Abstract

Nanoparticles from biodegradable polymers are considered one of the most promising systems for biomedical application as drug delivery systems. Therefore, the synthesis and characterization of a new aliphatic biodegradable copolyester named PBS/PBDL (poly(butylene succinate-*co*-butylene dilinoleate)) intended to the application as drug delivery system is reported in the thesis. Surfactant-free biodegradable and narrowly distributed, nanosized spherical particles (R_H < 60 nm) have been produced from the biodegradable material by applying a single-step nanoprecipitation protocol. The size of the generated polymer nanoparticles (PNPs) could be controlled by adjusting the polymer concentration, the choice of organic solvent, mixing different organic solvents or by changing temperature and ionic strength. By optimizing such parameters sub-100 nm uniform PNPs can be produced through this methodology including the advantage and ability to scale-up production. The nanoparticles structure was characterized in detail by employing a variety of scattering techniques and transmission electron microscopy (TEM). Combined static light scattering (SLS) and dynamic light scattering (DLS) measurements suggested that the nanoparticles comprise a porous core conferring them a non-compact characteristic. Their porosity enables water to be entrapped which is responsible for their pronounced stability and relatively fast degradation as followed by size exclusion chromatography (SEC). The polymeric nanoparticles could be loaded with the hydrophobic antitumoral drug paclitaxel (PTX) and doxorubicin (DOX) with a drug loading content of ~ 6–7% $w_{drug}/w_{polymer}$ and ~ 5% $w_{drug}/w_{polymer}$, respectively. The drug encapsulation and release modifies the inner structure of the nanoparticles, which holds a large amount of entrapped water in the drug-free condition. The controlled DOX release is pH-dependent and faster under slightly acidic conditions and the cell viability experiments demonstrated that the drug-free NPs are non-toxic, whereas the DOX-loaded NPs exert *in vitro* cytostatic efficacy on EL4 T cell lymphoma. Finally, the successful coverage of the hydrophobic PBS/PBDL NPs by the non-immunogenic and non-toxic hydrophilic *N*-(2- hydroxypropyl)methacrylamide (HPMA) copolymer makes them an alternative to the biodegradable FDA-approved polyester and PEG-shielded nanoparticles for biomedical application as drug delivery systems.

Keywords: paclitaxel, doxorubicin, biodegradable polyester, drug delivery systems, PHPMA, light scattering