## Review Form 3

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| Journal Name: | **International Journal of TROPICAL DISEASE & Health** |
| Manuscript Number: | **Ms_IJTDH_130803** |
| Title of the Manuscript: | **Effects of Repeated Oral Administration of Catha edulis Extract on Anxiety-like Behavior and Prefrontal Cortex-Malondialdehyde Level and Sex Differences to the Responses in Mice** |
| Type of the Article | **Original Research Article** |

**PART 1: Comments**

| | **Reviewer's comment** | **Author's Feedback** *(Please correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)* |
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| **Please write a few sentences regarding the importance of this manuscript for the scientific community. A minimum of 3-4 sentences may be required for this part.** | The manuscript carries some scientific importance in terms of findings especially on regular use of khat and effects on brain areas influencing behaviour. The findings also provide some insights into the possible mechanism of action leading to observed effects in the regular khat, more specifically production of oxidative stress at the level of the brain than, in part, influences anxiety-like behaviours among other psychostimulatory behaviours. The study also highlights sex as a co-variable in terms of effects of khat. | |
| **Is the title of the article suitable? (If not please suggest an alternative title)** | Title needs to be focused; it talks about 3 things: anxiety-like behavior, Malondialdehyde levels in prefrontal cortex and sex of mice. The title will appear more focused if it just talks about effects of khat on the brain in male and female mice | |

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| **Is the abstract of the article comprehensive? Do you suggest the addition (or deletion) of some points in this section? Please write your suggestions here.** | What exactly is the problem that drove the study? Specification on sex of animals and grouping is lacking. What does increased levels of malondialdehyde in the brain mean owing to the understanding that khat is a psychostimulant? | |
| **Is the manuscript scientifically, correct? Please write here.** | The manuscript is generally good and results finding elaborate. However, a few areas of concern:<br>**1.** There is need to specify sources and other details of the chemicals. Under section 2.3, how were housing conditions of temperature and humidity managed? This information is missed yet it is important especially on performance of animals hence can influence results. Under section 2.4, Why was tween 80 used for the control? Was the same vehicle used to reconstitute the khat doses? If so, please make it clear in the description. Was dosing done daily or how often? Under section 2.5, there is contradiction of information under 2.3 where you mention fresh leaves were prepared through freeze-drying for 2 days. How did you determine that you were strictly working with the prefrontal cortex? You have not mentioned about use of stereotactic atlas, for example. The process of brain tissue preparation for spectrophotometry is not clearly outlined; details are missed out.<br>**2.** There is need to add some literature on what khat does to the user in terms of metabolites produced hence observed effects. Some information of phytochemical composition of khat will provide the flow of information towards where the research is going.<br>**3.** Under section 2.8: Specify each statistical test for the measures analyzed. Kruskal-Wallis is mentioned under results but it is not illustrated here<br>**4.** Under results section, figure 2 is missed.<br>**5.** Under discussion, paragraph 1, authors state that female mice at lower dose showed stress and anxiety-like behaviors more than males but explanation is not given<br>**6.** Authors need to state how they determined anxiety and anxiogenic behaviours. What indicators were used to determine presence of such behaviours? These could have been just explorative behaviours, may be. | |
| **Are the references sufficient and recent? If you have suggestions of additional references, please mention them in the review form.** | References are sufficient | |
| **Is the language/English quality of the article suitable for scholarly communications?** | The language is suitable except a few grammatical errors pointed out in the manuscript | |
| **Optional/General** comments | **The manuscript requires minor changes** | |

## Review Form 3

**PART 2:**

| | **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)* |
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| **Are there ethical issues in this manuscript?** | *(If yes, Kindly please write down the ethical issues here in details)* | |

**Reviewer Details:**

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|---|---|
| Name: | **Albert Wafula Nyongesa** |
| Department, University & Country | **University of Nairobi, Kenya** |