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On the field of metallodrugs -new ruthenium compounds as anti-tumor agents

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The discovery of the anticancer properties of cisplatin by Rosenberg in the late 60's paved the way for the development of metal-based cancer therapy. Cisplatin and analogues are to date the only metal-based chemotherapeutics approved worldwide for clinical use. Although highly effective, dose-limiting side effects and the development of resistance to treatment severely limit their clinical value, and ruthenium compounds are a proven effective alternative.

We are engaged in the development of ruthenium complexes that combine stability and adequate solubility in aqueous media with a large spectrum of activity against several types of cancer models. In our approach, the problem of the known aqueous instability of monodentate ruthenium complexes is overcome by the use of a bi- or a multidentate ligand. We are currently screening ruthenium-based families exhibiting either piano-stool or octahedral structures for their chemotherapeutic potential. Organometallic {Ru(II)(η5-cyclopentadienyl)} derivatives are examples of the formerwhile Ru(III) complexes with tetradentateaminophenolate ligands are included in the latter. The activity of both ligands and complexes is investigated against human cancer cell lines with a different degree of chemoresistance. We have been working on the mode of action of these prospective metallodrugs, the possibility of drug distribution through the blood by means of serum protein binding (namely human albumin), addressing their cellular uptake and distribution, screening possible cellular targets, cellular morphological alterations and mechanism of cell death. Our compounds typically exhibit moderate to high cytotoxicity *in vitro*, in some cases largely surpassing that of cisplatin, and are active against cisplatin resistant cell lines. Our findings reveal distinct differences in cellular distribution in comparison to cisplatin and suggest that the major targets for these ruthenium complexes are possibly at the membrane and cytosol rather than the nucleus.

Biography

Ana Isabel Tomaz is presently a research assistant in the Organometallic and Bioorganometallic Group of the Center for Molecular Sciences and Materials at the Faculty of Sciences of the University of Lisbon (Portugal) in the field of medicinal inorganic chemistry, where she has been working on ruthenium complexes for cancer treatment. She completed her Ph.D. in 2003 from Instituto Superior Técnico at Technical University of Lisbon on potentially therapeutic vanadium compounds as insulin mimetics in the treatment of diabetes, and continued her postdoctoral studies on the field of metal complexes designed for therapeutic applications at University of Coimbra (Portugal).

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