OP14

THERANOSTIC NANOPARTICLES BASED ON PEO-POLYACETAL DIBLOCK COPOLYMERS FOR DRUG DELIVERY

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Introduction: Modern nanoparticle-based drug delivery systems are considered a promising therapeutic platform because of their potential to enhance the efficacy of drugs in anticancer and antiviral therapy. Besides their therapeutic action, modern nanoparticulate materials have been also used in biomedical imaging allowing drug targeting and the assessment of the therapeutic effect. Modern nanomedicine combines the above two actions in a single entity known as theranostic nanoparticles, which allow simultaneous diagnosis of the disease site, drug delivery to cure the disease and monitoring of the drug response [1-3].

Methodology: The block copolymer was synthesized via a two-step polycondensation reaction (figure 1), in the first step nitrobenzenedimethanol, hydroxyethyldisulfide, butyne diol and cyclohexyl divinyl ether were added in equimolar amounts with 1% PPTS. Next, for the synthesis of the block copolymer, 5 kDa monohydroxy terminated PEG was added to the preview's solution along with 1% PPTS. The block copolymer was isolated after precipitation and fractionation in hexanes. The quad-stimulus mediated degradation of the polymers either by UV (365 nm) photolysis or ultrasound (1 MHz) irradiation or in REDOX environment or by acidolysis at mildly acidic pH (ca. 5.2) was monitored using gel permeation chromatography. Micelles loaded with the model drug camptothecin (CPT) were prepared in aqueous medium and the ability of this micelles to serve as MRI contrast agents was evaluated using NMR. Furthermore, the release of the model drug CPT under the aforementioned stimuli was calculated using UV-Vis.

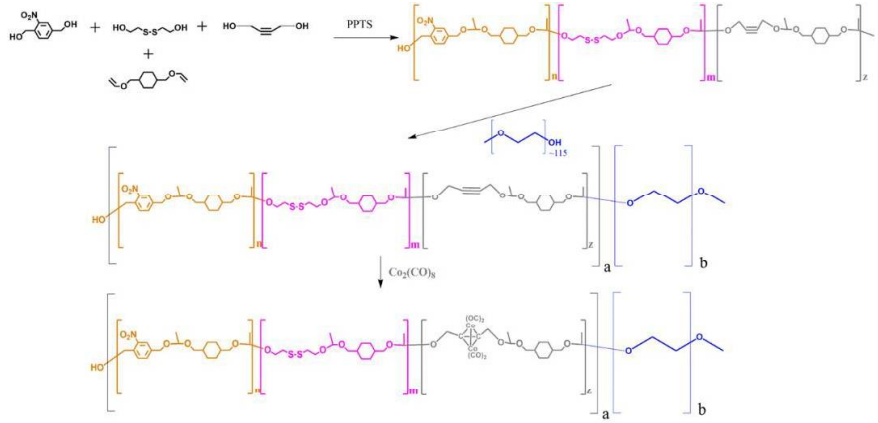

Figure 1: Synthetic procedure of the Polyacetal-PEO diblock copolymer.

Discussion: Polyacetals have a well-established hydrolysis profile under the mildly acidic conditions (pH 5.5) found in the late endosome. In an effort to introduce red-shifted photo-

lability on the backbone of the polymer in the visible, nitrobenzene comonomers were used (figure 1). Furthermore, we introduced disulfide bonds in the main chain of the polyacetal block which are redox labile. Ultrasound irradiation of the PEO-Polyacetal block copolymer has resulted in its degradation by the direct breaking of the acetal bonds. The polymer formed spherical nanoparticles in water with mean diameter of 130 nm determined by dynamic light scattering. The morphology of the nanoparticles was examined by SEM microscopy which confirmed their spherical shape and their relatively uniform size distribution. After 3 h of light irradiation (365nm) of 7 h ultrasound irradiation of the micelles at pH 7.4, 90 % release of the CPT was achieved (figure 2a). Conversely, the drug release rate was more pronounced when the pH was lowered to 5.2 (figure 2b). Furthermore, 60 h treatment of the nanoparticles with the reducing agent dithiothreitol has resulted in 50% and 70% release of the CPT at 7.4 and 5.2 pH, respectively (figure 2).

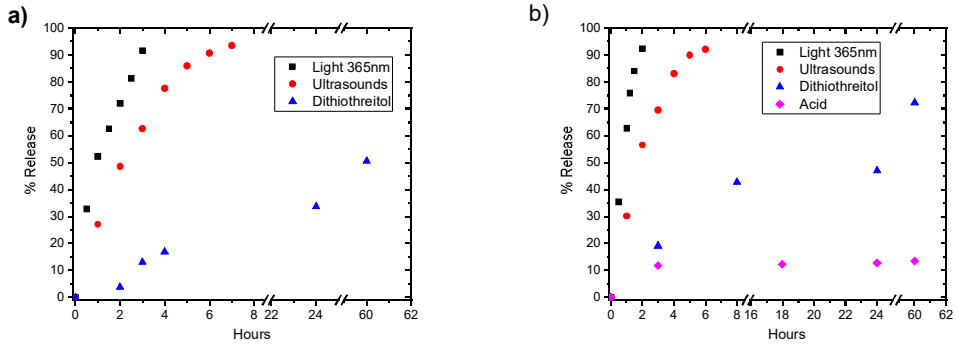

Figure 2: CPT release from the NPs upon the application of several stimuli.

Conclusions: We have developed a new multi-responsive polymer that responds individually to four different stimuli, while also exhibiting a super-paramagnetic behavior, and demonstrate its potential in the development of "smart" nanocarriers with ideal properties as contrast agents for MRI.

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