

Synthesis of Biopolymeric Nanoparticles Using Supercritical Carbon Dioxide as a Dispersion Medium

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ABSTRACT

The utilization of supercritical fluids (SCFs) can lead to the development of materials with unique chemical or physical characteristics that make them suitable for specialized applications. One such technique is synthesizing with supercritical fluids, where the unique fluid characteristics and properties of supercritical fluids are utilized. In this work, The Solution Enhanced Dispersion by Supercritical fluids (SEDS) process precipitation process has been employed to produce fine biopolymeric particles of Poly (L-Lactide) Acid (L-PLA) from dichloromethane (DCM) solution using CO₂ as antisolvent. Submicron particles of L-PLA with uniform morphology have been obtained at all successful SEDS conditions. The ongoing study highlights the potential of a gaseous antisolvent process as an attractive and scalable technology for the synthesis of ultrafine particles for specialty chemical applications.

Keywords: the solution enhanced dispersion, antisolvent, supercritical fluid, biopolymeric.

1 INTRODUCTION

Compared with conventional unit operations, techniques based on supercritical fluids (SCFs) can afford the peculiar features of the dense gases, such as high compressibility and diffusivity, very high evaporation rate and the possibility of fine tuning the solvent power through density modulation. The utilization of SCFs for the processing of pharmaceuticals, nutraceuticals and other products has attracted considerable interest in recent years as an emerging “green” technology [1], [2]. Crystallization using SCFs have several advantages over conventional liquid solvents/antisolvents crystallization as their physical properties such as density and solubility can be “tuned” within a wide range of processing conditions by varying both temperature and pressure.

Supercritical antisolvent techniques are considered highly effective for producing superior products of fine and uniform particles [2]. Moreover, SCFs can be easily separated from both organic cosolvents and solid products, providing a potentially clean, recyclable, and environmentally friendly technology [1]. Antisolvent

techniques such as the Compressed antisolvent (SEDS) process exploit the low solubility of most compounds in the antisolvent, in particular CO₂, which has to be miscible with the organic solvent.

SEDS precipitation can potentially overcome the limitations of liquid antisolvent processing, since very small micronic or submicronic particles can be obtained with narrow particle size distributions and with the complete elimination of the solvents. In the SEDS process, high pressure CO₂ is injected into the liquid phase solution, which causes a sharp reduction of the solute solubility in the expanded liquid phase. As a result, precipitation of the dissolved compound occurs. The potential advantages of the SEDS crystallization process lies in the possibility of obtaining solvent free, micrometer and submicrometer particles with a narrow size distribution [3]. By varying the process parameters, the particle size, size distribution and morphology can be “tuned” to produce a product with desirable qualities. This makes the SEDS technique attractive for the manufacturing of high-valued products, such as pharmaceuticals [4]. The scientific literature shows that SEDS treated materials can range from nanoparticles to microparticles to large empty particles [1–6]. The products can be amorphous or semi-crystalline; but, crystalline particulates have also been reported [1, 2]. Many of the SEDS produced powders range in the micron-size region that has been the target of several studies: many industrial applications require these particle dimensions to obtain the best process performance. For example, small particles in the 1–5 μm range with a narrow particle size distribution are needed for applications in pulmonary delivery and controlled release systems [7].

To contribute at a better knowledge of SEDS applicability to nanosized materials, the scope of this work is to demonstrate that the capability of producing fine particles is a general feature of the SEDS process and that it is possible to describe conditions of the SEDS parameters at which nanoparticles of controlled size and distributions can be obtained. Literature data together with an extensive SEDS experimentation have been performed to assess the possibility of obtaining general validity rules for fine particles production. The mechanism that can produce fine particles during SEDS has also been investigated.

2 EXPERIMENTAL

2.1. Materials

Precipitation with Compressed Antisolvent was carried out using one solute-solvent model systems: L-PLA with a minimum purity of 99.8% purchased from Sigma-Aldrich. Absolute DCM with a minimum purity of 99%, acquired from King saud university (KSU) central storages, was used to prepare the L-PLA solutions sprayed into the precipitator. Carbon dioxide of an instrument grade (99.99 % purity) was used as an antisolvent and further purified by passage through columns containing sieves (Aldrich).

