

## PEER-REVIEW REPORT

**Name of journal:** *World Journal of Gastrointestinal Pharmacology and Therapeutics*

**Manuscript NO:** 80867

**Title:** Cinnamic acid regulates the intestinal microbiome and short-chain fatty acids to treat slow transit constipation

**Provenance and peer review:** Invited Manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 06216741

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Doctor

**Reviewer's Country/Territory:** China

**Author's Country/Territory:** China

**Manuscript submission date:** 2022-10-15

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2022-10-24 00:54

**Reviewer performed review:** 2022-11-02 02:16

**Review time:** 9 Days and 1 Hour

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input checked="" type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

<b>Peer-reviewer statements</b>	Peer-Review: [ <input checked="" type="radio"/> ] Anonymous [ <input type="radio"/> ] Onymous
	Conflicts-of-Interest: [ <input type="radio"/> ] Yes [ <input checked="" type="radio"/> ] No

## SPECIFIC COMMENTS TO AUTHORS

The original findings of this manuscript and the new hypotheses that this study proposed was CA could treat STC effectively. The new phenomena that were found through experiments in this study was CA significantly improved the diversity and abundance of the beneficial microbiome. The figures in this manuscript are of average quality, with different fonts and drawing styles, and lack of original data for animal experiments. What is new in this study is the potential effect of CA through SCFAs, which can alleviate STC. However, the relationship between SCFAs and STC is also relatively recognized by scientific researchers, and innovation is not enough. The figure 5C,5D,5E diagram in Figure 5 were just a simple output of the result, without careful processing by the author. The original intention of the author's article is encouraging, but the way of data processing is too crude and needs to be carefully handled.

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**Provenance and peer review:** Invited Manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 01557050

**Position:** Editorial Board

**Academic degree:** AGAF, MD, PhD

**Professional title:** Professor

**Reviewer's Country/Territory:** Japan

**Author's Country/Territory:** China

**Manuscript submission date:** 2022-10-15

**Reviewer chosen by:** Dong-Mei Wang

**Reviewer accepted review:** 2022-12-02 10:01

**Reviewer performed review:** 2022-12-10 11:09

**Review time:** 8 Days and 1 Hour

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
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Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No

<b>Peer-reviewer statements</b>	Peer-Review: [ <input checked="" type="radio"/> ] Anonymous [ <input type="radio"/> ] Onymous
	Conflicts-of-Interest: [ <input type="radio"/> ] Yes [ <input checked="" type="radio"/> ] No

## SPECIFIC COMMENTS TO AUTHORS

1) General comments Dr. Jiang and Dr. Xiao, et al. investigated “Cinnamic acid regulates the intestinal microbiome and short-chain fatty acids to treat slow transit constipation”. The reviewer has some comments. 1. In Methods, please explain how the authors determined concentrations in the high-dose and low-dose of CA. 2. In Results, in Figure 2, the authors described thickness of the mucosa and muscular, mucosal inflammation, and secretory function and so on. In the RPU and CA groups, were the authors compared to the control or the model? Please describe the details of the results in the section of CA ameliorated the histopathological performance and secretory function of intestinal mucosa in STC mice in Results. 3. In Discussion, how mechanisms the authors considered the effects of CA on intestinal motility and intestinal microbiome, such as direct effects on the intestinal tract or indirect effects on the bloodstream after absorption. 4. The authors have plenty of data on intestinal microbiome, but these results are very complex. Please describe the intestinal microbiome that are clinically associated with constipation, with some discussion in Discussion.

## RE-REVIEW REPORT OF REVISED MANUSCRIPT

**Name of journal:** *World Journal of Gastrointestinal Pharmacology and Therapeutics*

**Manuscript NO:** 80867

**Title:** Cinnamic acid regulates the intestinal microbiome and short-chain fatty acids to treat slow transit constipation

**Provenance and peer review:** Invited Manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 01557050

**Position:** Editorial Board

**Academic degree:** AGAF, MD, PhD

**Professional title:** Professor

**Reviewer's Country/Territory:** Japan

**Author's Country/Territory:** China

**Manuscript submission date:** 2022-10-15

**Reviewer chosen by:** Ji-Hong Liu

**Reviewer accepted review:** 2023-01-11 09:55

**Reviewer performed review:** 2023-01-14 06:53

**Review time:** 2 Days and 20 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Peer-reviewer	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous

statements

Conflicts-of-Interest: [ ☐ ] Yes [ ☒ ] No

## SPECIFIC COMMENTS TO AUTHORS

1) General comments Dr. Jiang and Dr. Xiao, et al. revised “Cinnamic acid regulates the intestinal microbiome and short-chain fatty acids to treat slow transit constipation”. This article is informative and well presented. The reviewer has some comments. 1. Please add these two articles in Methods and add the reference numbers in the text. Also, please add them to references. These are two papers in which the authors indicated “Yan SL, Wang ZH, Yen HF, Lee YJ, Yin MC. Reversal of ethanol-induced hepatotoxicity by cinnamic and syringic acids in mice [published correction appears in Food Chem Toxicol. 2017 Jan;99:242]. Food Chem Toxicol. 2016;98(Pt B):119-126. doi:10.1016/j.fct.2016.10.025.” “Wang Z, Ge S, Li S, Lin H, Lin S. Anti-obesity effect of trans-cinnamic acid on HepG2 cells and HFD-fed mice. Food Chem Toxicol. 2020;137:111148. doi:10.1016/j.fct.2020.111148” 2. The authors revised in Discussion “Moreover, The abundance of Prevotella is positively correlated with the fiber content of the diet [32].” Please correct “Moreover, the abundance of Prevotella is positively correlated with the fiber content of the diet [32].”