Formation of Polymer Nano-particles in Supercritical Fluid Jets

A. Gokhale*, B. Khusid**, R. Dave***, R. Pfeffer****

*Department of Mechanical Engineering, aag6@njit.edu
** Department of Mechanical Engineering, boris.khusid@njit.edu
*** Department of Mechanical Engineering, rajesh.n.dave@njit.edu
**** Department of Chemical Engineering, robert.pfeffer@njit.edu
New Jersey Institute of Technology, University Heights, Newark, NJ 07102

ABSTRACT

The supercritical antisolvent (SAS) process is an emerging technology for the production of micro- and nanometer-sized particles for a wide variety of bio-medical pharmaceutical applications [1]. In this paper, polyvinylpyrrolidone (PVP) nanoparticles are synthesized using dichloromethane (DCM) and acetone as organic solvents to prepare polymer solution and carbon dioxide in supercritical phase is used as an antisolvent. Several capillary nozzles from 20 μm to 127 μm are used to inject the solution at different Reynolds number. Particles from sub-micron size to nano size are obtained depending upon operating parameters.

Keywords: Supercritical Fluids, biopolymers, nanoparticles, polyvinylpyrrolidone.

1 INTRODUCTION

In this method, an organic liquid solution of the compound of interest (e.g., a polymer in a liquid solvent) is sprayed through a nozzle into a chamber containing a highly compressed gas or supercritical fluid (e.g., carbon dioxide), which is miscible with the solvent, but is an antisolvent for this compound. The dispersion of the liquid solution in such a medium generates a high degree of supersaturation, leading to the formation of fine, uniform particles. This method takes distinguishing properties of supercritical fluids to exhibit significant solvent strength when they are compressed to liquid-like densities. By operating in the critical region, the pressure and temperature are used to regulate the fluid density, which, in turn, regulates the solvent power of a supercritical fluid. The recovery and separation of the antisolvent from the solvent and solid products is then performed by a simple depressurization step. In addition, SAS processing benefits from fast mass transfer in supercritical fluids due to their low viscosity and high diffusivity relative to liquids. Carbon dioxide is a common choice for SAS applications since it is non-flammable, non-toxic, inexpensive, and environmentally benign. The important features of SAS include the wide range of materials that can be processed and the variety of particulate morphologies that can be formed. Although numerous papers, published within the last decade, have contributed to the design of SAS apparatuses and the product development, SAS processes are still optimized empirically since very little has been achieved in mastering quantitatively the dynamics of phenomena underlying this process.

Recently published studies of the SAS formation of polymer particles are limited to the use of good polymer solvents or their mixtures and rather wide nozzles [2, 3]. In contrast, we study the precipitation of a polymer in a mixture of “good” and “poor” solvents injected through micro-nozzles. In good solvents, the intra-chain repulsion between the segments works to expand the polymer dimensions, as does the solvent-solute interaction. In less favorable solvents, the solvent-solute and solute-solute interactions have opposite signs. In poor solvents, these attractive and repulsive forces are no longer balanced, and the polymer chain collapses.

2 EXPERIMENTAL SET UP

Experiments are conducted on solutions of a high-molecular weight PVP, M=1,300,000, in a binary mixture of a good, dichloromethane (DCM), and poor, acetone, solvents.

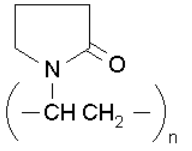

Figure 1. Chemical structure of polyvinylpyrrolidone

The solution is injected into a compressed carbon dioxide through a micro-nozzle. The operation temperature is maintained at 35°C while the operation pressure varies from 70 to 120 bar. The flow regime varies from dripping to spraying. The high-pressure chamber has double-sided (front and back) sapphire windows (320 mm × 16 mm) for flow visualization. The visualization system is comprised

of microscope lens, a high-speed CCD camera, a computer with the image capture software, and a Nd:YAG dual cavity pulsed laser that produces double shots with an exposure time from $5-\mu s$ to $15-\mu s$ delay (Fig. 2). The synthesis process is conducted as described below. CO_2 is continuously injected into the chamber at desired temperature and pressure and back pressure regulator is set for desired flow rate. After 15 minutes of continuous CO_2 injection, the solution is started injecting into the chamber at desired flow rate. The temperature inside the vessel is kept 35°C. After injecting the desired amount of solution, the solution pump is turned off and CO_2 injection is continued for 2 hours to ensure the dryness of the precipitated particles inside the chamber. After 2 hours, the CO_2 flow into the pressure chamber is turned off and chamber is slowly depressurized. Particles inside the chamber are collected in the air tight bottles for characterization.

