ABSTRACT

Amphiphilic copolymer nanostructures hold tremendous applications in biomedical and pharmaceutical fields. In aqueous media, an amphiphilic block copolymer with a stimuli-sensitive segment can form interesting self-assembled nanostructures capable of undergoing structural transformations and self-immolation when the stimuli changes. In this work, we have aimed to synthesize several nanoparticles from tailor-made polymeric prodrugs and core cross-linked nanoparticles from miktoarm star. These new nanoparticles can serve as carriers of anticancer drugs, having ability to release the payload preferentially in the environment of cancer cells. They can also be used to monitor cellular uptake in a real-time manner.

To achieve this goal, several new random and block copolymers with narrow dispersity were synthesized by the RAFT technique. Click chemistry and novel methods were used to conjugate drugs and fluorophores into polymeric side chains and to cross-link the nanostructures formed from these copolymers. A significant role for polymeric prodrugs and cross-linked nanostructures in medicinal therapy can be attributed to their ability to carry drugs and release their payloads upon reaching their target sites in response to external/internal stimuli, such as pH and redox levels.

We have synthesized a new amphiphilic block copolymer based on poly(ethylene glycol) methyl ether acrylate (PEGMA) and dopamine methacrylate (DOPMA). Then anticancer drug doxorubicin (DOX) was conjugated into the hanging catechol sidechains of the polymer with the help of 4-formylphenylboronic acid via boronic ester and aromatic amine bonds. The pH-responsive polymeric nanoparticles are stable in physiological pH and show pH-responsive release of DOX in the acidic microenvironment.

A fluorescent amphiphilic block copolymer poly(NVP)-*b*-poly(FPA-*r*-CA) (P2) was prepared via the RAFT technique. DOX was conjugated with the P2 through a pH-responsive aromatic imine bond resulting a self-indicating polymeric prodrug that was able to monitor cellular uptake in real-time.

In another work, a copper-catalyzed alkyne azide click reaction was utilized to synthesize a miktoarm fluorescent star polymer that was cross-linked in the presence of a redox-responsive cross-linker. The biotin-containing PEG was grafted onto the polymer chain to enhance targeting. A nanoparticle obtained from the above system was encapsulated with doxorubicin (DOX), followed by cross-linking. The synthesized structure was stable in high dilutions and capable of releasing DOX in a redox-responsive manner.

Key Words: Stimuli-responsive polymers, RAFT polymerization, Polymeric prodrugs, Self-indicating polymeric prodrug, Cross-linked nanostructures, Dopamine, Biotin, Doxorubicin.