

Response to Reviewers Comments

We thank the reviewers for their thoughtful and supportive comments. We have revised our manuscript in response to their suggestions and hope that this improved manuscript is acceptable for publication in *World Journal of Gastroenterology*

Reviewer #1: ESPS Manuscript NO: 52667 Title: Protective effects of panax notoginseng saponin on dextran sulfate sodium-induced colitis rats through P13K/AKT signal pathway inhibition General comments The authors described the effect of panax notoginseng saponin on experimentally induced colitis rats suggesting the possible mechanism of its protective effect. Title: It reflects the major topics and contents of the study. Abstract: It gives a clear delineation of the research objective and the results. Material and methods: The experimental model, study design and methods are well described. Appropriate statistical methods are selected. Results & Discussion: The data is clearly presented but results are organized in many small paragraphs that decreased the significance of the obtained results. Therefore, I suggest putting the main results into a few paragraphs. The discussion is well organized. Tables & Figure: Reflects the major findings. In conclusion, this is a very interesting research, which provides a novel therapeutic in the treatment of the inflammatory bowel disease.

Reply: Thanks for your valuable comments. We display the results in this way to show the results more clearly and we hope to show them more completely, but integration of them may cause a slight confusion in some parts.

Reviewer #2: Qingge Lu et al. aimed to explore the protective effects of PNS on rats against DSS-induced intestinal inflammatory injury through PI3K / AKT signal pathway inhibition. Colitis rat models were constructed through DSS induction, and the rats were divided into a control group, a DSS group, a DSS+PNS 50mg/k group, and a DSS+PNS 100mg/kg group. The intestinal injury, oxidative stress parameters, inflammatory indexes, tight junction

proteins, apoptosis, macrophage polarization, and TLR4 / NFκB signal pathway of colon tissues in the four groups were detected. The PI3K/AKT signal pathway in colon tissues of the rats was intervened using the PI3K/AKT signal pathway inhibitor, LY294002. They observed that PNS protected rats against DDS-induced intestinal inflammatory injury by inhibiting PI3K / AKT signal pathway, and therefore, they pointed out, it may be used as a potential drug for colitis because it exerted with good inhibitory effects on inflammation in DDS-induced colitis. Please note that DDS-induced colitis in animal may not reflect the same mechanism in intestinal inflammation in humans. This is because the nature history of DDS-induced colitis is due to mucous trauma which is very different from human's colitis which is "antibody- antigen reaction-against the mucous resistance of the individual patient".

Reply: Thanks for your valuable comments. The rat enteritis model cannot fully simulate the pathogenesis of human enteritis, and we have supplemented the lack of clinical human trials as a deficiency in the discussion. We will conduct further human trials in the future if possible.