2.2. Procedure

SEDS crystallization of L-PLA with compressed CO₂ was performed by preparing a predetermined volume of L-PLA solution at a saturation concentration, for the given operating temperature, and injected into the 50 ml crystallization vessel. When the system equilibrated thermally, the pressurization step by the injection of CO₂ was initiated, while the liquid phase mixing was taking place. A controlled CO₂ flow rate was maintained until the full liquid volumetric expansion of was achieved. Consequently, the CO₂ supply feed was stopped. Then, a washing/drying step was performed by flushing the liquid phase with an injected CO₂ at a constant flow rate for a minimum of five hours. Finally, the crystallization vessel was depressurized by venting the entire fluid mixture of the vessel, and the dry solid powder was collected for off-line particle size analysis. A schematic representation of the SEDS experimental apparatus is shown in Figure 1.

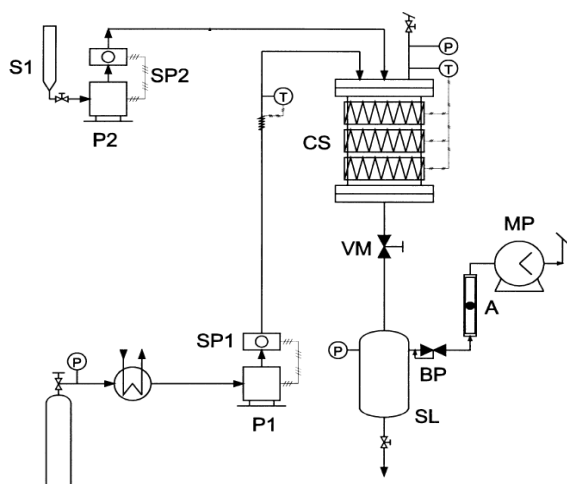


Figure 1. Schematic diagram of the of the SEDS apparatus: P1 and P2, high pressure pumps; SP1 and SP2, pressure dampeners; S1, liquid solution supplier; CS, precipitation vessel; VM, micrometering valve; BP, backpressure valve; SL, liquid separator; A, rotameter; and MP, wet test meter.

2.3. Characterization

Quantitative analysis of the precipitated particles was carried out using the following instruments: scanning electron microscopy (SEM, JEOL JSM-6610LV) provided particle morphology, size, size distribution (PSD), and degree of agglomeration. In order to achieve the best possible statistical representation of the formed particles in terms of particle size and size distribution, analysis of the photomicrographs were taken in several different regions of the collected sample, with a minimum of 1000 particles being used for each measurement.

3 RESULTS AND DISCUSSION

Crystallization using SCFs have several advantages over conventional techniques as their physical properties can be “tuned” within a wide range of processing conditions by varying both temperature and pressure. [1]. Moreover, the potential advantages of the SEDS crystallization process lies in the possibility of obtaining solvent free, submicron particles with a narrow size distribution [3-4]. The scientific literature shows that SEDS treated materials can range from microparticles to nanosized particles [1-4]. In this work, the feasibility of the SEDS crystallization process to produce ultrafine particles was studied. Moreover, the effect of the process parameters such as the antisolvent addition rate, temperature, solute concentration and solution addition rate on L-PLA particle size, size distribution morphology, and crystallinity was also investigated. In the presented results, the effect of antisolvent addition rate was analyzed at different levels of carbon dioxide addition rate, namely, 30, 40, 50, and 60 g/min, at 35 °C. Fig. 2. shows the SEM photomicrograph of the particles generated at the lowest addition rate, i.e., 30 gm/min, the particle size distribution was relatively bimodal and the particle sizes were relatively large with mean particle size of 2.53 μm.

