Influence of PCL Concentration and Solvent on Dimensions and Morphology of Electrosprayed Particles

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Introduction: Micro and nanoparticles are useful in medical science as drug delivery systems and for tissue engineering. Different polymers have been used to encapsulate or chemically bond with a range of drugs and also to produce nanoparticles with specific size and porous distribution. Polycaprolactone (PCL) is considered a non-toxic material with excellent biocompatibility and biodegradability. Also, PCL nanoparticles produced by electrospraying technique present high encapsulation capacity, controllable surface area, high porosity, and good cost-benefit. Electrospraying is an emerging process due to the fact to be carried out at room temperature, preventing the degradation of proteins and polymers. At the same time, the versatility of modifying the processing parameters like applied voltage, flow rate, and distance from the tip of the spinneret to collector, allows the operator to control the morphology, size, porosity, and distribution of the generated particles. The choice of the concentration of polymer in addition to the type and ratio of the solvent used also play an important role in the process. The objective of this study is to assess the influence of PCL concentration and solvent on the dimensions and morphology of electrosprayed particles.

Methods: PCL (Mw = 80,000 g mol^{-1}), Chloroform (CF, ≥ 99.5%), and N, N-Dimethylformamide (DMF, 99.8%) were purchased and used as received from Sigma-Aldrich (Saint Louis, MO, USA). In this study, the morphology and size of electrosprayed particles were evaluated at three PCL concentrations (2 wt%, 4 wt%, and 6 wt %) using three different solvent mixtures (1:1 CF/DMF, 3:1 CF/DMF, and 100% CF). Thus, nine groups of specimens with varying PCL and solvent concentrations (2 wt% PCL with 1:1 CF/DMF; 2 wt% PCL with 3:1 CF/DMF; 2 wt% PCL with 100% CF; 4 wt% PCL with 1:1 CF/DMF; 4 wt% PCL with 3:1 CF/DMF; 4 wt% PCL with 100 % CF; 6wt% PCL with 1:1 CF/DMF; 6 wt% PCL with 3:1 CF/DMF, and 6 wt% PCL with 100 % CF), containing three specimens per group were prepared. Homogeneous dissolution of the polymer pellets was accomplished using a bench rocker at room temperature. The electrospraying parameters used were an applied voltage of 15 kV, a spinneret-collector distance of 12 cm, a flow rate of 0.7 ml/h, and a 16 gauge needle. The polymer solutions were electrosprayed onto the grounded collector for 5 minutes. All samples were sputter-coated (Leica Microsystems, Vienna, Austria) with 8.0 nm Au-Pd coating and analyzed using a Scanning Electron Microscope (SEM, Carl Zeiss, Oberkochen, Germany). The diameter of the 30 random particles per sample was calculated from the obtained SEM micrographs using ImageJ software (U. S. National Institutes of Health, Bethesda, Maryland, USA). Statistical analysis was done using Two-Way ANOVA followed by Tukey for pairwise comparisons.

Results: SEM images showed a change in morphology and size of the particles among various tested groups. Within the 100% CF group, the samples with 2 wt% PCL concentration demonstrated relatively small (mean particle diameter = 9.90 µm) and wrinkled particles, while the samples with 6 wt% PCL showed bigger particles (mean particle diameter = 11.35 µm) with high porosity, as depicted in Figure 1. Also, with the increase in the PCL concentration, an increase in the number of fibers was observed among all the groups. The choice of solvent and the ratio of solvents used influenced the morphology of the particles. The use of DMF, which has partial solubility for PCL, produced smoother surface particles and increased the number of fibers.

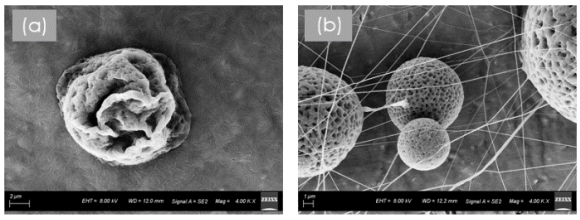

Figure 1. SEM micrographs of the electrosprayed microparticles from sample groups (a) 2 wt% PCL with 100% CF; (b) 6 wt% PCL with 100% CF

Two-way ANOVA demonstrated a statistically significant interaction between PCL concentration and solvents (P = <0.001) on the size of the particles. Among the levels of PCL concentrations and solvent mixture tested, pairwise comparisons using Tukey test showed a statistical significant variation in the mean particle diameter of nanoparticles between all the PCL concentration levels and solvent groups (P = <0.001), except between 4 wt % PCL vs. 6 wt% PCL. Pairwise comparisons using Tukey test also showed a statistical significant variation in the mean particle diameter of nanoparticles between all the nine groups of specimens tested with varying PCL and solvent concentrations (P < 0.050), except between the following groups as 4 wt% PCL with 1:1 CF/DMF vs. 4 wt% PCL with 3:1 CF/DMF, and 6 wt% PCL with 1:1 CF/DMF vs. 4 wt% PCL with 1:1 CF/DMF. The mean diameter of the particles for 1:1 CF/DMF, 3:1 CF/DMF, and 100% CF solvent ratios was 0.92, 2.49, and 9.90 µm for the 2 wt% PCL group; 3.77, 3.72, and 14.26 µm for 4 wt% PCL group, and 4.10, 5.46 and 11.35 µm for 6 wt% PCL group, respectively.

Conclusion: Morphology and dimensions of electrosprayed particles as well as the presence of fibers are significantly dependent on PCL concentration, choice of solvent, and solvent ratio. In the future, more electrospray parameters can be tested for potential drug delivery applications.