



TWO NOVEL UNUSUAL DITERPENES AND OTHER TERPENES FROM THE BARK OF XYLOPIA CALOPHYLLA (ANNONACEAE)

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Xylopia calophylla R. E. Fries is a species of the genus *Xylopia*, the second largest in the Annonaceae family, still scarcely studied in the literature. Known as “envira-vassourinha”, it occurs in igapó, várzea, and terra firme areas of the Brazilian Amazon. The hexane extract from the bark, obtained by maceration, was subjected to classical chromatographic techniques (CC, CCDA, and CCDP), resulting in the isolation of 12 terpenoid compounds, including two new diterpenes uncommon in Annonaceae. Structural elucidation was carried out by 1D/2D NMR experiments and mass spectrometry (MS), supported by literature data. The compounds were identified as terpenoids: three steroids (β -sitosterol, stigmasterol, and campesterol); three ketosteroids (stigmast-4-en-3-one or β -sitostenone, stigmast-4,22-dien-3-one, and campest-4-en-3-one); one oxygenated sesquiterpene (spathulenol); and five kaurane-type diterpenes, three known (kaurenoic acid, *ent*-15-oxokaur-16-en-19-oic acid, and xylopinic acid) and two new, named calophyllin A and calophyllin B, differing by the presence of an acetyl group ($-\text{COCH}_3$). The isolated compounds were evaluated against four human tumor cell lines (H1299, HepG2, MDA-MB-231, and SCC9) and one normal cell line (MRC-5). Only *ent*-15-oxokaur-16-en-19-oic acid and calophyllin B exhibited relevant activity, with IC_{50} values below 20 $\mu\text{g/mL}$ in all tumor cell lines. The most notable was *ent*-15-oxokaur-16-en-19-oic acid, which showed strong and promising activity against HepG2 ($\text{IC}_{50} = 5.63 \mu\text{g/mL}$) and H1299 ($\text{IC}_{50} = 9.55 \mu\text{g/mL}$). These findings, described for the first time for *X. calophylla*, demonstrate the potential of the new diterpenes as prototypes for antitumor agents and justify the continuation of phytochemical and biological studies, as well as expanding the chemosystematic knowledge of the species and the genus.

Keywords: *Xylopia calophylla*; diterpenes; terpenes; cytotoxic activity.

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