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7901 Stoneridge Drive, Suite 501,
Pleasanton, CA 94588, USA
Telephone: +1-925-223-8242
Fax: +1-925-223-8243
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
Manuscript NO: 36076
Title: Emodin and Baicalein inhibits sodium taurocholate-induced vacuole formation in pancreatic acinar cells
Reviewer's code: 01221925
Reviewer's country: Greece
Science editor: Ze-Mao Gong
Date sent for review: 2017-09-03
Date reviewed: 2017-09-06
Review time: 3 Days

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[ ] Accept
[Y] Grade B: Very good	[Y] Grade B: Minor language polishing	[ ] The same title	[ ] High priority for publication
[ ] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] Duplicate publication	[ ] Rejection
[ ] Grade D: Fair	[ ] Grade D: Rejected	[ ] Plagiarism	[Y] Minor revision
[ ] Grade E: Poor		[Y] No	[ ] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

This is an interesting paper regarding the use of CEB in a model of acute pancreatitis and the mechanism involved. Could the authors please respond to the following questions/comments? 1) Why were there only male rats used? 2) Have the authors compared the effect of CEB to the effects of each component by itself? 3) How were the doses chosen? 4) How was the 12hr time point chosen? Did the authors look at other time points? 5) What are the side effects of CEB? In humans what are the data for its use? 6) Could the authors include in the discussion a paragraph about the limitations of the study?

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
Manuscript NO: 36076
Title: Emodin and Baicalein inhibits sodium taurocholate-induced vacuole formation in pancreatic acinar cells
Reviewer's code: 00053888
Reviewer's country: United Kingdom
Science editor: Ze-Mao Gong
Date sent for review: 2017-09-03
Date reviewed: 2017-09-07
Review time: 4 Days

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[ ] Accept
[ ] Grade B: Very good	[Y] Grade B: Minor language polishing	[ ] The same title	[ ] High priority for publication
[Y] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] Duplicate publication	[ ] Rejection
[ ] Grade D: Fair	[ ] Grade D: Rejected	[ ] Plagiarism	[Y] Minor revision
[ ] Grade E: Poor		[Y] No	[ ] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

The authors have managed to isolate what they believe are the active ingredients in a Chinese herbal remedy used extensively for the treatment of severe acute pancreatitis. They have then gone about a well constructed scientific study using animal models and demonstrated that their compounds have a dose dependent effect in ameliorating the severity of the acute pancreatitis. The study is well designed, well carried out and well written. These compounds will undoubtedly suffer in the way many others have suffered. They will work well when given in close proximity to the stimulus for the attack but in clinical practice this will not be possible. The authors however make no promises that they will and recognise that further study is required.

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
Manuscript NO: 36076
Title: Emodin and Baicalein inhibits sodium taurocholate-induced vacuole formation in pancreatic acinar cells
Reviewer's code: 02445032
Reviewer's country: Spain
Science editor: Ze-Mao Gong
Date sent for review: 2017-09-03
Date reviewed: 2017-09-18
Review time: 15 Days

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[ ] Accept
[ ] Grade B: Very good	[Y] Grade B: Minor language polishing	[ ] The same title	[ ] High priority for publication
[ ] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] Duplicate publication	[ ] Rejection
[Y] Grade D: Fair	[ ] Grade D: Rejected	[ ] Plagiarism	[ ] Minor revision
[ ] Grade E: Poor		[Y] No	[Y] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

Severe acute pancreatitis (SAP) remains a serious clinical problem with significant morbidity-mortality. Identifying safe, effective and inexpensive drugs for the treatment of SAP remains necessary. In previous studies, emodin, baicalein and their combination have shown beneficial effects on SAP in experimental animals. This study aims to investigate the mechanisms of combined use of emodin and baicalein at cellular and organism levels with severe acute pancreatitis. The manuscript adheres to the Journal's standards and scope. Potentially, the paper is interesting to WJG readership and relevant to the field. However, many pieces of information are lacking, mainly in the description of procedures and results (including text, figure legends and abstract). These aspects should be revised in order to be acceptable for publication in WJG.

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READABILITY OF THE MANUSCRIPT and CONFORMITY WITH JOURNAL GUIDELINES 1.- The length of the title and running title is fine, but they both focus only on a very specific aspect of the work (vacuole formation). 2.- The abstract conforms to the preparation guidelines outlined in the Writing Requirements of Basic Study. However, it should be more informative. 3.- The references cited are relevant, appropriate and up-to-date. 4.- Language evaluation: Minor language polishing

SPECIFIC COMMENTS
Abstract Methods: brief description of procedures (pretreatment-treatment) should be included, both for rats and isolated cells. It should be mentioned that the cell study was made in cells prepared from healthy rats. Results: Make clear that (2.07 ± 1.20 vs 6.84 ± 1.13, $P<0.05$) refers to histopathologyscore, not amylase. In the results section of the abstract, numerical results for some parameters are included. In these cases, CEB doses or concentrations should be indicated.

