TITLE: CHANGES IN THE Attenuated Total Reflection (ATR) PROFILE CAUSED BY THE RIFAMPICIN ACTION AGAINST *Mycobacterium tuberculosis*

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ABSTRACT:

Tuberculosis (TB) is still a major public health threat, caused mainly by the acid fast bacillus *Mycobacterium tuberculosis (Mtb).* The standard TB treatment uses a combination of four drugs, which rifampicin (RIF) compose part of the scheme. The emergence of rifampicin-resistant and other drugs resistant mycobacteria leads to seek techniques towards the better understanding of drug action and the quick resistance detection. Recently, techniques involving spectroscopy and non-destructive method such as Raman, Attenuated Total Reflection (ATR), have been used in organic compounds, fungi and gram positive bacteria for differential diagnosis at the species level. Thus, the objective of this study was identify the main changes caused by the RIF action on *Mtb* H37Rv according to the time induction (0, 12, 24 and 48h) in Fourier Transform Infrared Spectroscopy (FTIR-ATR). The reference strain *Mtb* H_{37}Rv (ATCC 27294) was grown in Middlebrook 7H9-OADC; and induced by the minimal inhibitory concentration of RIF (0,004µg/mL). Aliquots were harvested at points 0, 12, 24 and 48 hour after induction. Bacteria were washed with Milli-Q water 3 times, 5000 rpm 2 min, and heat inactivated at 80 °C for 30 min. Samples spectra were performed using a FTIR spectrometer equipped with ATR accessory, in the spectral range between 4000 a 400 cm^{-1} with a resolution of 4 cm^{-1} and 128 scans. During RIF induction, were observed changes in the spectra over the time in regions comprising mycolic acids (2800-3000 cm^{-1}); region of the carbonyl ester groups in lipids (1735-1745 cm^{-1}); and region of the polysaccharides (900-1200 cm^{-1}). Therefore, FTIR-ATR spectroscopy could be an auxiliary tool for the drug action comprehension; RIF causes alterations in different components of mycobacterial metabolism, further than the ribosomal inhibition.

Keywords: FTIR-ATR, Spectroscopy, *Mycobacterium tuberculosis*, Rifampicin, tuberculosis