New ruthenium complexes as antitumoral agents

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Introdução

Nowadays, ruthenium compounds have received considerable attention because the complexes imidazolium-trans-dimethylsulfoxide-imidazole-tetrachlororuthenate(III) and indazolium-trans-bis(1H-indazole)-tetrachlororuthenate(III) entered human clinical trials [1, 2]. This fact stimulated us to search for new ruthenium compounds as antitumoral agents. This work reports on the synthesis, characterization, DNA interactions, and photocitotoxic activities of two new ligands and mixed-ligand complexes of ruthenium(II). Their general formula is [Ru(L)(phen)(dmso)(Cl)](PF_6), in which L= pqdS [N'-(6-oxo-1,10-phenanthrolin-5(6H)-ylidene)thiophene-2-carbohydrazide] for complex **1** and pqdO [N'-(6-oxo-1,10-phenanthrolin-5(6H)-ylidene)furan-2-carbohydrazide] for complex **2**.

Resultados e Discussão

The ligands were characterized by elemental analysis, vibrational, electronic, and ^{1}H NMR spectrometries. The complexes (Fig. 1) were characterized by elemental and conductivity analyses, vibrational, electronic, and ESI-MS spectrometries. The presence of the complexes in solution was confirmed by ESI-MS spectrometry in positive mode. Complex **1** give a main peak at m/z 728.6 assigned to $[Ru(pqdS)(phen)(dmso)(Cl)]^+$ (calculated mass 729.2) and complex **2** at 712.6 due to $[Ru(pqdO)(phen)(dmso)(Cl)]^+$ (calculated mass 713.2). The calculated isotopic distribution for the proposed species agrees with the experimental spectra. The molar conductivity values of 10^{-3} mol·L^{-1} solutions of **1** and **2** in nitromethane, at 25 ºC, are ΛM= 89.6 and 77.9 μS·cm-1, respectively, indicating that they are 1:1 electrolytes.

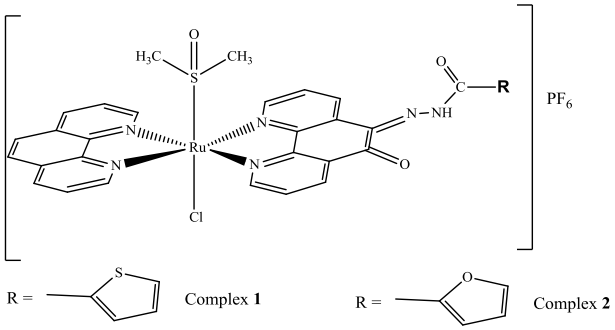

Figure 1: Proposed structures for complexes **1** and **2**.

The addition of calf thymus DNA to a solution of the complexes induces a hypochromic effect in their UV-Vis spectra indicating the formation of a ternary complex with DNA (Fig. 2). From the spectrophotometric data, the following binding constants were calculated 6.1 x 10^4 for **1** and 1.4 x 10^4 for **2**.

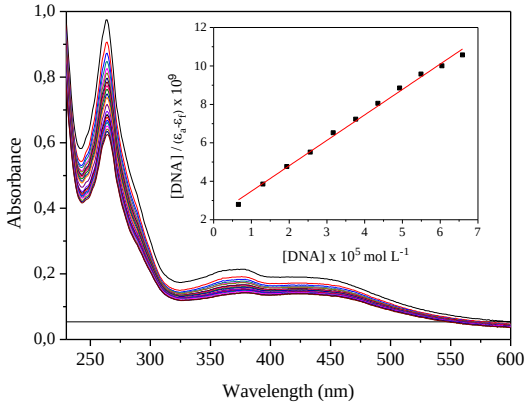

Figure. 2: Spectra of solutions containing complex **1** (2.5 × 10^{-5} mol L^{-1}) and increasing concentrations of DNA in HEPES buffer pH 7.4. [DNA]:[complex] ranging from 0 to 4. Inset: [DNA]/(ε_a - ε_f) *versus* [DNA].

UV-light exposure increases the cytotoxic activities of both compounds. The IC_{50} values obtained in the dark for complex **1** and **2** are 55.1 and 51.8 μmol L^{-1}, and after irradiation 18.8 and 17.3 μmol L^{-1}, respectively. Upon irradiation, there is an increase of approximately 3 times for both complexes.

Conclusões

These complexes can interact with DNA, an important target of antitumoral drugs. The cytotoxic activity of the complexes increased 3 times upon UV-light exposure which indicates that these compounds can be promising agents in photodynamic therapy.

Agradecimentos

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