Vascular contraction-stimulating effect of ruthenium-catecholamine complexes on rat thoracic aorta. Structure activity dependence and protein interaction

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Cancer is characterized by disorderly growth of cells. Angiogenesis, the new vessels formation, has an important role in this growth, such it is essential in tumor nutrition. Catecholamines participate in this process; however the mechanisms are not elucidated[1]. For this reason, we have immobilized catecholic site by coordination with the ruthenium ion. Thus, complexes of the kind "$[Ru(NH_3)_4(cat)]Cl$" were synthesized, where "cat" is dopamine, noradrenaline, adrenaline, isoproterenol or catechol. These complexes were characterized by many techniques, such as UV-vis, FTIR, Raman, NMR spectroscopies, mass spectrometry, HPCL and electrochemical analyses. As the most abundant protein of human blood is albumin (HSA) – 60% of the plasma composition; it is one of the main carrier proteins. So, the study of the interaction between HSA and these complexes is essential to evaluate toxicity, metabolism and bioavailability, and this analyze provides important information about the therapeutic efficacy of compounds as potential metallodrugs[2]. In this work, we have analyzed the interaction between ruthenium-catecholamine complexes and HSA by fluorescence spectroscopy. HSA were excited in λ 280 and 295 nm. The experiments were carried out at 298, 305 and 310 K. The results demonstrated a linear dependence between F_0/F and noradrenaline, adrenaline, dopamine and catechol complexes concentration, while only for Ru-isoproterenol complex we have found a linear dependence between $F_0/(F_0-F)$ and 1/[Q] in Stern-Volmer plot, for all temperatures. It was possible to obtain Stern-Volmer constants (Ksv) and the values decreased with the temperature increase, which suggests a static mechanism of interaction. The results showed the complex which has catechol as ligand had the smallest interaction with HAS (Ksv $4{,}5.10^3$ $mol^{-1}L$), while the complex with isoproterenol as ligand, showed the greatest interaction (Ksv $1{,}7.10^4$ $mol^{-1}L$). Additional studies of the vascular reactivity performed in thoracic aorta of rats, have allowed a view to understanding the interaction in adrenergic receptors. Similar behavior was found in vascular reactivity assays, once the complexes act as antagonist or partial agonist of the adrenergic receptors and ruthenium-catechol complex did not promote a vascular contraction, while the isoproterenol complex has promoted the maximum effect in lowest concentration (3.10^{-6} mol L^{-1}). It is possible to conclude from these results that the angiogenic mechanism of catecholamines is dependent of two binding-sites of catecholamines, since the coordination with ruthenium ion seems to modulate the biological effects.

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