## Review Form 3

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| JournalName: | AsianJournalofAdvancedResearchandReports |
| ManuscriptNumber: | **Ms_AJARR_130197** |
| TitleoftheManuscript: | **HistopathologicalandBiochemicalInvestigationsoftheBrainuponSub-acutePentazocineAdministration.** |
| TypeoftheArticle | |

**PART1:Comments**

| | Reviewer'scomment | Author's Feedback *(Please correct the manuscript and highlight that part inthemanuscript.Itismandatorythatauthorsshouldwritehis/herfeedback here)* |
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| **Pleasewriteafewsentencesregardingtheimportance of this manuscript for the scientific community. A minimum of 3-4 sentences may be required for this part.** | **Advantagesofthisresearch**<br>**Theresearchonthetoxicologicaleffectsofsub-acutepentazocineadministrationoffersseveral advantages:**<br>**1. InsightintoOpioidEffects:Thisstudyprovidesvaluableinsightsinto thebiochemicaland histopathological impacts of pentazocine, a commonly used analgesic among sickle-cell disease patients in Nigeria. By evaluating the effects on the cerebral cortex, the research highlights potential risks associated with opioid use, particularly in vulnerable populations suffering from chronic pain (Page 1).**<br>**2. Identification of Oxidative Stress: The findings indicate significant reductions in antioxidantenzymeactivities,suchascatalase(CAT)andsuperoxidedismutase(SOD),alongside increased levels of malondialdehyde (MDA), a marker of oxidative stress. This suggests that pentazocine may contribute to oxidative damage in the brain, which is crucial for understanding the drug's safety profile (Page 6).**<br>**3. Pathological Evidence: The study documents specific histopathological changes in the cerebral cortex, including neuronal cell loss and vacuolations, which provide concrete evidence of the drug's neurotoxic effects. This information is essential for healthcare providers to make informeddecisionsregardingpainmanagementstrategiesinpatientswhomaybeatriskofopioid dependence (Page 7).**<br>**Overall, the research underscores the need for careful consideration of pentazocine's use in clinical settings,particularlyregardingitspotentialneurotoxiceffectsandtheimportanceofmonitoringpatients for signs of oxidative stress and neuronal damage.** | |
| **Isthetitleofthearticle suitable? (Ifnotpleasesuggestanalternativetitle)** | **yes** | |

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| **Is the abstract of the article comprehensive? Do you suggesttheaddition(ordeletion)ofsomepointsinth is section? Please write your suggestions here.** | **yes** | |
| **Isthemanuscriptscientifically,correct?Pleasewrit e here.** | Toevaluatetheaccuracyandprecisionofthisstudy,severalimportantaspectsshouldbeconsidered:<br>1. Research Design: This studyhas utilized a randomized controlled trial (RCT) method, which helps reduce biases and increase the credibilityofthe results. The experimental groups were randomly assignedtofourgroups,includingonecontrolgroupandthreetreatmentgroupswithdifferentdosesof pentazocine.<br>2. Biochemical and Histopathological Methods: The study has used standard methods to evaluate theactivityofantioxidantenzymes(CATandSOD)andhistopathologicalexaminations.Thesemetho ds help ensure the accuracy and validity of the results, showing a decrease in enzyme activities and an increase in malondialdehyde (MDA) levels in the treatment groups.<br>3. StatisticalAnalysis:Thedatawereanalyzedusingone-wayanalysisofvariance(ANOVA)and post-hoc tests. These methods help determine the significance of the results and indicate that the observed differences between groups are statistically valid.<br>4. Limitations: One limitation of this study is the lack of assessment of systemic inflammatory markersintheblood,suchascytokines,todeterminebraintissueinflammation.Thispointismentioned in the conclusion of the study and highlights the need for further research.<br>Overall,thisstudyhasevaluatedthetoxiceffectsofpentazocineonthebraincortexusingappropriate design, valid methods, and accurate statistical analyses. However, it is important to consider its limitations as well. | |
| **Arethereferencessufficientandrecent?Ifyouhave suggestions of additional references, please mention them in the review form.** | Yes,butadd<br>1. Khamooshi F, Doraji-Bonjar S, Akinnawo AS, Ghaznavi H, Salimi-Khorashad AR, and Khamooshi MJ (2023)DarkClassicsinChemicalNeuroscience:ComprehensiveStudyontheBiochemicalMechani sms and Clinical Implications of Opioid Analgesics. Chemical Methodologies 7(12): 964-993. DOI: https://doi.org/10.48309/chemm.2023.414616.1731<br>2. KhamooshiF,AkinnawoAS,Doraji-BonjarS,andModarresi-AlamAR(2024)MitragynineChemistry: Extraction, Synthesis, and Clinical Effects. Chemistry Africa. DOI: 10.1007/s42250-024-00921-6 | |

