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METABOLOMIC PROFILE AND IN VITRO ANTI-INFLAMMATORY AND CYTOTOXIC ACTIVITIES OF LICARIA ARMENIACA EXTRACTS

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Licaria armeniaca (Lauraceae) is a tree up to 7 m, widely distributed in the Amazonian rainforest, Brazil. A specimen was collected in Belém, PA, and its tissues were extracted by an ultrasound-assisted method using Ethanol/ water as solvent. Each tissue was extracted according to optimal conditions as follows: leaves (Ethanol 64.9%, t: 26.1 min, 6.23% m/v), thin branches (Ethanol 73.8%, t: 31.3 min, 11.0% m/v) and thick branches (Ethanol 50.0%, t: 35.0 min, 11.0% m/v). The extracts were analyzed by LC-MS/MS and the data were converted from RAW standard data format (Waters corp., Milford, USA) to mzML format using MSConvert 3.0.2. Feature extraction of the resulting file was processed using MZmine 4. The output files were for the CANOPUS chemical classes prediction and statistical analysis. The leaf extracts showed a predominance of alkaloids (46.34%), amino acids and peptides (19.51%), and shikimate and phenylpropanoid derivatives (12.20%). For thin branches and thick branches, the major classes were alkaloids (35.97%), amino acids and peptides (20.86%), and carbohydrates (12.23%), and alkaloids (32.14%), amino acids and peptides (25.00%), and fatty acids (14.26%), respectively. The cytotoxic activity of the extracts was evaluated by the MTT method against three cancer cell lines: gastric ascites (AGP01), glioblastoma (AHOL), lung cancer (A549), and non-malignant murine macrophage cells (RAW 264.7). The cell availability was measured after 24h, and the samples with an IC_{50} value < 25 µg/mL were considered active. The leaf extract was selective to glioblastoma cell lines (IC_{50}, 11.52 µg/mL) while the thin and thick branches extracts were active against gastric ascites (IC_{50}, 15.71 and 13.59 µg/mL, respectively). However, the thick branches extract was the only activity against lung cancer (IC_{50}, 16.95 µg/mL). Regarding the cytotoxicity against normal cells (RAW 264.7), the thick branches extract displayed low toxicity. The in vitro anti-inflammatory activity was assessment using an LPS model stimulating macrophage cells with Lipopolysaccharide (LPS) to induce an inflammatory state, then testing the effect of extracts in reduction of inflammatory markers such as nitric oxide (NO) and anion superoxide. The reduction of nitrite concentration compared to LPS group was significant to leaf and thick branches extracts in all concentrations tested (6.25-25 µg/mL), meanwhile to thin branches extract was efficient only at 12.5 e 6.25 µg/mL. Regarding to superoxide anion formation, the extracts of thin and thick branches reduced in all concentrations tested. However, the leaf extract was effective only at 12.5 µg/mL.

Keywords: *alkaloids, amino acids and peptides, shikimate derivatives, MTT assay, LPS model.*