



PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 45484

Title: Unconjugated bilirubin alleviates experimental ulcerative colitis by regulating intestinal barrier function and immune inflammation

Reviewer’s code: 04025483

Reviewer’s country: Germany

Science editor: Jia-Ping Yan

Date sent for review: 2019-01-04

Date reviewed: 2019-01-04

Review time: 5 Hours

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 type="checkbox"/> Grade B: Minor language	(High priority)	<input 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 checked="" 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 checked="" type="checkbox"/> Major revision	<input checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

In this work, Zheng and co-workers assessed the role of unconjugated bilirubin (UCB) in the intestinal barrier function and immune inflammation in a mouse model of colitis (DSS colitis). Among their findings, the authors observed that treatment of colitic mice



**Baishideng
Publishing
Group**

7041 Koll Center Parkway, Suite
160, Pleasanton, CA 94566, USA
Telephone: +1-925-223-8242
Fax: +1-925-223-8243
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

with UCB, administered via gavage, led to an amelioration of colitis as assessed by disease activity scoring, body weight change, colon lengths and spleen weight. Further, UCB treatment led to an inactivation of the proteases trypsin and chymotrypsin, an increased expression of the tight junction protein occluding as well as a decreased serum expression of D-lactate, indicative of a restoration of intestinal permeability. Finally, the authors provide first evidence that UCB can inhibit the production of pro-inflammatory cytokines (TNF, IL1 β) and the TLR4-MyD88-TRAF6-NF- κ B signaling pathway. Major concerns: 1) Please clearly indicate the number mice used for every experiment and add this information to the respective figures 2) In addition to measuring serum D-lactate, did the authors also check for DAO? In addition to these indirect evidence, the authors should also make attempts to directly visualize restoration of the intestinal barrier e.g. via the use of fluorescently labeled dextran. 3) Why was UCB administered via Gavage and not by enema? Also, why was this dose chosen? Did the authors perform dosing curves prior to the experiments that are actually shown? 4) The authors should also analyze the role of UCD in chronic DSS colitis. If they could show that UCB can ameliorate also chronic DSS and eventually carcinogenesis (AOM-DSS model), this would tremendously increase the significance of their findings 5) The authors state that they have shown in prior studies that UCB can ameliorate the inflammation in trinitrobenzenesulfonic acid (TNBS)-induced colitis. However, the reference provided here is not correct. Please check and provide the correct reference. Minor concerns: 1) Figure 1 C: please add labeling to indicate which colon belongs to which treatment group 2) Language polishing both in style and grammar is necessary prior to publication

INITIAL REVIEW OF THE MANUSCRIPT

Google Search:

[] The same title



**Baishideng
Publishing
Group**

7041 Koll Center Parkway, Suite
160, Pleasanton, CA 94566, USA
Telephone: +1-925-223-8242
Fax: +1-925-223-8243
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

Duplicate publication

Plagiarism

Y] No

BPG Search:

The same title

Duplicate publication

Plagiarism

Y] No



PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 45484

Title: Unconjugated bilirubin alleviates experimental ulcerative colitis by regulating intestinal barrier function and immune inflammation

Reviewer’s code: 02821831

Reviewer’s country: Algeria

Science editor: Jia-Ping Yan

Date sent for review: 2019-01-21

Date reviewed: 2019-01-23

Review time: 11 Hours, 2 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 checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input checked="" type="checkbox"/> Yes
			<input type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

Interesting study. The authors must add in introduction the involvement of Pro Inflammntory cytokine and Nitric oxide in inflammatory proces in IBD (Rafa etal, 2013, Soufli et al,2016) The eventual modulation of inflammatory pathway



**Baishideng
Publishing
Group**

7041 Koll Center Parkway, Suite
160, Pleasanton, CA 94566, USA
Telephone: +1-925-223-8242
Fax: +1-925-223-8243
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

(TL4/NFKB) by probiotic agents needs some attention in by the authors(Toumi et al, 2014); The results are well argued; The clinical relevance of the study must be added in section Discussion

INITIAL REVIEW OF THE MANUSCRIPT

Google Search:

- The same title
- Duplicate publication
- Plagiarism
- No

BPG Search:

- The same title
- Duplicate publication
- Plagiarism
- No



PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 45484

Title: Unconjugated bilirubin alleviates experimental ulcerative colitis by regulating intestinal barrier function and immune inflammation

Reviewer's code: 03479673

Reviewer's country: India

Science editor: Jia-Ping Yan

Date sent for review: 2019-01-21

Date reviewed: 2019-01-28

Review time: 3 Hours, 7 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 type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input checked="" 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

I want to congratulate the whole your team for excellent and well planned study. As narrated in your study about novelty of this particular study question, it is worthwhile to seek answers of your questions in such a systematic and scientific manner. As if this



**Baishideng
Publishing
Group**

7041 Koll Center Parkway, Suite
160, Pleasanton, CA 94566, USA
Telephone: +1-925-223-8242
Fax: +1-925-223-8243
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

study takes proper shape in future research, I am sure it may give us a new direction in treatment and prevention of ulcerative colitis. Before accepting for publication there are few things which I would like to know. 1) How many mice were in each group? 2) How did you randomize these mice to particular group? And at what timeline of study randomization was done? 3) What was the calculated sample size you derived from the statistical calculation? And how did you calculate the same? 4) Blinding of the analyst was done or not? 5) Were the mice in all groups matching in their characteristics before starting the study intervention? Please provide the asked data in tabular form as well as in methods and results section. Then we can go ahead with your publication after this revision. And please recheck your manuscript for minor spelling errors again, as there are few. Thank you very much for submitting your work.

INITIAL REVIEW OF THE MANUSCRIPT

Google Search:

- The same title
- Duplicate publication
- Plagiarism
- No

BPG Search:

- The same title
- Duplicate publication
- Plagiarism
- No