

## ESPS PEER REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**ESPS manuscript NO:** 13959

**Title:** Growth inhibition and apoptosis induction by alternol in human pancreatic carcinoma cells

**Reviewer code:** 00005855

**Science editor:** Yuan Qi

**Date sent for review:** 2014-09-11 19:57

**Date reviewed:** 2014-10-08 15:57

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"/> Existing	<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 checked="" type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input checked="" type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

## COMMENTS TO AUTHORS

The authors investigated the effect of alternol on pancreatic cancer cells, and they demonstrated that alternol inhibited the growth of pancreatic cancer cells via cell cycle arrest and apoptosis induction. The present data suggest that the agent has the potential to be developed as an anti-tumor agent for the treatment of pancreatic cancers. There are several questions and issues to be addressed. Major 1. The present data suggest that alternol has effect on cell cycle arrest at S phase. Does the agent rather promote G1 to S transition? 2. Page 11. If the alternol activate Caspase 3, then degradation of pro-Caspase 3 should be demonstrated by showing increased fragments. 3. Does the p53 in the pancreatic cell lines mutated? Does an increase in the level of mutant p53 lead to restoration of its function? 4. The discussion section seems to be redundant, since the authors discussed one by one the steps of cell proliferation and cell cycle that are serially associated as signaling cascade. Minor 1. In the results section, description of methods that is redundant in the results section is found in every section. 2. In Page 12, the explanation of JC-1 should be in the method section and is redundant in the discussion section. 3. In Page 13, "the ratio of anti-apoptotic versus pro-apoptotic Bcl-2 proteins" should be read as "the ratio of anti-apoptotic versus pro-apoptotic Bcl-2 family proteins". 4. In the abstract: TdT-mediated dUTP nick end labeling (TUNEL). No need to abbreviate.

## ESPS PEER REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**ESPS manuscript NO:** 13959

**Title:** Growth inhibition and apoptosis induction by alternol in human pancreatic carcinoma cells

**Reviewer code:** 00034616

**Science editor:** Yuan Qi

**Date sent for review:** 2014-09-11 19:57

**Date reviewed:** 2014-10-04 17:50

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 checked="" type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> Existing	<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 checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Existing	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

## COMMENTS TO AUTHORS

Clear manuscript, would have expected though a more comprehensive discussion. Please review this section of your submission.

## ESPS PEER REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**ESPS manuscript NO:** 13959

**Title:** Growth inhibition and apoptosis induction by alternol in human pancreatic carcinoma cells

**Reviewer code:** 00503536

**Science editor:** Yuan Qi

**Date sent for review:** 2014-09-11 19:57

**Date reviewed:** 2014-10-05 11:09

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"/> Existing	<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	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input checked="" type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

## COMMENTS TO AUTHORS

The authors describes the anticancer effect of alternol on two pancreatic cancer cells. Since it is well known that the patients with pancreatic cancer show extremely poor prognosis, the data are encouraging. However, there are some concerns that need to be addressed. Major points 1. The authors used only pancreatic cancer cells for all assays. However, because they used no control of non-malignant cells, it is unclear whether the effect of alternol is cancer cell-specific. 2. The mechanism of anticancer effect of alternol seems to be somewhat different in two pancreatic cancer cells, which should be discussed more in the discussion. Minor point 1. Fig.1 should show the results of statistical analysis. 2. All the figures show the results from two cell lines independently. However, the data could be present in a more concise way. 3. In fig.5, the percentages of red and green shown in the graph seem to be inconsistent with the figures of flow cytometry. 4. In fig. 6, it is not clear what the y-axis represent in the graphs. Moreover, Western blotting should show the results from all the concentrations of alternol.

## ESPS PEER REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**ESPS manuscript NO:** 13959

**Title:** Growth inhibition and apoptosis induction by alternol in human pancreatic carcinoma cells

**Reviewer code:** 02842351

**Science editor:** Yuan Qi

**Date sent for review:** 2014-09-11 19:57

**Date reviewed:** 2014-10-11 20:17

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"/> Existing	<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	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input checked="" type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input checked="" type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

## COMMENTS TO AUTHORS

You can not draw the conclusion according the experiment, For it test the functions of alternol only in cell line. Please supplement picture about: "Alternol has shown a dose- and time-dependent inhibition for the proliferation of the PANC-1 and BxPC3 cells in vitro" Counting in the Cell viability assay is a subjective method. The author enumerate several molecules related to apoptosis and consider these molecules involve mechanism of apoptosis, but the author didn't test which one is the key factor further.

## ESPS PEER REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**ESPS manuscript NO:** 13959

**Title:** Growth inhibition and apoptosis induction by alternol in human pancreatic carcinoma cells

**Reviewer code:** 00502797

**Science editor:** Yuan Qi

**Date sent for review:** 2014-09-11 19:57

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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 checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> Existing	<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	BPG Search:	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

## COMMENTS TO AUTHORS

Points of criticism: 1. Statistical analysis of the results show that only the effect of alternol on apoptosis has a statistically significant strength ( $p < 0.01$ ), while the rest of the results depict a trend. 2. The manuscript needs linguistic improvement. Conclusion: The authors performed an experimental study in order to investigate in vitro the anti-tumoral effects of alternol. The design of the study has no systematic biases, the results, however, depict statistical strength only regarding apoptosis and show a trend towards antitumoral effect of alternol regarding other properties. This issue in combination with the fact that this study is an in vitro investigation should be strongly referred in the manuscript in order to be accepted in your journal.