

A manganese(IV) thiosemicarbazone complex as a potential anti-tuberculosis metallodrug candidate

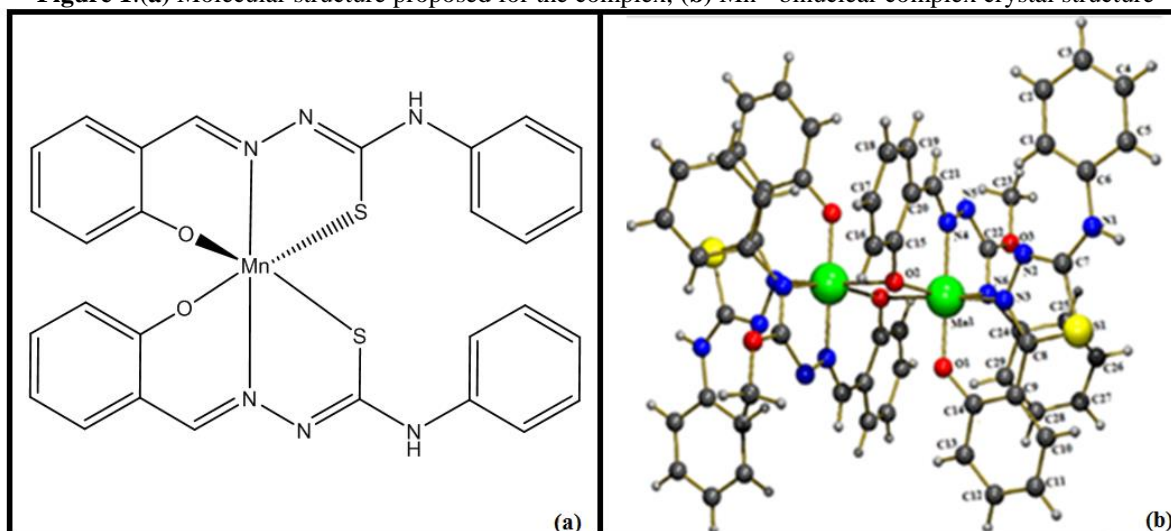
Jocely L. Dutra*, Victor M. Deflon

University of Sao Paulo, Institute of Chemistry of Sao Carlos, Brazil

*e-mail: jocely.dut@usp.br

Tuberculosis (TB) is an infectious disease caused by *Mycobacterium tuberculosis*, which kills millions of people each year. The first line currently available drugs for the treatment of TB were discovered more than forty years ago. Furthermore, the duration, complexity, adverse events in response to anti-TB drugs and the increasing incidence of multidrug resistant (MDR) and extensively drug resistant (XDR) have made the development of new anti-TB drugs urgently necessary[1,2]. Recent studies have shown that Mn^{II} complexes with thiosemicarbazones (TSCs) exhibit good activity against TB[3]. The Mn^{IV} complex was synthesized from $MnCl_2$, Et_3N and H_2phtsc (salicylaldehyde-4(N)-phenyl-3-thiosemicarbazone) in MeOH. The solid was characterized by different methods, including IR and UV-Vis spectroscopies, elemental analyses, magnetic susceptibility, conductometry and single crystal X-ray diffraction. The IR spectra show the absence of the band $\nu(O-H)$, at 3338 cm^{-1} for the ligand, and the shift of the band $\nu(C=N)$ from 1620 cm^{-1} to 1597 cm^{-1} , evidencing the absence of the free ligand upon coordination. The complex formed is neutral ($0,02\text{ }\mu\text{S}\cdot\text{cm}^{-1}$, $10\mu\text{M CH}_2\text{Cl}_2$) and the magnetic susceptibility is in accordance with a Mn^{IV} complex ($\mu_{\text{eff}} = 3,97\text{ BM}$). The structure proposed is depicted in **Figure 1(a)**. A few single crystals of a binuclear complex were obtained in a crystallization attempt of the product from MeOH/ CH_2Cl_2 solution by slow evaporation. X-ray structure analysis showed that the H_2phtsc was structurally modified, forming two different ligands in a binuclear complex (**Figure 1(b)**). While one ligand presented desulfurization and incorporation of a methoxide group (O,N,N coordination), the other one showed a cyclization by a nucleophilic attack of the sulfur atom on the imine carbon atom (O,N coordination).

Figure 1.(a) Molecular structure proposed for the complex, (b) Mn^{IV} binuclear complex crystal structure



References

- [1] <http://who.int/topics/tuberculosis/en/>, accessed in June 2016.
- [2] Boogaard, J. V.; Kibiki, G.S.; Kisanga, E. R.; Boeree, M. J.; Aarnoutse, R. E. *Antimicrob. Agents Chemother.* **2009**, *53*, 849-862.
- [3] Oliveira, C. G.; Maia, P. I. da S.; Souza, P. C.; Pavan, F. R.; Leite, C. Q. F.; Viana, R. V.; Batista, A. A.; Nascimento, O. R.; Deflon, V. M. *J. Inorg. Biochem.* **2013**, *132*, 21-29.

Thank CAPES, CNPq and FAPESP for supporting this work.