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CABREUVANOLS A-C, THREE NEW CASSANE-DERIVED DITERPENES FROM Myrocarpus frondosus AND THEIR ANTI-INFLAMMATORY EFFECTS

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Myrocarpus frondosus (Fabaceae) is a species native to South America, popularly known as Cabreúva, and has been traditionally used for its medicinal properties, especially anti-inflammatory properties [1]. This study aimed to isolate and characterize new metabolites from the bark of this plant, in addition to evaluate their biological activity. Thus, seven compounds were obtained by using successive chromatographic techniques. Three were new cassene diterpenes, trivially named Cabreuvanols A, B, and C (2–4), while the four known compounds were ayapin (1), afromosin 7-O-β-D-apiofuranosyl-(1→2)-glucopyranoside (5), tyrsifloside (6), and afromosin 7-O-β-D-glucopyranoside (7). Their structure was assigned by the mean of 1D/2D NMR and HR-MS data, while the absolute configuration of cabreuvanol A (2) was confirmed by X-ray crystallography. The crude extract, the fractions, and compounds 1-3 were evaluated for their cytotoxicity against mouse J774 macrophages and for their anti-inflammatory effects through inhibition of nitric oxide (NOx) production [2,3]. The crude extract and fractions showed low cytotoxicity and high capacity to inhibit NOx production, with a significance of 70% inhibition at the tested concentrations, for ethyl acetate (EAF) and dichloromethane (DCMF) fractions. The extract and these two fractions were more potent than the reference drug, dexamethasone, at a dose of 2.75 μg/mL (20.65 ± 0.87 μg/mL). The new compounds, cabreuvanols A and B also showed inhibitory effects. Compound 3 was more cytotoxic than others. Furthermore, anti-inflammatory activity was demonstrated in a murine model of acute lung inflammation (ALI) caused by LPS. In this model, the crude extract and fractions significantly reduced NOx levels, while compounds 1 and 2 moderately reduced NOx by 58.6 ± 4.7% and 23.4 ± 8.8%, myeloperoxidase (MPO) activity, exudation, and cell migration in bronchoalveolar lavage fluid, confirming the anti-inflammatory effect in vivo. The results indicate that Cabreúva is a source of bioactive diterpenoids with potential application in the development of anti-inflammatory agents.

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Keywords: *Myrocarpus frondosus, Structure elucidation, Diterpenes, Anti-inflammatory activity*

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