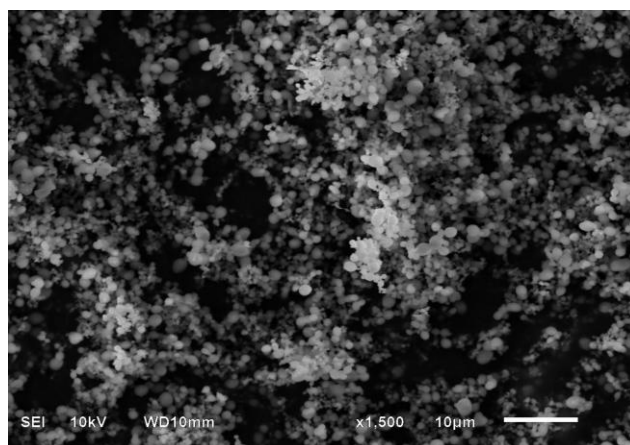


Figure 2. SEM photomicrographs of L-PLA produced by SEDS showing the effect of increasing antisolvent addition rate (30 gm/min).

At the higher carbon dioxide rate of 60 g/min (Fig. 3.), smaller particles with a low degree of agglomeration were obtained. However, the particles size distribution modality is comparable to the low carbon dioxide addition rate run but with a smaller mean particle size of 0.62 μm . It can also be observed that the primary particles have a *spherical*-shaped morphology. A faster rate of anti-solvent addition will generate higher levels of supersaturation, thus, higher levels of nucleation, and consequently, a larger number of smaller size particles with narrow particle size distribution.

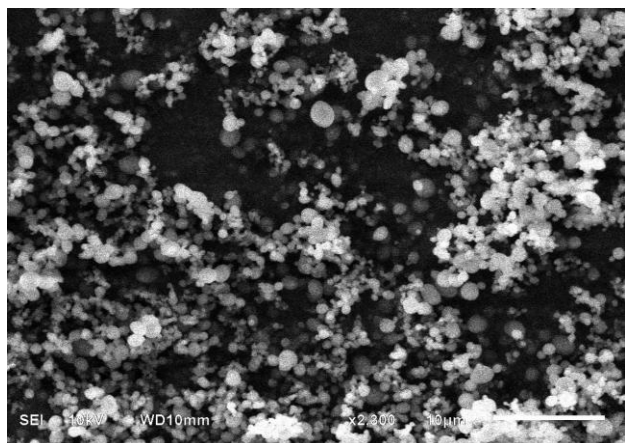


Figure 3. SEM photomicrographs of L-PLA produced by SEDS showing the effect of increasing antisolvent addition rate (60 gm/min).

Fig. 4. shows the SEM photomicrographs generated during experiments at 40 and 50 °C. It is clear that the mean particle size increases and the distribution is becoming very broad. Hence, increasing the temperature lowers the magnitude of the generated supersaturation during the SEDS process. Thus, larger particle sizes with broad particle size distributions are expected.

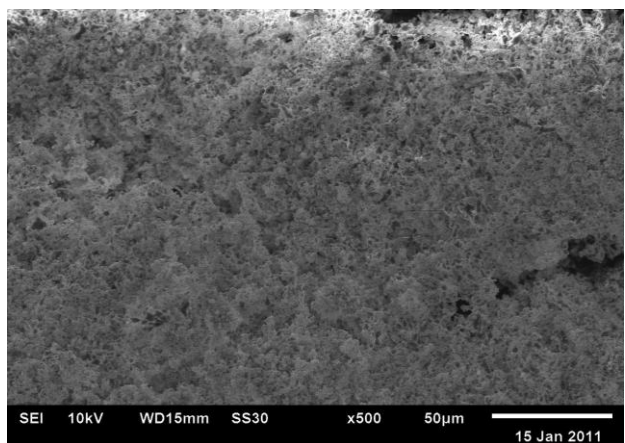


Figure 4. SEM photomicrographs of L-PLA produced by SEDS showing the effect of increasing temperature (40 °C).

4 CONCLUSIONS

This research showed that the production of ultrafine L-PLA particles could be achieved by means of the SEDS process. It was demonstrated that the particles size and size distribution can be strongly controlled through the manipulation of the process parameters. The higher the antisolvent addition rate, the smaller the size of the generated particles and the narrower the size distribution. In contrast, higher temperatures were found to increase the particles size and the level of agglomeration. The achieved experimental results necessitate further investigation for a better understanding of the theoretical underpinnings of the dynamics of the SEDS process and how the process parameters influence the volumetric expansion profile of the liquid phase, thus the magnitude of supersaturation, and consequently the characteristics of the final product.

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