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PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Oncology

Manuscript NO: 44659

Title: Qingjie Fuzheng Granules Inhibited Proliferation and Induced Apoptosis by Suppressing the PI3K/ AKT and ERK Signal Pathways in Colorectal Cancer Cells

Reviewer's code: 02575643

Reviewer's country: Italy

Science editor: Jia-Ping Yan

Date sent for review: 2018-11-20

Date reviewed: 2018-11-20

Review time: 9 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input checked="" type="checkbox"/> Accept	<input checked="" type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input checked="" type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

Interesting paper. QF granules have used in Chinese Medicine since antiquity. The major effect of this natural drug is an antiinflammatory action. This antiinflammatory action, inevitably, brings to cell Death and arrest of RNA transcritpion in vitro. The paper



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deserves publication, in times when the general public is looking for "natural remedies" and probably it will have a major marketing if well publicized. Probably, the major effect of QF granules on cancer patients will be an antiinflammatory action plus a placebo effect, which should not be underevaluated . Concerning the study, clearly the action should be analyzed in vivo. In the vitro study I would invite to add specific substance which could neutralize the antiinflammatory action of QF granules, to verify if QF granules have a direct action on cell cycle. In those days, we have to open our mind to new therapeutic possibilities. In this scenario to test an old traditional Chinese medicine, which has shown no side effects and a clear antiinflammatory action is Worthwhile. However, it is long way to show an effective anticancer action of the QF granules. The Authors should be encouraged to continue their studies. I would like to suggest to modify the title of the paper, adding at the end word "An hypothesis".

INITIAL REVIEW OF THE MANUSCRIPT

Google Search:

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Manuscript NO: 44659

Title: Qingjie Fuzheng Granules Inhibited Proliferation and Induced Apoptosis by Suppressing the PI3K/AKT and ERK Signal Pathways in Colorectal Cancer Cells

Reviewer's code: 02446498

Reviewer's country: Japan

Science editor: Jia-Ping Yan

Date sent for review: 2018-11-20

Date reviewed: 2018-11-26

Review time: 6 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input checked="" type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input checked="" type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input checked="" type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

In this manuscript, the authors examined the effect of Qingjie Fuzheng granule (QFG) in human colorectal cancer HCT-116 and HCT-8 cells. QFG decreased cell viability, inhibited cell proliferation and induced apoptosis. QFG treatment suppressed



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phosphorylated levels of PI3K, AKT and ERK. Although the results shows the anticancer effect of QFG clearly, I have several comments. 1. It's not clear whether the effect of QFG is selective for cancer cells or whether it's just toxic effect. The effect of QFG on non-malignant intestinal cells should be compared. QFG is used as a traditional Chinese medicine formula for patients. Animal experiments, such as a murine xenograft model of human colon cancer cells, will prove the anticancer effect of QFG. 2. Please provide information of plasma concentrations of QFG in human patients and compare them to the concentrations used in this experiments. 3. QFG consists of a mixture of four herbs as shown in Table 1. The effect of QFG should be compared to those of single component, combination of two, and combination of three. 4. Treatment with QFG induced apoptosis. Why weren't cells of sub G1 phase observed in Figure 2?

INITIAL REVIEW OF THE MANUSCRIPT

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Name of journal: World Journal of Gastrointestinal Oncology

Manuscript NO: 44659

Title: Qingjie Fuzheng Granules Inhibited Proliferation and Induced Apoptosis by Suppressing the PI3K/AKT and ERK Signal Pathways in Colorectal Cancer Cells

Reviewer's code: 02520845

Reviewer's country: Croatia

Science editor: Jia-Ping Yan

Date sent for review: 2018-11-20

Date reviewed: 2018-11-29

Review time: 9 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
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			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

ESPS Manuscript NO: 44659 Title: Qingjie fuzheng granules inhibited proliferation and induced apoptosis by suppressing the PI3K/AKT and ERK signaling pathway in colorectal cancer cells This very interesting investigation include appliance of TRC in

the treatment of colorectal cancer. The authors detailed described the effect of Quingjie fuzheng granules on the two type of colorectal cancer cells reveling the underlying mechanism that may provide benefit to the patient in the colorectal cancer treatment. Title: It reflects the major topics and contents of the study. Abstract: It gives a clear delineation of the research objective and the results. Material and methods: The study design and methods are well described; appropriate statistical methods are selected and made. Results & Discussion: The data are clearly presented and documented; every results are elaborated in the discussion section. Figures: Reflects the major findings; suggesting the short description of main result in figure legend. In conclusion, this is a very interesting research, which bring the new approach to treatment of colorectal cancer with appliance of TCM.

INITIAL REVIEW OF THE MANUSCRIPT

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