Nanostructured Polyanhydrides for Drug Delivery

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Polyanhydride copolymers have a unique combination of features that make them ideal for drug delivery applications. The hydrophobic nature of the polymer backbone excludes water from the bulk, however the anhydride bond is extremely labile with respect to hydrolytic degradation. Thus, the polymer erodes from the surface, rather than in the bulk. The erosion kinetics can be modulated by changing the hydrophobicity of the polymer, the copolymer composition, or the degree of crystallinity. However, the introduction of multiple phases complicates the release kinetics. In phase-separated systems such as semicrystalline polymers and microphase-separated copolymers, the individual phases may erode at different rates and may have different drug loadings. Thus an accurate description of the phase behavior is essential to precisely designing controlled release formulations and describing the release kinetics. Accurate description of the microstructure requires microscopic or spectroscopic techniques with the ability to discern length scales on the order of a few nanometers. We investigate the microstructure of copolymers based on 1,6-bis(*p*-carboxyphenoxy)hexane (CPH) and sebacic acid (SA). Solid-state NMR is used to determine the length scale of microphase separation in the copolymers. Synchrotron small-angle X-ray scattering (SAXS) experiments on blends are used to determine the CPH-SA segmental interaction parameter. The interaction parameter is used to predict the morphology of the microphase separation in copolymers via mesoscale molecular simulation. This technique can be used to aid rational design of new copolymers with tailored microstructures. SAXS experiments are also used to investigate the microstructure of copolymers and *in situ* crystallization experiments provide the crystallization kinetics. All of this information can be used to parameterize models of the erosion and drug release kinetics and to tailor the microstructure of polyanhydrides for the rational design of controlled release devices.