ANSWERING REVIEWERS

July 29, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 11281-review.doc).

Title: Mucocele of the appendix: Anti-proliferative Effects of Cinobufacini on HepG2 Cells Detected by Atomic Force Microscopy

Author: Qing Wu, Wei-Dong Lin, Guan-Qun Liao, Li-Guo Zhang, Shun-Qian Wen, Jia-Ying Lin

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 11281

The manuscript has been improved according to the suggestions of reviewers:
1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer
(1) TO REVIEWER 1
Question:"This is an original molecular research investigating the possible anti cancer effect of cinobufacini -a traditional Chinese medicine- on hepatocellular cancer cell lines. Previous studies of this traditional medicine pointed the possible involvement of apoptotic pathways in this drug's anticancer effect. Here the authors' study revealed the morphological cellular changes in cancer cells by atomic force microscopy after drug treatment with different concentrations. These findings also suggest apoptotic cell death. One significant limitation of this manuscript is there is no randomized clinical study that investigated the effect of the drug in hepatocellular cancer. In my opinion this should be

clearly underlined in the manuscript. My final opinion is acceptance of the manuscript."

Ans: We appreciate the reviewer's suggestion. In this work, we mainly studied the mechanism of anti-proliferative effects of Cinobufacini on hepatocellular cancer at the cellular level. Randomized clinical studies are necessary in our further work, we will be committed to this work

(2) TO REVIEWER 2

Question: "Atomic force microscopy provides qualitative and quantitative information on the architecture of cell membranes such as apoptosis. In this study, the changes in morphology and the biophysical properties of apoptosis should be supplemented."

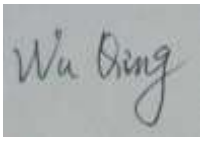
Ans: We appreciate the reviewer's suggestion. In this paper, we have proposed that the shrinkage and deep pores in cell membrane were similar to the symbols of apoptosis, which was marked in Page 10 with red words. "It appeared to be significant shrinkage and deep pores in cell membrane, which were similar to the symbols of apoptosis".

Reference: Jin H, Zhong X, Wang Z, Huang X, Ye H, Ma S, Chen Y, Cai J. Sonodynamic Effects of Hematoporphyrin Monomethyl Ether on CNE-2 Cells Detected by Atomic Force Microscopy. J Cell Biochem 2011;112:169-178. doi: 10.1002/jcb.22912. PMID:21053362

3 References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,



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