Abstract

The pharmacological properties of any drug are related to its ability to interact with macromolecular blood components. The interaction of human serum albumin (HSA) and apotransferrin (ATf) with six Ru II complexes containing ketoconazole (KTZ), which we have previously reported to be active against Leishmania major and Trypanosoma cruzi, has been investigated by monitoring the tryptophan fluorescence intensity of each protein upon incremental addition of the complexes. All the Ru-KTZ derivatives, namely cis-fac-[Ru II Cl 2 (DMSO) 3 (KTZ)] (1), cis-[Ru II Cl 2 (bipy)(DMSO)(KTZ)] (2), [Ru II (6-p-cymene)Cl 2 (KTZ)] (3), [Ru II (6-p-cymene)(en)(KTZ)]BF 4 2 (4), [Ru II (6-p-cymene)(bipy)(KTZ)]BF 4 2 (5), and [Ru II (6-p-cymene)(acac)(KTZ)]BF 4 2 (6) are able to quench the intrinsic fluorescence of HSA and ATf at 27 °C. Analysis of the spectroscopic data using Stern-Volmer plots indicates that in both cases the quenching takes place principally through a static mechanism involving the formation of Ru complex-protein adducts; further analysis of the fluorescence data allowed the estimation of apparent association constants and the number of binding sites for each protein and each compound. The results indicate that both HSA and ATf are possible effective transporters for Ru-KTZ antiparasitic drugs.

Keywords
Ruthenium, ketoconazole, antiparasitic, albumin, transferrin, fluorescence