

TITLE: ANTTITUBERCULAR ACTIVITY OF CHALCONES AND THEIR TOXICITY AGAINST HUMAN CELLS

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ABSTRACT: *Mycobacterium tuberculosis* is the causative agent of tuberculosis, disease considered a serious public health problem, with 10.4 million new cases and 1.8 million deaths in 2015. This bacterium can mainly affect the lungs, causing the most well-known form of the disease, pulmonary tuberculosis, but can also target other organs, characterizing extrapulmonary tuberculosis. One of the main problems related to tuberculosis is the multidrug resistant (MDR-TB) and extensively resistant (XDR-TB) strains. Chalcones constitute a class of substances widely distributed in nature and they exhibit numerous biological activities, including antibacterial, anti-inflammatory and antimycobacterial. Thus, the objectives of this study were evaluation of chalcones against *M. tuberculosis* and their cytotoxic activity against lung fibroblasts and murine macrophages. Chalcones were evaluated against the *M. tuberculosis* strain H37Rv (ATCC 27294) using the broth microdilution method with resazurin as a colorimetric indicator. Antitubercular potency was expressed as MIC₉₀ values (Minimum Inhibitory Concentration capable of inhibiting 90% growth). All chalcones were evaluated in concentrations ranging from 25.0 to 0.09 µM, using isoniazid as a reference antitubercular drug. Substances with MIC values equal to or lower than 10.0 µM were selected for the toxicity assays against lung fibroblasts non-tumorigenic MRC-5 (ATCC CCL-171) and murine macrophages J774A (ATCC TIB-67). For the cytotoxicity assay, resazurin was also used as a colorimetric indicator of cell viability, which is demonstrated by the IC₅₀ values (concentration capable of promoting 50% death of the lung cells or macrophages), which will be expressed in µM and using doxorubicin was as a positive control. All chalcones showed potent antimycobacterial activity, demonstrating MIC values between 12.68 and 2.01 µM, while isoniazid presented MIC₉₀ equal to 0.11 µM. Among the eight chalcones, six were selected for cytotoxicity assays. Chalcones **2** and **4** presented IC₅₀ of 30.30 and 26.64 µM for lung fibroblasts and **4** presented IC₅₀ of 90.98 µM for murine macrophages, indicating low toxicity for these cells. Thus, the results corroborate the antimycobacterial activity of chalcones and indicate low cytotoxicity in lung fibroblasts and murine macrophages, promoting the development of new active substances against *M. tuberculosis*.

Keywords: tuberculostatic, chalcones, *Mycobacterium tuberculosis*

Development Agency: Capes, Fapesp, CNPq, PROPG-Unesp