Author’s response to reviews

Title: Genotoxicity Evaluation of So-ochim-tang-gamibang (SOCG), a Herbal Medicine

Authors:

Mi Young Lee (mylee@biotoxtech.com)
Yang-Chun Park (omdpyc@dju.ac.kr)
Mirim Jin (mirimj@gachon.ac.kr)
Eunseok Kim (mybestcando@naver.com)
Jeong June Choi (c27022@dju.ac.kr)
In Chul Jung (npjeong@dju.ac.kr)

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Reviewer reports:

Przemysław Łukasz Mikołajczak (Reviewer 1): The manuscript titled "Genotoxicity evaluation of So-ochim-tang-gamibang (SOCG), a herbal medicine" is focusing on the study of potential genotoxicity of SOCG using three standard batteries of tests (1. bacterial reverse mutation test (Ames test), 2. in vitro mammalian chromosomal aberration test using Chinese hamster lung cells, 3. in vivo micronucleus test using ICR mice) as part of a safety evaluation. Authors found that SOCG is safe since it does not exhibit any genotoxic sings under the experimental conditions of the study. Since there is relatively little information concerning the genotoxicity of this product (mixture of 6 medicinal herbs as Cyperi Rhizoma (Cyperus rotundus L.), Lindera Radix (Lindera strychnifolia Fern.-Vill.), Aucklandiae Radix (Aucklandia lappa Decne.), Glycyrrhizae Radix (Glycyrrhiza uralensis Fisch.), Aurantii Fructus (Citrus aurantium L.), and Platycodi Radix (Platycodon grandiflorus Jacq. A.DC.), therefore the manuscript describes work on an interesting topic.

Answer>

We appreciate the reviewer's kind comments.

These following concerns need to be addressed:

A. Specific comments:
1. Since the SOCG is not popular in the rest of the world it should be of value to insert the information in what proportions is typically composed the product from these 6 herbs. There is an information about the ratio of the product on the chapter "Preparation of the SOCG" (8: 4: 1: 1: 4: 4), however, it is not clear whether the ratio is the same as in the commercially available product.

Answer>

Because SOCG is a prescription Korean medicine, which is prepared by specialized Korean medicine facility upon Korean medical doctors request in each time, there is no commercially available SOCG in the drug market. Although Korean medical doctors modify the mixture ratio depending on the patient’s condition, the mixture ratio used in our study, 8: 4: 1: 1: 4: 4, is the most widely used recipe prescribed by Korean medical doctors in clinical filed. We added a sentence that ‘This ratio is the standard formula in clinical application.’ in Materials and Methods (Page 6, line 8)

2. What was the solubility of SOCG in water, when up to the 5000 mg/kg dose was used in ICR mice, what was the volume of intragastrically administered SOCG or vehiculum? (see: chapter Methods, In vivo micronucleus test).

Answer>

Because water is the solvent for SOCG extraction, we choose distilled water as an excipient. SOCG was thoroughly dissolved in water up to 500 mg/ml, which is the highest concentration used in our experiment (5,000 mg/kg). We administered SOCG or vehicle in a volume of 10 ml/kg. We described the treatment volume in Materials and Method section (Page 11, line 8).

B. Minor errors:

1. It should be mentioned whether the values were expressed as arithmetic (?) means ± SD and what were the parameters in brackets ( SEM?) (see: Table 1)

Answer>

According to reviewer’s recommendation, we added the mean±Standard deviation in table 1

2. Please explain abbreviation : NOA ( see: Table 3)

Answer>

According to reviewer’s recommendation, we provided the full spelling of the abbreviations in a footnote of Table 3.
3. Some mistakes and errors in references:


Answer>

Thank you for reviewer’s advice. We had corrected the references. Because some references were added, the number of Ref 13 is changed to Ref 19 in the revised manuscript.

Angel Treasa Alex, Ph.D. (Reviewer 2): Minor Essential Revisions

Methods

1. The rationale for the selection of specific bacterial strains may be discussed/reference to be cited

Answer>

According to reviewer’s opinion, we added the rationale and references in Materials and Methods (Page 8, line 14)

2. The rationale for the selection of cell line may be discussed/ reference to be cited

Answer>

According to reviewer’s opinion, we added the rationale and references in Materials and Methods (Page 9, line 19)

Reference

Ref 5 - page numbers missing

Ref 8 - follow standard format

Answer>
Thank you for reviewer’s advice. We had corrected the references. Because some references were added, the number of Ref 8 is changed to Ref 14 in the revised manuscript.

A.H.M. Khurshid Alam, PhD (Reviewer 3): The manuscript entitled Genotoxicity Evaluation of So-ochim-tang-gamibang (SOCG), a Herbal Medicine has been well studied and can be accepted. However, the author needs to reduce the method section. The authors also need to provide some information regarding combination use of herbal medicines and their genotoxicity in introduction section.

Answer>

According to reviewer’s suggestion, we had shorted the Materials and Methods, especially the sections of bacterial reverse mutation test (Ames test), in vitro mammalian chromosomal aberration test, and in vivo micronucleus test. Also, we described the genotoxicity of herbal medicines in Introduction section (Page 5, line 3).