TITLE: DRUG REPOSITIONING: ACTIVITY OF HIV ANTI-RETROVIRAL AGENTS AGAINST *Mycobacterium tuberculosis*

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ABSTRACT:

Mycobacterium tuberculosis (MTB) is a bacterium that causes tuberculosis disease (TB) and responsible for thousands of deaths each year globally. In addition, this number is much higher when HIV co-infection (TB/HIV) occurs compared to individuals without HIV co-infection. Strategies recently used in TB drug development include reevaluation of existing drugs to use them to treat TB in order to obtain drugs with less toxicity and more efficient for the TB treatment. Therefore, the aim of this study was to evaluate the activity of HIV-anti-retroviral agents against MTB $H_{37}R_V$. The minimum inhibitory concentration (MIC) of Nevirapine (NVP) and Tenofovir disoproxil fumarate (TDF) against the reference strain MTB $H_{37}R_V$ (ATCC 27294) was determined by Resaruzin Microtiter Assay Plate. The drugs were serially diluted in Middlebrook 7H9 supplemented with Oleic Albumin Dextrose Catalase (ranging from 250 to 1.96 µg/ml) and plated in microplates. Isoniazid (INH) was used as the reference drug. Then 100 µL of standardized bacterial inoculum (turbidity equal to 1.0 McFarland scale and diluted 1:20) was added and incubated at 35 °C for 7 days. After this period, 0.02% resazurin was added to each well and the microplates were incubated for additional 24h at 35 °C. The change of resazurin color from blue to pink, by its reduction, was considered as the presence of bacterial growth. MIC was defined as the lowest drug concentration where no resazurin color change was observed. Both NVP and TDF showed MIC >250 µg/ml against MTB $H_{37}R_V$, while the isoniazid control exhibited MIC 0.06 µg/ml. People living with TB/HIV co-infection experience a large burden of adverse effects caused by the concomitant treatment for TB and HIV. In order to reduce the number of drugs used in the TB/HIV therapy, here we sook to verify whether the HIV anti-retroviral agents also had activity against MTB. However, NVP and TDF did not showed interesting activity against MTB when compared to the reference drug, INH.

Keywords: *Mycobacterium tuberculosis*; anti-retroviral agents; anti-bacterial agents; drug repositioning

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