ABSTRACT

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Title of diploma thesis: Novel phthalocyanine photosensitizers for photodynamic therapy of tumorous diseases

Oncological diseases are considered to be a serious global problem for many years. One of the most significant factors of their expansion in human population is an increasing life expectancy. Higher incidence of physical and chemical carcinogens and better diagnostic methods of malignant neoplasms are farther possible factors. According to World Health Organisation (WHO) almost 8 million people in the world die from oncological disease every year, whereas 1.7 million of them are Europeans. Malign tumours in Czech Republic, as well as in the world, are the second most frequent causes of death right after cardiovascular diseases, in both genders. Despite increasing incidence of malign tumours in the world, the mortality rate is decreasing. This decline is connected especially with higher quality of medical care together with availability of new diagnostic and therapeutic means.

Thus the therapy of cancer is an important subject of biomedical research. Scientists have been trying to discover an effective and highly selective therapy which is capable of targeting cancer cells with a minimal impact on healthy tissue. Photodynamic therapy (PDT) has a potential to meet these requirements. PDT is currently in a stage of preclinical and clinical studies that are essential for its next development. It's clinically employed in USA, Canada, Japan and also in some european countries so far.

PDT requires three key elements: the photosensitizer (PS), the red region of a visible light and the oxygen. These components are nontoxic on their own, but their combination initiates photochemical reaction which is the key step of this approach. Products of photoreaction are highly reactive oxygen species (ROS) inducing damage to cell components and eventually cell death. Besides the direct cytotoxic effect, PDT induces also inflammation and disruption of tumor vasculature.

The aim of this study was an evaluation of new PS from the group of phtalocyanines and their aza-analogues which could be used in a clinical application of PDT. Cytotoxic efficiency was evaluated *in vitro* using human cervical carcinoma cell line (HeLa). Cell viability after incubation with PS and illumination by a red light was assessed by neutral red uptake assay.

Fluorescence microscopy and microscopy in differential interference contrast were employed for evaluation of morphological changes after activation of PS by light. Visualization of mitochondrial changes due to PDT by the fluorescence probe MitoTracker Green and detection of changes in nucleus by combination of propidium iodide (PI) and the fluorescence probe Hoechst 33342 were used. For the subcellular localization assay also the fluorescence probe LysoTracker Blue was used.

The results of the experiments demonstrated relatively low activity of observed PS from the group of phtalocyanines against selected cell line. Cytotoxic activity of its aza-analogue was not confirmed. Appropriate combination of photosensitizer and carrier couldn´t be found due to high toxicity of selected carriers (obseved in Cremophor EL, various types of Si nanoparticles) or due to their limited capacity for photosensitizer (observed in liposomes).