Answering reviewers

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 31883

Title: Intestinal anti-inflammatory activity of Ground Cherry (Physalis angulata L.) standardized CO2 phytopharmaceutical preparation

Reviewer's code: 03476668

Comments: The manuscript by Almeida-Junior et al entitled "Intestinal anti-inflammatory activity of Ground Cherry (Physalis angulata L.) standardized CO2 phytopharmaceutical preparation" explains the effect of Ground Cherry (Physalis angulata L.) standardized supercritical CO2 extract in trinitrobenzenesulphonic acid model of rat intestinal inflammation. This is very well done study, very supportive, results are excellent, and observations do support the conclusion.

Answer: Thank you. We appreciate the reviewer's positive comment.

Specific comments:

1. In the abstract section, the route of administration must be added.
Answer: Thank you, we added this information in the abstract.

2. In Abstract, also the abbreviated form of MPO and AP need to be mentioned in parenthesis.
Answer: Thank you, we added this information in the abstract.

3. Results should be separated in different section according to findings and figures.
Answer: Thank you. We reviewed the article according all rules described in the WJG guidelines and requirements.

4. What is the purpose of examining Muc proteins, should be described.
Answer: Thank you. However, in our manuscript we only analyzed the MUC mRNA abundance. This evaluation was explained in the manuscript. In fact, we did not examine Muc proteins

5. Since half-life of cytokines is very less, the level of cytokines must be determined in blood.
Answer: Thank you. We considered this possibility but the detection of cytokines in serum has two major limitations (Sullivan *et al*, 2000). Cytokines often circulate as proteins bound to soluble receptors, carrier proteins, or inhibitors, which may mask their easy detection by enzyme-linked immunosorbent assay (ELISA) (Dugue *et al*, 1996) associated with that many cytokines are undetectable in serum because they are produced locally and have a very short half-life (Sullivan *et al*, 2000). So, in order to avoid these limitations, we measured cytokines in the affected tissues. Moreover, we do not have blood samples to do a new analysis. In addition,

for this evaluation it will be necessary a complete new experiment. This is not possible. Nevertheless, we appreciate the suggestion and do not rule out the possibility of conducting further experiments in the future in order to measure these cytokines in the blood.

Sullivan *et al*. Measurement of Cytokine Secretion, Intracellular Protein Expression, and mRNA in Resting and Stimulated Peripheral Blood Mononuclear Cells. Clinical and Diagnostic Laboratory Immunology. 2000

Dugue *et al*. Preanalytical factors and the measurement of cytokines in human subjects. Int. J. Clin. Lab. Res. 1996

6. What is the effect of 25 mg/kg PACO2 in the modulation of cytokines?

Answer: Thank you. The $PACO_2$ at 25mg/kg was not capable to modulate any cytokine. We added this information in results section in manuscript.

7. Since this is short-term study, the activated form of NF-kB, MAPK and other protein should be examined instead of total mRNA.

Answer: Thank you for your suggestion. Proteins are synthesized from mRNA templates by a process that has been highly conserved throughout evolution. Alterations in mRNA tend to occurs first in mRNA and later in protein synthesis and/or release. Precisely because this study is a short-term study, we prioritize to first analyze if occurs any alterations in transcription (mRNA synthesis) to later, in further experiments, analyze alterations in protein itself.

Reviewer's code: 02941439

Comments: The article entitled "Intestinal anti-inflammatory activity of Ground Cherry (Physalis angulata L.) standardized CO2 phytopharmaceutical preparation" is good work, perfectly analysed, presented the results and discussed them perfectly. The final decision is acceptable.

Answer: Thank you. We appreciate the reviewer's positive comment.