Crystal structure, cytotoxicity and *in vitro* antileishmanial activity of novel Sb(V)- and Bi(V)-based organometallic complexes against Sb-sensitive and resistant *Leishmania*

Arshad Islam[1,2], Bruno Rodrigues do Prado[1], Weverson Ferreira[1], Juliane Sousa Lanza[2], Bernardo Lages Rodrigues[1], Rubens do Monte-Neto[3], Fréderic Frézard[2], Cynthia Demicheli[1*]

[1]*Department of Chemistry, Institute of Exact Sciences, Federal University of Minas Gerais (UFMG), Belo Horizonte, Brazil,* [2]*Department of Physiology and Biophysics, Institute of Biological Sciences, Federal University of Minas Gerais(UFMG),*[3]*René Rachou Research Centre – Fiocruz Minas*

*e-mail: demichel@netuno.lcc.ufmg.br

In the efforts to explore innovative, innocuous and cost-effective drugs for the treatment of leishmaniasis and to overcome the currently prevalent problem of drug resistance, novel organoantimony(V) dicarboxylates and amino acid-derivated hydroxamic acids *i.e.*, $[Ph_3M1(L1)_2]$ (**1**), $[Ph_3M1(L2)_2]$ (**2**), $[Ph_3M1L3]$ (**3**), $[Ph_3M1(L3)_2]$ (**4**) and organobismuth(V) $[Ph_3M3(L1)_2]$ (**5**), and $[Ph_3M2(L2)_2]$ (**6**), were synthesized where L1 = deprotonated 3-(dimethylamino)benzoic acid (HL1); L2 = deprotonated 2-acetylbenzoic acid (HL2); L3 = deprotonated alanine hydroxamate (HL3); M1 = triphenylantimony(V) and M2 or M3= triphenylbismuth(V) from triphenylbismuth(V) dichloride or triphenylbismuth(V) carbonate salts. Complexes were characterized by elemental analysis, IR, UV-*Vis* and NMR. Crystal structures of **1** and **5** were determined by single crystal X-ray diffraction. *In vitro* antileishmanial assessments exhibited that all complexes were active against Sb-sensitive (SbS) *Leishmania infantum* and *L. amazonensis* promastigotes at a faint concentration (IC_{50} 2.1–14.3 μM) but the organobismuth(V) salts and their dicarboxylate complexes remained, comparatively, the most active against both of SbS *Leishmania* strains. In contrast to the organobismuth(V) (IC_{50} 2.1–2.5 μM), the organoantimony(V) dicarboxylates and hydroxamates were active against both of SbS *Leishmania* strains at slightly higher concentrations (IC_{50} 4.4–14.3 μM and 6.7-10.7 μM respectively) but were found, comparatively, less cytotoxic (CC_{50} 37.2–39.7 μM and 38.13-165.8 μM, respectively) than organobismuth(V) ones (CC_{50} 0.81–8.0 μM) towards murine macrophages. The organoantimony(V) complexes (**1** and **2**) also exhibited antileishmanial activity better than Glucantime® against intracellular amastigote from both SbS *Leishmania* strains, at ~9.5–8.1 μM, a concentration below the cytotoxic concentration. Astonishingly, the *in vitro* evaluation of organoantimony(V) complexes (**1**, **2**, **5** and **6**) in Sb-resistant (SbR) *Leishmania* promastigotes of both strains resulted in the growth inhibition of their 50 % cells at ~0.37–10.0 μM concentration. Collectively, organoantimony(V) complexes were more selective than organobismuth(V) ones, both against promastigotes and amastigotes forms of SbS *L. infantum* and *L. amazonensis*, as well as against their SbR promastigotes. Financial support: FAPEMIG and CNPq.