580e Polymersome Encapsulated Hemoglobin (Peh): a Novel Type of Oxygen Carrier

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Bovine hemoglobin (Hb) was encapsulated inside polymer vesicles (polymersomes) to form encapsulated Hb (PEH) dispersions. PEH particles are 100% surface PEGylated with longer PEG chains and thicker hydrophobic membranes as compared to conventional liposomes. Polymersomes were self-assembled from poly(butadiene)-poly(ethylene glycol) (PBD-PEO) amphiphilic diblock copolymers with PBD-PEO molecular weights of 22-12.6 kDa, 5-2.3 kDa, 2.5-1.3 kDa, and 1.8-0.9 kDa. The first two diblock copolymers possessed linear hydrophobic PBD blocks, while the later possessed branched PBD blocks. PEH dispersions were extruded through 100 and 200 nm pore radii membranes. The size distribution, Hb encapsulation efficiency, P50, cooperativity coefficient and methemoglobin (metHb) level of PEH dispersions are consistent with the values required for efficient oxygen delivery in the systemic circulation. The influence of different molecular weight diblock copolymers on the physical properties of PEH dispersions was analyzed. PBD-PEO copolymers with molecular weights of 22-12.6 kDa and 2.5-1.3 kDa completely dissolved in aqueous solution to form polymersomes, while the other two copolymers formed a mixture of solid copolymer precipitates and polymersomes. PEHs self-assembled from 22-12.6 kDa and 2.5-1.3 kDa PBD-PEO copolymers possessed Hb loading capacities greater than PEG-LEHs, PEGylated actin-containing LEHs, and non-modified LEHs, although their sizes were smaller and their hydrophobic membranes were thicker. The Hb loading capacities of these polymersomes were also higher than lipogel encapsulated hemoglobin particles and nanoscale hydrogel encapsulated hemoglobin particles. PEH dispersions exhibited average radii larger than 50 nm, and exhibited oxygen affinities comparable to human erythrocytes. Polymersomes did not induce Hb oxidation. The interaction between Hb and the membrane of 2.5-1.3 kDa PBD-PEO polymersomes improved the monodispersity of these particular PEH dispersions. These results suggest that PEHs could serve as efficient oxygen therapeutics.