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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

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Abstract

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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 ($AlCl_3$) 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 ($AlCl_3$ 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 $AlCl_3$-induced groups and the control group at any of the three time points (7, 14, or 21 days). Regarding acute toxicity, neither the test group (100 mg/L) nor the control group recorded any deaths or abnormalities. Therefore, no LC_{50} value could be determined. These findings confirm the acceptance of OKA as an inducer in the zebrafish model of AD and highlight the significance of the safe and non-toxic nature of L. garciae bark's methanolic extract for future ethnopharmacological investigations. © 2023 The Author(s)

Author keywords

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

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