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PART 1:

Journal Name:	British Journal of Pharmaceutical Research
Manuscript Number:	**2013 BJPR 3505**
Title of the Manuscript:	**CHRONIC ANTI-INFLAMMATROY ACTIVITY OF ETHANOLIC EXTRACT OF LEAVES OF CLERODENDRUM VISCOSUM BY CARRAGEENIN INDUCED PAW OEDEMA IN WISTAR ALBINO RATS**

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- This form has total 9 parts. Kindly note that you should use all the parts of this review form.

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PART 2: 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	This study by Chandrashekar and Rao investigates the role of ethanolic extract of the leaves of Clarodendrum viscosum (EELCV) on carrageenin-induced rat paw oedema. EELCV at doses of 75, 150, and 300 mg/Kg was given orally from 10 days before up to 60 min. before carrageenin injection. Indomethacin was used as reference drug. The Authors show that EELCV at highest doses used is able to reduce oedema formation, suggesting that the anti-inflammatory effect is probably due to the presence of phenolic compounds in EELCV. There are several concerns that will need to be addressed. Specific comments are listed below: 1) The Authors stated that (see Results and Discussion, lines 108-110; Conclusion, lines 148-149): "oral administration of EELCV at doses of 150 and 300 mg to Wistar Albino rats showed significant (P=0.01) and moderate anti-inflammatory activity (P=0.05). This sentence is misleading. This is probably due to a misinterpretation of statistical analysis. In fact, ANOVA of the data reported in Table 1 with the Dunnett post hoc test for multiple groups (Graph Pad Instat 3 software) demonstrate that EELCV both at 150 mg/Kg and 300 mg/kg significantly reduced the oedema at 3h by 64% (P<0.01, n=10) and by 46% (P<0.05, n=10) respectively. A significant inhibition was also observed at 4h. The Authors should check the statistical analysis. 2) The data in graph 1 (effects of EELCV at 3h) are different from those reported in table 1 (eg. indomethacin, EELCV 150 mg, etc). The Authors should explain this point. In addition, statistical analysis is missing. 3) The Authors stated: "The peak effect of the carageenin induced paw oedema was observed at the 3rd hr after the injection", see pag. 2 lines 77. This sentence is not correct. The peak was observed at 4h as reported in table 1.	

	4) The Authors reported that the percentage of inhibition of the oedema at 3h was 66.44% and 63.75 at the dose of 150 mg/kg and 300 mg/kg respectively (see abstract). However, different values of inhibition are reported in Results and Discussion (53.19%, and 38.28%). Checking the data of table 1, the percentage of inhibition of EELCV at doses of 150 and 300 mg should be 64% ($P<0.01$, $n=10$) and by 46% ($P<0.05$, $n=10$). 5) There are no data which show the target by which EELCV exerts its effects. Carragennin oedema is a model of non immune acute inflammation mainly sustained by the release of prostaglandins and nitric oxide following the induction of COX-2 and iNOS protein expression in activated leukocytes infiltrated into the carrageenin-injected rat paw (Di Rosa et al., J Pathol, 1971, 104, 15-29; Ialenti et al., Eur J Pharmacol, 1992, 211, 701-706; Salvemini et al., Br J Pharmacol 1996; 118: 829–838). The manuscript could be improved if the Authors demonstrate the effect of EELCV on COX-2/iNOS expression in inflamed paw tissues by Western blot (for example see D'Acquisto et al., Gene Therapy Gene Therapy 2000 7, 1731-1737). 6) Finally, it is well known that the long-term use of anti-inflammatory drugs is associated with significant untoward effects on the gastrointestinal tract (as correctly reported by the Authors). Consequently, the Authors should be performed experiments to verify the effect of chronic administration EELCV on gastric mucosal (for example see Wallace et al., Gastroentrerolgy 1194, 107; 173-179).	
Minor REVISION comments		
Optional/General comments		

Note: Anonymous Reviewer