Abstract

The research in the field of drug delivery systems has been extensively studied in the past decades. One of the fields where this principle is applied, is anticancer therapy. Many drug delivery systems (DDS) are based on macromolecular carriers, which are able to accumulate in the tumor tissue due to the enhanced permeability and retention (EPR) effect. Those macromolecular carriers are mostly based on polymer nanoparticles, polymerosomes, dendrimers, polymer micelles or water-soluble polymer conjugates. An interesting polymer material applicable in DDS is poly[*N*-(2-hydroxypropyl)methacrylamide] (PHPMA), which is highly hydrophilic, biocompatible and non-fouling to plasma proteins. PHPMA copolymers enable incorporation of functional groups for covalent drug attachment via stable or stimuli (e.g. pH or enzymatic activity) sensitive bonds. Modern approaches to anticancer therapy are e.g. photodynamic therapy (PDT), which uses photosensitisers, compounds able to generate cytotoxic reactive oxygen species (ROS) upon irradiation. Another trend is the usage of inhibitors of antiapoptotic proteins (IAP), which are able to increase the therapeutic effect in combination with classical cytostatics. In the treatment of advanced or highly resistant tumors, combination of such therapies is key to successful treatment. The topic of the diploma thesis presented is the design, synthesis and physico-chemical characterization of new DDS applicable in anticancer therapy. Water-soluble polymer conjugates bearing prodrugs for PDT, 5-aminolevulinic acid (5-ALA) or its hexyl ester (HAL) connected to a PHPMA carrier via pH sensitive hydrazone bond, were successfully synthetized. The first generation of those conjugates was based on polymer carriers of a size below the renal filtration limit, while the second generation was based on high molar mass polymers containing biodegradable bonds. Moreover, a successful synthesis of PHPMA systems bearing IAP inhibitor LCL-161 linked via hydrazone bond or enzymatically cleavable linker Val-Cit-pAB was successfully completed. Finally, the synthesis of biodegradable graft copolymer PCL-*g*-PHPMA, which self-assembles into micellar structure in aqueous solutions, was successfully performed. The micelles were used to encapsulate IAP inhibitor AZD-5582. All prepared systems will be biologically tested to prove their efficacy, and thus confirm their potential as DDS in anticancer therapy.

Keywords: polymer, RAFT polymerization, drug, photodynamic therapy, multidrug resistance

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