



Section: 03

Antiproliferative and Anti-*H. pylori* Activities of Coumarin-Enriched Fractions from *Calophyllum brasiliense* Oil

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The genus *Calophyllum* comprises approximately 200 species of tropical trees. In Brazil, the most representative species is *Calophyllum brasiliense* (guanandi). Pre-clinical studies have attributed several properties to extracts of *C. brasiliense*, with a notable emphasis on its antitumor activity, which is the focus of this research. Its main chemical constituents include xanthones, coumarins, chromanones, flavonoids, and terpenoids. Evidence has demonstrated that chromanones isolated from guanandi exhibit activity against *Helicobacter pylori*, a bacterium considered a primary risk factor for gastric adenocarcinoma (GAC). This study aimed to fractionate the oil of *C. brasiliense* to obtain coumarin-enriched fractions and to evaluate their antiproliferative activity against gastric adenocarcinoma (GAC) cells and antibacterial activity against *Helicobacter pylori*. The sample, produced by the rural producer Rubens Szpilman, was subjected to a liquid-liquid partition, yielding hexanic and methanolic fractions. The methanolic fraction was purified by column chromatography (Sephadex LH-20) using methanol as the mobile phase, which generated four fractions. Following analysis by thin-layer chromatography, the first three fractions were combined and set aside, while fraction 4 was selected for structural elucidation by mass spectrometry and for biological assays of cytotoxicity (AGS and L929 cells) and antibacterial activity (*H. pylori*). The results indicated that fraction 4 exhibited an IC_{50} of $41.25 \pm 0.85 \mu\text{L}/\text{mL}$ against AGS cells, with a selectivity index of 1.58. The cisplatin control showed an IC_{50} of $6.54 \pm 0.78 \mu\text{L}/\text{mL}$ with a selectivity index of 1.02. For *H. pylori*, the Minimum Inhibitory Concentration (MIC) and Minimum Bactericidal Concentration (MBC) were both $8 \mu\text{L}/\text{mL}$. The amoxicillin control presented an MIC of $0.0062 \mu\text{L}/\text{mL}$ and an MBC of $0.125 \mu\text{L}/\text{mL}$. Analysis by (+)-ESI-FT-ICR mass spectrometry provided the exact molecular formula ($C_{22}H_{22}NaO_5$) for the molecular ion at m/z 425.13609 [$M+\text{H}^+$] and mass fragments at m/z 375 ($M-\text{CO}$) and 347 [(100%), $M-\text{C}_4\text{H}_3$], indicating the presence of 4-phenyldipyranocoumarins as the class of substances responsible for the observed biological activities.

Keywords: *Calophyllum brasiliense*, Coumarins, Chromanones, Gastric Adenocarcinoma, Mass Spectrometry.

