UNIVERSITI TEKNOLOGI MARA

PHYTOCHEMICAL STUDY OF *Calophyllum canum* HOOK. F. ex T. ANDERSON AND ITS NEUROPROTECTIVE EVALUATION IN AN *in vitro* PC12 CELL-BASED STROKE MODEL

MAS ATIKAH BINTI LIZAZMAN

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ABSTRACT

Previous phytochemical and biological studies have revealed *Calophyllum* species are rich in phenolic constituents specifically xanthones and coumarins which possess a wide range of biological activities. For example, cytotoxicity, HIV-1 reverse transcriptase inhibitory activity, antisecretory, and cytoprotective properties as well as antinociceptive, molluscicidal, and antimicrobial effects. However, there are very few studies conducted on *C. canum*, the *Calophyllum* species from Sarawak. The evaluation of their neuroprotective properties has been least studied as well. Hence, this study is aimed to develop a chemical and biological database on the entities found in the *C. canum*. Several chromatographic techniques have been implemented for the isolation of pure compounds from the stem bark *C. canum* extracts. For instance, vacuum liquid chromatography, gravity column chromatography, and gel filtration chromatography were employed for fractionation of the plant extracts whilst radial chromatography was for the purification of the compounds. The structures of these compounds were identified and elucidated using advanced spectroscopic techniques such as 1D and 2D nuclear magnetic resonance, infrared, ultraviolet, mass spectroscopy, and comparison with the reported data. The phytochemical study of *C. canum* has led to the isolation of eight xanthones namely: 5-methoxytrapezifolixanthone, 5-methoxyananixanthone, euxanthone, trapezifolixanthone, ananixanthone, 6-deoxyisojacareubin, caloxanthone C and 1,5-dihydroxy-3-methoxy-4-isoprenylxanthone, together with three common triterpenoids, *β*-sitosterol**,** friedelin, and stigmasterol. The two xanthone isomers, 5-methoxytrapezifolixanthone, and 5-methoxyananixanthone were isolated from the plant extract for the first time. Caloxanthone C, 5-methoxytrapezifolixanthone, 5-methoxyananixanthone, 1,5-dihydroxy-3-methoxy-4-isoprenylxanthone, and stigmasterol were discovered from the hexane extract. Meanwhile, euxanthone, 6-deoxyisojacareubin, *β*-sitosterol, and friedelin were found in the chloroform extract. Both ananixanthone and trapezifolixanthone were isolated as major constituents from both hexane and chloroform extracts. The selected compounds, trapezifolixanthone, ananixanthone, euxanthone, *β*-sitosterol, and friedelin were tested for their neuroprotective properties in the stroke model. The most significant neuroprotective property was demonstrated by ananixanthone, *β*-sitosterol, and friedelin which portrayed the same order of reduction of caspase 3/7 activity as the known neuroprotectant DPAT. The findings have highlighted the therapeutic potential of trapezifolixanthone and ananixanthone as neuroprotective agents.

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