UNIVERSITI TEKNOLOGI MARA

CYTOLOGICAL AND MOLECULAR ANALYSIS OF ANTI-TUMOUR BIOACTIVITIES OF *Urginea maritima* (L.) BAKER AQUEOUS EXTRACT ON HUMAN MALIGNANT NEUROBLASTOMA WITH ITS NEUROPROTECTION ABILITY

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ABSTRACT

This study was conducted with the hypothesis that the phytochemical closely related to Libyan medicinal herb, *Urginea maritima* (L.) Baker constituents within water-based extract would own appropriately powerful properties that contribute to intrinsic regulation specific antitumour activities in human malignant SH-SY5Y neuroblastoma cells. The purpose of the present study was to explore the characterisation and identification of the major phytochemical of the *U. maritima* aqueous extract. Additionally, the study also aimed to evaluate their effectiveness on the cellular and molecular mechanism associated with the main anti-tumour criteria. Through utilising several *in-vitro* techniques on both the experimental cell line models involving (2×10^4 to 1×10^6 cells/ml) with the quality of $\geq 90\%$ viability of SH-SY5Y neuroblastoma and RA differentiated (neuron- model) cells. Evaluation of the impact of the active extract ingredients was conducted based on morphological observation, biochemical, cellular function and gene expression profile, and the analysis was carried out for its estimation within different concentrations and durations. Neuroblastoma is a well-known extra-cranial solid tumour and one of the most deadly malignancies in childhood. Indeed, neuroblastoma with high-risk stages is extremely heterogeneous and very aggressive metastases. Although the most intensive multimodal therapies are available, but the key for the successful medical intervention of malignant neuroblastoma is still a challenging task. In this regard, the present investigation data for the first time clearly emphasise the significantly specific anti-tumour activities including viability and proliferation inhibition at a time-dose dependent manner with an estimated IC_{50} value at 10µg/ml, 1µg/ml and 100ng/ml after an incubation at 24, 48 and 72hrs respectively, with less neurotoxicity among the neuron model cells. Efficient apoptosis-causing and the induction of a more pronounced G1 phase arrest. More importantly, the investigation highly supported the ability of novel biological activities of this natural product, as it elucidated that the extract *in-vitro* could directly induce a neuronal differentiation mechanism. Based on the gene expression profiling was performed using the Human Affymetrix microarray module evaluating the biological significance of the *U. maritima* experiments. Following this Gene Ontology (GO) analysis and the major significant pathway through a Database (D.A.V.I.D) was decided. Further, the most promising results were also verified using RT-PCR. The expression profile results established extensive detail on the gene expression that encoded groups of proteins attributed to death receptors interrelated to intrinsic apoptosis pathway involving *bad*, *bid*, *bbc3*, and also elevated caspase-9 for treating malignant SH-SY5Y neuroblastoma population, which are in accordance with our previous findings and confirmed the research hypothesis. Furthermore, the studied extract strengthens cellular machinery correlated with neurogenesis, differentiation and development, bio action due to stimulation of *wnt* signal pathways with overexpression of numerous *wnt* ligands including *wnt3A*, *wnt7A*, *wnt7B* and *wnt11*. Collectively, these novel findings reveal that the active constituents of this unusual natural product, medicinal herb *U. maritima* exhibited dual effects on the neuron cells. Indeed, this preferential ability through diverse bioactivities provides an interesting basis for widespread medical application and a promising therapeutic candidate against neurological diseases, more specifically against neuroblastoma disorders.

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