Tailoring nitrosyl ruthenium complexes for improve cellular uptake: Synthesis, characterization and biological assays

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The research in the nitric oxide (NO) field has been considerably expanded, including the application of new NO drugs to medicine[1]. Ruthenium nitrosyl complex has been investigated to the ability of release nitric oxide inside the cells in a controlled manner. The present study is focused on synthesize nitrosyl ruthenium complexes containing modified amino acids as methionine, lysine and arginine, and study biological activity of them.

New nitrosyl ruthenium compounds have been synthesized by reaction between amide and carboxylic acid to functionalize ruthenium complex with amino acid as biomolecule. Ligand were characterized by ^{1}H NMR, 2D NMR (correlations) and mass spectrometry. Ruthenium complexes were characterized by Uv-vis and FTIR spectroscopy, elemental analysis, cyclic voltammetry and mass spectrometry. Photochemical release of NO was conducted. Compounds were tested against B16F10 (murine melanoma) and normal cells L929 (fibroblast). Besides of that, complexes were also tested against amastigotes forms of *T. cruzi*. Elemental analysis and MALDI-TOF/TOF mass spectrometry has confirmed the structure of all studied compounds. The cell viability results showed Ru-etpy (precursor) and Ru-Lys (complex containing modified lysine) were not cytotoxic in L929 cells (normal cells), indicating these complexes can be used as chemotherapeutic agents. In B16F10 cells cytotoxicity increase around 20 % for compound Ru-Lys in comparison to compound Ru-etpy, which could be attributed to the cellular uptake of amino acid bonded to the ruthenium. Complexes associated with benznidazole in a ratio of 1:1, demonstrated similar activity to benznidazole against amastigotes forms of *T. cruzi*.

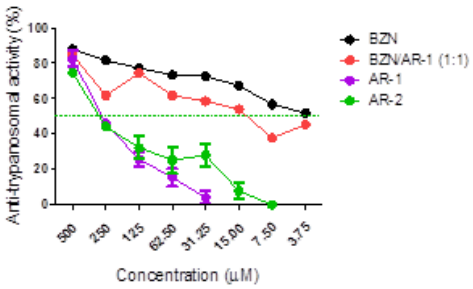

Figure 1. Comparison between complexes and complexes associated with benznidazole against amastigotes forms of *T. cruzi*. (BZN = benznidazole, BZN/AR1 (1:1) = Ru-etpy and benznidazole in proportion of concentration 1:1, AR-1 = Ru-etpyNO_2, and AR-2 = Ru-etpyNO.

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