1 ABSTRACT

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Tumor diseases are a global health problem and one of the most common causes of death in developed countries. Therefore, considerable effort is devoted to research and develop novel anticancer drugs. Common conventional therapies, such as chemotherapy, radiotherapy, surgery, or their combination, are often associated with severe side effects and high treatment costs. Photodynamic therapy (PDT) is therefore being increasingly recognized as an alternative treatment modality for the treatment of many malignant and non-malignant conditions. PDT is a clinically approved non-invasive treatment which consists of two relatively simple procedures: administration of a photosensitive drug and subsequent radiation of the tumor by light to activate the photosensitizer (PS). The activated photosensitizer reacts with molecular oxygen to form highly reactive oxygen species (ROS). This creates a state of oxidative stress in the tumor which leads to tumor cell death, tumor (micro)vasculature shutdown and induction of anti-tumor immune response.

The aim of this work is to evaluate the photodynamic activity of novel amphiphilic anionic PSs at the cellular level under in vitro conditions and based on the results to assess their cytotoxic effect. Cytotoxicity experiments were performed on human malignant cervical cell line HeLa using neutral red uptake assay on 96-well plates. The toxicity experiments were performed both after the irradiation with activating light and without the presence of activating light (dark toxicity). Uptake profiles of PSs to the cells were also performed by measuring fluorescence in the cell lysate. Detection of morphological changes at the level of whole cells and subcellular structures were studied by using a fluorescence and confocal laser scanning microscopy.

The results of individual experiments on the HeLa tumor cell line have shown high photodynamic activity after irradiation and very low inherent toxicity of all studied compounds. The most suitable properties were achieved with HK22Zn-COONa (EC50 = 0,306 ± 0,180 μM, TC50 > 1000 μM, TC_{50}/EC_{50} > 3268). Uptake of the substances into the cells was rapid in the first two hours than reaching stead-state. For all investigated substances, photodynamic activation of PS resulted in significant morphological changes indicating ongoing cell death.