authors have any explanation for this discrepancy? Similarly, there are divergent results of S8%, which increases male's weight gain, but not in females. All these differences between sexes are interesting and should be discussed.
  o Ln 323: "honey might reduce weight gain by modulation of appetite-regulating hormones such as leptin,..." If this was the mechanism, then the intake of diet would have been reduced, in fact this happens in the case of females fed H20%. Moreover, as the authors have measured plasma leptin levels, they should discuss these results here
  o Ln 343-4:" further studies involving liver histology and liver function test is needed for a conclusive report" Could you perform these studies in your samples?
  o Ln 352-353: If the authors have not measured the weight of subcutaneous adipose tissue, they cannot make this assumption
  o Ln 370-2: "The increase in insulin may also be as a result of insulin resistance which is affirmed by the observed significant increase in TNF-α (TNF-α induces insulin resistance by inhibiting insulin signal transduction)". The authors must evaluate insulin resistance, at least by determining the expression/activation of a key molecule in the insulin signaling pathway, such as Akt, to be able to
affirm it. The increase in TNF-alpha is only an indirect evidence.

Minor points:
- Ln 26: rat strain must be mentioned, and it is not necessary to include the scientific name for the rat
- Ln 26: groups of 5 rats each
- Ln 27: which sugar was used? Table sugar? Sucrose?
- Ln 29: "in equivalent weight to honey", please, rewrite
- Ln 47-50: please, rewrite the sentence, it is not clear
- Ln 80: taste, instead of test

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

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Quality of written English
Please indicate the quality of language in the manuscript:

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