Reviewer's report

Title: Acute and repeated dose 28-day oral toxicity studies of a Siddha medicine "Nuna Kadugu" in Sprague Dawely rats

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Reviewer: Akihiro Hagiwara

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Comments to Author:

Author: Ramaswamy, R.S.. et al.

Title: Acute and repeated dose 28-day oral toxicity studies of a Siddha medicine “Nuna Kadugu” in Sprague-Dawley rats.

The introduction and discussion sections are well described, but the materials and methods section and results section should be precisely noted.

1. P6L27-32 (section 2.7. Repeated dose 28-day oral toxicity study)
Parameters concerning blood clotting/potential were not performed in the present study. As OECD Guideline 407 stipulated that these should be made at the end of the test period. Would you please note the comment briefly.

2. P7L11-14 (section 2.8. Histopathology)
Many tissues (such as spinal cord, lung, lymph nodes, accesary sex organs etc.) were not collected in the present study. As OECD Guideline 407 defined that these should be preserved in the most appropriate fixation medium for all animals, would you please note the comment briefly. If preserved all tissues described in the guideline, please note accurately.

The epididymides and thymus were not weighed in the present study. As OECD Guideline 407 stipulated that they should be weighed for all animals, would you please note the reason briefly.

Would you please note clearly the description concerning histopathological examination for low and mid dose groups. Were hisopathological examinations in low and mid dose groups performed in the present study?

5. P7L21 ~ 25 (section 2.9. Statistical analysis)
Would you please note the statistical analysis for the significances of intergroup differences in incidences of findings from ophthalmology, urinalysis, macroscopic pathology and histopathology.

6. P7L27 ~ P8L6 (section 3.1. Standardisation of NK), Table 1 and Figure 1.
Would you please describe the characterization and specification of the test material more precisely. Description concerning impurity should be noted briefly, and Table 1 should be deleted. Please explain the 7 peaks appeared in Figure 1.

7. P8L17 ~ 18 (section 3.3. Repeated oral toxicity study:), and Fig. 3

Body weight data was presented in Fig. 3, however data obtained from both sexes were shown all together, and body weight data at commencement of the experiment were not given. Body weight data in males and females should be present separately. Would you please improve Fig. 3.

8. P8L18 ~ 19 (section 3.3. Repeated oral toxicity study:), and Fig. 4-5

Food and water data were presented in Fig. 4 and 5, respectively, however data obtained from both sexes were shown all together. Food and water consumption data in males and females should be presented separately. Would you please improve Figs. 4 and 5.

9. P8L19 ~ 23 (section 3.3. Repeated oral toxicity study:), and Table 2.

Hematology data was presented in Table 2, however data obtained from both sexes were shown all together, and numbers of rats examined were not given. Hematology data in males and females should be presented separately. Explanations for abbreviations such as RDW-CV, PLT, MPV, PWV, PCT and P-LCR were not appeared in Table 2 and in Materials and methods section. Would you please improve the materials and methods section, and Table 2.

10. P8L23 ~ 29 (section 3.3. Repeated oral toxicity study:), and Table 3 and 4.

Plasma biochemical profile data and serum electrolyte data were presented in Table 3 and Table 4, respectively, however data obtained from both sexes were shown all together, and numbers of rats examined were not given. These data in males and females should be presented separately.

11. P8L29 ~ 31 (section 3.3. Repeated oral toxicity study:), and Table 5.

Relative organ weight data was presented in Table 5, however data obtained from both sexes were shown all together, and numbers of rats examined were not given. These data in males and females should be presented separately.

12. P8L31 ~ P9L1~3 (section 3.3. Repeated oral toxicity study:), and Fig. 6 ~ 13.

Details of the histopathological data were not shown in this article. Histopathological data should be tabulated, and analyzed statistically. Would you please delete all photos (Fig. 6 ~13), because of no meaning (all photos are normal findings).

Level of interest: An article of limited interest

Quality of written English: Needs some language corrections before being published

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.