Project NCN PRELUDIUM "Novel BODIPY derivatives and ruthenium complexes conjugates as photosensitizers for bacterial inactivation in the *in vivo Caenorhabditis elegans* model"

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The growing antibiotic resistance among bacteria is becoming an increasing threat to public health worldwide every year. Multi-drug resistant bacteria. strains such as *Enterococcus spp*., *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumanii*, *Pseudomonas aeruginosa*, and *Enterobacter spp*. cause numerous infections and can develop many mechanisms of resistance to antibiotics. Therefore, the research for the new therapeutic methods which will not induce resistance is of great importance. Photodynamic antimicrobial therapy (PACT) could be one of such methods. An essential advantage of PACT is the low probability of inducing resistance among bacteria, in contrast to antibiotics. PACT requires three factors: a drug called photosensitizer (PS), oxygen, and light. PS after exposure to light produces reactive oxygen species (ROS), which are responsible for cell death. PACT is a promising therapeutic option for treating antibiotic-resistant microbes, but currently no photosensitizers are approved for antimicrobial photodynamic treatment. For this reason, the development of novel compounds for PACT represents an urgent need for research.

Boron dipyrromethene derivatives (BODIPY) are organic compounds that gain growing importance as photosensitizers due to many favorable characteristics, including intensive absorption of light and good stability. Also, the structure of these compounds can be easily changed, which allows for modification of their properties. Ruthenium polypyridyl complexes are another promising candidates for the application in PACT. They possess several favorable properties, including stability, water-solubility, efficient singlet oxygen generation which is one of the most important reactive oxygen species in PACT.

The aim of the proposed project is to obtain novel photosensitizers that would combine the advantages of both BODIPY compounds and ruthenium complexes to increase the potential of application in photodynamic antimicrobial therapy. Noteworthy, both of these compounds separately were proved to exhibit promising antimicrobial activity, but their conjugates have not been tested for PACT application before. Synthesis of several novel BODIPY-Ru-complexes conjugates is planned. It is believed that obtained conjugates could be efficient photosensitizers possessing a high affinity towards bacteria, especially Gram-negative ones, thereby contributing to the development of novel agents for the inactivation of the most dangerous antibiotic-resistant strains. The photodynamic activity of obtained compounds against bacteria will be evaluated both *in vitro* and *in vivo.* The animal model of *Caenorhabditis elegans* will be used for *in vivo* studies. *C. elegans* is a worm that can be infected by microorganisms similar to mammals, including humans. Therefore, there is a probability that novel antimicrobials drugs with promising activity evaluated in *C. elegans* model could also be successful in humans.

The realization of the project will be divided into few steps:
a) Synthesis of BODIPY and ruthenium complexes conjugates.
b) Isolation, purification, and characterization of obtained compounds.
c) Evaluation of physical-chmical properties of obtained compounds.
d) Assessment of photodynamic activity of obtained compounds against bacteria *in vitro.*
e) Assessment of photodynamic activity of obtained compounds against bacteria *in vivo* using *Caenorhabditis elegans* model.