Reviewer's report

**Title:** Enhanced antitumor efficacy of cisplatin in combination with HemoHIM in tumor-bearing mice.

**Version:** 1  **Date:** 25 November 2008

**Reviewer:** Vladimir Trajkovic

Reviewer's report:

The study by Park et al. examined the ability of the herbal composition HemoHIM to enhance cisplatin antitumor activity and reduce its toxicity. While the presented results are encouraging, there are some important issues concerning the experimental design and interpretation of results, which require authors' attention.

Major compulsory revisions:

1. The preparation and characterization of HemoHIM should be explained in more details or the relevant reference cited. More specifically, the authors should explain the rationale for mixing the polysaccharide fraction with the original extract from which the polysaccharide fraction was obtained. Do original extract and ethanol-soluble/insoluble fractions display any effects, and if so, how do they compare to those of HemoHIM?

2. The authors claim that HemoHIM enhances both NK and Tc antitumor activity in melanoma-bearing mice in the absence of cisplatin (Fig. 4). One would therefore expect that HemoHIM alone would suppress tumor progression in vivo. However, the authors do not show nor mention the effect of HemoHIM alone on melanoma growth in vivo. Why?

3. It is unclear why the authors use one system (inoculation of mitomycin-treated B16 melanoma cells) to assess the influence of HemoHIM alone on NK and Tc activity (Fig. 4), and a different one (inoculation of untreated B16 cells) to determine the effect of HemoHIM on NK and Tc activity in cisplatin-treated mice (Fig. 5A, B). This is very confusing and the rationale for such an approach must be stated. Moreover, as it is clear that HemoHIM injection alone can increase NK and Tc activity (Fig. 4), why the HemoHIM alone group was omitted in the experiment with cisplatin (Fig. 5A, B)? It is difficult to estimate the cooperation between cisplatin and HemoHIM in activating Tc and NK cells if the effect of HemoHIM alone is not determined in the same experimental setting. The same goes for the effects on tumor size (Fig. 2) and cytokine (IFN-gamma and IL-2) secretion (Fig. 5C, D). The effects of HemoHIM alone on these parameters simply must be examined in order to accurately evaluate its cooperation with cisplatin.

4. There are spelling and grammatical errors throughout the paper. The language should be checked by a native English speaker or someone proficient in English.
Minor essential revisions:

1. Page 6: The principle underlying the cell viability assessment by CCK-8 needs a brief explanation.

2. Page 10, last line of paragraph 1: replace "figure 4C" with "figure 2C"?

3. Page 23: In the legend for Figure 5, it says that "the lymphocytes of the three mice in each group were pooled." If the lymphocyte pools were investigated, how the SD values were obtained? Were there several pools of three animals in each group, or the replicates of one pool were investigated?

Discretionary revisions:

1. The histopathology in Fig. 6 indicates the ability of HemoHIM to prevent cisplatin-induced renal damage. However, did the authors perform any quantification of the histopathology analysis? Are some other parameters of renal function available (e.g. urine protein/creatinine or glucose/creatinine ratio)? These additional data might strengthen the authors' claim about the kidney-protective effect of HemoHIM.

**Level of interest:** An article whose findings are important to those with closely related research interests

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

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests.