Biophysical characterization of layer-by-layer synthesis of aptamer-drug microparticles for enhanced cell targeting.

ABSTRACT

Targeted delivery of drug molecules to specific cells in mammalian systems demonstrates a great potential to enhance the efficacy of current pharmaceutical therapies. Conventional strategies for pharmaceutical delivery are often associated with poor therapeutic indices and high systemic cytotoxicity, and this result in poor disease suppression, low surviving rates, and potential contraindication of drug formulation. The emergence of aptamers has elicited new research interests into enhanced targeted drug delivery due to their unique characteristics as targeting elements. Aptamers can be engineered to bind to their cognate cellular targets with high affinity and specificity, and this is important to navigate active drug molecules and deliver sufficient dosage to targeted malignant cells. However, the targeting performance of aptamers can be impacted by several factors including endonuclease-mediated degradation, rapid renal filtration, biochemical complexation, and cell membrane electrostatic repulsion. This has subsequently led to the development of smart aptamer-immobilized biopolymer systems as delivery vehicles for controlled and sustained drug release to specific cells at effective therapeutic dosage and minimal systemic cytotoxicity. This article reports the synthesis and in vitro characterization of a novel multi-layer co-polymeric targeted drug delivery system based on drug-loaded PLGA-Aptamer-PEI (DPAP) formulation with a stage-wise delivery mechanism. A thrombin-specific DNA aptamer was used to develop the DPAP system while Bovine Serum Albumin (BSA) was used as a biopharmaceutical drug in the synthesis process by ultrasonication. Biophysical characterization of the DPAP system showed a spherical shaped particulate formulation with a unimodal particle size distribution of average size ~0.685 μm and a zeta potential of +0.82 mV. The DPAP formulation showed a high encapsulation efficiency of 89.4 ± 3.6%, a loading capacity of 17.89 ± 0.72 mg BSA protein/100 mg PLGA polymeric particles, low cytotoxicity and a controlled drug release characteristics in 43 days. The results demonstrate a great

promise in the development of DPAP formulation for enhanced in vivo cell targeting. *Biotechnol.*