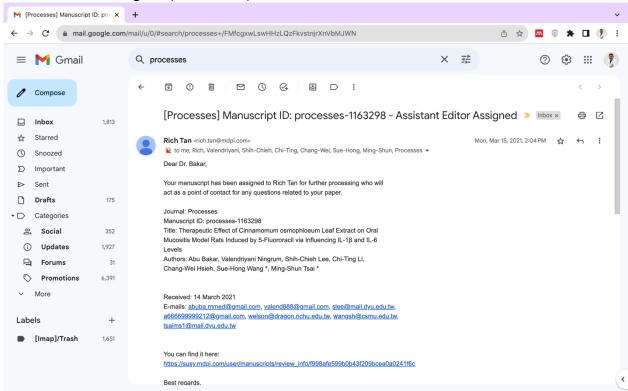
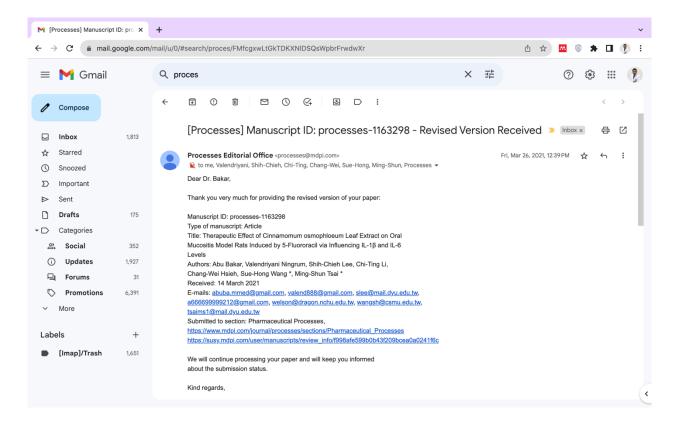
## **Bukti korespondensi Processes**

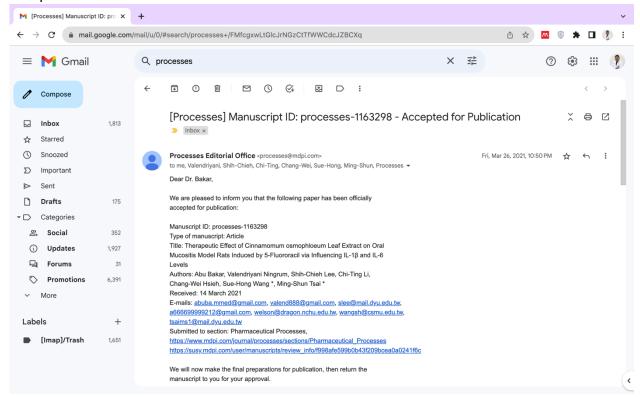
Assistant Editor Assigned (submission)



## Revised Version Received (Revision)



## Accepted for Publication



## Response to Reviewer

Comments and Suggestions for Authors

The authors studied the CO leaf extract affect for oral mucositis and revealed the relationship of pro-inflammatory cytokine level.

Normally, natural extract product has fewer side effects in the human.

Therefore, this research has high potential for therapeutic purpose.

To publication in Processes journal, manuscript need some scientific modification as below.

**Point 1:** Dose CO have side effect report for human when they used high dose? If you have, add more information and reference papers in Introduction section.

**Response 1:** Thank you for your valuable feedback on our manuscript. We have added the information and reference of CO side effect report for human in the Introduction (line 64-65) and Reference No.12.

**Point 2:** Body weight was significantly decreased in only treatment of CO 100 mg/ml. How about only CO 50 mg/ml? If body weight was not big difference between WT and CO 50 only, CO 50 is best condition for this research.

**Response 2:** Thank you for your suggestion. Treatment with 100 mg/mL CO only (100 only) showed increase in body weight of about 10 % ( $32 \pm 5$  g) similar to the WT group and no significant difference (line 173-174). From our unpublished results, the body weight of the CO 50 only (50 only) group was also similar to the WT group, and no significant difference was found between the WT, 50 only and 100 only groups. From results of this study, we found dosedependent therapeutic effect of the 5-FU+50 and 5-FU+100 groups. Therefore, we conclude that CO 100 is the best condition for this research.

**Point 3:** Result 3.3 Food and water intake part (line 119 to 220). Line 200 to 220 sentences need rearrange. Explain of Fig3A, and 3B was changed. Authors should correct the 3.3 result section to the correct explanation.

**Response 3:** Thank you for your valuable feedback. We have followed your suggestion and changes have been made accordingly (line 221-241).

**Point 4:** Fig 6. Although authors remarked 5μm in left side of image, this is an unusual mark for scale bar. I recommend put 5μm of scale bar in the image.

**Response 4:** Thank for your valuable feedback. We have followed your suggestion and labelled the scale bars in the panels of upper region. The images in the lower region are all  $5\mu$ m in size (Fig. 6).

**Point 5:** Result 3.7 is main mechanism for CO in this research. However, Result 3.7 section deficient the conclusion for Fig7. Although authors explained relation of IL-1 $\beta$  and TNF- $\alpha$  in

Discussion part, to understand this result more easily, author should add the meaning of the result in section 3.7.

**Response 5:** We thank your valuable feedback on our manuscript. We have added the meaning of the Fig. 7 result in the Result section 3.6 (line 398-408).

**Point 6:** IACUC approved number for animal experiment should be need in Material and Method section.

**Response 6:** Thank you for your valuable feedback. The approved number for animal experiment have been written in the Material and Method section 2.2.1 Animal Preparation as "All animal experimental protocols were followed in accordance with the guidelines of the Institutional Animal Care and Use Committee of Da-Yeh University (protocol number: 109004)" (line 88-91).