ABSTRACT

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Title of bachelor thesis: Experimental evaluation of photodynamic efficiency of phthalocyanine photosenzitisers and cell death assessment

Tumor diseases represent on of the largest group of malignant illnesses in the world. Their incidence is slowly shifting from developed countries to third world countries and therefore they represent the most widespread health problems, often leading to the death of patients. Intensive research and development of new and effective anticancer drugs and treatment methods is devoted because of the spread and mortality of these diseases. One of the intensively researched modern method is photodynamic therapy (PDT), which is utilizing photosenzitizers (PSs). To ensure the maximum efficiency, effectiveness of PDT and maximalization of results, it is necessary to observe three basic parameters – effective PS, light and oxygen. These individual components do not represent danger to the patients on their own, but their combination brings positive effect in the cancer treatment. The principle of the method is administration of an inactive PS to the patient with subsequent irradiation by light of suitable wavelength. PS is activated during the irradiation and the reaction with oxygen leads to a photochemical reaction with the formation of highly toxic reactive oxygen species (ROS). ROS are toxic to the target cells and trigger cell death in irradiated tissues.

Development of novel PSs and testing their effectiveness in the fight against malignant and non-malignant forms of tumor is important. The aim of my work was to determine the activity of two novel amphiphilic cationic PSs on HeLa cell line at different drug-light intervals (0, 4 and 12 h). Subsequently, the efficacy was also further valuated on additional malignant cell lines (MCF-7 and HCT-116) and on the human endothelial cell line EA.hy926. Evaluation of cell death pathway was performed as well – the method is based on the continuous detection

of cell death processes by exposure of phosphatidylserine (PhSer) on the outer leaflet of the membrane using luminescent and fluorescent detection reagents.

The results of my work show that compound P41 with DLI = 4 h (EC_{50} = 0,037 ± 0,009 μM) is the most effective from the studied compouds on HeLa cell line with analogous promising results at DLI = 12h. In comparison with P39 compound, with the results a little bit highert than P41, both of the studied compounds shown their efficiency as well on the MCF-7, HCT-116 and EA.hy926 cell lines.

Key words: photodynamic therapy, photosenzitizer, cell death, cytotoxicity, phtalocyanines