

Reviewer:

Gathering knowledge of traditional Chinese medicine and evaluating its action on the innate immune response seeking to improve the evolution of patients with sepsis is an interesting path that may bring new discoveries. However, there are still gaps to be filled by new studies.

Dear editor and reviewer:

Enclosed please find the revised manuscript “NO.: 69962 Magnolol protects against acute gastrointestinal injury in sepsis by down-regulating RANTES”. We greatly appreciate the comments and have learned a lot from the reviewers. Appropriate changes made in the revised manuscript.

We found that in our study, inhibition of serum TNF- α levels by magnolol was only partial, i.e., 50–60% inhibition vs. Model group and there may be enough circulating TNF- α for host defense. It appears that magnolol has more than a single anti-inflammatory effect in the treatment of sepsis. Some studies have reported that drugs with anti-inflammatory actions, such as antioxidative agents, could regulate immunity dysfunction with apparent safety to infectious peritoneal cavity in sepsis. As we know, PAMPs can leading to the initiation of innate immune and inflammatory responses. TLRs are a group of evolutionarily conserved and membrane-bound pattern recognition receptors that recognize various PAMPs including microbial nucleic acids, lipids, proteins, lipoproteins, and glycoproteins. We have found magnolol could down-regulates RANTES levels by inhibiting of the TLR4-regulated NF- κ B signaling pathways. Taken together, these findings suggest that magnolol may have a immunomodulating role of in sepsis. We will test this idea in subsequent experiments.

We feel that these changes are more persuasive and strongly support our statement in the manuscript. We hope the reviewers agree with our answers and the new version of this manuscript meets the standard of the prestigious

journal of **World Journal of Clinical Cases**. Thank you very much for your consideration.

Sincerely yours,

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