Summary of Ph. D. thesis "II - electronic Ru(II) complexes with selected ligands as potential antitumor agents"

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The Ph. D. thesis titled: "II - electronic Ru(II) complexes with selected ligands as potential antitumor agents" refers to the synthesis of arene Ru(II) complexes with amino/hydroxycoumarins, chromone and pyrazole derivatives and identification of their structure based on spectroscopic methods and others physicochemical properties, as well as characterization of their cytotoxicity. The new nineteen arene Ru(II) complexes have been synthesized and described. Each of the synthesized ligands and complexes were characterized by spectroscopic methods, such as: ^{1}H NMR, MS, IR, elemental analysis and crystallographic techniques. The lipophilicity, which was expressed as log*P* value was also determined. For the selected Ru(II) complexes the oxidation-reducing properties were determined using cyclic voltammetry. Log*P* was determined by use of RP-TLC method and it was observed that the complexes possess average lipophilicity with the exception of complexes **1e** and **3e**, for which the log*P* value is negative and that indicates the hydrophilicity of these complexes. The cyclic voltammetry measurement of complexes **1a**, **2a**, **4a**, **1b**, **3b** showed that processes connected with oxidation and reduction of Ru(II) ion are quasi reversible. Spectrofluorimetry was also performed for selected complexes, and it was found that the complexes exhibited a weaker intensity of fluorescence compared to the aminocoumarins. Based on the UV-Vis spectral analysis, the thermodynamic stability of the obtained compounds was determined by performing spectrum after 0, 24 and 48 h and it was found that under experimental conditions most of the compounds were stable. The structure of complexes **1a**, **1g**, **1j** was confirmed by crystallographic techniques.

Apart from the chemical part, the work also consists of the biological part. The viability of HeLa, K562, CFPAC tumor cell lines after treatment with **1a**, **2a**, **4a**, **1b**, **3b** complexes and ligands **a**, **b** was determined with us use of MTT assay. The tested compounds were found not to be toxic at all. In addition, the cytotoxicity of all complexes and ligands was tested by use of MTT assay against HL-60, NALM-6, WM-115, COLO205 human, tumor cell lines. The tested compounds and ligands showed poor cytotoxicity, except for single compounds. It is important to emphasize the particular activity of the ligand **i** and the complex **2j** for which the IC_{50} values were below 100 μM against of all examined cell lines (with the exception of ligand **i**, for which the IC_{50} was 186,74 ± 20,33 μM against of HL-60 cells). Ligand **i** and complexes **1e**, **3e**, **1i**, **1j**,

2j, **2c** were selected for determination of DNA damage in lymphoblastic leukemia cells - NALM-6, by use of comet assay. The obtained results show that the most interesting examined compound is ligand **i** for which the percentage of DNA damage increases with the concentration of the compound in the tested sample. For the other compounds no such dependence was observed.

To conclude, the obtained complexes were characterized in terms of their structural and biological properties. There was no relationship observed between the structure (position of the substituents and their character) and the biological activity of the obtained compounds. It was only established that complexes had better cytotoxicity compared to the ligands. However, these differences in most cases were not significant. Also no significant diffrences were observed in case of change of arene substituent. Differences in cytotoxicity between coumarins with amino and hydroxyl substituents are not enough significant to suggest that compounds containing hydroxyl substituents strengthen their cytotoxicity.