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| **Isthelanguage/Englishqualityofthearticlesuitable for scholarly communications?** | Middle,Itneedspolishingand somesentencesthatarecompletelyredinthesimilarityfinderlinkbelowneedto be corrected.<br>http://dl.daneshlink.ir/Ms_AJARR_130197.pdf | |
| **Optional/General**comments | **BenefitsoftheResearch**<br><br>**1. Increaseawarenessaboutthetoxiceffectsofpentazocine:Thisresearchfocusesonstudying thetoxiceffectsofpentazocineonthebraincortexandshowsthattheuseofthisdrugcan leadtoadecreaseintheactivityofantioxidantenzymessuchascatalase(CAT)and superoxide dismutase(SOD), andanincrease in the levelofmalondialdehyde(MDA), indicating oxidative stress.**<br>**2. Histopathologicalanalyses:Theresultsoftheresearchindicatethatthetherapeuticgroup s treatedwith pentazocine havesignificant histopathologicalchangesin thebraincortex, including loss of nerve cells and accumulation of granular cells.**<br>**3. Attentiontoclinicalneeds:Thisresearchhighlightstheneedforfurtherinvestigationsintothe negativeeffectsofpentazocineinpatientswithsicklecelldiseaseandrecommendscautionto physicians and pharmaceutical companies in the use of this drug.**<br><br>**LimitationsoftheResearch**<br><br>**1. Limitationinassessingsystemicinflammation:Onelimitationofthisresearchisthelackof evaluationofsystemicinflammationmarkersintheblood,suchascytokines,todetermine brain tissue inflammation.**<br>**2. Animalmodel:Theuseofanimalmodels(Wistarrats)maynotfullygeneralizetheresultsto humans,asthephysiologyofhumansandmiceisdifferent,whichcouldleadtolimitationsin the application of the results.**<br>**3. Lackoflong-termeffectsassessment:Thisresearchfocusesontheshort-termeffectsof pentazocineanddoesnotconsiderthelong-termeffectsandsideeffectsresultingfrom prolonged use of this drug.**<br><br>DearEditor,<br><br>AboutthisManuscript,<br><br>The study investigates the toxicological effects of sub-acute pentazocine administration on the cerebral cortex, particularly in the context of its use among sickle-cell disease patients in Nigeria.Twenty-eightadult Wistarrats weredividedintofourgroups, withonecontrolgroupreceivingnormalsalineandtheothersreceivinggradeddosesofpentazocine(30 mg/kg,60 mg/kg, and 90 mg/kg) for 14 days. Resultsindicated a decrease incatalase (CAT) and superoxide dismutase (SOD) activities, alongside anincrease in malondialdehyde (MDA) levelsin the brain tissues of treated groups, suggesting moderate toxicity and potential inflammatory responses in the brain.<br><br>BenefitsoftheResearch<br><br>1. Increaseawarenessaboutthetoxiceffectsofpentazocine:Thisresearchfocusesonstudyingthet oxiceffectsofpentazocineonthebraincortexandshowsthattheuseofthis drug can lead to a decrease in the activityof antioxidant enzymes such as catalase (CAT) and superoxide dismutase (SOD), and an increase in the level of malondialdehyde (MDA), indicating oxidative stress.<br><br>2. Histopathologicalanalyses:Theresultsoftheresearchindicatethatthetherapeuticgroupstreated withpentazocine have significanthistopathological changesinthebraincortex, including loss of nerve cells and accumulation of granular cells.<br><br>3. Attentiontoclinicalneeds:Thisresearchhighlightstheneed forfurtherinvestigationsinto thenegativeeffectsofpentazocineinpatients withsicklecelldiseaseandrecommends caution to physicians | |

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| | and pharmaceutical companies in the use of this drug.<br><br>LimitationsoftheResearch<br><br>1. Limitationinassessingsystemicinflammation:Onelimitationofthisresearchisthelackofevaluationofsystemicinflammation markersintheblood, suchascytokines,to determine brain tissue inflammation.<br><br>2. Animal model:Theuseofanimal models(Wistarrats) maynotfullygeneralizetheresultstohumans,asthephysiologyofhumansand miceisdifferent, whichcouldleadto limitations in the application of the results.<br><br>3. Lackoflong-termeffectsassessment:Thisresearch focuses ontheshort-termeffectsofpentazocineand doesnotconsider thelong-termeffectsand sideeffectsresulting from prolonged use of this drug.<br><br>Thisresearchisofscientificvalueandpublicationvalueforthefollowingreasons:<br><br>1. Importantandrelevanttopic:Theresearchfocusesontheeffectsofthetoxicdrugpentazocineonpatients withsicklecelldisease.Thistopicishighlyimportantduetothe prevalence of addiction to this drug in Nigeria and its impact on brain health.<br><br>2. Valid methodology:Theuseofarandomizedcontrolledtrial (RCT)andbiochemicalandhistopathologicalanalysesenhancesthecredibilityoftheresults.Thisresearchhas employed standard methods to evaluate antioxidant enzyme activity and histopathological examinations.<br><br>3. Significantresults:Theresultsindicateadecreaseinantioxidantenzymeactivity andanincreaseinmalondialdehyde(MDA)levelsinthetreatment groups,clearlyindicating oxidative stress and brain damage caused by pentazocine.<br><br>4. Recommendations forfuturereseach:Theresearchhighlightsthe needforfurtherinvestigationsintosystemicinflammatorymarkersandthelong-termeffectsofpentazocine, which can contribute to future research and improve pain management in patients with sickle cell disease.<br><br>Consideringthesepoints,thisresearchcanserveasacrediblesourceinthefieldoftheeffectsofpainmedicationsonbrainhealthandpainmanagementinpatients,andit hasvalue for publication and dissemination. | |

**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: | **Ferydoon Khamooshi** |
| Department, University & Country | **University of Zabol, Iran** |