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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
Manuscript NO: 36732
Title: FO alleviates liver injury induced by intestinal IR via AMPK/SIRT-1/Autophagy pathway
Reviewer's code: 00506276
Reviewer's country: Poland
Science editor: Ke Chen
Date sent for review: 2017-11-07
Date reviewed: 2017-11-10
Review time: 3 Days

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[Y] Grade A: Priority publishing	Google Search:	[ ] Accept
[ ] Grade B: Very good	[ ] Grade B: Minor language polishing	[ ] The same title	[ ] High priority for publication
[Y] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] Duplicate publication	[ ] Rejection
[ ] Grade D: Fair	[ ] Grade D: Rejected	[ ] Plagiarism	[ ] Minor revision
[ ] Grade E: Poor		[Y] No	[Y] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

In this study authors demonstrate that fish oil has protective effect in liver injury induced by intestinal ischemia-reperfusion in vivo as well as on hepatocyte HepG2 injury induced by LPS in vitro. In vivo, fish oil improved liver histology and liver enzyme activities, increased AMPK phosphorylation and SIRT-1 expression, increased the expression of autophagy markers, and reduced serum TNF-alpha and liver MDA concentrations. In vitro, fish oil attenuated LPS-induced injury of HepG2 cells by improving AMPK-SIRT-1 signaling. Together, the data suggest that fish oil-contained n-3 PUFAs exert the protective effect by activating AMPK-SIRT-1 pathway and improving autophagy. The topic is interesting and a lot of results are presented. However, there are also some important concerns. 1) It would be reasonable to include additional group of rats receiving FO but not subjected to I/R procedure.

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Intraperitoneally injected fish oil could have some effects on the signalling pathways of interest also in healthy rats. 2) Why fish oil was administered intraperitoneally? Oral administration would be more reasonable if clinical/therapeutic implications are considered. In addition, it could not be excluded that ip. administered FO has some local irritating/proinflammatory effects. It would be convenient to compare the effects of FO with that of other lipid suspensions. 3) FO was administered before I/R injury. It is unlikely to reproduce this schedule in patients. Protective effect of FO administered during/after I/R would be more promising. 4) Some details about MDA assays should be provided. What method)colorimetric?, HPLC?) was applied? How specific was the method for MDA itself vs. other lipid peroxidation products? Were any antioxidants added during tissue processing to prevent lipid peroxidation in vitro? 5) In vivo studies were performed in the rat whereas in vitro experiments in human HepG2 cells. Were antibodies used for Western blotting species-specific or the same antibodies used in both sets of experiments? According to current description, only one antibody was used for each protein which raises concerns about their species specificity. The name of secondary antibodies should also be specified. 6) Was total AMPK measured or only phospho-AMPK? 7) qRT-PCR: it is stated that RNA was isolated from lungs; why? How the results of qRT-PCR were calculated? 8) According to Fig. 5 SIRT-1 siRNA and AMPK siRNA have similar effect on SIRT-1 and Beclin expression but aSIRT-1 siRNA had greater effect on TNF and MDA. This suggests that the mechanism of the effects of AMPK and SIRT-1 only partially overlap, and that autophagy itself does not mediate all the protective effects of SIRT-1. This issue should be discussed. 9) Both SIRT-1 and AMPK siRNAs abolish injury-induced up-regulation of the respective proteins but have no effect on their baseline levels (in the absence of injury). This observation is surprising; gene knockdown should reduce baseline level of the respective protein. 10) Protective effect on the liver could be secondary to reduced injury of the intestine as evidenced by histology results. Thus, the effect of FO on the liver could be the indirect one. Minor comments: 1) The abbreviation “FO” should be replaced by full name in the title. 2) “MDA activity” should be changed to “MDA concentration”. 3) It is unclear what is actually presented on figure 4 left bottom panel. One cannot measure “p-AMPK mRNA”. AMPK phosphorylation is the post-translational modification; mRNA encodes AMPK irrespectively of its later phosphorylation.

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
Manuscript NO: 36732
Title: FO alleviates liver injury induced by intestinal IR via AMPK/SIRT-1/Autophagy pathway
Reviewer's code: 00069015
Reviewer's country: China
Science editor: Ke Chen
Date sent for review: 2017-11-07
Date reviewed: 2017-11-13
Review time: 6 Days

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[ ] Accept
[ ] Grade B: Very good	[Y] Grade B: Minor language polishing	[ ] The same title	[ ] High priority for publication
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[ ] Grade E: Poor		[Y] No	[Y] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

1. In the Introduction section, the authors should briefly introduce the circumstance of clinical treatment for liver injury induced by intestinal IR, and compare the therapeutic effect of FO to the drugs already in use. 2. In the section of Results 3.1, paragraph 1, line 3, the authors said "the damage of liver was significantly improved by pretreating with FO emulsion, and the histopathological score was significantly reduced compared with the I/R group", which was inconsistent with the results exhibited in Fig. 1. 3. The paper proved that FO can alleviate liver injury induced by intestinal IR. To prove this protective function was dependent on AMPK/SIRT-1/Autophagy pathway, the authors should exhibit more evidence to confirm it. 4. The authors should label each figure clearly, such as the results of histopathological analysis in Fig.1 and western blot analysis in Fig 3, Fig. 4 and Fig 5. 5. The quality of western bolt analysis in this paper

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should be improved. 6. There are some grammatical and spelling errors. Please modify.