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Journal Name:	International Journal of Biochemistry Research & Review
Manuscript Number:	2015_IJBcRR_16387
Title of the Manuscript:	IN VITRO AND IN VIVO EFFECT OF QUERCETIN ON HEPATOCYTE TRANSMEMBRANE N+, K+- ATPase ACTIVITY IN RATS
Type of the Article	Original Research Article

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PART 1: Review Comments

	Reviewer's comment	Author's comment (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)
Compulsory REVISION comments	50 mg/kg weight of animal for in vivo experiment is too high. It can't be correlated with the clinical use of quercetin. PH should be pH Using post 4,000 rpm supernatant and 100-180 ug protein for Na,K-ATPase activity measurement are not justified. High speed post supernatant and minimum amount of protein should be used for the enzyme activity assay. Methods are not clear, need to make is more explicit. Fig.1. Better to show the activity instead of percent activity in the x-axis. Is there any difference between nature of binding of ouabain and quercetin to Na,K-ATPase? Fig. 2. Except IV administration the effect is not significant relative to control. What is the justification of inclusion of all these data.	Thank you for your various comments. We beg to differ that 50 mg/kg body weight animal "is too high" in <i>in vivo</i> experiment. Generally, a casual look of various <i>in vivo</i> animal experiments will reveal that doses higher than 50 mg/kg have and are being used in animal experiments. What determines the dosage in <i>in vivo</i> experiments is the determination of safe dose, which is usually done through preliminary acute toxicity test to determine the LD₅₀. For quercetin in particular, various works have been done that show that quercetin has a very wide safety margin both in laboratory animals and human. 50 mg/kg body weight is still very much within the safety margin of quercetin usage in <i>in vivo</i> animal study. On using post 4,000 rpm supernatant and 100-180 ug protein for Na,K-ATPase activity, we have noticed a typographical error on our part. It ought to read 100-120 ug protein (the correction has been effected). We have also added a reference to justify this (ref 26). The methods we used are standard methods which have been justified by different references. Fig. 1. The use of percent activity for the plotting



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		of graph is justifiable, see reference 27. On the difference in nature of binding of ouabain and quercetin, we will like to say that it is outside the scope of this present study. Fig. 2. Please take a second look at the graph carefully, for it showed that though there were no significant differences among the negative control of the different routes of quercetin administration, but there was significant difference between each route of quercetin administration compared to the corresponding negative control. It also showed significant difference between oral and intraperitoneal, oral and intravenous, and between intraperitoneal and intravenous. Please study the graph, and results and discussion again. Thank you again for your comments.
<u>Minor</u> REVISION comments		
<u>Optional/General</u> comments	Can't be considered in its present form. Needs major revision including new experiments, rewriting methods etc.	We are of the opinion that the methods used in the study are the standard methods with references for justification. The experiments done in this study are enough for the scope of the study. Thank you.