Reviewer’s report

Title: Effects of semicarbazide-sensitive amine oxidase inhibitors on morphology of aorta and kidney in diabetic rats

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Reviewer: Eliane Hiromi Akamine

Reviewer's report:

The authors aimed to evaluate the effects of aminoguanidine (AG) and 2-bromoethylamine (2-BEA) on the SSAO activity and on the prevention of diabetic vascular complications. In addition, the mechanisms involved were also explored. The main findings were that both AG and 2-BEA inhibited the aortic SSAO activity. The diabetic rats showed higher plasma and aortic SSAO activity and plasma methylamine levels than normal control rats. Treatments with AG and 2-BEA prevented the SSAO activity and promoted further increase in the plasma methylamine levels in diabetic rats, although it had not prevented the changes in blood glucose and weight. Moreover, the treatments with AG and 2-BEA prevented the changes in the plasma NO and endothelin-1 levels and morphology of the aorta and kidney. The study is interesting. However, I have several concerns particularly in relation to conclusions.

1) The authors concluded that "AG and 2-BEA were common SSAO inhibitor with low toxicity" (line 27, page 13). How was the toxicity tested?

2) Also, the authors concluded that "AG and 2-BEA might exert their effects by reducing the production of toxic FA and H2O2 by a significant inhibition of the SSAO-catalyzed oxidative deamination" (lines 31-35, page 13). Since formaldehyde levels were not changed by either diabetes or treatments, there are other sources of formaldehyde as discussed and the H2O2 was not measured, the conclusion is not correct.

3) The results do not allow to associate the effects of AG and 2-BAE to SSAO inhibition. Beyond formaldehyde, oxidative deamination by SSAO generates other aldehydes. The measurement of those other aldehydes could aid to explain, at least in part, the effects of AG and 2-BAE because aldehydes can induce endothelial injury through the production of advanced glycation end-products (AGEs). H2O2 measurement and AGEs (since AG inhibits its formation) could also be useful.

4) Please give the rationale for the evaluation of the morphology of kidney and its relation with the diabetic vascular complications. The implications of effects of the treatments on the changes in the morphology of aorta and kidney should be discussed. Actually, the authors evaluate some indirect markers of vascular dysfunction (NO and endothelin-1 levels were measured in plasma instead of aorta) and morphological changes in aorta rather than diabetic vascular complications. The term diabetic vascular complications should be avoided and replaced by other more appropriate.

5) The results shown in the figure 2 and figure 3 should be presented as column graphs. If the authors want to evaluate the effect promoted by treatments with AG and 2-BAE along 8 weeks in the same
group, the results may be shown in a XY axis graph.

6) What were the effects of the SSOA inhibition on the formaldehyde and methylamine and the consequences of the accumulation of these products in the normal control rats? The results of NC+AG and NC+2-BEA groups should be shown in the figures 4, 5 and 6. If the treatments did not change the parameters analyzed in normal control rats, this information should be given in the description of the results.

7) Since streptozotocin-induced diabetes is a well established model of type 1 diabetes mellitus, the first paragraph could be removed and instead the authors should discuss the fact that the treatments have not prevented the changes in the blood glucose, which has an implication in the vascular complications.

8) Please revise the English, paying attention on the incorrect/inappropriate terms (for example: signal, line 26, page 2; expect, line 28, page 2; suicidal, line 50, page 3).

9) Please revise the incomplete sentence at the first line of the page 4.

10) There is a symbol showing an incorrect difference between DM+2-BEA and DM groups in the figure 6b. Please review it.

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.

No

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

No

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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Please indicate the quality of language in the manuscript:

Not suitable for publication unless extensively edited

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