Materials and Methods 1. General: Centrifugation conditions would be better described if expressed in units of gravity (times gravity or × g) rather than revolutions per minute, rpm. 2. First paragraph in the Materials and Methods section may be entitled Animals instead of Materials (no materials are mentioned or described). 3. Therapeutic effects of CEB. - Line: 5: low-dose instead of high dose; line 8: high-dose instead of lowdose (names “high” and “low” do not correspond with the doses). - Please, specify route of administration of CEB (intravenous??) and when it was administered after taurocholate (immediately??) 4. Isolation of rat pancreatic acinar cells - The title of this subsection should be “Isolation of pancreatic acinar cells from healthy rats” - In their Pancreapedia article (ref 18), Williams et al mention many different digestion enzymes to be used for the isolation procedures. Please, give details of the collagenase used in this study (manufacturer, type and concentration/activity used for the digestion). Include also details for the trypsin inhibitor (manufacturer, concentration/activity used). 5. Cell vitality assay. - MTT assay. If a commercial kit was used, please give details of the name and manufacturer. If it was not a kit, please include a literature reference. - This subsection (as a whole) is very confusing. When comparing the text of this paragraph with the corresponding one in the Results section and the corresponding figure (Figure 2), I have come to determine that 3 diffrerent experiments have been done: 1) NaTC alone (different concentrations and different incubation times); 2) NaTC 8 mM for 30 min (?) after 10-min pretreatment with different concentrations of CEB; 3) CEB alone (time?) at different concentrations. Still, I am not sure that this is what the authors really performed…The protocols used (design of the different experiments) are scarcely described (substances involved, pretreatment or not, times, concentrations, etc). The

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subsection may be completely rewritten. 6. Cell ultrastructural observation. I feel curious about the reason why in the cell viability experiments, after the 10-min pretreatment with CEB, the authors used 8 mM NaTC/30 min as a damaging factor, whereas in the cell ultrastructural study, the damaging factor was 1 mM NaTC/1 min. Maybe the readers would thank some explanatory note about this. 7. Intracellular Ca2+ measurement. Please indicate manufacturer for the fluo-3 AM probe. 8. Quantified IP3R expression. Please, indicate manufacturer for the RNA and protein extraction kit, and provide some literature reference for the RT-PCR and Western blotting protocol.

Results 1. Serum amylase and inflammatory response. CEB decreased serum IL-6 in SAP rats EXCEPT AT THE LOW DOSE. This should be made clear. 2. Cell viability. Lines 7-8 of this page should read: "The pre-treatment with CEB could increase the vitality in cells treated with 8 mM NaTC, and showed dose- dependent protective effects at …" and then (following lines): "Moreover, CEB alone had no adverse effect on the normal cells at either….) 3. Vacuoles. - Line 9 from the bottom of the page: indicate NaTC concentration. ("after one-minute with ….. mM sodium taurocholate" - Line 4 from the bottom of the page: indicate CEB concentration and pretreatment time.

Discussion 1. Last page of the text, line 4 from the top of the page: "We used pancreatic acinar cells prepared from healthy rats that were induced by sodium taurocholate as an …"

Figures and figure legends General: The figure legends should help making the figure comprehensible without reference to the text. In this sense, I think that the authors should give a brief description of the experimental groups/treatments/pretreatments, including times, concentrations, etc). 1. Figure 2.iii: an explanatory note on the reason why vitality results of the experiments with CEB alone (Fig 2.iii) are nor expressed in the same way as in the previous experiments (Figures 2.i and 2.ii) may be appreciated by the readers. 2. Figure 2 legend (ii): "CEB pretreatment increased (instead of decreased???) vitality in cells treated with 8 mM sodium taurocholate and showed dosedependent protective effect…" 3. Figure 3i B and C: According to the legend, the sharp increase in cytosolic calcium ofin the first 2 seconds is due to addition of NaTCI. Have the authors explored the possibility that this is some artefact??? 4. Figure 4i: title on Y-axis: "mRNA relative expression (% of control)" 5. Figure 4ii: Have the authors quantified the IP3R protein bands and normalized to respective β-actin control?? A bar chart with these data (perhaps in addition to the image) should be more illustrative and informative.