Neuropharmacological Assessment of *Calophyllum inophyllum* Against Alzheimer's Disease: In vitro, In vivo and In silico Approaches

Abstract

Alzheimer's disease (AD) is a progressive neurodegenerative disorder and the leading cause of dementia worldwide, posing a substantial medical and socioeconomic burden. Existing therapeutic options mainly offer symptomatic relief and fail to effectively halt disease progression, underscoring the urgent need for novel, multitargeted, and safer therapeutic agents. Natural products, owing to their chemical diversity and polypharmacological potential, represent a promising source for Alzheimer's drug discovery. *Calophyllum inophyllum*, a tropical medicinal plant widely used in traditional medicine, has demonstrated anti-inflammatory, antioxidant, and enzyme-inhibitory properties, suggesting potential relevance in neurodegenerative disorders. However, systematic evaluation of its neuroprotective effects with in-vivo relevance remains limited.

This study aims to conduct a comprehensive neuropharmacological assessment of *C. inophyllum* using integrated in vitro, in vivo, and in silico approaches to explore its therapeutic potential against Alzheimer's disease. Methanolic extracts of the leaf, and stem bark will be fractionated based on solvent polarity using n-hexane, chloroform and ethyl acetate, and the resulting fractions will be screened for antioxidant activity and acetylcholinesterase and butyrylcholinesterase inhibition using established biochemical assays. Fractions exhibiting significant bioactivity will be further evaluated in a scopolamine-induced Alzheimer's disease mouse model to assess their effects on memory, learning, and oxidative stress-related biochemical markers.

Advanced analytical techniques, including HPLC, LC-MS and GC-MS, will be employed to identify the major bioactive constituents present in the most potent fractions. Furthermore, molecular docking and ADME prediction studies will be conducted to elucidate the molecular interactions of identified compounds with key Alzheimer's-related targets and to assess their drug-likeness.

By integrating experimental and computational findings, this research is expected to provide mechanistic insights into the neuroprotective potential of *C. inophyllum* and identify promising lead compounds for further development. The outcomes of this study may contribute to the discovery of plant-derived, multitarget therapeutic candidates for the management of Alzheimer's disease.