297a Supercritical CO2 Based Formation of Drugs and Proteins Nanoparticles and Microencapsulation for Sustained Release

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<>**Abstract**

Purpose: To produce nanoparticles of drugs and proteins using supercritical CO_2, encapsulate the obtained nanoparticles into polymer microparticles using a non-aqueous method and study their sustained *in-vitro* drug release.

Methods: A hydrophilic drug, dexamethasone phosphate and a protein, lysozyme were chosen for this study. Briefly, the active pharmaceutical ingredient (API) was dissolved in an organic solvent, which is miscible with supercritical CO_2. This solution was then injected through a 100 μ nozzle in supercritical CO_2 with ultrasonic field for enhanced molecular mixing (Supercritical AntiSolvent precipitation with Enhanced Mass transfer - SAS-EM technique). Supercritical CO_2 rapidly extracts the organic solvent leading to instantaneous precipitation of the API in the form of nanoparticles. The nanoparticles were then encapsulated in poly(lactide-co-glycolide) polymer using anhydrous s/o/o/o technique. This resulted in a well-dispersed encapsulation of the API nanoparticles in polymer microspheres with higher encapsulation efficiencies. *In-vitro* drug release from these microparticles was studied.

Results: Using supercritical CO_2 as an antisolvent, API nanoparticles were obtained in the range of 250-300 nm. Upon encapsulation in PLGA, composite microspheres of size ~50-70 μm were obtained. The *in-vitro* drug release of these nanoparticles/microparticles composites showed sustained release of the API over an extended period of time (~700 hours) with almost no initial burst release.

Conclusions: API nanoparticles can be produced using the SAS-EM technique. When microencapsulated, these particles can provide sustained release of a therapeutic drug or protein without initial burst effects. Since the entire process is completely anhydrous, it is applicable to a variety of hydrophilic drugs, peptides and proteins.

Keywords: sustained/controlled drug release, dexamethasone phosphate, lysozyme, PLGA, SAS-EM, s/o/o/o, supercritical carbon dioxide, nanoparticles, microparticles.