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NEW INSIGHTS INTO THE CHEMICAL CONSTITUENTS OF THE BARK OF GUATTERIA MEGALOPHYLLA (ANNONACEAE)

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Guatteria megalophylla Diels (Annonaceae) is a tree species distributed in Colombia, Ecuador, Peru, Guyana, and Brazil, with records from the states of Acre, Amazonas, Pará, and Rondônia. Previous studies have reported the presence of alkaloids in the stem, such as *O*,*O*-dimethylcurine, 12'-*O*-methylcurine, and isocondodendrine, as well as antioxidant activity in ethanolic extracts of the stem and leaves. The chemical composition of the leaf essential oil has also been investigated, along with its *in vitro* and *in vivo* antileukemic potential against HL-60 cells [1]. This study represents the first phytochemical investigation focused specifically on the bark of this species. The hexane and methanolic extracts of the bark were prepared by maceration, and the alkaloid fraction was obtained from the methanolic extract through acid–base treatment. These analyses led to the isolation of 13 compounds, identified by 1D/2D ^{1}H and ^{13}C NMR spectroscopy and gas chromatography–mass spectrometry (GC–MS). The hexane extract was fractionated by classical chromatography, using open-column chromatography and preparative thin-layer chromatography (PTLC), yielding the steroids campesterol, stigmasterol, β-sitosterol; the ketosteroids stigmast-4-en-3-one or β-sitostenone, stigmast-4,22-dien-3-one, and campest-4-en-3-one; and the oxygenated sesquiterpenes 1,10-*epi*-cubenol and caryophyllene oxide (8). The alkaloid fraction was further separated by high-performance liquid chromatography (HPLC), leading to the isolation of the alkaloids 9-hydroxyguatterfiesine, (–)-pallidine, melosmine, liriodenine, and the oxygenated sesquiterpene oxyphyllenodiol A. The hexane and methanolic extracts, as well as the neutral and alkaloid fractions, were evaluated for *in vitro* cytotoxic activity against HepG2 (human hepatocellular carcinoma) and HCT116 (human colon carcinoma) cell lines. Although none of the extracts or fractions exhibited strong cytotoxicity, the alkaloid fraction showed the highest inhibition (49.7% and 32.97% against HepG2 and HCT116, respectively), compared with the methanolic extract (19.64% and 3.71%). The discovery of these compounds in *G. megalophylla* not only provides the first chemical characterization of its bark but also strengthens the phytochemical framework of the genus *Guatteria*, underscoring its pharmacological potential.

Keywords: *Guatteria megalophylla*; alkaloids; sesquiterpenes; steroids and ketosteroids.

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References: [1] COSTA, R. G.A., *et al. In vitro* and *in vivo* growth inhibition of human acute promyelocytic leukemia HL-60 cells by *Guatteria megalophylla* Diels (Annonaceae) leaf essential oil. **Biomedicine & Pharmacotherapy,** 122, 2020.