Junior Science Communications
Faculty of Applied Sciences, UiTM Shah Alam
https://journal.uitm.edu.my/ojs/index.php/JSC

E-ISSN 2637-0689
Vol 47 2025

Colloquium on Applied Sciences 2 2024
8-14 July 2024, Faculty of Applied Sciences, UiTM Shah Alam, Malaysia

Acetylcholinesterase Activity and Histopathological Effects of Caffeine in *Plasmodium berghei* ANKA-infected ICR Mice

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Structured Abstract

Background: Malaria has been a global concern, recorded with 241 million cases and 627,000 deaths in 2020. It is a common and life-threatening infectious disease caused by parasites of the *Plasmodium* genus and transmitted by the female *Anopheles* mosquito. In Malaysia, cases rose to 404 in 2022, with cerebral malaria being one of the most severe complications related to malaria. Caffeine, known as an adenosine receptor antagonist, is being used as a treatment in this study to investigate its potential as an antimalarial activity. Therefore, this study aims to determine AChE activity and the histopathological effects of caffeine in the brains of *P. berghei* ANKA-infected ICR mice.

Methods: The methodology involves Ellman *et al*., (1961) with slight modification and histopathological study. Sixteen ICR mice were divided equally and prepared into four groups: the normal control, *P. berghei* ANKA-infected (negative control), infected CQ-treated (positive control), and infected caffeine-treated. Mouse brains were then homogenized, and the supernatant was collected for AChE activity determination. For histopathological analysis, the brain was fixed in 10% formalin, processed for 10 hours, embedded in paraffin wax, and sectioned using a microtome. H&E staining was then performed, and morphological changes within the tissues of the mice were observed under a light microscope.

Results: The result shows that 5 mg/kg b.w. of caffeine treatment was able to modulate the levels of AChE activity (1.260±0.106 mol/min) as compared in *P. berghei* ANKA-infected animals (1.335±0.121 mol/min), where the AChE activity level increased due to parasitic infection. Histopathological study revealed that infected caffeine-treated mice showed a reduced number of hemozoin pigments and no presence of PRBCs compared to *P. berghei* ANKA-infected.

Conclusion: In conclusion, caffeine treatment in *P. berghei* ANKA-infected ICR mice was able to increase AChE activity and reduce PRBCs and hemozoin pigment. Hence, caffeine might be developed as an antimalarial drug due to neuroprotective and neurotoxic effects that influence therapeutic approaches.

Keywords: Malaria, Acetylcholinesterase Activity, Histopathological Studies, Caffeine, *P. berghei* ANKA

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