Author's response to reviews

Title: A Comparative Study on the Hepatoprotective Action of Bear Bile and Coptidis Rhizoma Aqueous Extract on Experimental Liver Fibrosis in Rats

Authors:

Ning Wang (nwang@hku.hk)
Yibin Feng (yfeng@hku.hk)
Fan Cheung (cheungfan@hku.hk)
Oi-Yee Chow (dcoy@hku.hk)
Xuanbin Wang (xuanbin.w@163.com)
Weiwei Su (lsssww@126.com)
Yao Tong (tongyao@hku.hk)

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Author's response to reviews: see over
Dear Editor,

**A Comparative Study on the Hepatoprotective Action of Coptidis Rhizoma Aqueous Extract and Bear Bile on Experimental Liver Fibrosis in Rats**

I enclose herewith the manuscript of the above captioned research paper, which is original and is not being considered elsewhere. As shown in the title, the paper focuses on a comparative study on hepatoprotective effect of Coptidis Rhizoma Aqueous Extract (CRAE) and bear bile on liver fibrosis models in rats, which we think will meet with the scope of your journal. To the best of our knowledge, this is the first report showing CRAE and its active compound, berberine can be substitutes of bear bile (BB) and its active compound, taouroursodeoxycholic acid (TUDCA) for liver fibrosis models. We also demonstrated that CRAE and berberine have antioxidative effect, which could be one of mechanisms for their hepatoprotective action and anti-liver fibrosis. We believe these findings can contribute to substitutes of bear bile in treatment of liver diseases.

Bear bile use in Chinese medicine is a worldwide problem and the abuse of bear bile brings lots of pain to bear. Farming and getting bile from bear is cruel and inhuman. Thus, searching for an alternative to bear bile is under keen concerns in modern days. It is difficult to replace bear bile by chemical composition, but it is possible to replace bear bile by pharmacological action in some clinical indications. Both bear bile and coptis can be used in liver diseases. Our study found that both CRAE and berberine exert anti-fibrotic property as well as BB on the liver fibrosis in various rat models. CRAE and berberine could reduce the peroxidative stress in liver through increasing the superoxidase dismutase (SOD) activity. We hope these findings can shed light on the potentials of CRAE and berberine as alternatives to bear bile in the treatment of liver fibrosis.

We responded the comments from editor as below,

- *Thank you for providing us with a license number for the company from whom you purchased the bear bile used in your study. However, as I am sure you can appreciate, we wish to ensure that your study took place within a full ethical framework. We would therefore ask you to confirm that this license number entitles the Hang Hing Company to sell bear bile. Could you also provide us with some more information regarding the legalities of the selling of bear bile?*

Response: Thanks for your comments. I understand that using bear bile should follow the restricted ethical regulations and concerns so I confirm that the license number I put in this manuscript could entitle the Hang Hing Company to sell bear bile in Hong Kong. In Hong Kong, the government has forbidden the trade of bear bile products without license since 2006 by the implementation of The Protection of Endangered Species of Animals and Plants Ordinance (the Ordinance). The Ordinance put the medicine containing bear derivates under control but allows the existing stock to be traded after the agents have registered for a trading license (pp.19, Kaitlyn-Elizabeth Foley et al.: Pills, Powders, Vials and Flakes: the bear bile trade in Asia, [http://www.trafficj.org/publication/11_Pills_Powders_Vials_Flakes.pdf](http://www.trafficj.org/publication/11_Pills_Powders_Vials_Flakes.pdf)).
• We notice that you have previously published a paper on a similar topic subject in the Journal of Ethnopharmacology (Hepatoprotective effects of Coptidis rhizoma aqueous extract on carbon tetrachloride-induced acute liver hepatotoxicity in rats. J Ethnopharmacol 2009, 124: 130-6. Ye X, Feng Y, Tong Y, Ng KM, Tsao SW, Lau GKK, Sze C, Zhang Y, Tang J, Shen J, Kobayashi S). Could we please ask you to clarify their advance of your current submission over this previous publication.

Response: Thanks for your comments. They are the two different studies concerning the possible uses of Coptidis Rhizoma in the liver diseases. Our published study focused on the protective effect of Coptidis Rhizoma on acute liver injury, which may be the problem induced by some toxins or drugs. The induction of acute hepatic damage may be severe but regarding the rapid regeneration of hepatocyte, the problem may be not as difficult to be solved as hepatic fibrosis, which is our focus in the current submitted paper. In this study, we used three different animal models (only one model was used in our published paper) to mimics liver fibrosis induced by different risky factors. It should be a more comprehensive study to investigate the anti-fibrotic action of Coptidis Rhizoma. In addition, in the current submitted paper, we compared the therapeutic potency of Coptidis Rhizoma and Bear bile, the antiquity Chinese Medicines but now being forbidden to use with regards of animal welfare and animal protection. This is the first attempt to find some scientific evidences for herbal alternatives to bear bile.

• We recommend that you ask a native English speaking colleague to help you copyedit the paper. If this is not possible, you may need to use a professional language editing service. For authors who wish to have the language in their manuscript edited by a native-English speaker with scientific expertise, BioMed Central recommends Edanz (www.edanzediting.com/bmc1). BioMed Central has negotiated a 10% discount to the fee charged to BioMed Central authors by Edanz. Use of an editing service is neither a requirement nor a guarantee of acceptance for publication. For more information, see our FAQ on language editing services at http://www.biomedcentral.com/authors/authorfaq/editing.

Response: Thanks for your comments and suggestions. We have asked a native speaker to check and polish our manuscript carefully.

I believe that the information provided in this manuscript will be of interest to the readers of your journal, and thus would be most grateful if you would kindly consider our manuscript for publication in your journal.

Thank you for your kind consideration.

Yours sincerely,
Yibin Feng, PhD
Associate Professor,
School of Chinese Medicine,
Li Ka Shing Faculty of Medicine,
The University of Hong Kong