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pH-Responsive Nanoparticles for Drug and Gene Delivery

By

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Stimuli-sensitive polymers that respond to temperature, pH, light, ionic strength, and electric or magnetic fields are attractive for use in drug delivery, diagnostics, and sensing. Much attention has been paid to the use of pH-sensitive polymers for oral drug delivery, gene delivery, and insulin delivery, where a physiological pH shift facilitates swelling. In this research, pH-sensitive poly N,N-dimethylaminoethyl methacrylate (DMAEMA) / 2-hydroxyethyl methacrylate (HEMA) nanoparticles were prepared for the triggered release of paclitaxel within a tumor microenvironment. Monodispersed nanoparticles were synthesized by forming an O/W emulsion followed by photopolymerization. Particles were characterized by transmission electron microscopy, dynamic light scattering, electrophoresis, and cytotoxicity. High release rates and swelling ratios are achieved at low pH, low crosslinking density, and high content of DMAEMA. Cell viability studies indicate that pH-sensitive DMAEMA/HEMA nanoparticles are not cytotoxic and may be used as an efficient, feedback-regulated drug delivery carrier. DMAEMA/HEMA nanoparticles were also used as gene carriers with nearly 100% encapsulation rate due to their ability to swell at low pH which may overcome the obstacles of endosomal release and low transfection efficiency of nonviral gene delivery vectors. Once internalized via the endocytosis pathway, the nanoparticles undergo osmotic swelling facilitating endosomal escape of DNA to the cytoplasm. For intracellular tracking, particles were conjugated with quantum dots and examined by confocal microscopy at different time points. To examine the efficacy of DMAEMA/HEMA nanoparticles in facilitating endosomal escape of pDNA encoded EGFP, HeLa cells were incubated with DNA-loaded nanoparticles for 24 and 48 h. Enhanced gene transfection and particle uptake were achieved by modulating matrix elasticity and pH sensitivity. After a 48 h incubation, the transfection efficiency obtained by using DNA-loaded DMAEMA/HEMA nanoparticles was 45 ± 4.8%, in comparison to 40 ± 3.1% for PEI/DNA complexes. Our results show that elastic and pH-sensitive DMAEMA/HEMA nanoparticles enable higher gene expression at 24 and 48 h than polyethyleneimine (PEI)/DNA and poly-L-lysine (PLL)/DNA complexes without the drawback of cytotoxicity.

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