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SCIENCE DIRECT
J. of Supercritical Fluids 37 (2006) 287–291
THE JOURNAL OF Supercritical Fluids
www.elsevier.com/locate/supflu

Preparation of fine particles of poly(*N*-vinyl-2-pyrrolidone-*co*-2-methylene-1,3-dioxepane) using supercritical antisolvent

Sungwoo Choi, Kangmin Lee, Soyoung Kwon, Hwayong Kim *

School of Chemical and Biological Engineering and Institute of Chemical Processes, Seoul National University, San 56-1, Shilim-dong, Kwanak-ku, Seoul 151-744, Republic of Korea

Received 17 June 2005; received in revised form 21 September 2005; accepted 16 November 2005

Abstract

Fine particles of poly(*N*-vinyl-2-pyrrolidone-*co*-2-methylene-1,3-dioxepane) (poly(NVP-*co*-MDOP)) were produced by means of aerosol solvent extraction system (ASES). Dichloromethane (DCM) was used as solvent and supercritical carbon dioxide was used as antisolvent. Mean diameter of obtained polymer particles ranged from 0.18 to 0.26 μm. The effects of temperature, pressure and solution flow rate on the particle size were investigated. And the relation of particle size and initial drop size was also considered. The size and morphology of particles were investigated by scanning electron microscope.

Keywords: Aerosol solvent extraction system; *N*-Vinyl-2-pyrrolidone; 2-Methylene-1,3-dioxepane; Supercritical carbon dioxide

1. Introduction

Various biocompatible and/or biodegradable polymers have been studied for drug delivery systems, tissue engineering, sutures, etc. [1–3]. One of them is poly(ε-caprolactone) that has the repeating molecular structure that consists of five non-polar methylene groups and a single relatively polar ester group. Poly(ε-caprolactone) is formed with 2-methylene-1,3-dioxepane (MDOP) by the free radical polymerization that was reported to proceed 100% ring opening [4]. However, it is difficult to prepare spherical poly(ε-caprolactone) particles at room condition because of its low glass transition temperature. MDOP can copolymerize with vinyl monomers by convenient free radical to obtain copolymers with biodegradable poly(ε-caprolactone) units in the backbone chain. Some research groups studied about synthesis of copolymers of MDOP and other monomer [5–7]. In our lab copolymer of MDOP with *N*-vinyl-2-pyrrolidone (NVP) was synthesized [8].

Recently various processes to prepare fine particles have been researched. And several processes using supercritical fluids are introduced in review articles [9–11]. Aerosol solvent extraction system (ASES) is one of those processes. It consists of atomizing a solution of the substrate in an organic solvent into a precipitator and causing precipitation of product by rapid mass transfer of supercritical fluid and organic solvent.

ASES process has been applied by various research groups to polymers, superconductor precursors, pharmaceuticals and fullerene [12–16]. Most research groups reported experimental results and the effects of parameters such as pressure, temperature and concentration of solution. Some research group worked to investigate the phenomena in ASES process. Werling and Debenedetti researched into mass transfer of supercritical fluid and solvents [17,18]. Bristow et al. studied supersaturation [19] and Rantakylä et al. studied the effect of initial droplet size [20]. However, Rantakylä et al. did not consider the effect of other parameters when they analyzed the effect of a certain parameter.

In our lab, poly(NVP-*co*-MDOP) was synthesized and particles of the polymer are prepared using ASES process to investigate the effect of pressure, temperature and solution flow rate. And the effect of initial droplet sizes on the particle sizes was analyzed.

* Corresponding author. Tel.: +82 2 880 7406; fax: +82 2 888 6695.
E-mail address: hwayongk@snu.ac.kr (H. Kim).

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doi:10.1016/j.supflu.2005.11.023

2. Mathematical model

When a liquid jet emerges from a nozzle, it can be broken. Two factors contribute to the jet break up. One is the Reynolds number (*Re*) which is the ratio of inertial force and friction force.

$$Re = \frac{d_o U_L \rho_L}{\mu_L} \quad (1)$$

where d_o is nozzle diameter (m), U_L is liquid velocity (m/s), ρ_L is liquid density (kg/m^3), and μ_L is liquid viscosity (kg/m s). The other is the Weber number (*We*) which is the ratio of kinetic energy and surface energy.

$$We = \frac{d_o U_L^2 \rho_L}{\sigma} \quad (2)$$

σ is interfacial tension between gas and liquid (kg/s^2).

The Ohnesorge number (*Oh*) is defined with *Re* and *We*:

$$Oh = \frac{\sqrt{We}}{Re} \quad (3)$$

The larger *Oh* and *Re* indicate the jet stream is better atomized [21].

