Review Form 3

Journal Name:	**Journal of Complementary and Alternative Medical Research**
Manuscript Number:	**Ms_JOCAMR_121371**
Title of the Manuscript:	**MODULATORY EFFECTS OF MORPHINE AND XYLOPIA AETHIOICA EXTRACT ON KAPPA OPIOD RECEPTORS (KOR), Δ OPIOID RECEPTOR (DOR), PAIN HYPERSENSITIVITY AND MOTOR FUNCTIONS IN WSTAR RATS**
Type of the Article	**Original Research Article**

Review Form 3

PART 1: **Review Comments**

Compulsory REVISION 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)*
Please write a few sentences regarding the importance of this manuscript for the scientific community. Why do you like (or dislike) this manuscript? A minimum of 3-4 sentences may be required for this part.	**This manuscript is important for the scientific community as it explores the potential of Xylopia aethiopica extract as a natural alternative to opioids for pain management. By demonstrating significant analgesic effects and improved motor functions in animal models, the study offers a promising solution to the problems of opioid dependence and tolerance. The molecular docking studies provide insights into how bioactive compounds from Xylopia aethiopica interact with opioid receptors, paving the way for future drug development and safer pain relief options.**	
Is the title of the article suitable? (If not please suggest an alternative title)	**Yes**	
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.	**Yes**	
Are subsections and structure of the manuscript appropriate?	**Yes**	
Please write a few sentences regarding the scientific correctness of this manuscript. Why do you think that this manuscript is scientifically robust and technically sound? A minimum of 3-4 sentences may be required for this part.	This manuscript is scientifically robust and technically sound due to its well-structured experimental design, use of established methods for assessing pain and motor functions, and thorough statistical analysis. The inclusion of molecular docking studies strengthens the findings, and the detailed methodologies ensure the reliability and credibility of the results.	
Are the references sufficient and recent? If you have suggestions of additional references, please mention them in the review form. -	**Yes**	

Minor REVISION comments **Is the language/English quality of the article suitable for scholarly communications?**	Yes	
Optional/General comments	**Sample Size and Statistical Power**: • The study mentions the use of Wistar rats but does not specify the number of animals per group. A small sample size can reduce the statistical power and reliability of the results. • Recommendation: Clearly state the number of animals used in each group and justify the sample size with a power analysis. **Control Group Variability**: • The control group exhibited some variability in response times and motor functions, which may suggest inconsistencies in the experimental setup or inherent variability in the subjects. • Recommendation: Ensure rigorous standardization of experimental conditions to minimize variability. Consider using larger control groups to account for natural variations. **Lack of Detailed Methodology**: • The methods for inducing pain and administering treatments are briefly described but lack sufficient detail. For example, the exact protocols for the tail flick test, Rotarod test, and molecular docking studies are not thoroughly explained. • Recommendation: Provide a detailed description of all experimental procedures, including specific parameters for pain induction, testing protocols, and molecular docking methodologies. **Potential Bias in Pain Induction**: • The method of pain induction using electroconvulsive stimuli and a hot plate may introduce variability and potential bias in pain perception measurements. • Recommendation: Consider using multiple standardized methods of pain induction and assessment to validate the findings and reduce bias. **Ambiguity in Dose-Response Relationship**: • The study explores the effects of different doses of Xylopia aethiopica and morphine, but the rationale for selecting these doses and their relevance to clinical settings is not clearly discussed. • Recommendation: Provide a justification for the chosen doses, including any preliminary dose-finding studies. Discuss how these doses relate to potential therapeutic doses in humans. **Molecular Docking Analysis**: • The molecular docking analysis is briefly mentioned, but the selection criteria for the compounds, the docking parameters, and the validation of the docking results are not thoroughly detailed. • Recommendation: Include comprehensive details on the molecular docking process, such as the selection of compounds, docking parameters, validation methods (e.g., cross-docking or comparison with known ligands), and interpretation of binding affinities.	

	Inconsistent Terminology and Measurement Units: • There are inconsistencies in the terminology used (e.g., "anagelsymeter" vs. "analgesimeter") and in the presentation of measurement units (e.g., time in seconds). • Recommendation: Ensure consistent use of terminology and units throughout the manuscript to avoid confusion and enhance clarity.	

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)*
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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