



PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 54350

Title: Optimal dosing time of Dachengqi decoction for the protection of extrapancreatic organs in experimental acute pancreatitis

Reviewer's code: 00503176

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Professor

Reviewer's Country/Territory: Croatia

Author's Country/Territory: China

Manuscript submission date: 2020-01-21

Reviewer chosen by: AI Technique

Reviewer accepted review: 2020-01-22 09:45

Reviewer performed review: 2020-01-22 10:20

Review time: 1 Hour

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input type="checkbox"/> No



Peer-reviewer statements Peer-Review: [Y] Anonymous [] Onymous Conflicts-of-Interest: [] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

This is a thorough report on two experiments conducted by researchers with the expertise in the field. The animal experiments are generally not too complex, but measurements (PK in tissues and plasma; inflammation markers etc.) are complex and sophisticated. The manuscript provides a novel insight into the topic. I have no comments on the design of animal experiments and I have no comments on the measurement methods - all seems to be appropriate and valid. I have only a few minor comments. 1. English is generally adequate, but there are sporadic typos across the manuscript - should be re-checked. 2. I would NOT agree that using serial Student t-tests (or their non-parametric analogues) is appropriate in these experiments. Both experiments are, generally, settings in which (for each outcome) one-way analysis of variance (parametric or non-parametric) is appropriate. 3. One problem that arises in this very complex work (considering the number of outcomes/analytes) - is the question of the overall type 1 error. Just as an example - there are like 6-8 analytes compared across 4 groups (each with a control, mostly). this is at least some 20 statistical tests (in a single experiment) - multiplicity is an obvious issue. I agree that it would be TOO CONSERVATIVE to include a very strict method for controlling FWER, but something should be done - for example: amilase levels - comparison of 3 groups vs. control: one-way ANOVA followed by pairwise comparisons BUT with some form of ADJUSTMENT for the number of post-hoc test. The same for interleukin levels. AND Whenever possible - report EXACT p-values. For PK data...one thing is not very clear - how was the "mathematics" done? It is generally accepted that for example - Cmax, AUC and elimination rate constant follow log-normal distribution. This would mean: for each



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analyte, use ANOVA on ln-transformed data, and compare each group vs. the control - and report the differences as Geometric means ratios. you can provide for example 90% CIs around the ratios (no need for post-hoc adjustments- to be flexible) - and AVOID reporting P-values. The P-values are...of less relevance or no relevance here. GMRs would provide information on PERCENT (relative) DIFFERENCE between groups and the idea about the size of the difference. E.g., ratio (90%CI) of 1.50 (1.20-1.85)..would suggest around 50% higher exposure (e.g., if Cmax or AUC is analyzed). It is often forgotten that P-index IS NOT A MEASURE of an effect. and sometimes - like here, at least regarding PK data - the primary interest is getting insight into the extent of difference between different administration timings. Avoiding focus on p-values in this setting (with so many tests) - I believe it is very important - anyone aware of the multiplicity problem will immediately recognize that at least some null-hypotheses were rejected - simply by chance. However, if effects are provided, "p-values" become less relevant - For example...a ratio of 1.70 with CIs form 0.90 to 2.50 would have $P > 0.05$ - but it is clear that there IS an effect (a difference), of around 70%...it is just that the precision of the estimate is poor since there were 6 animals per group. But in such a case "high p-value" - DOES NOT exclude the fact that the difference (between dosing schedules or any other factor levels) - most likely exists.



RE-REVIEW REPORT OF REVISED MANUSCRIPT

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Author's Country/Territory: China

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Reviewer chosen by: Yu-Qiao Wang

Reviewer accepted review: 2020-04-01 18:09

Reviewer performed review: 2020-04-01 18:17

Review time: 1 Hour

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 checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input checked="" type="checkbox"/> Accept	<input 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



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SPECIFIC COMMENTS TO AUTHORS

This is a very complex experiment. The authors have generally adequately responded to my comments and revised the manuscript . I have no further comments

INITIAL REVIEW OF THE MANUSCRIPT

Google Search:

- The same title
- Duplicate publication
- Plagiarism
- No

BPG Search:

- The same title
- Duplicate publication
- Plagiarism
- No