

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 33218

Title: Solid lipid nanoparticles delivering anti-inflammatory drugs to treat inflammatory bowel disease: effects in an in vivo model

Reviewer's code: 02411089

Reviewer's country: Turkey

Science editor: Ya-Juan Ma

Date sent for review: 2017-02-10

Date reviewed: 2017-02-17

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input checked="" type="checkbox"/> Grade A: Excellent	<input checked="" 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 checked="" type="checkbox"/> No	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		BPG Search:	<input 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

Congratulations on your work and paper. They are both valuable. I'd just suggest the review of the study by a pharmacologist.

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 33218

Title: Solid lipid nanoparticles delivering anti-inflammatory drugs to treat inflammatory bowel disease: effects in an in vivo model

Reviewer's code: 02439036

Reviewer's country: Spain

Science editor: Ya-Juan Ma

Date sent for review: 2017-02-10

Date reviewed: 2017-03-05

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 checked="" type="checkbox"/> Grade B: Very good	<input checked="" 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"/> Duplicate publication	
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	<input checked="" type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor		<input 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

Dianzani et al reported the effects of co-loaded dexamethasone and butyrate in SNL on the in vitro inflammatory response and in an in vivo DSS-IBD model. Manuscript is well written, figures are precise and the idea is of great interest in the field. However, further clarifications should be approached to improve the quality of the manuscript. Major comments: 1) It is intriguing that same authors have previously analyzed the effect of dexamethasone –SNL and butyrate –SNL in a clinical trial (Serpe et al. European Journal of Pharmaceutical Sciences:39 (2010)) but they have not done the same comparison here. According to their experience and also the material availability, the comparison between DX –SNL , Butyr –SNL and DX+Butyr –SNL could have provided a more relevant conclusion. Otherwise, the combination of DX and Butyrate without nanoparticles could have also provided interesting information. In the current manuscript, it is not clear whether the effect is due to the combination of the two drugs or the presence of the nanoparticle. 2) The in vitro and in vivo effects of DX, Butyrate and DX+Butyrate –SNL



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on cytokines is not the same. Could they discuss further this point. 3) It would be of interest to show gut-tissue images from the DSS-mice treated with DX, with Butyrate and with the DX+Butyrate—SNL 4) Do the authors have any further information about the modulation of CAM proteins in HUVEC? Minor comments: Please correct some misspelling words

PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 33218

Title: Solid lipid nanoparticles delivering anti-inflammatory drugs to treat inflammatory bowel disease: effects in an in vivo model

Reviewer's code: 02984371

Reviewer's country: Canada

Science editor: Ya-Juan Ma

Date sent for review: 2017-02-23

Date reviewed: 2017-03-15

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 checked="" 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 checked="" 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 checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

Name of Journal: World Journal of Gastroenterology ID: 02529335 Manuscript Type: Frontier Solid lipid nanoparticles delivering anti-inflammatory drugs to treat inflammatory bowel disease: effects in an in vivo model Review General comments: This is a very interesting article discussing a novel drug delivery using of dexamethasone cholesteryl butyrate solid lipid nanoparticles in in vitro and in vivo models. In vitro analysis of cell adhesion of inflammatory cells and cytokine production was performed. In vivo analysis of mice with colitis was performed. Abstract/core tip/introduction: Extensive English language editing needed Introduction: Important to discuss budesonide MMX and how this delivery mechanism is different, including advantages and disadvantages. It is not common knowledge that Butyrate monotherapy is effective in IBD. Please elaborate on the data behind this statement (i.e. Butyrate use in clinical trials in human subjects) Unclear statement, please elaborate "SLN have been proposed as a rational, effective and economic system to improve



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butyrate therapy[28-30]. Their use in cancer therapy has been already figured out in preclinical and clinical trials” Statement of study aim: would make separate paragraph within introduction Would be more specific that just “in vitro” “in vivo”. What type of in vitro/in vivo models? Methods: Extensive English language and spelling errors must be corrected. Meaning of abbreviations HUVEC and PBMC must be outlined in the text. What type of patients were HUVEC extracted from. Their characteristics should be outlined. Where were the experiments done? and over what time period?, which years? Must be explicit in text. In vitro cell adhesion assay: Please explain logic for using to incubate cells with IL-1B instead on TNF. TNF is well know to be implicated in IBD and its blockade is, so far, a cornerstone of therapy. In vivo model of colitis: It is not clear why only the colitis induced mice received sterile phosphate-buffered saline solution. Please clarify. How many mice in each group? Results: Language editing needed Must explain jurkat cells relevance in the methods Cell adhesion: should use comparative statistical analysis between different drugs used for continuous variable (% inhibition of cell adhesion) In vitro cytokine production: should provide P values for statistical comparison In Vivo models Should mention numbers when discussing comparisons of reductions in DAI (i.e X% vs Y% $p=z$) When animals were sacrificed, were colonic specimens examined? This would be interesting to compare. Discussion: Language editing needed Should discuss why no significant differences in in vitro assays was seen at higher concentrations Please discuss limitations of study