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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
ESPS manuscript NO: 15795
Title: Biological evaluation of Geranium schiedeanum, a new hepatoprotective agent against the toxic action of ethanol during liver regeneration
Reviewer's code: 00002232
Reviewer's country: Spain
Science editor: Ya-Juan Ma
Date sent for review: 2014-12-09 09:04
Date reviewed: 2014-12-16 22:10

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
[Y] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] Duplicate publication	[ ] Rejection
[ ] Grade D: Fair	[ ] Grade D: Rejected	[ ] Plagiarism	[Y] Minor revision
[ ] Grade E: Poor		[Y] No	[ ] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

Madrigal-Santillán et al. investigated the protective effect o an extract of Geranium schiedeanum (exGs) in regenerative livers of rats receiving ethanol as hepatotoxic. For this purpose, the authors measured ALT, AST, albumin, bilirrubin and lipid peroxidation in both plasma and liver. All these parameters were measured in partially hepatectomized rats at day 8 after the surgical procedure. Rats treated chronically with ethanol and exGs showed a significant decrease in mortality, oxidative stress and biochemical parameters of liver damage; compared with rats non treated with exGs. In addition, the treatment with exGs was associated with an increase in liver regeneration. The authors concluded that exGs modulate oxidoreduction processes and enhance liver regeneration in rats with liver damage induced caused by ethanol consumption. The experimental design is appropriate and the subject is clinically relevant. I only have some observations concerning the study. 1)How do the authors explain the regenerative effect caused by exGs? Is it due to an enhacement in hepatocellular hypertrophy, hepatocellular hyperplasy or both? Oxidative stress may modify the activity of signaling pathways involve in both processes. Therefore, experiments assessing changes in the cell

cycle (Ki67, cyclin D, PCNA…) or in hepatocellular cell area at days 0, 2 and 4 would improve the quality of this study. 2)It would be interesting to compare results of hepatocellular apoptosis and/or necrosis in ethanol-treated rats after partial hepatectomy (e.g.: 0, 2 and 4 days) with or without exGs treatment. These results would support more robustly the author's conclusions. 3)The appropriate test for comparison and visualization of mortality is the method of Kaplan and Meier and the comparison of curves with the log-rang test. This statistic strategy provides more information than Student t test and/or ANOVA.

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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
ESPS manuscript NO: 15795
Title: Biological evaluation of Geranium schiedeanum, a new hepatoprotective agent against the toxic action of ethanol during liver regeneration
Reviewer's code: 00225294
Reviewer's country: Spain
Science editor: Ya-Juan Ma
Date sent for review: 2014-12-09 09:04
Date reviewed: 2015-01-26 03:01

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

COMMENTS TO AUTHORS

The work is a preliminary and phenomenologic study of the effect of a potential hepatoprotective extract from Geranium schiedeanum, against ethanol toxicity. Main points: 1. The definition of the extract is of Paramount importance 2. Authors need to provide additional inputs on the hepatoprotection: cyclins involved in cell proliferation, fibrosis and molecular signatures for this (MMPs, TIMs, etc) 3. Molecular markers of inflammation/toxicity due to ethanol. In the absence of these details, it is difficult to establish the scientific relevance of the experimental details given in the manuscript.

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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
ESPS manuscript NO: 15795
Title: Biological evaluation of Geranium schiedeanum, a new hepatoprotective agent against the toxic action of ethanol during liver regeneration
Reviewer's code: 00068007
Reviewer's country: Spain
Science editor: Ya-Juan Ma
Date sent for review: 2014-12-09 09:04
Date reviewed: 2015-01-09 01:05

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
[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

Major points: - The aim of this study is to investigate the hepatoprotective effect of the Gs extract on the toxicity induced by EtOH in partial post-hepatectomy liver regeneration in rat. However, since some of the assayed parameters are altered by partial hepatectomy (without ethanol administration), it is convenient to include a PH-Gs group of rats in this study to separately study the protective effects of Gs extract during liver regeneration in the absence of ethanol. - The authors suggest a probable capacity of the Gs extract to preserve the normal structure of the liver, a histological study of the liver of the animals should be carried out in order to confirm this hypothesis. - Why AST is decreased while ALT is increased in the of liver PH-EtOH rats? - Why is the total antioxidant status increased in liver after partial hepatectomy? - In comparison with the PH and PH-EtOH groups, the total antioxidant status/capacity is increased in the serum but decreased in the liver of PH-Gs-EtOH rats. What is the explanation for this effect? - What is the difference between the total antioxidant status (TAS) measured in serum and total antioxidant capacity (TAC) measured in liver? What is measured in each one? Minor points: - In the conclusion of the abstract: "diminution of free

radicals and a greater presence of antioxidant agents in the samples analyzed." instead of "diminution of free radicals a greater presence of antioxidant agents in the samples analyzed."

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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology
ESPS manuscript NO: 15795
Title: Biological evaluation of Geranium schiedeanum, a new hepatoprotective agent against the toxic action of ethanol during liver regeneration
Reviewer's code: 00225231
Reviewer's country: South Korea
Science editor: Ya-Juan Ma
Date sent for review: 2014-12-09 09:04
Date reviewed: 2015-01-12 15:02

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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		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

This manuscript entitled, "Biological evaluation of Geranium schiedeanum, a new hepatoprotective agent against the toxic action of ethanol during liver regeneration" was designed to evaluate the effect of an extract of Geranium schiedeanum as a potential hepatoprotector agent against the toxicity induced by alcohol in the partial post-hepatectomy liver regeneration model in rat. They showed that administration of the extract significantly reduced the unfavorable effect of ethanol on liver regeneration, the level of enzymes, and the metabolic processes that regulate glucose and lipid levels, as well as the mortality of the animals treated. And they concluded that the effect can be clearly related with the modulation of oxidoreduction processes by agents contained in the extract. The comments are as follows; 1. The hepatic protective function of geranium in livers treated by EtOH after PH is shown to be significant. However, in writing a manuscript, several mistakes are found. 2. Page 7, line 9: In "Total antioxidant concentration (TAC) was determined utilizing the Randox Kit (Randox Laboratories Ltd., U.K.) and is reported in mmol/L.", "Total antioxidant concentration (TAC)' looks like a mistake of "total antioxidant status (TAS)". 3. Page 9, line 2: In "while bilirubin

values increased to 0.11 mg/dL in this group.", "increased" looks like a mistake of "decreased" to see the context. 4. Page 9, line 24: In "Contrariwise, rats of the PH-Gs-EtOH group exhibited a significant diminution in serum as well as in ALT levels,", "a significant diminution in serum as well as in ALT levels" is not properly written. 5. Page 9, line 26: In "On comparing the ALT levels of this group with those of the group adminstered Et,", Et looks like a mistake of EtOH. 6. Page13, line 15: It is needed to show data on "Surprisingly, alcohol administration at early stages of liver regeneration in rats with PH diminishes the serum activity of these enzymes" 7. Page14, line 20: In "The increase in TAS (serum) and in TAC (liver) found in our study is in agreement with that previously cited, indicating that EtOH favors OS in this model, demonstrated by the high TBARS levels found (Figure 4).", looks like mistakes of "The decrease in TAS (serum) and increase in TAC (liver) found in our study is in agreement with that previously cited, indicating that EtOH favors OS in this model, demonstrated by the high TBARS levels found (Figure 5). 8. Why is AST level lowered in PH-EtOH group compared to others in Figure 2 (lower panel)? Discussion is needed. 9. If you have tissues of the experiment, I suggest you to show data on expression level of Ki-67 or PCNA that are markers of liver regeneration.