

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 71180

Title: Anti-inflammatory effects of quercetin via inhibiting tumor necrosis factor- α -induced matrix metalloproteinase-9 expression in normal human gastric epithelial cells

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 00070760

Position: Peer Reviewer

Academic degree: MD

Professional title: Full Professor

Reviewer's Country/Territory: China

Author's Country/Territory: Taiwan

Manuscript submission date: 2021-09-02

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-09-02 19:56

Reviewer performed review: 2021-09-12 18:29

Review time: 9 Days and 22 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 Grade E: Do not publish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 checked="" type="checkbox"/> Accept (General priority) <input 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

These results indicated that TNF-induced MMP-9 expression mediated the anti-inflammatory effects of quercetin in gastric mucosal epithelial cells, both in a dose- and time-dependent manner. These new findings suggest that quercetin significantly downregulates TNF--induced MMP-9 expression in GES-1 cells via the c-Src-ERK1/2 and c-Jun or NF-B pathways. The works are informative and interesting.. With a dose- and time-dependent manner, how about the safety of the use of Quercetin and quercetin-rich diets as food supplements? Quercetin can suppress the expression of MMP-9 and prevent the early pathological changes associated with gastric inflammation. Does an overdose of quercetin aggravate gastric injures else, such as ulcer, GC and so on?

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 71180

Title: Anti-inflammatory effects of quercetin via inhibiting tumor necrosis factor- α -induced matrix metalloproteinase-9 expression in normal human gastric epithelial cells

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05194092

Position: Associate Editor

Academic degree: MSc, PhD

Professional title: Professor

Reviewer's Country/Territory: China

Author's Country/Territory: Taiwan

Manuscript submission date: 2021-09-02

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-09-03 07:54

Reviewer performed review: 2021-09-13 02:14

Review time: 9 Days and 18 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 type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input checked="" 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 checked="" 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

In this manuscript, the authors used TNF- α -induced GES-1 cells to investigate the in vitro antimetastatic and anti-inflammatory activities of quercetin. MMP9 expression damages the extracellular matrix including components of basement membrane, inducing gastric disease. The manuscript indicated that TNF- α induced MMP9 expression and through c-SRC/ERK1/2/NF κ B pathway, and quercetin suppressed the TNF- α -induced MMP9 expression and could be a potential food supplement for preventing gastric inflammation. However, there are many issues with the current form of the manuscript as indicated below: Major revision for consideration

1. In the paragraph under "Omics approach to identifying inflammation-related proteins involved in GC", the website "https://www.abcam.com/human-inflammation-antibody-array (40 Targets)" is empty, please check it again.
2. The author used TNF- α to induced MMP9 expression, but there are no data showing that MMP9 did cause cell damage under 30 ng/ml TNF- α . And the data from Figure1 also only show the relevance between MMP9 and gastric cancer.
3. What is MMP inhibitor? The method part did not mention the catalog and supplier, please add the information.
4. In figure2, MMP9 inhibitor did decrease the expression of MMP9 induced by TNF- α , but actually in order to prove the effect of TNF- α , TNF- α inhibitor instead of MMP9 inhibitor should be used.
5. Please check the grammar of sentence "...if so, the mechanisms responsible" under the paragraph "Effects of quercetin on the expression of MMP-9 induced by TNF- α in GES-1 cells".
6. In figure6D, the abbreviation "Q" did not explain in the legend.
7. In figure7D, the response of



**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>

TNF- α -induced NF- κ B translocation reduced in 60min and did not follow the time dependent manner, why? 8.The figure9 overclaimed the effect of quercetin, the experiments above did not prove that quercetin directly inhibit the c-Sac or MAPKs pathway, the changes in these pathway may cause by upstream pathway. 9.The author said "...quercetin has been reported to inhibit the lipopolysaccharide-induced MMP-9 expression observed in lung inflammation and the production of pro-inflammatory cytokines", in this paper, author change the cell line and inducer, so what is the innovation of this paper?