

PEER-REVIEW REPORT

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Title: Cryptotanshinone inhibits CagA-induced proliferation and metastasis of gastric cancer and HP CagA-positive strains caused mucosal erosions

Reviewer's code: 02535296

Position: Peer Reviewer

Academic degree: MSc, DSc

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Reviewer's Country/Territory: Italy

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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 Grade E: Do not publish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 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 checked="" type="checkbox"/> Yes <input 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 paper “Cryptotanshinone inhibits CagA-induced proliferation and metastasis of gastric cancer and *Helicobacter pylori* CagA-positive strains caused mucosal erosions” by Zhangming Chen et al. describes the use of compound cryptotanshinone (CTS) for the treatment of gastric cancer caused by *H. pylori*. The presentation is clear and the results properly presented. The practical effects of CTS on the experiments in vitro (and in vivo on a mouse model) suggest that this compound could in principle become an effective drug against gastric cancer. As noted in the introduction, CTS has been shown effective in the treatment of other types of tumors. Less convincing is the explanation presented by the authors about the molecular mechanism of action of CTS in gastric cancer, and in particular its link with CagA. It is known that CTS acts as an irreversible inhibitor of SHP2, and this is the effect observed on the growth of GC cells. But the link between CagA and SHP2 is indirect, demonstrated only by the presence of CagA-IgG (Table 1). Is the phosphorylation of SHP2 directly performed by CagA, or does CagA induce the phosphorylation process? Can the author, for example, test that CTS does not act directly on CagA, blocking SHP2 phosphorylation? Perhaps this part in the discussion could be somehow attenuated, making it more hypothetical. Other points:

- The meaning of Table 2 is not clear (at least for me), a legend should be included. What’s the difference among the four groups?
- If the hypothesis of the authors is correct, the cartoon of Fig. 7 should be redrawn. The message of the paper, if I understand correctly, is that CTS blocks the activity of SHP2 (in particular of SHP2-P), blocking GC proliferation etc. CTS should be moved to the lower part of the figure.