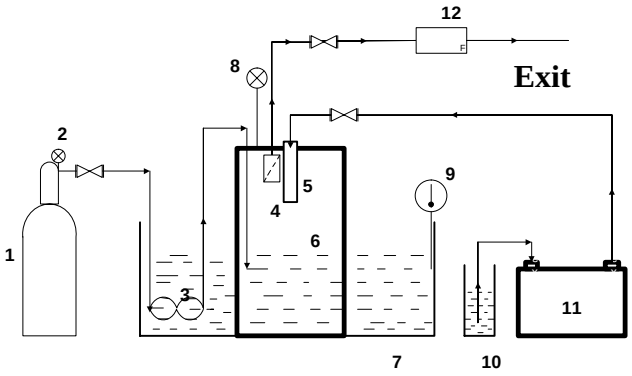

Figure 2. Schematic diagram of experimental setup. $_1$ CO_2 cylinder, $_2$ pressure regulator, $_3$ coil, $_4$ frit, $_5$ capillary nozzle, $_6$ pressure chamber, $_7$ water bath, $_8$ pressure gauge, $_9$ thermometer, $_{10}$ solution tank, $_{11}$ solution pump, $_{12}$ flow meter.

High pressure carbon dioxide cylinders (Bone Dry, 99.9% pure) are purchased from MG Industries. Acetone (HPLC Grade, 99.5+ %), dichloromethane (HPLC Grade, 99.7+ %) and polyvinylpyrrolidone (PVP) are purchased from Alfa Aesar. PVP is soluble in dichloromethane and insoluble in acetone (Alfa Aesar) and it is confirmed by checking solubility of PVP in DCM and acetone by laser scattering instrument.

Analytical methods include scanning electron microscopy (Leo 1530VP) for particle morphology; laser scattering instrument (Coulter N4$_+$) and sigma scan pro software for particle size and size distribution.

3 RESULTS AND DISCUSSION

The paper is focused on the effects of the solvent composition and operational parameters on the particle morphology and properties. In particular, increasing the acetone content in the solvent is found to suppress the particle aggregation, eliminate their surface irregularities, and decrease the average size (Fig. 3). The particle size is also decreasing with decreasing the chamber pressure.

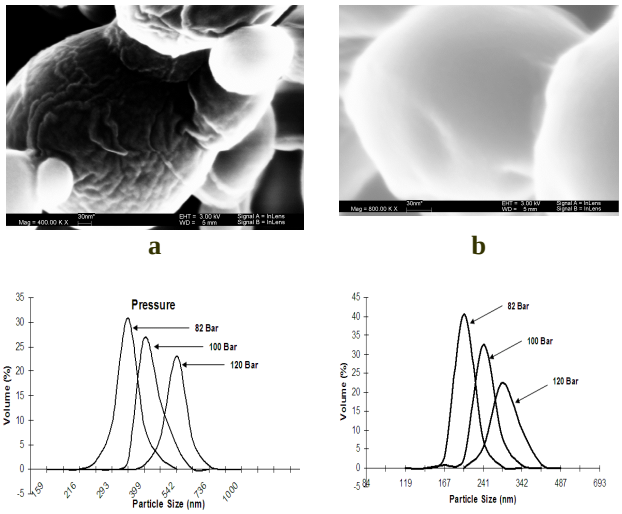

Figure 3. The particle morphology and size distribution of 2 wt % PVP solution in (a, c) DCM and (b, d) DCM-20 wt % acetone mixture; flow rate 0.2 ml/min; chamber pressure 82 bar; nozzle ID (a, b) $127\mu m$, (c, d) $40\mu m$.

With smaller nozzle diameter, particle size reduces as well as particle size distribution gets closer. Figure below represents SEM image of precipitated PVP particles and particle size distribution.

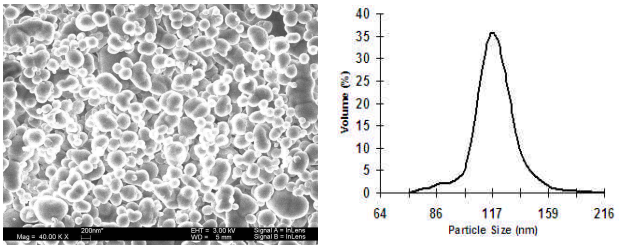

Figure 4. The PVP particles precipitated from 2% PVP solution in DCM-40 wt % acetone mixture; 20 μm nozzle ID, flow rate 0.2 ml/min; chamber pressure 82 bar and temperature 35°C.

4. CONCLUSION

Poor solvent (acetone) helps in reducing agglomeration as well as fast drying. In our case, particle drying time is around 2 hours when only good solvent is used but reduces to 30 minutes when mixture of good and poor solvent is used to make a polymer solution. Smaller nozzle leads to smaller droplets formation which leads to smaller size of particles. Near critical point of mixture, particle morphology and size distribution is favorable and with increase in pressure above critical point, particle size increases. Below critical point of mixture, no particle formation is observed.

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