TITLE: EFFECT OF *TRIS*-(1,10-PHENANTHROLINE)IRON(II) ON DIFFERENT METABOLIC STAGES OF *MYCOBACTERIUM TUBERCULOSIS* AND ACTION AGAINST RESISTANT TUBERCULOSIS

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ABSTRACT:

Tuberculosis (TB) is considered the world's deadliest transmissible disease according to the World Health Organization (WHO). The high incidence is mainly related to the emergence of resistance to the main classes of antimicrobials, and to the fact that about 2 billion people have latent infection worldwide. The need to develop new drugs that are active in these peculiar forms of the disease represents a great challenge for the control and treatment of TB. Therefore, this work aimed to determine the activity of the metal complex, *tris*-(1,10-phenanthroline)iron(II) ($[Fe(phen)_3]^{2+}$) against *Mycobacterium tuberculosis*, the main agent causing TB. The Minimum Inhibitory Concentration (MIC_{90}) of the complex was determined against the sensitive bacterial of *M. tuberculosis* $H_{37}Rv$ and against 7 strains of clinical isolates monoresistant, with multiple (MDR-MDR) or extensive (MDR-TB) resistance through the Resazurin Microtiter Assay (REMA), in which the complex was exposed to the mycobacterial culture, obtaining after 7 days of incubation, the concentration that inhibited 90% of the growth of *M. tuberculosis*, by fluorescence reading in Cytation 3 (Biotek®). The MIC_{90} of the complex was also determined against non-replicating bacilli by the Low Oxygen Recovery (LORA) method using *M. tuberculosis* in plasmid-containing latency, capable of emitting luminescence, the incubation was performed for 10 days in anaerobic chambers, followed by recovery in an oxygenated environment for another 28 h and then the luminescence reading in Cytation 3 (Biotek®). The first line drugs for TB treatment, rifampicin and isoniazid, were used as controls and all the trials were performed in triplicates. The complex exhibited a MIC_{90} value of 5.32 μg/mL against metabolically active sensitive strains and a value of 12.27 μg/mL against latent bacteria. The activity against resistant bacteria was equal or better in 4 strains and less effective in the other 3 tested, compared to activity against sensitive bacteria. In view of the results, it is possible to characterize the complex ($[Fe(phen)_3]^{2+}$) as a promising drug candidate for TB treatment, since it was effective against *M. tuberculosis* in both its active and latent metabolic state and in front resistant bacteria, a profile that highlights him in the face of the challenge in the control and treatment of the disease, as the rates of antimicrobial resistant TB have been declared a worldwide threat by the WHO.

Keywords: Tuberculosis, *M. tuberculosis*, Resistance, Latency, New Drugs.

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