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Journal Name:	<u>British Journal of Medicine and Medical Research</u>
Manuscript Number:	2013_BJMMR_8559
Title of the Manuscript:	Hepatic Antioxidant Effect of Paroxetine in Rats Exposed to Chronic Restraint Model
Type of the Article	Research article

General guideline for Peer Review process:

This journal's peer review policy states that **NO** manuscript should be rejected only on the basis of '**lack of Novelty**', provided the manuscript is scientifically robust and technically sound.

To know the complete guideline for Peer Review process, reviewers are requested to visit this link:

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PART 1: Review Comments

	Reviewer's comment	Author's comment <i>(if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)</i>
Compulsory REVISION comments	<p>This is, in summary, a paper aimed to investigate the hepatic antioxidant effect of paroxetine in rats exposed to chronic restraint model.</p> <p>The manuscript is interesting and well-conducted; however, some revisions are needed as currently presented. The authors may find as follows my comments/suggestions.</p> <p>Some statements within the Introduction section are too generic and need to be more deeply clarified. For example, the authors stated that selective serotonin reuptake inhibitors were generally preferred over tricyclic antidepressants and monoamine oxidase inhibitors due to lesser adverse effects, good compliance, and comparable efficacy with these older drug groups. First, they are requested to specify whether they refer to animal models or human studies. Also, to more comprehensively support that all existing antidepressant drugs may be comparable in terms of efficacy, the authors may find as follows</p>	<p>1- according to animal studies and human clinical trials</p> <p>1. Many thanks for the references however, Zafir, A., Ara, A., and Banu, N. (2009). In vivo antioxidant status: a putative target of antidepressant action. Prog. Neuropsychopharmacol . Biol. Psychiatry 33, 220–228. doi: 10.1016/j.pnpbp.</p>



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	<p>some useful and detailed studies that may be consulted (Sanchez et al; Int Clin Psychopharmacol. 2014 (in press); Seitz DPet al., Int J Geriatr Psychiatry. 2010; Cipriani et al., J Clin Psychiatry. 2008; Katzman et al., J Clin Psychiatry. 2007; Arroll et al., Ann Fam Med. 2005).</p> <p>Similarly for the following statement in the same section: “Chronic stress exposure is associated with neurodegeneration and a marked change in anti oxidant enzymes”. More details are needed to support this statement.</p> <p>The authors also stated in the Discussion section that paroxetine antidepressant effect against anhedonia-induced by glucocorticoids could be related to suppression of oxidative stress that is associated with dexamethasone administration. The mentioned assumption is quite interesting but needs to be further discussed by the authors. I suggest to develop this statement including specific and more focused evidence.</p> <p>Methods section, the authors should provide a more detailed rationale about their decision to measure at the end of the study, liver transaminases ALT and AST as well as the hepatic levels of GPx, catalase and TBARS in order to test the hepatic antioxidant</p>	<p>2008.11.010</p> <p>2. David D J P , M Bourin, G Jegou, C Przybylski, P Jolliet and A M Gardier (2003). Effects of acute treatment with paroxetine, citalopram and venlafaxine in vivo on noradrenaline and serotonin outflow: a microdialysis study in Swiss mice. Br.J. Pharmacol.,140,1128–1 136</p> <p>Provide me with a lot of information about comparable effects of antidepressants in terms of efficacy and I mentioned them with their supportive information.</p>
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	<p>effect of paroxetine. This is a crucial point that needs to be further addressed in order to improve the way in which the main topic of the present manuscript has been investigated.</p> <p>Discussion section, when the authors mentioned the existing relationship between depression and immune system, they should also cite recent studies about this topic (Mills et al., J Child Psychol Psychiatry. 2013; Serafini et al., Eur Neuropsychopharmacol, 2013; Hashmi et al., J Pak Med Assoc. 2013).</p> <p>Finally, the authors should be more candid in reporting the main limitations of the present study. I suggest to include a separate section in which they may describe the major shortcomings related to the major conclusion of their study. Overall, the assumption that paroxetine possesses an anti-oxidant action that helps in protection of livers of chronic restrained rats is interesting but the mentioned points need to be further developed in order to make the manuscript more easy to follow.</p>	<p>2- I modified the paragraph of stress and mood to be in a possible explanatory form as regards this point.</p> <p>3- I modified the methodology to be in a more possible descriptive form to my aim of the work</p> <p>4- I removed the unnecessary statement about the HPA axis, may be mentioned in another study that will be more concerned to the relationship between stress and immunity.</p> <p>5- I modified the conclusion paragraph</p>
<u>Minor</u> REVISION comments	No further minor revisions.	
<u>Optional/General</u> comments		