Reviewer's report

Title: Role of 1,5-anhydro-D-fructose in C57BL/6J mice challenged with high-fat diet

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Reviewer: Sof Andrikopoulos

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Obesity and high fat diets impair glucose tolerance and contribute to disease states such as Type 2 diabetes. Interventions that can promote better glucose tolerance are therefore desirable to prevent progression to diabetes. Previous studies have shown that AF can act in an anti-oxidant manner and can improve glucose tolerance and insulin secretion in chow-fed mice. In this study the authors have used a naturally occurring sugar called 1,5-Anhydro-D-fructose (AF) to treat mice fed a high fat diet and assessed body weight gain, glucose tolerance and insulin secretion. The results showed that feeding mice AF did not affect body weight gain, glucose intolerance caused by high fat feeding or rates of insulin secretion. The authors suggest that the lack of AF may be the result of the route of administration (via drinking water) and/or that the dose may be have been lower than required. This is a well-written and presented study that shows a lack of effect in this high fat fed mouse model. I have the following comments to make:

Compulsory Revisions

1. It has been suggested that high fat does not cause oxidative stress (Moore et al. Diabetes 53, 2610–2616, 2004). It is therefore possible that if AF is acting as an antioxidant that it would not improve glucose tolerance under these conditions. This point could be further discussed.

2. In a previous study these authors have shown that the improvement in glucose tolerance and insulin secretion following AF treatment was associated with an increase in GLP-1 levels. It is likely that with high fat feeding the potentiating effect of AF to induce GLP-1 is blunted. This point should also be discussed.

3. The plasma insulin levels shown in Fig 2A and Fig 2B should be presented on the same scale to highlight the blunting effect of a high fat diet on insulin release.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests:

I declare that I have no competing interests.