

Currently, cancer is one of the most common causes of premature death. In addition to surgical intervention, cancer treatment relies heavily on chemotherapy. 50% of chemotherapy schemes currently use cisplatin and its very close analogous (e.g. oxaliplatin, carboplatin). Despite the obvious advantages of cisplatin therapy (as its effectiveness) it has two very clear disadvantages, side effects and drug resistance (the appearance of tumor insensitivity to the drug). The disadvantages of cisplatin are related to the way it binds to DNA. Cisplatin creates relatively strong, irreversible covalent bond directly between the metal and the purine bases in DNA. Therefore, it is very important to search for such complexes of various metals, which, thanks to the introduction of appropriate organic ligands, will exhibit a mechanism of interaction with DNA other than cisplatin. Another very important aspect in modern drug chemistry is also the possibility of controlling the cytotoxic properties of a compound with the use of an external factor, i.e. light. Then, a much stronger response of cancer cells to the presence of a light-induced drug than healthy cells may improve therapeutic indices. For any new group of compounds in order to be characterized as a photo-excited chemotherapeutic agent, it is first necessary to analyse in detail how the molecules of this group of compounds behave under the influence of excitation with light in the visible range. Such research requires a combination of various spectroscopic methods (including the use of ultrafast spectroscopy techniques) with biological studies. Therefore, the objectives of this project focus on the synthesis and study of the photodynamics and biological properties of platinum(II), ruthenium(II), iridium(III) and rhenium(I) complexes, with a new group of organic ligands, namely 4-substituted derivatives 2,6-bis(thiazol-2-yl)pyridines, which are structural analogues to the 4'-substituted 2,2':6',2''-terpyridines.

2,2':6',2''-terpyridine is one of the most important building blocks currently used in the synthesis of transition metal coordination compounds. Compared to 2,2'-bipyridine or 1,10-phenantroline, the structure of 2,2':6',2''-terpyridine allows the synthesis of isomerically pure, linear metal complexes. Therefore, complexes of this tridentate ligand exhibit beneficial supramolecular, photophysical, electrochemical, biological, kinetic, and magnetic properties and are increasingly used in material engineering, drug chemistry, pharmacy, and optoelectronics. In the context of anticancer therapy, terpyridine derivatives introduced into complexes of various transition metals change the way of interaction of these complexes with DNA from covalent towards less destructive non-covalent interactions. Moreover, by introducing appropriate structural modifications (e.g. appropriate substituents), it is possible to design the terpy-like molecule in such a way that it exhibits photophysical properties favourable for phototherapy. In the implementation of the project, we decided to use two groups of the appropriate substituents to ensure the expected photodynamic and cytotoxic effect. The first is substituents based on large conjugated aromatic rings, and the second group consists of substituents containing a strong N-donor moiety. In both groups, the substituents attach to 2,6-bis(thiazol-2-yl)pyridine directly or via an acetylene or a phenylene linker. Numerous literature reports confirm the effectiveness of introducing the substituents proposed in the project in the context of improving emission properties and anti-cancer activity. For example, large aromatic rings such as anthracene or pyrene in the coordination compound molecules have the ability to intercalate between base pairs of deoxyribonucleic acid of cancer cells, contributing to their natural death mechanism (apoptosis). On the other hand, they act as energy reservoirs, causing the metal compound to exhibit much stronger photoluminescence with extended lifetime. Strong N-donor substituents, such as those based on the triphenylamine moiety, also significantly affect parameters such as quantum efficiency of photoluminescence and under the influence of light intensify the generation of singlet oxygen in cancer cells and can be used in photodynamic therapy.

The properties of terpyridine and its complexes can be modified by replacing the peripheral pyridine rings with another heterocyclic rings, e.g. with a thiazoles present in the 2,6-bis(thiazol-2-yl)pyridine structure (proposed in this project). Preliminary studies have shown that transition metal compounds with 2,6-bis(thiazol-2-yl)pyridines can be very attractive in terms of both optical properties as well as anti-cancer properties. However, the lack of more extensive research, especially in the context of photophysical properties, means that the potential of this group of compounds still remains undiscovered. Hence, the main task of this project is to design compounds that could be used as light-induced cytostatics by combining research aimed at fully defining photodynamics with biological studies.