

Abstract

The discovery of antitumor activity of cisplatin was one of the major chemo-pharmaceutical discoveries of the nineteen-sixties. It enabled new ways of treating cancer patients, as well as opening the doors of research of drugs based on a metal ion. Research of platinum substances advanced, providing several new drugs for approved clinical use in the next two decades. They managed to reduce the magnitude of cisplatin's most severe side effects, but failed to address the lack of selectivity, both fast emergent and innate resistance and other shortcomings of the drug. In parallel with platinum-based drug research, research in compounds with other metal centers proceeded at pace. Among the first candidates for clinical trials were octahedral ruthenium(III) compounds, among which NAMI-A and KP1019 proved most interesting. NAMI-A has recently failed the second phase of clinical trials, while the second phase of trials for KP1019 and its related formulations is still ongoing. Modern ruthenium compounds are mainly based on organometallic ruthenium(II) with the most known compounds being RM175 and RAPTA-C. Both are currently undertaking preclinical trials. Among the newest, the almost unseen phototherapeutical TLD1433 has blazed into clinical trials in the recent years, its structure resembling those of well-known ruthenium dyes.

In order to undertake a categorization of basic physico-chemical and biologic properties, I synthesized three series of compounds – organoruthenium complexes with diketonates and pta, organoruthenium complexes with quinolones and pta and organoruthenium complexes with nitroxoline analogues. Their properties were characterized by means of various spectroscopic and analytical techniques such as nuclear magnetic resonance, infrared spectroscopy, high resolution mass spectrometry and CHN elemental analysis. Crystal structures of compounds were determined by X-ray single crystal diffraction and analyzed in relation to similar compounds of the class. In collaboration with other researchers I studied their biological activity (antibacterial, cytotoxic, cathepsin-inhibiting properties, etc.). The use of phosphine ligand pta had an expected significant impact on the biological properties of tested compounds.

Keywords: ruthenium coordination compounds, organoruthenium compounds, diketonates, quinolones, crystal structures, biological activity