



PEER-REVIEW REPORT

Name of journal: World Journal of Clinical Cases

Manuscript NO: 61978

Title: Tetramethylpyrazine inhibits proliferation of colon cancer cells in vitro

Reviewer's code: 05773965

Position: Peer Reviewer

Academic degree: PhD

Professional title: Professor

Reviewer's Country/Territory: Germany

Author's Country/Territory: China

Manuscript submission date: 2021-01-14

Reviewer chosen by: Jin-Lei Wang

Reviewer accepted review: 2021-02-19 10:01

Reviewer performed review: 2021-02-24 15:59

Review time: 5 Days and 5 Hours

| | |
|---------------------------------|---|
| 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 Grade E: Do not publish |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 |
| 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 |



**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

SPECIFIC COMMENTS TO AUTHORS

In this article, Li et al. investigated the anti-cancer activity of Tetramethylpyrazine (TMP), a component of the traditional Chinese medicine Chuanxiong Hort on colon cancer cell lines. To fulfill their aim, they assessed the cell viability, proliferation, cell cycle progression as well as apoptosis. They show that TMP acts most significantly on two colon cancer cell lines, SW480 cells and HCT116 cells. TMP was able to decrease colon cancer cells proliferation in a dose- and time-dependent manner through inducing a cell cycle arrest at the G0/G1 phase. Also, TMP induces the apoptosis of the colon cancer cells. Despite the well written manuscript, some recommendations would help to better highlight the importance of the study and are necessary to support their claims: Major:

1. In the introduction, the text starting from “Although” line 82 till line 92 lacks references.
2. In the experiments addressed in the first part of the results, did the author study the colon cancer cells at different time points (24 hours or 72 hours for example)? If not, why was the 48 hours’ time point chosen to assess the cell viability and IC50?
3. Concerning the concentrations of TMP used in the experiments, did the author base the choice of concentration on any previous study? For example, Zheng et al. (2011) have used concentrations of TMP similar to those used in this study. Also, in the second part of the results, the concentrations of TMP used to examine cell viability and morphology were stated differently in the materials and methods section; it would be flawless if this is better clarified and corrected.
4. In figure 3C, the authors should present their data in a different way to support their statement of time and dose dependence for TMP . With the current presentation, the dose dependence is clearly visible, whereas the time dependence remains difficult to interpret as there is also not statistics. The authors may consider splitting the data in two different graphs.
5. The authors mention that TMP at a concentration of 600 µg/ml most efficiently induces cell cycle arrest and apoptosis. Is that based on any further experiments? From the figures,



TMP of concentration 1200 $\mu\text{g}/\text{ml}$ showed the highest effect. Song et al. (2013) have shown that TMP could have some side effects in vivo upon increasing TMP concentration further above 100 μM . Is it similar in this case so that the author relied on 600 $\mu\text{g}/\text{ml}$ being the most efficient without side effects? This should be made clearer in the text. Also, it is recommended to specify exactly the statistical significance of these 2 results and show it on the graph. Please adapt the text and figures accordingly. 6.

In the discussion, it would be more convincing to point out the in vivo effect of TMP in other cancer types in which it induced similar alterations to those uncovered by the present study. For example, Zhou et al. (2017) have shown that upon treating mice with TMP, they detected a decrease in tumor growth due to the inhibition of cell proliferation. For the discussion it would be interesting if the authors could speculate based on their current and past data if similar could be the case in colon cancer? Also, it might help to write some lines about the advantage of TMP compared to other natural products that have been shown to act on cancer cells. Minor: 1. The authors state in the beginning that they aimed to assess the mechanisms by which TMP act. Did the author assess for any cell cycle regulators (CDK4, p16...) or apoptotic markers (caspases 3 for example). If so, then it would be a nice addition to extend on that. 2. In Figs 4+5 concerning the cell cycle and apoptosis analysis, did the authors check for different time points? If not, why did they rely only on the 24 hours assessment instead of 48h? 3.

The graphs throughout the paper would profit from unified design and colors. 4.

Line 159: please fix the font and change case status of "statistical analysis" to be similar to the previous titles 5. Line 164: Replace Graphgraph by Graph pad



RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: World Journal of Clinical Cases

Manuscript NO: 61978

Title: Tetramethylpyrazine inhibits proliferation of colon cancer cells in vitro

Reviewer's code: 05773965

Position: Peer Reviewer

Academic degree: PhD

Professional title: Professor

Reviewer's Country/Territory: Germany

Author's Country/Territory: China

Manuscript submission date: 2021-01-14

Reviewer chosen by: Man Liu

Reviewer accepted review: 2021-03-30 15:02

Reviewer performed review: 2021-03-30 15:14

Review time: 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 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 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

Major: Figure/Images raw data needs to be provided to the journal as well as the Figure



**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

still need to be improved in terms of resolution and quality.