

HOSTED BY



Contents lists available at ScienceDirect

Journal of King Saud University – Science

journal homepage: www.sciencedirect.com

Original article

Neurotoxicity of aluminium chloride and okadaic acid in zebrafish: Insights into Alzheimer's disease models through anxiety and locomotion testing, and acute toxicity assessment with *Litsea garciae* bark's methanolic extract



Siti Zaleha Raduan^{a,d}, Qamar Uddin Ahmed^{b,*}, Abdul Razak Kasmuri^a, Muhamad Rusdi Ahmad Rusmili^a, Wan Azizi Wan Sulaiman^c, Mohd Farooq Shaikh^{e,j}, Muhammad Hamdi Mahmood^f, Syed Najmul Hejaz Azmi^g, Mohammad Z. Ahmed^h, Shadab Kazmiⁱ

^a Department of Basic Medical Sciences, Kulliyah of Pharmacy, International Islamic University Malaysia (IIUM), 25200 Kuantan, Pahang, Malaysia

^b Drug Discovery and Synthetic Chemistry Research Group, Department of Pharmaceutical Chemistry, Kulliyah of Pharmacy, IIUM, 25200 Kuantan, Pahang, Malaysia

^c University College MAIWP International, 68100, Batu Caves, Kuala Lumpur, Malaysia

^d Department of Para-clinical Sciences, FMHS, UNIMAS, 94300 Kota Samarahan, Sarawak, Malaysia

^e Neuropharmacology Research Laboratory, Jeffrey Cheah School of Medicine and Health Sciences, Monash University Malaysia, 47500 Bandar Sunway, Selangor Darul Ehsan, Malaysia

^f Department of Basic Medical Sciences, FMHS, UNIMAS, 94300 Kota Samarahan, Sarawak, Malaysia

^g Applied Sciences Department, College of Applied Sciences and Pharmacy, University of Technology and Applied Sciences-Muscat, P. O. Box 74, Al-Khuwair, 133, Oman

^h Department of Pharmacognosy, College of Pharmacy, King Saud University, Riyadh, Saudi Arabia

ⁱ Department of Child Health, School of Medicine, University of Missouri, Columbia, MO, USA

^j School of Dentistry and Medical Sciences, Charles Sturt University, New South Wales, Australia

ARTICLE INFO

Article history:

Received 18 April 2023

Revised 18 June 2023

Accepted 14 July 2023

Available online 20 July 2023

Keywords:

Alzheimer's disease
Adult zebrafish
Aluminium chloride
Okadaic acid
Litsea garciae
Acute toxicity

ABSTRACT

Alzheimer's disease (AD) is a complicated neurodegenerative disorder that presents significant challenges for the development of effective therapeutic interventions. Understanding disease mechanisms and exploring potential treatments require the use of animal models that accurately replicate the pathology of AD. In this study, we investigated the potential of two neurotoxin inducers, aluminium chloride (AlCl₃) and okadaic acid (OKA), to validate the zebrafish as a model organism for AD. AD can impact locomotor activity and induce anxiety-like behaviors. To assess these behaviors, a 6-minute novel tank test was conducted. Zebrafish were administered with low, medium, or high doses of neurotoxic agent (AlCl₃ or OKA) intraperitoneally twice weekly for 21 days. Behavioral activities were recorded at three time points: day 7 (short duration), day 14 (moderate duration), and day 21 (extended duration). The behavioral task required the evaluation of four endpoints. Methanolic extract of *Litsea garciae* bark was selected as a potential plant for the treatment of AD in this study, based on its previously demonstrated antioxidant effect. However, the acute toxicity of this plant has not been previously assessed. Therefore, this research was aimed to investigate the acute toxicity of the *L. garciae* bark's methanolic extract in adult zebrafish. The extract was immersed in a static system following OECD Test Guideline No. 203, and the acute toxicity test involved monitoring the adult zebrafish for 96 h for any deaths or apparent abnormalities. Regarding the behavioural task, the groups induced with 100 nM of OKA demonstrated significant differences in all measured parameters compared to the control group at the 21-day time point. In contrast, none of the parameters were significantly different between the AlCl₃-induced groups

Abbreviations: AD, Alzheimer's disease; AlCl₃, Aluminium chloride; OKA, okadaic acid; NTT, Novel tank test; LG, *Litsea garciae*; CREAM, Central Research and Animals Facility; IACUC-IIUM, Institutional Animal Care & Use Committee IIUM; SBC, Sarawak Biodiversity Centre; OECD, Organisation for Economic Cooperation and Development; LC₅₀, lethal concentration; pH, potential of hydrogen.

* Corresponding author.

E-mail address: quahmed@iium.edu.my (Q.U. Ahmed).

Peer review under responsibility of King Saud University.



Production and hosting by Elsevier

<https://doi.org/10.1016/j.jksus.2023.102807>

1018-3647/© 2023 The Author(s). Published by Elsevier B.V. on behalf of King Saud University.

This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).