Study demonstrates antitumor action of substance present in Brazilian green propolis

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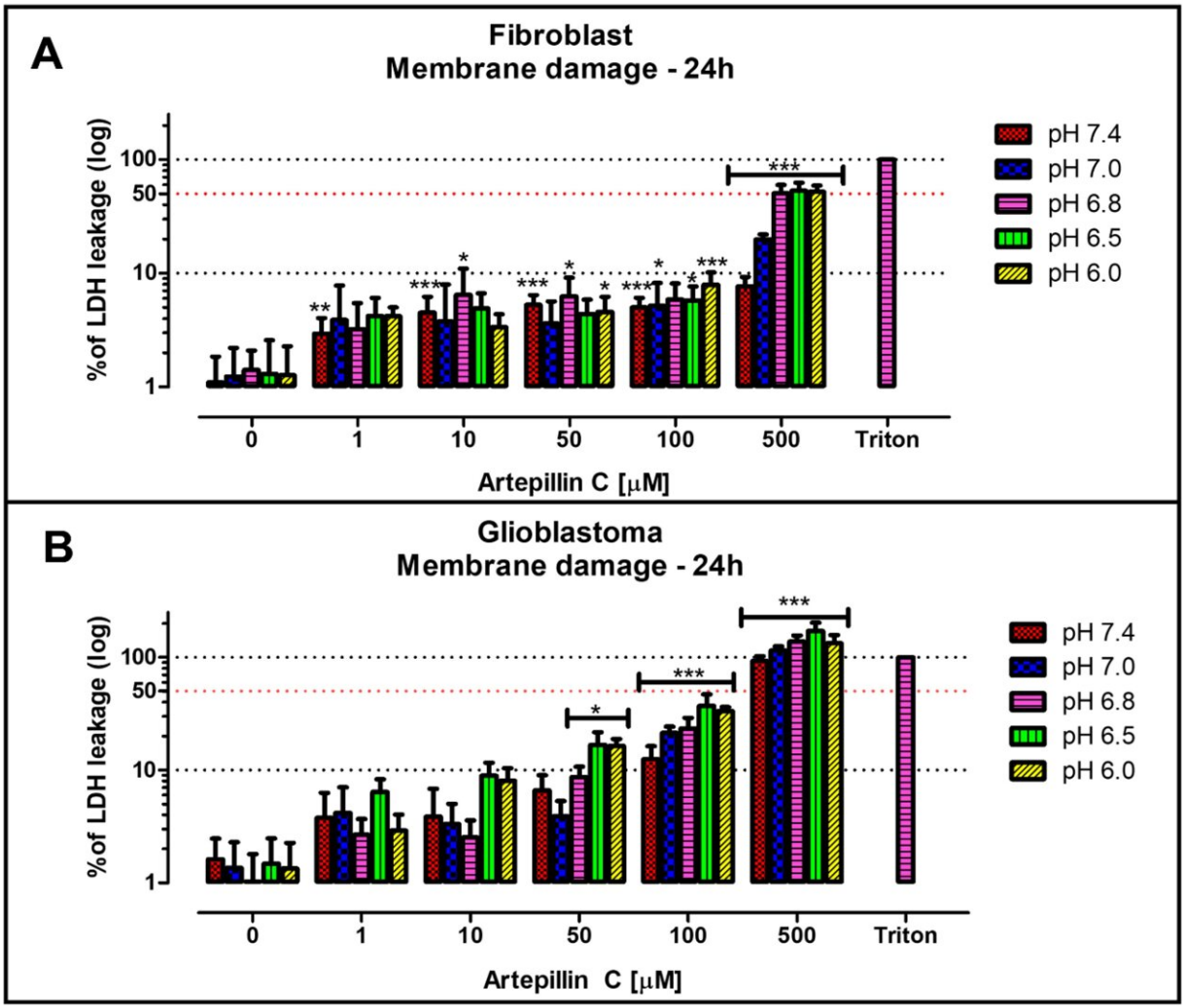

LDH assay representing the percentage of membrane integrity damage obtained for fibroblast (**A**) and glioblastoma (**B**) cell lines, after 24 h incubation, exposed to 0, 1, 10, 50, 100, and 500 μM of Artepillin C. Triton was used as the positive

control for membrane damage assays, since it solubilizes lipids, releasing 100% of LDH. * for p Life (2023). DOI: 10.3390/life13112186

Propolis has long been used in traditional medicine and has won attention from the scientific community following proof of its health benefits, which include antioxidant, anti-inflammatory, antimicrobial, antitumor, and immunomodulatory properties. Its composition varies according to origin, geographic location, and the bee species that produces it.

Researchers affiliated with São Paulo State University (UNESP) in Brazil and the University of Southern Denmark (SDU) set out to analyze Brazilian green propolis, which is produced by the Africanized honeybee (Apis mellifera).

Its main component is artepillin C (3,5-diprenyl-4-hydroxycinnamic acid), a phenolic compound primarily found in the resin of Baccharis dracunculifolia, a native Brazilian plant (popular name alecrim-do-campo) known to have antitumor properties.

"Prior research showed that artepillin C can alter model biological membranes, thin films around living cells, especially when we vary the pH of the medium in which they are placed," said Wallance Moreira Pazin, a professor in the Department of Physics and Meteorology at UNESP's Bauru School of Sciences (FC).

The researchers decided to find out how healthy cells and tumor cells behaved biochemically when brought into contact with artepillin C, focusing for this purpose on fibroblasts—the primary cells in the healing and maintenance of connective tissue—and glioblastoma cells, respectively. Glioblastoma is the most common primary brain cancer.

The culture medium's pH was also varied to see whether a more acidic microenvironment would lead to different effects of artepillin C. "This is relevant because tumor tissue converts glucose into lactic acid and makes the extracellular microenvironment more acid," said Pazin, first author of an article on the research published in the journal *Life*.

They next performed a meticulous analysis of the effects of the propolis on cell membranes, using an optical microscope to observe the integrity, fluidity, and morphology of the membranes. The analysis showed that artepillin C interacted intensely with tumor cells, altering their fluidity and potential for reorganization. It also triggered autophagy, a cleansing process that involves the degradation of worn, abnormal, or malfunctioning cellular components.

According to Pazin, the study contributes to a deeper understanding of the substance's action mechanisms and provides insights for future research leading to innovative treatments for cancer.

"However, although in vitro trials have demonstrated high efficiency for this molecule's biological activities, oral or topical administration to patients would be hindered by certain particularities, such as low absorption and bioavailability," Pazin said. "In this context, strategies to enhance its therapeutic action will be required in order for progress to be possible in the use of artepillin C against tumors. An example would be the deployment of nanocarriers for controlled release."

More information: Wallance M. Pazin et al, pH-Dependence Cytotoxicity Evaluation of Artepillin C against Tumor Cells, *Life* (2023). DOI: 10.3390/life13112186

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