DESCRIPTION FOR THE GENERAL PUBLIC

Search for effective anti-cancer therapy and effective antibiotics remains a challenge for modern medicine. Therefore, photodynamic therapy (PDT) and photodynamic antimicriobial therapy (PACT) are one of the most intensively developing approaches. PDT is a complementary method to surgery, radiation therapy, chemotherapy, immunotherapy and hormonotherapy of cancer diseases. Strong interest in oncological PDT results from its specific mechanism of action, a high therapeutic efficacy in both palliative and primary treatment, while ensuring patient safety. To the main advantages of PDT belong: its low toxicity to healthy tissues, not known drug resistance mechanisms and good cosmetic results. The treatment consists of several steps: (i) administering a drug known as a photosensitizer, (ii) a process of its accumulation in the target tissue (e.g. tumor), (iii) selective exposure to radiation of appropriate wavelength using a laser or fiber optic probe. The result is a light-activated photodynamic reaction between the drug and oxygen, leading to the formation of reactive oxygen species, including singlet oxygen, which is considered to be the major cytotoxic agent causing necrosis of the target tissue or microorganisms death.

Clinically applied photosensitizers are characterized by a low selectivity towards diseased cells in comparison to normal cells. Low selectivity causes side-effect, such as prolonged photosensitivity which manifests with painful burns when PDT treated patients are exposed to a strong light source. This effect persists for up to several weeks due to slow elimination of photosensitizers from the body, which is another disadvantage of this group of drugs.

Although gradual introduction of new photosensitizers into clinical treatment, none of them fulfill the requirements of an ideal drug. PDT is a promising method of treatment, but further progress is dependent upon technological improvement of radiation sources, adequate light dose delivery (dosimetry) and the search for new compounds possessing features of an ideal photosensitizer. Particularly promising characteristics exhibit macrocyclic compounds from the porphyrinoid group, including phthalocyanines. These are synthetic analogs of porphyrins consisting of four izoindole rings linked with nitrogen bridges. On the other hand, the lipophilicity of porphyrinoids results in poor solubility in biological fluids and a high tendency to form aggregates, thus low bioavailability limits their use. The main course of actions to obtain the ideal photosensitizer is focused on their chemical modification. Bicyclic sesquiterpenes such as azulene and guaiazulene are naturally occurring compounds possessing many interesting photochemical properties, including photosensitizing ability.

The aim of this project is to obtain new photosensitizers consisting of norphthalocyanine/phthalocyanine and sesquiterpene moieties. Both sesquiterpenes and phthalocyanines reveal promising photosensitizing properties, which allow to assume that their conjugation can result in novel effective photosensitizers. It was assumed that the combination of photosensitizers from different chemical groups in one therapeutic system may exhibit a synergistic photosensitizing effect, a desired stability, an improved solubility and a low tendency to form aggregates. The next stage of research will involve the determination of physico-, photo- and electrochemical properties of obtained conjugates. The spectroscopic analysis will confirm the identity of resulting compounds, evaluate their photostability and assess ability to generate reactive oxygen species, which are crucial features for successful photosensitizers. These studies will determine the potential utility of obtained conjugates in medicinal chemistry and pharmacology.

The effectiveness of obtained conjugates will be evaluated in *in vitro* tests using human tumor cell lines and different microorganisms (bacteria, fungi). In these studies the obtained photosensitizers will be administered to cancer cell or microorganism cultures. After incubation which enables their penetration into the cells, the cultures will be exposed to the appropriate dose of visible radiation (radiation source, the wavelength of light, intensity), and then the cell survival will be assessed. The results will be compared to experiments carried without prior exposure to the radiation. These tests will determine whether tested conjugates can be considered as potential photosensitizers for medical applications.