

ESPS PEER REVIEW REPORT

Name of journal: World Journal of Hepatology

ESPS manuscript NO: 12723

Title: Therapeutic approach for non-alcoholic fatty liver disease: focus on drug mechanism and treatment outcome

Reviewer code: 02444976

Science editor: Ling-Ling Wen

Date sent for review: 2014-07-25 20:34

Date reviewed: 2014-08-05 15:04

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 checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> Existing	<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"/> 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"/> Existing	<input checked="" type="checkbox"/> Minor revision
		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

COMMENTS TO AUTHORS

The authors have written a review on drug mechanism and treatment outcome in NAFLD. The paper is well written but needs minor English review. I have several comments regarding specific drugs: Pioglitazone- there is a concern re this class of drugs concerning risoglitazone and an increase in cardiac mortality. Metformin-the authors should consider a comment that there is no evidence of an effect on hard clinical end-points such as mortality Vitamin E-the authors should insert a comment that it is recommended for treatment in non-diabetics since in diabetics there are concerns re an increase in mortality in diabetics. Lipid-lowering- I think there is a need to mention that initial resistance to using statins due to a concern following reports of hepatic side-effects with early statins . There is now sufficient data from real world use of statins to confirm that hepatotoxicity is extremely rare. Clistazol- I suggest the authors include a reference showing a decrease in hepatic steatosis, inflammation and fibrosis in a CDAA mouse model. Fujita et al Gut 2008;57:1583-91. PUFA-I suggest they cite in addition a good review by Bouzianis et al Nutr Rev 2013;71:753-71. MUFA-there is evidence that a high MUFA diet attenuates hepatic steatosis in obese rats. Hak et al Prostaglandins Leukot Essent fatty Acids 2013;89:301-40.

ESPS PEER REVIEW REPORT

Name of journal: World Journal of Hepatology

ESPS manuscript NO: 12723

Title: Therapeutic approach for non-alcoholic fatty liver disease: focus on drug mechanism and treatment outcome

Reviewer code: 02715281

Science editor: Ling-Ling Wen

Date sent for review: 2014-07-25 20:34

Date reviewed: 2014-08-06 12:52

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"/> Existing	<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"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair		BPG Search:	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Existing	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

no

ESPS PEER REVIEW REPORT

Name of journal: World Journal of Hepatology

ESPS manuscript NO: 12723

Title: Therapeutic approach for non-alcoholic fatty liver disease: focus on drug mechanism and treatment outcome

Reviewer code: 02444760

Science editor: Ling-Ling Wen

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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 checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> Existing	<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"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input checked="" type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

The manuscript of 'Therapeutic approach for non-alcoholic fatty liver disease: focus on drug mechanism and treatment outcome' reviews the pathogenesis and treatment of non-alcoholic fatty liver disease (NAFLD), with the emphasis on drug mechanisms and therapeutic outcome. Being summarized by this review, insulin resistance (IR), oxidative stress, and adipokine-based inflammation take the central place in the spectrum of NAFLD, especially non-alcoholic steatohepatitis (NASH). Thiazolidinedione, Metformin, Vitamin E, Pentoxifylline, Fibrates, Ezetimibe, and other options (i.e., Cilostazol, polyunsaturated fatty acids (PUFAs), monosaturated fatty acids (MUFAs)) serve as effective agents for the therapy of NAFLD. These results add a new level to our knowledge about NAFLD, and may be valuable for both experimental research and clinical interference of this ever-growing disease. Major comments 1. As described by the review, 'The pathogenesis of NAFLD development is closely associated with insulin resistance and dyslipidemia, especially hypertriglyceridemia', and 'Increased serum levels of free fatty acid (FFA) and glucose can cause oxidative stress in the liver.....and lead to ectopic fat accumulation, especially in the liver.' These mechanisms related to two-hit hypothesis have already been well established by previous reviews. However, some novel pathological disorders that underlie NAFLD, such as gut microbial alternation, gut-liver crosstalk, endoplasmic reticulum stress, and TLR/MyD88 signaling-mediated innate immune response, are not mentioned. 2. Drug-based treatment of NAFLD reflects the other



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topic of this review. Both mechanisms and outcome of TZDs, Metformin, Vitamin E, Pentoxifylline, Fibrates, and Ezetimibe has been detailedly discussed. But this review seems to ignore some up-to-date progression in this field. For example, GLP-1 has recently been uncovered, both experimentally and clinically, to serve as important regulator of serum glucose, dyslipidemia, and NAFLD. Minor comments 1. Secondary Title, which explains the pathogenesis (insulin resistance - FFA flux and hyperinsulinemia, role of oxidative stress - Mitochondrial dysfunction, inflammation and adipokines) and different therapeutic drugs, is suggested in the text.