Dear reviewer expert 1,

We are very grateful to the incisive comments and suggestion on our study and manuscript. We have carefully revised the original paper according to the reviewers' questions and suggestions. All changes made in the manuscript are highlighted in yellow. In addition, the point-by-point responses to the reviewers' comments and questions are listed below:

Comments and Suggestions for Authors

In this study, the authors investigate the anti-inflammatory effects of caffeic acid phenethyl ester (CAPE) using a zebrafish model of alcohol-induced liver inflammation. The research combines in vivo experimentation, transcriptomic analysis, molecular docking, and gut microbiota profiling to elucidate the molecular mechanisms underlying CAPE's effects. This work represents a valuable contribution to the understanding of natural bioactive compounds in the context of inflammation and metabolism, and it opens the door for further development of CAPE as a potential therapeutic agent.

1. L54: Replace the incorrect phrase "alcoholic-induced" with "alcohol-induced". The same error appears again in L68.

We sincerely apologize for these mistakes. Both instances of "alcoholic-induced" have been corrected to "alcohol-induced" in the revised manuscript (highlighted in yellow). Thank you for pointing out this error.

2. L57: Correct the grammatical structure. It should read: "Zebrafish are characterized…", using the plural form in scientific contexts.

You are absolutely right. We have revised the sentence to "Zebrafish are characterized…" in the revised version of the manuscript. This change has been highlighted in yellow.

3. L71: Replace "is identified" with the correct form: "has been identified" to maintain proper verb tense.

We have made the suggested correction. The phrase "is identified" has been changed to "has been identified" in the revised manuscript, and the modification is highlighted in yellow.

4. L82: Grammar issue: "Our previous study have revealed" should be corrected to "Our previous study has revealed…".

Thank you for catching this grammatical error. The sentence has been corrected to "Our previous study has revealed…" in the revised manuscript, and the change is clearly highlighted in yellow.

5. The Materials and Methods section is clearly and concisely written. However, I suggest the authors include a schematic diagram of the experimental design, summarizing the treatment groups, sampling, and analyses performed. This would significantly improve clarity text for readers.

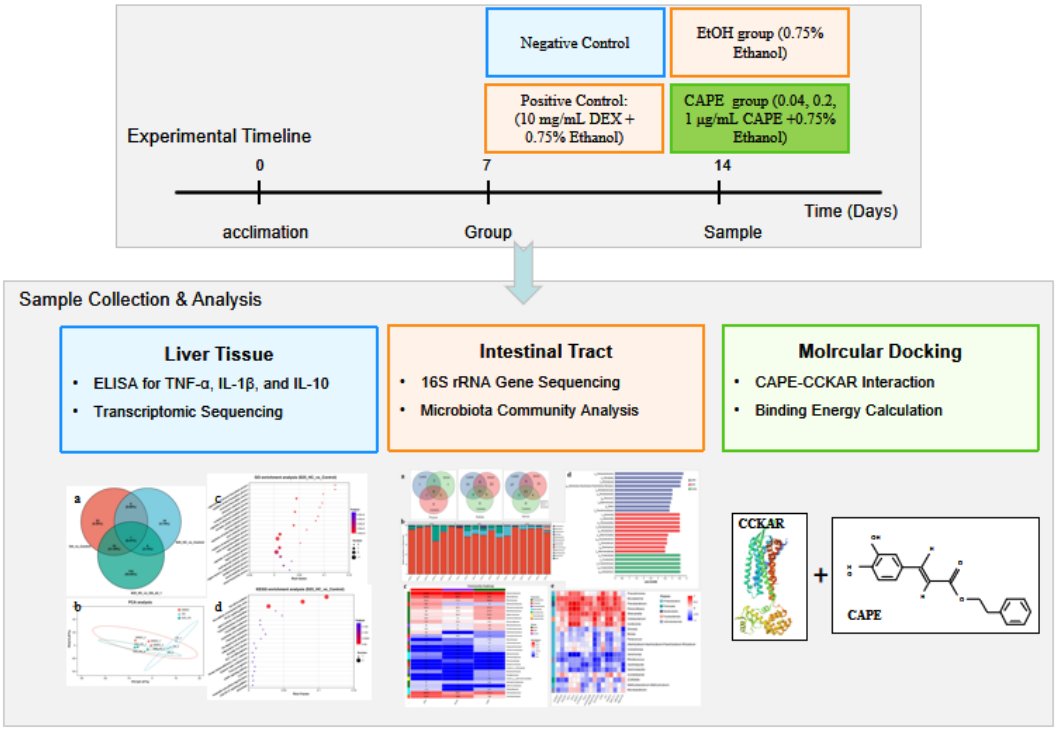
Thank you for your constructive suggestion to improve the clarity of our experimental design. We have added a schematic diagram as a supplementary file, "Materials and Methods" (highlighted in yellow), as shown in the figure, which visually summarizes:

Treatment groups: Control, EtOH group, CAPE doses (0.04/0.2/1.0 μg/mL), and positive control (DEX + alcohol).

Sampling: Liver/intestinal tissues collected at day 14.

Analyses: Transcriptomics, 16S rRNA sequencing, ELISA, and molecular docking.

The diagram aligns with the text to help readers follow our workflow. We believe this will enhance the manuscript's clarity.



Experimental Design Schematic of CAPE Study in Zebrafish

6. L132–136: Since you included a positive control group, I recommend identifying the group with "normal fish-rearing water" as the negative control for clarity and consistency in experimental terminology.

We have followed your recommendation. In the revised manuscript, the group with "normal fish-rearing water" has been clearly labeled as the negative control group throughout the text, especially in the Results and Discussion sections. This modification has been highlighted for easy identification.

7. L150: Improve the wording by replacing "via MJZol total RNA extraction kit…" with "mRNA was isolated using the MJZol kit…".

The wording has been revised as you suggested. The sentence now reads "mRNA was isolated using the MJZol kit…" in the revised manuscript, and this change is highlighted in yellow.

8. L222: Avoid starting the sentence with “And.” A more appropriate transition would be: “Moreover, the regulatory effects of CAPE…”

We have made the suggested change. The sentence now begins with “Moreover” in the revised manuscript, and the modification is clearly highlighted.

9. L257–263: It is advisable to provide full terms followed by abbreviations in parentheses the first time they appear in the text, e.g., Biological Process (BP), Cellular Component (CC), etc.

We have carefully reviewed the manuscript and added the full terms followed by abbreviations in parentheses for all relevant terms upon their first appearance. This includes Biological Process (BP), Cellular Component (CC), etc. All these changes are highlighted in yellow in the revised manuscript.

Once again, we would like to express our heartfelt gratitude for your meticulous review and constructive suggestions. We believe that these revisions have greatly enhanced the quality and clarity of our manuscript. If you have any further questions or suggestions, please do not hesitate to let us know.