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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 35253

Title: Optimal timing for the oral administration of Da-Cheng-Qi Decoction based on the pharmacokinetic and pharmacodynamic targeting of the pancreas in rats with acute pancreatitis

Reviewer's code: 00504345

Reviewer's country: Bulgaria

Science editor: Yuan Qi

Date sent for review: 2017-07-24

Date reviewed: 2017-08-03

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	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"/> The same title	<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"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> No	

COMMENTS TO AUTHORS

Please, Look on the attached file with views and questions.

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Name of journal: World Journal of Gastroenterology

Manuscript NO: 35253

Title: Optimal timing for the oral administration of Da-Cheng-Qi Decoction based on the pharmacokinetic and pharmacodynamic targeting of the pancreas in rats with acute pancreatitis

Reviewer's code: 00503345

Reviewer's country: Canada

Science editor: Yuan Qi

Date sent for review: 2017-08-02

Date reviewed: 2017-08-08

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	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	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Duplicate publication	publication
<input type="checkbox"/> Grade D: Fair	<input checked="" type="checkbox"/> Grade C: A great deal of	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor	language polishing	<input checked="" type="checkbox"/> No	<input type="checkbox"/> Minor revision
	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input checked="" type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

In this manuscript the authors have examined the pharmacokinetics of the absorbed components of the Da-Cheng-Qi decoction (DCQD) used in Chinese medicine for the treatment of early acute pancreatitis (AP). A single-dose of DCQD was administered intragastrically to rats at different times after induction of AP. Blood and pancreatic concentrations of DCQD components were monitored. The effects of intragastrically administered DCQD on IL-6 and IL-10 serum levels and pancreatic tissue damage were evaluated 24 hours after intragastric administration of DCQD. The data suggest that absorption of DCQD components is improved if administered at least 12 hours after induction of AP. DCQD affects the balance of IL-6 and IL-10, thereby promoting resolution of inflammation, and reduces pancreatic damage when administered 12 hours after AP induction. General comments: Overall the manuscript is wordy and not



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easy to read. The pharmacokinetic/pharmacodynamic data are informative but additional discussion is needed as absorption of DCQD components could be influenced by the time of day that the decoction was administered to rats (see comments below). Data on the secretion of pro- vs anti-inflammatory cytokines add very little to what is already published. The data shown regarding damage to pancreatic tissue are not consistent with previous data showing that a similar dose of intragastrically administered DCQD 2 hours after AP induction confers some protection against pancreatic tissue damage (Refs. 4 & 5). The discrepancy should be discussed. Specific comments: a) Materials and Methods: The composition of the internal working solution and the composition of the “double-solvents” should be provided. b) It is correct to provide the concentration of the DCQD components extracted from blood or serum (?) in $\mu\text{g/mL}$. However, for solid tissues it is counterintuitive to provide a concentration in ng/mL (table 1). The data should be normalized according to protein content or tissue weight. c) The circadian clock can influence the absorption and the effects of drugs. Was DCQD intragastrically administered to groups of rats at the same time of day? d) The authors recently published two studies showing that DCQD (12 mg/kg) orally administered 2 hours after induction of AP could reduce pathological scores in the pancreas. Here, it is shown that DCQD (12 mg/kg) orally administered 4 hours after induction of AP has no effect on pancreatic tissue damage. These discrepancies should be discussed.