

ESPS Peer-review Report**Name of Journal:** World Journal of Gastrointestinal Oncology**ESPS Manuscript NO:** 7666**Title:** In vitro study on estrogenic effects of biologically active polyphenols contained in food matrices on a model of colorectal cancer cells**Reviewer code:** 00503405**Science editor:** Ling-Ling Wen**Date sent for review:** 2013-11-28 12:50**Date reviewed:** 2014-01-26 23:03

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input checked="" type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

COMMENTS TO AUTHORS

In the original article of Pampaloni et al. (In vitro study on estrogenic effects of biologically active polyphenols contained in food matrices on a model of colorectal cancer cells) the authors aimed to study the biological effects of two phytoestrogens on cell growth and on expression of estrogen receptor beta in (ER-beta pos. and neg) colon cancer cell lines. The aims, methods and results are all clear, the figures help the understanding. The main result of the study, namely the possibility that quercetin and genistein can exert their effect on the used CRC cell lines by activating molecular mechanisms regarding regulation of ER β expression, inducing a noticeable increase, is new and well documented. Some stylistical revision is however needed. The abstract must be expanded with the main results and conclusion of the study. The text must be re-formatted according to the guidelines of WJGO. English language needs minor polishing. After minor revision, I suggest to accept the manuscript for publication in WJGO.

ESPS Peer-review Report

Name of Journal: World Journal of Gastrointestinal Oncology

ESPS Manuscript NO: 7666

Title: In vitro study on estrogenic effects of biologically active polyphenols contained in food matrices on a model of colorectal cancer cells

Reviewer code: 02543800

Science editor: Ling-Ling Wen

Date sent for review: 2013-11-28 12:50

Date reviewed: 2014-01-30 10:22

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input checked="" type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

COMMENTS TO AUTHORS

The manuscript presented an interesting study. I have a few comments: 1) The abstract doesn't read like an abstract, but more like an introduction. 2) Figure legends are buried in the text, making it difficult to read. 3) The manuscript used the word "protective" in many places. The observation of quercetin and genistein in suppressing cancer cell growth does not mean they can protect normal colonic mucosa from developing CRC. 3) The last paragraph said "Results obtained on our CRC cellular models, although they must be confirmed by in vivo studies, not only support what has been observed in other hormone sensitive cancers [51-52], but would also further prove and confirm the protective role of ER β on estrogen sensitive tissue such as breast, ovary, prostate, and colorectal mucosa, introducing the possibility that the same results we have obtained could also be found for other hormone sensitive tissues [53-56] In conclusion, our study on the effects of quercetin and genistein has confirmed the epidemiological and experimental data which show the protective action of both the tested phytoestrogens against CRC, by acting on tumoral cell growth and by modulating the expression levels of mRNA. In particular, our study revealed, for the first time in research on CRC, a significant effect of quercetin on expression levels of ER β at a concentration comparable to that found at the level of colorectal mucosa following a daily intake of 16 mg of quercetin/day." This paragraph has some overstatements. First, the manuscript didn't present any direct evidence to confirm the protective role of ERbeta on estrogen sensitive tissue. The upregulation of ERbeta is a consequence of quercetin treatment. It can't be assumed that the effect of quercetin on CRC tumor cell growth is mediated by ERbeta unless an experiment with and without ERbeta being blocked or



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knocked down/out was done. Second, as above, I don't think one could conclude that quercetin and genistein have the protective role. Therefore, this paragraph and similar overstatements in the manuscript should be revised.

ESPS Peer-review Report**Name of Journal:** World Journal of Gastrointestinal Oncology**ESPS Manuscript NO:** 7666**Title:** In vitro study on estrogenic effects of biologically active polyphenols contained in food matrices on a model of colorectal cancer cells**Reviewer code:** 00183059**Science editor:** Ling-Ling Wen**Date sent for review:** 2013-11-28 12:50**Date reviewed:** 2014-02-07 20:13

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)		BPG Search:	<input type="checkbox"/> Minor revision
<input checked="" type="checkbox"/> Grade E (Poor)	<input checked="" type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

1) The author mentioned that these compound inhibit the cell growth through the binding to ER. If the author really would like to say that, binding assays between compound and ER are needed (eg, thermal shift assay, biacore assay and so on) or the author could refer the previous publication which shows binding. 2) If the author would like show that these compound effect specifically ER, it might be better to show the comparison between HCT8- β 8 and HCT8-pSV2neo in cell viability assay and q-PCR experiment. 3) In the luciferase assay and q-PCR experiment, the author collected the sample at 48hrs and 6days, respectively. Actually this time point to collect the sample is too late. If compounds are incubated with the cells 48hrs or 6days, a lot of genes had already turned on and the author can not avoid the off target or indirect effect. Thus, it is better to show in the earlier time point. 4) If the author could test the another colorectal cancer cell line and there is a correlation between sensitivity to compound and ER expression level, it would be interesting.

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Name of Journal: World Journal of Gastrointestinal Oncology

ESPS Manuscript NO: 7666

Title: In vitro study on estrogenic effects of biologically active polyphenols contained in food matrices on a model of colorectal cancer cells

Reviewer code: 00070821

Science editor: Ling-Ling Wen

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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
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COMMENTS TO AUTHORS

This study maybe has some guiding significance for the future preventive therapy of colorectal cancer. And the preliminary results from this research are encouraging. But I think the authors should revise or answer those questions. 1. The authors only gave the box-and-line drawings instead of the details research data. Please provide the each step images of the in-vitro cell culture experiments. 2. The structure of article is too loose, especially the part of DISCUSSION. And the part of INTRODUCTION is too long. It made the scientific thesis less prominent. It does harm to the readers' reading and comprehension. 3. The words of article should be polishing. 4. Some references are outmoded; please provide the recent literatures as possible. And revise the references according to demanded format by editors of journals.