



PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 39217

Title: Moxibustion treatment modulates the gut microbiota and immune function in a dextran sulphate sodium -induced colitis rat model

Reviewer’s code: 02941672

Reviewer’s country: Japan

Science editor: Xue-Jiao Wang

Date sent for review: 2018-04-09

Date reviewed: 2018-04-15

Review time: 5 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input 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 checked="" 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 type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

This paper has impact to elucidate the mechanisms how moxibustion effect for UC. It is novel to find that moxibustion improved gut microbiome and cytokine expression. However, there are several points for revision as follows. 1, There is discrepancy



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between microbiome diversity and inflammatory cytokine expression (Ex, Fig5d and Fig 8 or 9). The author described that gut microbial variation may affect mucosal immunity, but it cannot be concluded. 2, The "A", "B", "C", ... in Fig 4 and 5 needs to be changed to "HC", "UC", "UC7" .. like other figures.

INITIAL REVIEW OF THE MANUSCRIPT

Google Search:

- The same title
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- Plagiarism
- No

BPG Search:

- The same title
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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 39217

Title: Moxibustion treatment modulates the gut microbiota and immune function in a dextran sulphate sodium -induced colitis rat model

Reviewer’s code: 00503255

Reviewer’s country: Japan

Science editor: Xue-Jiao Wang

Date sent for review: 2018-04-16

Date reviewed: 2018-04-17

Review time: 17 Hours

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 type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good		<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	(General priority)	Peer-reviewer’s expertise on the topic of the manuscript:
<input type="checkbox"/> Grade E: Do not publish	<input type="checkbox"/> Grade D: Rejection	<input checked="" type="checkbox"/> Minor revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Major revision	<input checked="" type="checkbox"/> General
		<input type="checkbox"/> Rejection	<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

The authors investigated the gut microbiome profiling and the expression of inflammatory cytokines in serum and colon mucosa of healthy rats and DSS induced UC rats with or without moxibustion treatment and reported that reduced diversity, gut



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microbial dysbiosis, increased inflammatory cytokines and decreased anti-inflammatory cytokines in DSS induced US rats and showed that these effects could be alleviated by moxibustion treatment. Based on these findings, they conclude that moxibustion exerts its therapeutic effect by modulating the microbiome and intestinal mucosal immunity. The paper is well-written and has interesting findings. Some points should be revised.

1. page 3, line 11-12: This sentence did not show what samples the authors used for cytokine analysis in this study. "in colon mucosa and serum" should be added after "the expression of inflammatory cytokines". ", respectively" should be added after "by PCR and ELISA".

2. references: Page numbers should give full-spelling. For example, the reference No.1:"688-93" should be changed to "688-693".

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Name of journal: World Journal of Gastroenterology

Manuscript NO: 39217

Title: Moxibustion treatment modulates the gut microbiota and immune function in a dextran sulphate sodium -induced colitis rat model

Reviewer’s code: 00506397

Reviewer’s country: United States

Science editor: Xue-Jiao Wang

Date sent for review: 2018-04-13

Date reviewed: 2018-04-25

Review time: 12 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input checked="" type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input 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 checked="" 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

SPECIFIC COMMENTS TO AUTHORS

Microbial dysbiosis is an important factor in the pathogenesis of inflammatory bowel disease including ulcerative colitis (UC). Xiao-Mei Wang et al., show that moxibustion treatment for 7 days significantly restored the colonic mucosa and reduced submucosal



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inflammatory cell infiltration in rats eliciting UC, caused by intake of dextran sulphate sodium from drinking water. The salutary effects of moxibustion on colitis were mediated via concomitant restoration of healthy gut microbiota and altered expression of cytokines associated with pro- and anti-inflammatory states. Specifically, moxibustion therapy led to reduced alpha diversity of the microbiome, associated with altered ascorbate, aldarate and amino acid metabolism. The authors concluded that alleviation of UC by moxibustion was mediated via its ability to alter the gut microbiome and intestinal mucosal immunity. Although the findings reported in this manuscript support the overall conclusion, the authors need to address a number of concerns as outlined below: 1. The Abstract and Core Tip sections must be carefully revised to indicate that the salutary effect of moxibustion treatment was restricted to 7-day regimen and that 14-day treatment fared far worse. Also, the authors should more SUCCINCTLY state their cytokine expression data in both Abstract and Core Tip sections. The Abstract should convey the central message of this work without burdening the readers with the details of the PCR and ELISA data, and statistics. 2. The authors need to outline the experimental methodology more clearly. For example, with regard to the model of UC developed with 7 days of 4% DSS administered in drinking water, authors need to explain in Materials and Methods why it was necessary to keep giving rats 1% DSS in their drinking water? Was the quality and quantity of UC different in the absence of continued presence of DSS in water? 3. How did the authors determine histopathological scores (shown in Fig. 3). The colonic tissue sections, stained with H&E shown in Fig. 2 should be labelled (with arrows or other markers) to indicate key features that reveal differences in the healthy tissue versus abnormal tissue architecture seen in UC with or without treatment. 4. Figure Legends need to be more clearly described so the reader can understand the intended explanation of the data contained in the Figures. As an example, it would be helpful for the reader if arrows or some other



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markers indicated the change pointed out by the authors (infiltration of mononuclear cells or disorganized glands) in Figure 2. 5. The authors should make judicious use of abbreviations throughout the manuscript, without unnecessary repetition. For example, OC in the Core Tip and other sections of the manuscript. 6. The Method of collection of blood plasma is unclear as written "Blood plasma were collected by abdominal aortic." Please clarify this. 7. In the Discussion, authors write that "This finding suggests that short-term (7 day) but not long term (14 day) moxibustion treatment may significantly affect the gut microbiome." What is the possible explanation of this suggestion and what type of experimental strategies will be able to discern the mechanism of this difference? Do the quality/quantity of the evolving microbiome and its metabolic consequences (between days 7 and 14) in the GI tract support this suggestion? Please speculate why longer duration of treatment is not helpful and put this observation in a proper context of previously published observations.

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