The Cytotoxic Action of Doxorubicin in Combination With Brazilian Geopropolis on Human Epidermoid Carcinoma Cells (HEp-2)

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Two of the greatest challenges in cancer therapy today are the systematic toxicity of many chemotherapeutic agents and the development of resistance to these drugs by cancer cells. The toxicity of doxorubicin limits its clinical applications in a dose-dependent manner, especially in cases of drugs-resistant cancers. Our objective was to analyze the action of geopropolis associated with doxorubicin on epidermoid carcinoma cells of the human larynx (HEp-2). The samples produced by Melipona Fasciculata Smith were obtained from an apiary in Palmeirândia, Maranhão, Brazil. The cytotoxicity was assayed by MTT on VERO cells (ATCC CCL-81) after 72 hours incubation. HEp-2 cells were incubated in the presence of geopropolis (25 µg/mL), doxorubicin (1 µM), and the combination of geopropolis and doxorubicin, with and without verapamil (5 µM). Cell viability was assayed after 24, 48 and 72 hours by the MTT assay. Apoptosis and necrosis were evaluated by flow cytometry using Annexin V and propidium iodide (PI). Doxorubicin showed no cytotoxic effects on VERO cells. However, the association of doxorubicin with geopropolis significantly decreased the viability of HEp-2 cells in relation to the isolated variables (p < 0.05), inducing apoptosis in 25% of the cells, and necrosis in 23%. The geopropolis/doxorubicin mix co-administered with verapamil displayed high cytotoxicity compared to the control (p < 0.05). The geopropolis/doxorubicin mixtures appeared to induce a cytotoxic action in tumour cells in a time-dependent manner. The cytotoxicity in combination with verapamil may indicate a blocking of channel proteins important for cell survival and resistance to anticancer agents, favoring the action of the combination geopropolis/doxorubicin. Therefore, these results suggest that geopropolis may exhibit a promising synergistic role in chemotherapy by lowering the minimum therapeutic concentrations.

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