Electrospray synthesis of PLGA TIPS microspheres

Conference or Workshop Item

Electrospray Synthesis of PLGA TIPS Microspheres

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We successfully demonstrate the synthesis of polymer microspheres using a single electrospray source, and show their physical characterisation. Electrospray has proven to be a versatile method to manufacture particles, giving tight control over size with quasi-monodisperse size distributions. It is a liquid atomisation technique that generates a monodisperse population of highly charged liquid droplets over a broad size range (nanometres to tens of microns). The droplets contain liquid precursors for the in-flight synthesis of particles, and control over the trajectory of these droplets can be precisely manipulated with the use of electric fields to drive them to a grounded substrate.

This study reports a method to synthesize poly(lactic-co-glycolic) acid (PLGA) microspheres using the electrospray and thermally induced phase separation (TIPS) techniques, followed by subsequent freeze-drying, for particle production. These microspheres are of interest as vehicles for controlled drug release systems.

Materials and Methods

A 5% w/v polymer solution of PLGA (Purasorb PDLG 5004A, 50:50 DL-lactide/glycolide copolymer) was prepared using a solvent formulation of dimethyl carbonate (DMC), formic acid and deionized (DI) water with the following ratio, 99:0.5:05 v/v. The solution was electrosprayed in the cone-jet mode at 1ml/hr using a dual-electrode configuration (i.e. needle and extractor plate) and one 19G needle source positioned concentrically 1mm above a 0.4mm diameter extractor hole. Care was taken to avoid misalignment between the nozzle and the extractor hole, which may cause the jet to discharge asymmetrically leading to an electrical short between the two components.

The electrodes were maintained at different potentials to achieve the desired electric field with $V_{needle} > V_{extractor} > V_{collector}$ (ground). The voltages applied to the needle and extractor were 10.2kV and 7.0kV, respectively. The electric field driving the droplets between the extractor electrode and the collector was high enough to avoid reversal of the droplet motion near the extractor (satellite trapping). Particles were collected in a liquid nitrogen bath (40mm below the extractor plate) held within a non-stick Teflon casing. Particles were subsequently lyophilised for 24 hours to produce porous, spherical particles (Figures 1A and 1B).

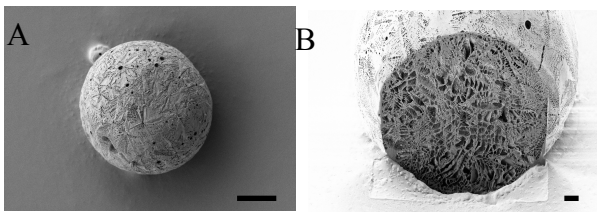

Figure 1 – (A) SEM micrograph of a PLGA TIPS microsphere. Scale bar 10μm. (B) FIB-SEM slice through a microsphere. Scale bar 2μm.

Results and Discussion

SEM images revealed the successful synthesis of freeze-dried polymer particles. Particle size was measured using a particle size analyser (Morphologi G3, Malvern Instruments, UK), and results revealed a median particle size of 14μm. Spectroscopic analyses (Alpha 300R Confocal Raman Microscope, WiTec, Germany) revealed identical spectra for the electrosprayed PLGA and PLGA as-received. Hence, the electrospray process did not alter the composition of the polymer. Further, imaging the internal structure of electrosprayed PLGA particles using confocal Raman microscopy yielded images similar to those in Figure 1B; such structures were not present for PLGA as-received.

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