Reviewer’s report

Title: Short-term treatment with taurolidine is associated with liver injury

Version: 0 Date: 07 Jun 2017

Reviewer: Frantisek Trejtnar

Reviewer's report:

The manuscript brings experimental data which may be interesting for medicinal scientific community. In addition, the presented data might be applicable to determine safety of a clinically important compound. A complex of relevant in vitro and in vivo methods was employed in the study. The manuscript is divided in standard sections and meets Journal’s requirements. However, several shortcomings can be find through the submitted manuscript:

Major comments:

1. Why did the authors use the geometric mean as statistical parameter (p.10, l.9)? The adequate method of evaluation for the performed tests should employ arithmetic means. The reviewer recommends to recalculate experimental data and use arithmetic means for statistics. ANOVA test should be utilized for statistical evaluation of differences between the experimental groups.

2. The results in Fig. 1, part A and part B are presented as associated continuing data. However, these data are independent, not continuing, obtained parallel using different concentrations of taurolidine. These parts of Fig. 1 have to be changed in column graphs similarly as data presented in parts C and D of the figure.

Minor comments:

1. The HepaRG cells is better to seed at a density 2.6 x 10^4 cells/cm^2. But the used amount 2.7 x 10^4 cells/cm^2 (p.6, l.61) can be acceptable even a higher number of the seeded cells can lead to stopping of their differentiation.

2. The hydrocortisone-hemisuccinate concentration employed for HepaRG cell culturing (p.7, l.5) should be 50 uM instead of 50 mM.

3. Information on weight and age of the used rats should be added to the part "Animal preparation and experimental setting" (p. 6).
4. Was the liver removed from anesthetized but living animals (p.6, l.34)? The presented formulation is not clear. There is no information on how and when the animals were euthanized.

5. The authors use systematically the term "Taurolidine". However, it is clear from the context that they mean compound called taurolidine. Standard generic name should be written using low initial letter. Such unclear designation can be confusing. For example, the doses of taurolidine in Methods (p.6, lines 24-28) expressed as mg/kg probably mean amount of taurolidine but not a formulation called Taurolidine. It has to be clearly explained and corrected.

6. The sentence "As previously described, cell differentiation was induced and cells used up to four weeks." (p.7, l.14-17) is not clear. How long did the differentiation take place? When were the cells taken for experiments? These details should be clarified.

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

No

**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 recommend additional statistical review

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