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ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 7338

Title: MK-0626, a selective DPP-4 inhibitor, attenuates hepatic steatosis in ob/ob mice

Reviewer code: 00542353

Science editor: Gou, Su-Xin

Date sent for review: 2013-11-14 17:24

Date reviewed: 2013-12-05 22:32

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input checked="" type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<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"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)		BPG Search:	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input checked="" type="checkbox"/> Minor revision
		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

COMMENTS TO AUTHORS

In the present study Ohyama et al evaluated in vivo effects and mechanism of action of a DPP-4 inhibitor (MK-0626) on hepatic steatosis in ob/ob mice. The major finding of this experimental study was that MK-0626 attenuated liver steatosis. Interestingly authors demonstrated that this effect is not due to a decrease in food intake and/or body weight. They suggested that possible mechanisms are the inhibition of hepatic lipogenic gene expression, the enhancement of triglyceride secretion from the liver and the increase of serum adiponectin levels. Although some other studies already demonstrated effects of DPP-4 inhibitors in the prevention of liver steatosis, in this study authors evaluated several potential underlying mechanisms. This is a very interesting study about a field of growing interest. The study design is clear and adequate for the aim. Results are very well presented and are consistent with methods. Conclusions are supported by data. Some minor changes are needed: 1. Please consider to report a recent study supporting your findings (Akaslan SB et al *Metab Syndr Relat Disord.* 2013 Aug;11(4):243-50) 2. The evidence of the effect on adiponectin levels has been already reported (*Clin Sci (Lond).* 2010 Jun 8;119(6):239-50). This study should be cited. 3. Overall, some data on this issue already exist. Thus, authors should further stress more innovative aspects of their study.



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ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 7338

Title: MK-0626, a selective DPP-4 inhibitor, attenuates hepatic steatosis in ob/ob mice

Reviewer code: 02822536

Science editor: Gou, Su-Xin

Date sent for review: 2013-11-14 17:24

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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	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"/> Existed	<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"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	<input type="checkbox"/> Grade D: rejected	BPG Search:	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> Existed	<input type="checkbox"/> Minor revision
		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

COMMENTS TO AUTHORS

Incretin analogues are being increasingly used in type II diabetic patients. One of the beneficial effects that have been detected with these molecules are related to the hepatic alterations provoked by insulin-resistance, that are steatosis and nonalcoholic steatohepatitis (NASH). There is enough evidence to support that, but there isn't sufficient knowledge about the pathophysiological mechanisms that are involved In this manuscript the authors tried to elucidate which are the possible mechanisms implicated, conducting an experimental research in steatotic ob/ob mice, treated with MK-0626, a selective DPP-4 inhibitors. They concluded that the enhancing AMPK activity (that express increased cellular energy) results in an inhibition of hepatic lipogenic gene expression. I think that it is an elegant experimental model that has to be considered for publication. I only have minor considerations: In the introduction, there have to be substituted "Other symptoms of metabolic....." by " Other comorbidities of metabolic.....". I think is more correct In the summary paragraph, another substitution should be " ...an effective strategy for patients with hepatic steatosis" by "an effective strategy for patients with hepatic steatosis induced by type II diabetes" In table 2, in the lean mice group, there are a very low levels of plasma insulin and HOMA-score. Do the authors can explain these results?