There are many types of atomizer, and various empirical equations for the initial droplet size are proposed for each type. The most important properties of liquid atomization are surface tension, viscosity, and density. For a liquid injected into a gaseous medium, the only thermodynamic property generally considered of importance is the gas density. The important variables of liquid flow are the velocity of the liquid jet or sheet and the turbulence in the liquid stream. The gas flow variables to be considered are the absolute velocity and the relative gas-to-liquid velocity [21]. In case of atomizer used in our experiment (the type of air-blast atomizer), the equations which estimate the initial droplet size consist of two terms of relative velocity and surface tension and have the same form even though parameters of each equation are not same. So the use of these equations is justified for the description of the qualitative relationship between the initial droplet size and the processed particle size. We chose the equation suggested by Lorenzetto and Lefevre to calculate the initial drop size because of the similarity of atomizer [22].

$$\mathrm{SMD} = 0.95\left[\frac{(\sigma m_L)^{0.33}}{\rho_L^{0.37}\rho_G^{0.30}U_{GL}}\right]\left(1+\frac{m_L}{m_G}\right)^{1.70} + 0.13\left(\frac{\mu_L^2 d_o}{\sigma\rho_L}\right)^{0.5}\left(1+\frac{m_L}{m_G}\right)^{1.70} \quad (4)$$

where the subscript G and L represent air, liquid, and *m* is flow rate (kg/s). SMD is the acronym of 'Sauter mean diameter'. It defined as follows:

$$\mathrm{SMD} = \frac{\sum N_i D_i^3}{\sum N_i D_i^2} \quad (5)$$

N_i is the number of drops in size range *i* and D_i is the middle diameter of size *i*.

According to the equilibrium thermodynamics, the interface does not exist above the critical point. Hence, when considering a slow process of CO_2 dissolution in a solvent portion above the critical point, the solvent portion might be regarded as an effective droplet without the interface and interfacial tension [17,18]. However, the interface is often formed very rapidly. And it may create error to analyze this phenomenon with the equilibrium thermodynamics [23]. Lengsfeld et al. made a study of surface tension of DCM and CO_2 [24]. The experiments were carried out at the critical point of the mixture, and they found that interfacial tension of DCM in CO_2 at 8.5 MPa and 308 K approximated to 0.00001 kg/s^2.

3. Experimental

3.1. Materials

NVP (min. 99%) was supplied from Aldrich. MDOP (min. 98%) was supplied from Fluka. 2,2-Azobisisobutyronitrile (AIBN, min. 98%) was supplied from Junsei Chemical and recrystallized in methanol. DCM (min. 99.6%) was supplied from Aldrich. Carbon dioxide (min. 99.5%) was supplied from Korea Industrial Gases.

3.2. Apparatus and methods

3.2.1. Copolymerization of NVP with MDOP

Detailed apparatus and method for copolymerization of NVP with MDOP is reported in Ref. [8]. NVP and MDOP are polymerized in supercritical carbon dioxide using heterogeneous precipitation method with AIBN as the initiator. The weight ratio of NVP to MDOP is 9:1. Residual monomers were removed before ASES process.

3.2.2. ASES process

A schematic diagram of the semi-continuous ASES apparatus is shown in Fig. 1. The volume of the precipitator is about 100 mL

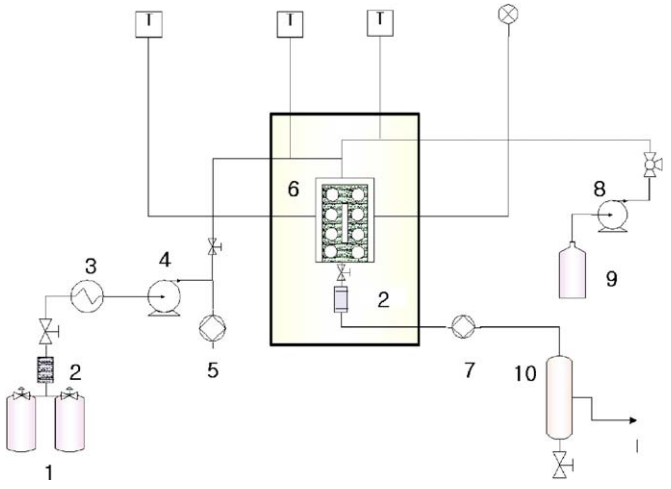

Fig. 1. Schematic diagram of the experimental apparatus: (1) carbon dioxide bomb, (2) filter, (3) heat exchanger, (4) high pressure pump, (5) relief valve, (6) precipitator, (7) back pressure regulator, (8) high pressure pump, (9) solution reservoir, (10) separator.