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Wan Chai, Hong Kong, China

ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 6598

Title: Effects of resveratrol and other polyphenols in hepatic steatosis

Reviewer code: 02526292

Science editor: Ma, Ya-Juan

Date sent for review: 2013-10-25 19:31

Date reviewed: 2013-10-28 01:55

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"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

The manuscript by Aguirre et al makes the remarkable attempt to summarize all is known about the effects of resveratrol and other polyphenols on hepatic steatosis. The manuscript is well structured, with distinct in vitro and in vivo (rodents) sections orderly presented. Also, 1 study on humans is presented. The manuscript suffers of few conceptual flaws and lacks of insight, which need to be addressed. Specific comments: - page 4: NAFLD definition excludes alcohol consumption. Alcohol consumption gives rise to AFLD. NAFLD and AFLD are distinct clinical entities, although histologically similar. Re-phrase. - pages 4-5: the "two-hit" hypothesis of Chris Day is old and now completely outdated, since the discovery that the major trigger for NAFLD to NASH development is played by the the gut microbiota and inflammatory infiltrates annexed (see for short summary Podrini C et al. Curr Pharm Des 2013). Re-write this part. - page 5: genetic factors contributing to NAFLD are starting to be understood (PNPLA3 etc) and could be briefly discussed (see Anstee QM, Nat Rev Gastroenterol Hepatol 2013) - on page 7 a classification of polyphenols is offered in details. On page 8, resveratrol is presented simply as a phytoalexin and this category does not fall among the ones presented in page 7. - Tables: it would be useful, together with reporting the first author of the studies also the reference number. It eases the reading. - Throughout the manuscript, several studies are described in which resveratrol activates SIRT1 and/or AMPK. Activation does not mean that SIRT1/AMPK mediate the effect of resveratrol. Mediating the effects means that if you block/inhibit SIRT1 and/or AMPK resveratrol does not have an anti-lipidogenic effect in the liver. I don't have time to do this for the authors, but they should go through each study they cite on this and state things correctly according to what has been done experimentally. Activation does not mean mechanism in biology/medicine. - page 13: "clearly lower" repeated twice - Rafa de Cabo has



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done much deal of study on the effect of resveratrol on rhesus monkeys. Authors should check these publications to describe if liver effects were reported therein. - human studies on resveratrol: authors must also report negative data : "Resveratrol supplementation does not improve metabolic function in nonobese women with normal glucose tolerance." Yoshino J, Cell Metab 2012 - delipidating is a very odd term. Better to use anti-lipidogenic?



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Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 6598

Title: Effects of resveratrol and other polyphenols in hepatic steatosis

Reviewer code: 00009616

Science editor: Ma, Ya-Juan

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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	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"/> 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"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

Nil



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ESPS Peer-review Report

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Reviewer code: 00542353

Science editor: Ma, Ya-Juan

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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 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 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"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

In this interesting review, Aguirre et al evaluated major literature data about effects of resveratrol and other polyphenols in the prevention of hepatic steatosis. The review is well written. As highlighted by Authors, most of data derive from in vitro studies and animal studies and major results are that polyphenols present hepatoprotective effects because they reduce liver fat accumulation and decrease oxidative stress and inflammation. Some points need to be addressed:

1. Major limitation of the present review is that criteria for searching strategy of literature are not reported. In particular, considering that there is a lack of data on humans, a complete report of literature on in vitro and animal studies is mandatory. Authors should include in the text a "searching strategy" paragraph and they should update the review with all available data on this issue.
2. In the introduction section, describing major complications correlated to NAFLD, Authors mainly focused the attention on the risk of hepatocarcinoma. However, some details about the link between NAFLD and venous/arterial thrombosis should be reported.
3. Wine is one of the most important sources of resveratrol. Your data suggest that resveratrol is able to reduce liver weight, triacylglycerols and oxidative stress. However, wine intake is one of the major causes of hepatic disease establishment and evolution. Studies on cardioprotective effects of alcohol suggest that different dosages and different pattern of drinking are able to led to opposite effects (Semin Thromb Hemost. 2011;37:875-84). Authors should discuss this aspect also for NAFLD.