A NEW COBALT(III) COMPOUND AS A CARRIER PROTOTYPE FOR ANTITUMOR PRODRUGS

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Co^{3+} complexes are promising compounds as Prodrugs Activated by Hypoxia due to the high crystal field stabilization energy of d^6 low spin system, which allows the formation of inert complexes. The kinetic stability is necessary to achieve the reducing environment and release the drug only after being reduced, which happens because of the liability of the d^7 system of Co^{2+} complex.[1] Herein, we present the cytotoxic assays and reactivity studies of $[Co^{III}(L)(TzCl)](BF_4)_2$ (**L** is [(*bis*(1-methylimidazol-2-yl)methyl)(2-(pyridyl-2-yl)ethyl)amine] and **TzCl** is (1-(4-chlorophenyl)-1H-1,2,3-triazole-4-carbaldehyde oxime), a carrier prototype for antitumor prodrug. Synthesis and characterization data of the title complex were previously described.[2]

Diffraction results showed it is a mononuclear complex with Co^{3+} coordinated to four atoms of nitrogen of **L** and to an atom of nitrogen and an atom of oxygen of **TzCl**. Elemental analysis and infrared spectroscopy corroborated to the X-ray structure. The electronic spectra in acetonitrile showed one ILCT at 243 nm (ε /(mol^{-1} L cm^{-1}) = 26879) and one LMCT around 369 nm (ε /(mol^{-1} L cm^{-1}) = 5208). In the same medium, the E_{pc} found was -0.31 V *vs* NHE.

Light and dark stability of $[Co^{III}(L)(TzCl)](BF_4)_2$ were analyzed by electronic spectroscopy in buffered aqueous medium. Data showed higher stability in the dark (88%) than under light (78%) after seven days. The reduction reaction of the complex with ascorbic acid was monitored by electronic spectroscopy. The oxygen and pH dependence were analyzed varying oxygen concentration and applying three different mediums (pH 6.2, 7.0, and 7.4). Results confirmed the reduction of $[Co^{III}(L)(TzCl)](BF_4)_2$ by ascorbic acid and showed higher initial rates at pH 6.2 and lower oxygen concentration.

Under atmosphere oxygen concentration, no cytotoxic activity for lung and breast cell lines was observed, although, an aged solution of the title compound presented 60% cellular viability, at 100 µM. The aged solution of $[Co^{III}(L)(TzCl)](BF_4)_2$ was more toxic than the solution of **TzCl**, which may be due to the additivity toxicity of the complex formed after the drug being released.

Based on these results we conclude that the complex $[Co^{III}(L)(TzCl)](BF_4)_2$ presents a good reactivity and can be considered a promising carrier of cytotoxic agents to the hypoxia region of cancer cells.

References:

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