

Format for ANSWERING REVIEWERS



March 7, 2014

Title: Therapeutic Uses of Animal Biles in Traditional Chinese Medicine: An Ethnopharmacological, Biophysical Chemical and Medicinal Review

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Jin-Lei Wang, Director, Editorial Office
Baishideng Publishing Group Co., Limited
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Dear Director Wang:

Thank you very much for your kind letter of January 20, 2014. We were happy to know that after some modifications, our manuscript will finally be acceptable for publication in World Journal of Gastroenterology.

Also, I was very pleased to speak with you on the phone to discuss with you our concerns on the revised manuscript on February 11, 2014.

Enclosed please find a revised manuscript and a letter detailing each change in response to the concerns of the editors and the reviewers. We appreciate the rigorous evaluation of our work by you and the reviewers. A detailed list outlining the changes we have made, is as follows:

Responses to the comments of the Editors in the letter of January 20, 2014:

1. We have correctly formatted the title, abstract, text, and reference in the revised manuscript according to the Instructions for Authors.
2. To assist the reviewers, we have denoted revisions in **red color**.
3. Two pages of completed and signed Copyright Assignment form.

Responses to the comments of Reviewer 1:

1. Thanks for the comments. Page 6, Line 5 from the bottom: The error has been

corrected.

2. Page 7, Paragraph 2, Line 7: This sentence has been modified. We state, "Cholesterol is present in highly variable proportions in all biles including arthropods. The latter are incapable of cholesterol synthesis, but biotransform other sterols into cholesterol."

3. Page 45, Paragraph 1, Line 6: This sentence has been modified. We state, "The polar hydroxyl functions generally are α -axial or equatorial and an aliphatic side chain is conjugated with glycine or taurine in C₂₄ bile acids or sulfated in C₂₇ bile acids."

Responses to the comments of Reviewer 2:

1. Thank the reviewer for his/her critical comments and suggestions. This reviewer raised a concern on whether there is any reason for the ordering of biles in the text.

On Page 4, Paragraph 2, we have clearly stated, "*Here, we explore critically the extensive literature on TCM and Chinese materia medica, some extending back over two millennia. We investigate the old and the latest archaeological and paleozoological evidence from China, with particular focus on the medicinal uses of animal biles and their components. We attempt to answer the following questions: (i) during what periods of Chinese history were each of the animal biles introduced as therapeutic agents? (ii) which animal biles were used first for their therapeutic purposes, and which of these were most extensively employed? (iii)...*" Therefore, in the text, we discuss the use of animal biles based on a chronological list in China from the earliest times together with their origins as documented in Chinese materia medica. As a result, it is very easy for readers to find important information: which animal bile was first used to treat diseases by Chinese and in which books these animal biles with the medicinal use and therapeutic effect can be found. In the text, we discuss why dog bile was first used based on archaeological and paleozoological evidence. Moreover, it is very convenient for readers to check back to the original books that described the therapeutic usages of animal biles.

Actually, for extra convenience, (i) Table 1 and Figure 2 provide a chronological list of animal biles used therapeutically in China from the earliest times, including Chinese name (Pin Yin), English name, Latin nomenclature, earliest recorded book, year and author, bile salt and bile alcohol composition, and bile pigment composition; (ii) Table 2 has provides a list of diseases treated by animal biles in traditional Chinese medicine. All of the described information in the manuscript should greatly benefit interested readers because it is now facile for them to ascertain useful information regarding Chinese literature, therapy of disease, and chemical compositions of animal biles.

2. This reviewer made a suggestion that it is better to classify and serialize biles according to groups of organisms and to reorder biles in Table 1 and bile acids in Figure 1 to correspond to the revised main text.

As we discussed above, we did not change the order of biles in Table 1. However, we add a

new Table 3 showing a list of animal biles according to groups of organisms (i.e., mammals, birds, reptiles, amphibians, fish and arthropods) used therapeutically in China.

In addition, based on the reviewer's suggestions, Figure 1 has been revised, in which perspective structures of major bile acids in selected animal biles according to groups of organisms: (i) mammals (humans, bears, pigs and mice); (ii) birds; (iii) reptiles (snakes and turtles); (iv) amphibians (toads and frogs); and (v) fish.

Once again, thank you very much for your timely and favorable consideration.

Sincerely yours,

A handwritten signature in black ink, appearing to read 'David Q.-H. Wang', written in a cursive style.

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