**Reviewer’s report**

**Title:** Pharmacokinetic Study of Single- and Multiple-dosing with Metolazine Tablets in Healthy Chinese Population

**Version:** 0  **Date:** 24 Oct 2016

**Reviewer:** Melanie Felmlee

**Reviewer’s report:**

The manuscript by Li et al evaluates the pharmacokinetics of metolazone after single and multiple oral doses, as well as a food effect study. The authors utilized non-compartmental analysis of determine the influence of dose and gender on pharmacokinetic parameters. The study design and analysis methodology was suitable for the goals outlined by the authors; however, I have a few concerns about the manuscript and presentation of the data.

1) The figures are unclear due to the connecting lines that are present between all data points. It would be advisable to remove figure 7 (mean data) and present mean ± SD data in the earlier figures, possibly combining all of the single dose data into a single figure. This would make it easier for the reader to evaluate differences between doses. Within figure 5 there should be a distinction made between the fed and fasted data points. The figure legends should also contain additional information so that they stand alone from the text of the manuscript.

2) The manuscript should be revised for English grammar and readability. In some cases there are run-on sentences and paragraphs containing a single sentence.

3) Methods, page 6. Were women on hormonal birth control included in the study?


5) Methods, page 10. What parameters were used for the linear regression model to determine dose proportionality? Why was superposition not considered?

6) Results, page 12-13. The paragraph contains data that was included within the tables. The numbers can be removed with a reference to the table.

7) Results, page 14. Elimination half-life of 8.97 hours (line 59) is not consistent with the data in Table 1, which listed the elimination half-life as 7.61 hours.

8) Discussion, page 17. Include any comparative literature data on the pharmacokinetics of metolazone or similar compounds.

**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.

I am able to assess the statistics

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

Needs some language corrections before being published

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