Investigating the Apoptotic Mechanisms Activated in Glioblastoma Cells by Pre-Screened Cytotoxic Plants: Innovations for Novel Drug Discovery

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Glioblastoma multiforme (GBM) remains the most aggressive primary brain tumor, with a median survival of 12–15 months despite multimodal therapy. Identifying compounds that selectively induce tumor cell death through distinct apoptotic pathways may improve treatment. This study investigated the cytotoxic and molecular effects of crude polar extracts from three Southwest Florida plant species (Byrsonima lucida, Pinus elliottii, and Ulmus alata) on LN-229 human glioblastoma cells. MTT assays across 24 h to 72 h were used to assess cell viability. All extracts demonstrated dose- and time-dependent cytotoxicity. B. lucida produced the strongest effect, reducing viability to ~19% and ~50% at 1 mg/mL after 48 h and 72 h, respectively. P. elliottii demonstrated moderate cytotoxicity (66% survival at 72 h), while U. alata showed minimal effects (>90% survival). Apoptotic gene expression was quantified using RT-qPCR to investigate mechanisms of cell death. B. lucida treatment induced strong apoptotic signaling, including a 4-fold upregulation of CASP3 and a 288-fold increase in BAX expression, consistent with caspase-dependent apoptosis. In contrast, P. elliottii produced a 20-fold downregulation of CASP3 despite a 32-fold increase in BAX, suggesting caspase-independent cytotoxic pathways. ELISA confirmed these trends, showing a 24% increase in CASP3 protein levels in B. lucida-treated cells and a 58% decrease in P. elliottii-treated samples. These results demonstrate that plant-derived bioactive compounds can induce glioblastoma cell death through mechanistically distinct apoptotic pathways. The effects observed suggest that combination therapies targeting both caspase-dependent and caspase-independent pathways may represent a promising strategy for future GBM treatment.

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