TITLE: *IN VITRO* COMBINATION OF β-LAPACHONE AND ACETYLCYSTEINE AGAINST *Mycobacterium tuberculosis*

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ABSTRACT: The tuberculosis treatment presents several problems related to the use of drugs that present high toxicity, lack of patient adherence and consequent increase of resistant clinical isolates. The search of a new therapeutic scheme involves performing tests that determine the antimycobacterial activity when pharmacological agents are combined. β-lapachone is a natural quinone that demonstrates great pharmacological potential, presenting excellent activity against *Mycobacterium tuberculosis*. Acetylcysteine (AC) is a drug that is used as adjuvant in some therapies, especially in patients with respiratory diseases. It has also been shown that this drug decreases pulmonary pathology and inflammatory status, favors the immune response to control *Mycobacterium tuberculosis* replication, and reduces the burden of mycobacterial infection in the lung. Considering the advantages of both compounds, the aim of this study was to evaluate the minimum inhibitory concentration (MIC) of β-lapachone and AC alone and the effect of the combination of these two compounds against *M. tuberculosis*, using Resazurin Microtiter Assay Plate (REMA) and checkerboard method. The experiment was carried out in triplicate, using reference strain *M. tuberculosis* H_{37}Rv (ATCC 27294). β-lapachone (stock solution in dimethylsulfoxide, 10,000 µg/mL) and AC (Fluimucil®, 100,000 µg/mL) were used in concentrations ranging from 31.25 to 0.12 µg/ml and 12,500 to 195.31 µg/mL, respectively. Fractional inhibitory concentration index (FICI) of values ≤ 0.5; 0.5 - 4 and ≥ 4 were considered synergistic, indifferent and antagonistic, respectively. β-lapachone and AC presented MIC 1.95 µg/mL and 1,562.5 µg/mL, respectively. β-lapachone + AC combination showed synergism against *M. tuberculosis* H_{37}Rv,with a FICI = 0.375. The association of these compounds showed promising results that encourages more studies seeking ways to improve tuberculosis therapeutic scheme.

Keywords: tuberculosis, quinone, acetylcysteine, checkerboard