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Journal Name:	Journal of Pharmaceutical Research International
Manuscript Number:	**Ms_JPRI_42430**
Title of the Manuscript:	**Mechanism of Anticonvulsant Effects of Ethanol Leaf Extract and Fractions of Milicia Excelsa (Moraceae) in Mice.**
Type of the Article	**Original 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.
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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	**The authors investigated anticonvulsant effects of various fractions of Milicia excelsa (welw.) C.C. Berg using 3 models of epilepsy.** **There are several concerns particularly with regards to methods and results** **Introduction: Authors have not provided sufficient evidence to support their hypothesis that Milicia excelsa (welw.) C.C. Berg produces anticonvulsant effects. Evidence to indicate the possible anticonvulsant efficacy of this plant should be included. Are there any studies on isolated chemicals from this plant with pharmacological effects that indicate possible anticonvulsant activity?** **The objectives of this study are not clear. It seems that the 1st part of experiments was designed to screen various fractions for antiepileptic activity and the 2nd to investigate the mechanisms of action. However, all three chemoconvulsants used in this study have well established mechanisms of action. Therefore if the test drug shows efficacy against a particular chemoconvulsant-induced epilepsy the mechanism can be predicted without the 2nd part of the experiment.** **Methodology is very confusing. To test the drug in each of the models there are 5 groups and 3 of them have received test drug (EME) in 3 different doses. Rationale to choose these doses is not stated.** **None of the other fractions (HF, EAF, BF, and AF) were tested under methods 2.5.1, 2.5.2 and 2.5.3, although the objective stated on page 3, lines 44 and 45 is "……..to investigate the anticonvulsant potential of the ethanol leaf extract, 45 HF, EAF, BF, and AF using mice models."** **Study design described to investigate mechanisms of action is extremely poor. Why was AF used instead of other fractions? Line 106 states use of "most active fraction (AF)". How authors reached that conclusion??** **Authors have investigated 3 mechanisms including GABA antagonism, 5-HT antagonism and NOS inhibition. However, it is not clear what prompted authors to explore only these 3 mechanisms. And the mechanisms were investigated only in PTX model, the rationale for which is not stated.** **No control groups with only inhibitors without extract? It appears from table 4, such groups were probably included. If this is true, L-NNA + diazepam group is missing Number of animals per group?** **Results are not at all in line with methods.** **For example:** **3.1 Effects of HF, EME, EAF, BF and AF of Milicia excelsa on…. But the table does not show the effects of HF and method describes only use of EME. Same is true for the results of other models. Methods have stated 5 groups of animals in 2.5.1, 2.5.2 and 2.5.3 but the corresponding results in tables 1, 2 and 3 show 11 groups.** **Table 1, column 4 row 11 shows a value of 1587.5 ± 2125. SEM is bigger than mean. Is it 2125 or 212.5?**	

	Table 3 shows effect of pentobarbitone but corresponding method descriptions states use of diazepam. Diazepam is stated as "DZP" at places and "DPZ" at other places. **Line 223: "Since AF produced consistent anticonvulsant effects in all the convulsion models used" is wrongly stated. No protective effect of AF was seen in SCN model (table 3).** **Line 251-2512 state that the magnitude of activity of the fractions was of the order AF > EAF > HF > BF. Nowhere in the manuscript effects of HF and BF are presented. So how authors reach this conclusion?** **Authors propose that AF acts via three mechanisms that were investigated. However, it is hard to understand how aqueous fraction which is expected to contain all water soluble constituents manages to cross the blood brain barrier and exert the said effects. Authors should provide the explanation for the same.** **The discussion is largely based on the evidence for similar activities of other plants. Authors should rather focus on the extracts investigated, their possible constituents and targeted mechanisms.**	
Minor REVISION comments	There are several grammatical errors that need correction. Some of the results could have been better presented in graphs	
Optional/General comments	The manuscript is poorly written with several inconsistencies particularly with regards to methods and results. The conclusion which states high efficacy of aqueous fraction is hard to understand because aqueous compounds do not easily cross the blood brain barrier.	

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