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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Hepatology

ESPS manuscript NO: 17589

Title: Systematic Review: Preventive and Therapeutic Applications of Metformin in Liver Disease

Reviewer's code: 00043980

Reviewer's country: United States

Science editor: Yue-Li Tian

Date sent for review: 2015-03-16 09:08

Date reviewed: 2015-04-11 22:47

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 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 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 type="checkbox"/> No	

COMMENTS TO AUTHORS

We have examined this new review article. Our comments for the authors are summarized below.

Methods: It is unclear how the authors chose Hepatitis B, Hepatitis C, NAFLD, HCC, and cholangiocarcinoma as the diseases that were reviewed, when considering the prevalence of alcoholic cirrhosis. In NAFLD: the metformin biochemical explanation is longer than necessary and takes away from the important points of the review article. Paragraph starting with "In the pediatric context as well...", please indent start of paragraph. Hepatitis B: Statement of "although, no clinical studies exist, it may be that metformin is beneficial in insulin-resistant patients with HBV" is contradictory and perhaps better worded as "based on in vitro studies, metformin may have potential benefit for patients with hepatitis B, however clinical trials are needed to further explore this therapy."

Hepatic Malignancies: Please indent first sentence of first paragraph starting with "The PI3K/Akt/mTOR pathway is often..." Please indent sentence starting with "In already-diagnosed HCC, the clinical literature..." "...literature is sparse. A retrospective clinical study determined that in patients with already-established HCC, though duration of exposure prior to diagnosis was not



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available" unclear what this sentence is trying to say. Paragraph starting with: "Physicians are often hesitant to use metformin in cirrhotic pateints..." please indent start of paragraph. Suggest changing sentence "Hence, using metformin as a chemopreventive agent against HCC is very reasonable in patients with chronic liver disease" to "Hence, using metformin as a chemopreventive agent against HCC is a reasonable option in patients with chronic liver disease". Conclusion: Please indent start of paragraph.



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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Hepatology

ESPS manuscript NO: 17589

Title: Systematic Review: Preventive and Therapeutic Applications of Metformin in Liver Disease

Reviewer's code: 01562153

Reviewer's country: Taiwan

Science editor: Yue-Li Tian

Date sent for review: 2015-03-16 09:08

Date reviewed: 2015-03-25 20:41

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 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		[Y] No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

Metformin is the most commonly prescribed medication in the treatment of type 2 diabetes mellitus. Recently, the use of metformin has shown potential as a preventive and therapeutic agent for a broad spectrum of conditions, including liver disease and hepatic malignancies. In this systematic review, the authors analyze the literature behind the potential use of metformin across the spectrum of liver disease and malignancies. They concluded that there is insufficient evidence to recommend use of metformin in the adjunctive treatment of chronic liver diseases including non-alcoholic fatty liver disease and hepatitis C, and that there is good evidence for a chemopreventive role against hepatocellular carcinoma among patients with diabetes and chronic liver disease. Thus, the authors suggested that metformin should be continued in patients even with cirrhosis to provide this benefit. This manuscript was well prepared. The references were well reviewed and discussed. Thus, this article could offer useful information to the clinicians for managing liver diseases.



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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Hepatology

ESPS manuscript NO: 17589

Title: Systematic Review: Preventive and Therapeutic Applications of Metformin in Liver Disease

Reviewer's code: 00070897

Reviewer's country: China

Science editor: Yue-Li Tian

Date sent for review: 2015-03-16 09:08

Date reviewed: 2015-04-14 15:15

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 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
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<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> No	<input type="checkbox"/> Major revision
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		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> No	

COMMENTS TO AUTHORS

The authors reviewed metformin effects in various liver diseases. This is very helpful for future research and the potential applications of metformin in liver disease.



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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Hepatology

ESPS manuscript NO: 17589

Title: Systematic Review: Preventive and Therapeutic Applications of Metformin in Liver Disease

Reviewer's code: 01518980

Reviewer's country: United States

Science editor: Yue-Li Tian

Date sent for review: 2015-03-16 09:08

Date reviewed: 2015-04-22 21:52

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 checked="" type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
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<input type="checkbox"/> Grade E: Poor		[Y] No	<input checked="" type="checkbox"/> Major revision
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		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

Specific comments 1. The review should start with a general review of the actions of metformin and not a description of NAFLD development which is not relevant to the topic. 2. The word adipokine is used when in fact the correct word is adiponectin. 3. The review needs to be carefully edited for a large number of grammatical and typographical errors, inconsistent formatting, incomplete sentences and a reference list replete with errors.



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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Hepatology

ESPS manuscript NO: 17589

Title: Systematic Review: Preventive and Therapeutic Applications of Metformin in Liver Disease

Reviewer's code: 00186136

Reviewer's country: Brazil

Science editor: Yue-Li Tian

Date sent for review: 2015-03-16 09:08

Date reviewed: 2015-04-07 04:08

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input checked="" 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
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		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

The manuscript is well written and very interesting