

# Response to Reviewer 1 Comments

**Point 1.** Abstract: The following sentences should be reviewed and rewritten to avoid redundant info. They pretty much say the same. "This article provides an overview of the key components of ginger, such as 6-gingerol, 6-shogaol, zingerone, and 6-paradol. It also examines the mechanism of action and research advancements of ginger in the treatment of various gastrointestinal cancers. The aim of this study is to investigate the mechanisms of action of the main components of ginger and their potential clinical applications in treating gastrointestinal tumors."

**Response 1: Based on the reviewer's comments, I have removed the duplicate statements in the abstract.**

**Point 2.** Introduction: a. Figures have to be numbered in the order of the apparition in the manuscript. Please revise. Figures 2 (page 4), 3 (page 4) and 4 (page 5) were inserted before Figure 1 (page 21). b. Also, in the main manuscript, is written "Figure 2 depicts the types of ginger...", but in Figure 2 there is only one type. Please revise. c. Please clarify the content of the following sentences. "Through bioinformatics methods, we used TCMSP (<https://www.tcm-sp-e.com/tcm-sp.php>), DAVID online database(<https://david.ncifcrf.gov/>), Cytoscape3.9.1 software and bioinformatics online platform (<http://www.bioinformatics.com.cn/>) to perform enrichment analysis of the active components and their action targets of ginger (see Figure 3). The results showed that most genes were enriched in the Pathway in cancer". Was this performed in this review, as a study? Apparently so. Then, this should also belong to the aim and be presented as results. Please revise the aim of your review, by the end of Introduction and avoid redundancy.

**Response 2: a. I've numbered the figures in the order in which they appear in the manuscript.**

**b. I have modified the caption of Figure 1 to read "Types of tumors treated with ginger."**

**c. I have put them after the introduction, rewritten this section and added supplementary material as mentioned by the reviewer. This part of the Network Pharmacology analysis explains why we are looking at ginger for the treatment of gastrointestinal cancers and provides the research basis for this study.**

**Point 3.** Page 5: Please clarify: "After hydrogenation, shogaol can be converted to shogaol."

**Response 3: I apologize for the error, I have corrected it to read, "After hydrogenation, shogaol can be converted to paradol."**

**Point 4.** Page 7: Please define abbreviation PMA (Phorbol Myristate Acetate) before its first use.

**Response 4: I have added the definition of PMA: "Phorbol 12-myristate 13-acetate"**

**Point 5.** "Conclusion and prospects" a. This subparagraph appears way too long. Conclusion should be short and crispy. Please avoid redundancy. b. The authors could insert a subparagraph with "Strength and limitations" of this review. Many sentences from the conclusion could go there. c. Also, they could insert a subparagraph with "Perspectives on future research" and introduce there many sentences from "Conclusion".

**Response 5: a. The conclusions have been trimmed in response to the reviewers' comments.**

**b. The section "Strengths and limitations" has been added and the statement in the "Conclusions" has been used.**

**c. A small paragraph entitled "Perspectives on future research" had been inserted at the end, and a number of sentences had been introduced from the "Conclusions".**

**Point 6.** Figure 1 should be inserted earlier in the manuscript, not in Conclusion. Please rewrite figure legend for Figure 1 and give a full description. Please make the upper part of Figure 1 readable. The lower part of Figure 1 is very ingenious and synthesizes a lot of the content of the manuscript.

**Response 6: I've changed the order in which the figures appear, modified the figure legends and elaborated on the figures.**

**Point 7.** Please be more generous in explaining the Figure legend for Figure 3.

**Response 7: I have explained the Figure legend of Figure 3 in detail**

**Point 8.** I did not find any scientific evidence for the esophageal cancer. Please revise/clarify.

**Response 8: Sorry I have deleted the reference to esophageal cancer and corrected the reference to laryngeal cancer on page 10: "In another study, the anticancer activity of 6-shogaol in laryngeal cancer (Hep-2) cells was investigated. The study revealed that 6-shogaol induces apoptosis in Hep-2 cells through oxidative damage and the regulation of apoptotic markers "**

## Response to Reviewer 2 Comments

**Point 1.** Abbreviations used should be with its full name when it firstly appears in the paper.

**Response 1: I have added the definition of PMA: "Phorbol 12-myristate 13-acetate"**

**Point 2.** Figure legends. Description to help a figure stand alone is encouraged to be added.

**Response 2: A description has been added to the figure to aid understanding, as suggested by the reviewers**