Author’s response to reviews

Title: Toxicological Evaluation of Therapeutic and Supra-therapeutic Doses of Cellgevity® on Reproductive Function and Biochemical Indices in Wistar Rats

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ANSWERS TO REVIEWERS COMMENTS

Authors wish to appreciate the commendation given to our present research. To the best of our knowledge, we hope the following answers would help present our research in a suitable format as suggested by the reviewers and others. Also, some suggested revisions are highlighted in RED in the manuscript.

Reviewer 1

Comment

The methods section needs some reorganizing and additional information. For instance, the subheading Statistical analysis was neglected by authors. The description of the statistical test should be included. In addition, provide the information about the statistical program (name, version) used in this study.
Answer:

We strongly apologize for this omission. The statistical analysis has now been included in the methods section. Also, the description of the statistical test as well as version used has been included.

Comment

What is a "normal" or "traditional dose" that humans would be exposed to when using Cellgevity®? In other words, how do the doses used in the study compare to human exposure?

Answer:

The "normal" or "traditional dose" that humans would be exposed to when using Cellgevity is 14.3mg/kg as contained in the medication leaflet. However, some individuals commonly take higher doses than the normal or traditional dose. Hence, the investigation of supra-therapeutic dose in this study.

Comment

What was the rationale for choosing the doses 14.3 and 28.6 mg/kg? Generally, at least three test groups and a control group should be used. The results do not show a dose response.

Answer:

As reflected in the title of this manuscript, we used therapeutic (14.3mg/kg or 28.6mg/kg) and supra-therapeutic (1000, 2000 or 3000 mg/kg) doses. The therapeutic dose used in this study is within the recommended dose range by the manufacturer. However, we have the understanding that some people take this medication above the recommended dose on the justification that it has no adverse effect. Our major goal as stated in the manuscript was to investigate the effect of therapeutic and supra-therapeutic doses on reproductive function and biochemical indices in Wistar rats. The manuscript contained the results obtained on supra-therapeutic dose and the authors are of the opinion that these findings will guide on the appropriate use of this medication.
Comment

What was the rationale for choosing mice in acute toxicity test? The study design used by authors is not very similar to the OECD 423 or 425 toxicity tests. Please add reference to OECD.

Answer:

In general, it is recommended that acute toxicity testing be carried out with either of the two animal species (mice or rats), OECD Guidelines for Testing of Chemicals. No 420 (OECD, 1992). However, mice are often used for accurate results because of their nature and strength compare to rats (Wang et al., 2007; Awodele et al., 2012). Please find details in our previous article (Awodele et al., 2012) and elsewhere.


Comment

Please discuss the lack of effect of the treatment with 2000 mg/kg and 3000 mg/kg of CGV on luteinizing hormone levels.

Answer:

Authors have discussed the lack of effect of the treatment with 2000 mg/kg and 3000 mg/kg of CGV on luteinizing hormone levels in our manuscript.
Comment

Please revise the figure legends. You can delete "Values in parenthesis represent % change… decrease". Also, authors should express all measurements in conventional units.

Answer:

All the figure legends have been revised as suggested. Authors apologise for the use of “values in parenthesis represent % change… decrease". We have expressed all measurements in conventional units.

Comment

Figures 2 and 3 - Include in the y axis the unit of measurement.

Answer:

Figures 2 and 3 now have their units of measurement on the y axis.

Comment

Figure 4 - Change the design of this graph. Present the body weight in the y axis and the doses in the x axis. Attention to the unit of measurement for weight.

Answer:

Figure 4 has been re-oriented. The body weight is now on the y axis and the doses on the x axis as suggested. The animal weight was expressed in g/kg unit.

Comment

I would also recommend that some improvement should be made to the presentation of the tables. Not have vertical lines at its lateral borders. Tables may be easier to understand by including the doses in lines and the parameters in columns.

Answer:

We appreciate the above recommendations and have used the same to improve the quality of our tables.
Reviewer 2

Please include a section in your discussion about the limitations of the study and to what extend the conclusions about the dosage could be extended to humans.

Answer:

1. Authors have included in our discussion some of the possible limitations of our study.

2. Also, we gave insight of the extent to which the dosage could be extended to humans.

Thank you.

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