The Effects of Polymer Lengths and Cryoprotectants on the Size and Stability of PCL-PEG Nanoparticles

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Understanding the factors that affect nanoparticle formation can be instrumental in engineering nanoparticles that will be effective in treating a broad range of diseases. Studies have shown that size of the nanoparticle plays a major role in the biodistribution. Maintaining smaller nanoparticles is also key to the cellular uptake of these particles. Nanoparticle size can be modified based on the hydrophilic-to-hydrophobic ratio of the nanoparticle, which was tested by preparing polyethylene glycol (PEG)-polycaprolactone (PCL) polymeric nanoparticles using flash nanoprecipitation. Then, the size distribution of the nanoparticles was measured using dynamic light scattering analysis. Nanoparticles were formed with either PEG(2k) or PEG(5k) and a varying hydrophobicity. In both types of particles, using a hydrophobicity between 40-60% yielded nanoparticles around 50 nm. In PEG(2k) particles, increasing the hydrophobicity from 58% to 81% increased the particle size from 50 nm to 200 nm. Increasing the hydrophobicity past 75% resulted in particles that were larger than 125 nm, suggesting that a hydrophobicity between 40-60% is ideal. Freeze-drying the nanoparticles with cryoprotectants can also affect their stability and size post-redispersion. We tested this by freeze-drying nanoparticles with either Trehalose, Poloxamer 188, or both in nanoparticle-to-cryoprotectant ratios (w/w) ranging from 1:1.125 to 1:10. An increased nanoparticle-to-cryoprotectant ratio and using both trehalose and poloxamer 188 rather than only one of the two minimized the size change post freeze-drying. These findings suggest that altering the ratio of hydrophilic to hydrophobic block and using a cryoprotectant can significantly alter the structure of a nanoparticle. This work was supported by NIH R37AI051024, R01AI117776, R01CA15506, and P30ES005022.