ABSTRACT

Bioinorganic medicinal chemistry is receiving an increasing amount of attention since the discovery of the cytostatic property of cisplatin in the late 1960s. Despite a widespread use of platinum-based chemotherapeutics new compounds were developed also with different metal ions included (gallium, iron, copper, titanium, palladium, gold, ruthenium and others). Among them, ruthenium-based complexes are the most promising alternatives with several lead compounds such as KP1019, RAPTA and TLD-1433 complexes which have already entered different stages of clinical trials or are on the right track to get there. In general, ruthenium complexes show also other numerous interesting properties, which find various applications in abundant aspects of life. They are used in the field of catalysis where Grubbs´ catalysts play a leading role and in the field of Grätzel solar cells, where ruthenium polypiridine complexes are used as dyes responsible for sunlight absorption.

The goal of my research was to synthesize different types of ruthenium coordination compounds with *N*,*N*-, *N*,*O*- and *N*,*N*,*N*-donor ligands – organoruthenium complexes, ruthenium complexes with trithiacyclononane, ruthenium polypiridine complexes and ruthenium complexes with tridentate ligand. The aim was also to study their physico-chemical properties by means of different spectroscopic techniques such as infrared and UV-Vis spectroscopy, high resolution mass spectrometry, elemental analysis CHN and nuclear magnetic resonance. The crystal structures of the compounds were determined by X-ray single crystal diffraction and the stability of compounds in aqueous and dmso solutions was studied. In collaboration with various research groups from Slovenia and abroad the interactions of novel compounds with aldo-keto reductases (AKR1C1–1C3) and 15-lipoxygenase-1 (15-LOX-1) were studied. The results of the enzyme inhibition tests reveal that some of novel ruthenium compounds inhibit the activities of AKR1C isoenzymes as well as 15-LOX-1. The enzyme kinetic analysis showed uncompetitive inhibition, which indicates that the inhibitor binds to the substrate bound enzyme.

Keywords: synthesis, ruthenium coordination compounds, crystal structures, enzyme inhibition, AKR1C isoenzymes, 15-lipoxygenase-1