SUMMARY

Concomitant microbial infections are a major threat to people struggling with cancer. Given the increasing drug resistance of bacteria and the increasing resistance of cancer cells to common chemotherapeutic agents, it is important to search for new compounds that can be more universal, i.e., antimicrobial and anti-cancer at the same time. Administration of compounds with expected therapeutic properties to the skin or mucous membranes can unpredictably affect the opportunistic activity of natural microflora as well as pathogens that often cause wound infections in cancer patients. One way to address this problem is to modify known chemical compounds or synthesize new ones. In this context, I decided that it is worthwhile to be interested in complexes of arene ligands with ruthenium(II) ions, which have a completely different mechanism of action than previously used drugs.

This dissertation is divided into three parts. In the first part, I describe the synthesis of a series of chloride and hexafluorophosphate complex containing a ruthenium(II) ion in combination with p-cymene and selected carbathioamidopyrazole ligands with different substituents at the C-3 and C-5 positions of the pyrazole ring. In this part, the stability of the tested compounds in aqueous solution was tested and their lipophilicity was determined. In the second part, describing the study of biological properties, the focus was on the antimicrobial and anticancer activity of the synthesized compounds. The biostatic and biocidal activity of the tested complexes and their substrates against selected strains of Gram(+) and Gram(-) bacteria and fungi was determined and the obtained results were compared with selected antibiotics. The satisfactory antibacterial activity formed the basis for a very interesting research to determine the synergistic properties. The obtained results showed that the tested compounds in some combinations increased the efficacy of antibiotic therapy by 2 - 4 times. For the most promising compounds, additional experiments were conducted to determine the mechanisms of bacteriostatic or bactericidal activity. For this purpose, their ability to induce bacterial cell death and their effect on DNA, cell wall, and cell membrane were determined. In addition, a microbial viability assay and microscopic examination were performed using appropriate fluorescent dyes, and antioxidant capacity was determined using selected non-enzymatic free radical assays. Anticancer activity was evaluated by cytotoxicity assays against cancer and normal cell lines. These studies showed high efficiency of the synthesized complexes, and their competitiveness with cisplatin (commonly used in medicine against melanoma cell lines) with significantly lower toxicity against normal cell lines deserves special attention.

Later in the work, the DHET, DAF - FM and H₂DFDA probes were used in the study of cancer lines to analyze the effects of the compounds of interest on the level of reactive oxygen species and reactive nitrogen species generation, and the DAUDA and TMA - DPH probes to determine changes in cell membrane fluidity. Studies on mitochondrial membrane depolarization of cells showed pro-apoptotic properties of the complexes. Other steps performed in the anticancer part fused on the use of PARP-1 polymerase interaction to determine genotoxicity and to study the mechanism of intercalation with DNA. In addition, a structure-activity relationship analysis (SAR) was performed considering the physicochemical properties of the complexes and their cytotoxic activity against the tested cancer lines and selected strains of microorganisms.