

Title: TIOSSEMICARBAZONES: DETERMINATION OF ANTI- *Mycobacterium tuberculosis* ACTIVITY IN THREE IMPORTANT DIFFERENT BIOLOGICAL CONDITIONS.

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Abstract:

Tuberculosis (TB) is an infectious disease caused mainly by *Mycobacterium tuberculosis* (MTB). Factors such as the emergence of resistant strains make urgent the search for new compounds as potential drugs. In this sense, the Medicinal Inorganic Chemistry has been shown an important tool in Drug Design against infection diseases. The compounds were previously synthesized by Chemistry Institute/USP. Minimum Inhibitory Concentration (MIC) was determined against MTB strain H37Rv (ATCC 27294) using Resazurin Microtiter Assay (REMA) according to Palomino *et al*, 2002 – in three important different conditions: acid pH; 2% albumin; 10% FBS. The results were observed by visual colorimetric change and fluorescence (TECAN Spectrafluor[®]) in response to cell metabolism. Ratio was calculated between the MIC condition and MIC pH 6.8. The most common method to determine protein MIC shift is the use of serum supplements and albumin, because albumin is the serum protein most commonly involved in significant binding of drugs, others such as alpha 1-acid glycoprotein, lipopeptides and globulins may also be involved. In addition, into macrophage we found an acid pH in order to determine the behavior of the compound in an acid pH, which is very important since MTB is able to permanence into macrophage for many years. The results were: [Co(atc-Ph)₂]Cl.MeOH (MIC pH 6.8: 12.50 µg/mL; MIC pH 6.0: 22.02 µg/mL [ratio:1.76]; MIC 2% albumin: 13.88 µg/mL [ratio:1.11]; MIC 10% FBS: 17.91 µg/mL [ratio:1.43]); [Co(atc-Et)₂]Cl (MIC pH 6.8: 12.50 µg/mL; MIC pH 6.0: 23.27 µg/mL [ratio:1.86]; MIC 2% albumin: 21.82 µg/mL [ratio:1.75]; MIC 10% FBS: 17.16 µg/mL [ratio:1.37]). The cut-off ratio is 2.0 and less than 2.0 we considered the compound did not present significant variation in the activity. If the compound presents a significant loss of activity, it may suggest that this compound interacts irreversibly with some component of the plasma studied and it will likely occur *in vivo*. If the reverse occurs, only one can suggest that it probably will not occur *in vivo*. So, we identify a new prototype drug candidate compounds active against MTB.

Keywords: tuberculosis, cobalt, activity

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