

TITLE: ANTIMICOBACTERIAL AND ANTI-INFLAMMATORY ACTIVITY OF NATURAL PRODUCTS AS TREATMENT FOR SEVERE PULMONARY TUBERCULOSIS

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ABSTRACT:

Tuberculosis (TB) is a serious public health problem with highest number of deaths among adults worldwide aggravated by the emergence of multidrug-resistant (MDR) *M. tuberculosis* strains (Mtb). Severe forms of TB are associated with exacerbated inflammation, increasing the severity of pulmonary pathology. This scenario encourages the use of adjuvant therapy based on anti-inflammatory interventions and the search for new substances combining anti-TB and anti-inflammatory properties. In this work, we evaluated natural products of the *Eugenia umbelliflora*, *Psidium cattleianum*, *Myrciaria floribunda* and *Passiflora pentagona* from the Restinga de Jurubatiba National Park, for the antimycobacterial and anti-inflammatory properties. Suspensions of BCG and *Mtb* H37Rv in culture medium were incubated with crude extracts, fractions and substances of the plants cited before (4-500 µg/ml) for 5 days. LPS-stimulated RAW 264.7 macrophages were incubated with the same samples for 24 hours to evaluate the capacity to inhibit production of inflammatory mediators (NO and TNF-α) and the cytotoxicity. Inhibition of NO and TNF-α production was evaluated in the Griess and indirect bioassay assay with L929 fibroblasts respectively, and cell viability was verified by the MTT method. The antioxidant assay was performed using sodium nitroprusside. Antimycobacterial activity was evaluated against the *Mtb* H37Rv (10^6 CFU) and compared to the anti-TB drug rifampicin. **RESULTS:** The samples exhibiting *dual* activity were selected. Hexanic fraction of *E. umbelliflora* was the most active in the inhibition of mycobacterial growth (MIC₅₀ 32.5±1.7 µg/mL) and NO production (IC₅₀ 25.6±1.4 µg/mL). Dichloromethane fraction of *M. floribunda* was the second most active sample, and also showed antioxidant properties (IC₅₀ 6.8±1.7 µg/mL). The extract and fraction in ethyl acetate of *P. cattleianum* showed only anti-inflammatory activity while the hexanic fraction of *P. pentagona* exhibited only antimycobacterial activity. The selected fractions with *dual* activities are being used for the isolation of active substances and future tests in experimental murine model of pulmonary TB.

Keywords: Tuberculosis, Inflammation and Natural Products

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