Photodynamic therapy (PDT) is known to be a prospective modality for cancer treatment. A regular PDT includes laser irradiation of the tumor following a systemic injection of the photosensitive dye – a photosensitizer (PS) that preferentially accumulates in the neoplastic tissue. Under the light exposure and in the presence of oxygen, the PS produces reactive oxygen species (ROS) destructive for the tumor. For successful clinical application, PS should meet a few general requirements. Particularly, it should be water-soluble to be injected intravenously, have strong absorption in the red or near-infrared region for deeper penetration into tissue, have high singlet oxygen generation (SOG) quantum yield and low dark cytotoxicity, selectively accumulate in the tumor and weakly in the skin, and can be rapidly eliminated from the body. PS in the polymeric formulations has been shown to have an enhanced fluorescence quantum yield and generate more singlet oxygen due to disaggregation of PS and prevention of photobleaching. Besides, a polymer is able to improve the permeation of the PS through cellular membranes. It is known that a number of factors influence PS biodistribution and pharmacokinetics in animal body including those related to the PS (molecular weight, charge, formulation etc.) and design of the experiment (drug dose, administration route, tumor model), which makes it difficult to compare the results of different studies. Therefore, the applications of the PS-polymer systems to fluorescence diagnostics and PDT are not widely explored. The only clinically approved polymer-based formulation with chlorin is Fotolon composed of chlorine e6 and PVP. In this work, a comparative study of Ce6, three Ce6-polymer systems and Photodithazine (PDZ) has been performed. Polyvinylpyrrolidone (PVP), polyvinyl alcohol (PVA) and pluronic F108 have been used for dissolution of Ce6. Dynamics of accumulation of the PSs in a mouse cervical carcinoma and clearance from normal tissue after i.v. injection have been investigated in vivo using fluorescence imaging. At the same time plasma concentrations of PS have been measured. Based on the in vivo imaging data and the plasma drug level, the time point at 4 h post-injection has been chosen for quantitative biodistribution analysis, and the amounts of PS in the tumor and normal tissues have been estimated by the chemical extraction method. The study was carried out to test the ability of three Ce6-polymer conjugates to target the tumor. Mouse cervical carcinoma inoculated subcutaneously in mice was used as a tumor model.

The results showed that none of the polymers significantly changed fluorescence kinetics in the tumor. It is important that concentration of the Ce6 formulated with polymers in the tumor tissue was comparable with clinically used photosensitizer Photoditazine, but uptake in the skin was less. At the same time, tumor-to-skin ratios of the Ce6-polymer systems were similar to free Ce6. We concluded that the use of the polymeric formulation is reasonable for fluorescence diagnosis and PDT of cancer.

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