

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 85636

Title: Linolenic acid-metronidazole inhibits the growth of *Helicobacter pylori* through oxidation

Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05072111

Position: Peer Reviewer

Academic degree: PhD

Professional title: Assistant Professor

Reviewer's Country/Territory: Poland

Author's Country/Territory: China

Manuscript submission date: 2023-05-31

Reviewer chosen by: AI Technique

Reviewer accepted review: 2023-06-14 05:31

Reviewer performed review: 2023-06-26 07:08

Review time: 12 Days and 1 Hour

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 Grade E: Do not publish
Novelty of this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
Creativity or innovation of this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation

Scientific significance of the conclusion in this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
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
Re-review	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

The original article entitled "Linolenic acid-Metronidazole inhibits the growth of *Helicobacter pylori* through oxidation" focuses on determining the molecular mechanisms of the antibacterial activity of the linolenic acid-metronidazole combination against *Helicobacter pylori*. Overall, I find the manuscript interesting and accurately describing the experiments carried out to discover this mechanism. To further improve the quality of the manuscript, several modifications are suggested: 1. "Although metonidazole is a relatively cheap ..." -> Although metonidazole is a widely used and cost-effective 2. Please modify the sentences: "Therefore, Lla-Met could be used for preparing antibiotics. It is ideal. But the antibacterial mechanism of the Lla-Met compound remains unclear, this study explored this mechanism", as currently it is difficult to understand the meaning. 3. Section 1.3. -> please provide the model of microscope used here. 4. Please modify the sentence: "a final concentration of 10 ug/mL PI at 37 oC protected from the light 30 min", as currently it is difficult to understand the meaning. 5. Please modify the sentence: "Lla-Met induced the expression of ROS, MdaB, and SodB, all anti-oxidation-related genes in Table 2" -> I believe that it should be stated



**Baishideng
Publishing
Group**

7041 Koll Center Parkway, Suite
160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
<https://www.wjgnet.com>

that Lla-Met is inducing production of ROS in *H. pylori*, and therefore an increased expression of MdaB and SodB, both of which are associated with protection against the oxidative stress. 6. Please modify the sentence: "In this paper, the mechanism of linolenic-metronidazole compound was demonstrated to involve inhibiting *H. pylori* growth by up-regulating superoxide dismutase MdaB and SodB genes, resulting in excessive ROS accumulation" -> logical mistake. It should be stated that linolenic-metronidazole compound demonstrated antibacterial activity against *H. pylori* by inducing excessive ROS accumulation, which was not buffered by up-regulating antioxidant-related MdaB and SodB genes. 7. Please modify the sentence: "The results showed that excessive accumulation ROS could affect viability of *H. pylori* by 20.5% ..." -> The results showed that excessive accumulation of ROS could affect viability of *H. pylori* by reducing it to 20.5% ...

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Reviewer's code: 04861666

Position: Peer Reviewer

Academic degree: BSc, MSc, PhD

Professional title: Assistant Professor

Reviewer's Country/Territory: India

Author's Country/Territory: China

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Review time: 7 Days and 17 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
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SPECIFIC COMMENTS TO AUTHORS

As a result of the excessive and improper utilization of antibiotics, the prevalence of drug-resistant *H. pylori* strains, including those resistant to multiple drugs, is steadily rising. This situation has detrimental effects on the management and treatment of *H. pylori* infections. Consequently, the development of novel anti-*H. pylori* agents has become an urgent necessity. In the current study, authors have used a combination of linoleic acid-metronidazole (Lla-Met) for the managing *H. pylori*. Fortunately, a positive aspect is that *H. pylori* strains do not developed resistance to Lla-Met. Authors have used different assay to explore the mechanism of their action and concluded that Lla-Met kills *H. pylori* mainly by inducing oxidative stress, DNA damage, PS ectropionation, and changes on cell morphology. Comments 1. Authors should include details about the combination of Lla-Met, such as the formulation ratio and instructions on how to make it. 2. How many replicates were used for each experiment?