

Identification of Bioactive Metabolites from *Ficus carica* and Their Neuroprotective Effects of Alzheimer's Disease

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Abstract : Neurodegenerative disease including Alzheimer's disease is a major cause of long-term disability. Oxidative stress is frequently implicated as one of the key contributing factors to neurodegenerative diseases. Protection against neuronal damage remains a great challenge for researchers. *Ficus carica* (commonly known as fig) is a species of great antioxidant nutritional value comprising a protective mechanism against innumerable health disorders related to oxidative stress as well as Alzheimer's disease. The purpose of this work was to characterize the non-polar active metabolites in *Ficus carica* endocarp, mesocarp, and exocarp. Crude extracts were prepared using several extraction solvents, which included 1:1 water: ethylacetate, acetone and methanol. The dried extracts were then solvent partitioned between equivalent amounts of water and ethylacetate. Purification and fractionation were accomplished by high-throughput chromatography. The isolated metabolites were tested on their effect on human neuroblastoma cell line by cell viability test and cell cytotoxicity assay with acrolein. Molecular weights of the active metabolites were determined via LC-HRESIMS and GC-EIMS. Metabolomic profiling was performed to identify the active metabolites by using differential expression analysis software (Mzmine) and SIMCA for multivariate analysis. Structural elucidation and identification of the interested active metabolites were studied by 1-D and 2-D NMR. Significant differences in bioactivity against a concentration-dependent assay on acrolein radicals were observed between the three fruit parts. However, metabolites obtained from mesocarp and the endocarp demonstrated bioactivity to scavenge ROS radical. NMR profiling demonstrated that aliphatic compounds such as γ -sitosterol tend to induce neuronal bioactivity and exhibited bioactivity on the cell viability assay. γ -Sitosterol was found in higher concentrations in the mesocarp and was considered as one of the major phytosterol in *Ficus carica*.

Keywords : alzheimer, *Ficus carica*, γ -Sitosterol, metabolomics

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