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Original Research Paper

Morphology control of amino acid particles in interfacial crystallization using inkjet nozzle

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ABSTRACT

The aim of this study is to apply the inkjet technique to liquid–liquid interfacial crystallization. Instillation with an inkjet nozzle was compared with the batch process in order to evaluate the effectiveness of the inkjet technique for controlling particle morphology. The effects of amino acid solution concentration and organic solvent type on particle properties were investigated for instillation with an inkjet nozzle. The morphology of alanine and glycine particles was observed by scanning electron microscopy and X-ray powder diffraction. The inner structure of alanine and glycine particles was investigated by cutting particles with an ion milling machine. Controlling particle size by adjusting the droplet size in the instillation with an inkjet nozzle was found to be feasible. Most alanine and glycine particles produced by instillation were spherical, whereas most particles produced by the batch process were non-spherical. A higher concentration of amino acid in the solution may lead to the generation of solute particles at the spherical interface. It was found that the surface structure of alanine particles changed when using two kinds of organic solvents as anti-solvents. In addition, instillation allowed for β-glycine to be identified and the crystal polymorph of the particles to be controlled.

1. Introduction

Powder and fine particles are commonly used in industrial applications, such as the preparation of food, pharmaceutical products and cosmetics [1,2]. The physical and chemical properties of powder particles strongly influence the characteristics of products prepared from powder in manufacturing. Therefore, the ability to control particle morphology, shape and size distribution is essential in industrial applications [3]. For example, the particle morphology of a drug affects its dissolution rate and adsorption rate [4]. Colloids with precisely controlled spherical shape and highly uniform particle size distribution are also promising for manufacturing functional materials [5]. Thin films and composite particles have been fabricated by controlling the structure of ordered particles [6].

Bottom-up technology is often used for controlling particle properties in such fabrication processes. There have been studies on controlling particle properties in bottom-up techniques such as crystallization and sol–gel methods, for the purpose of obtaining various particle properties [7–9]. Crystallization can be carried out through separation and particle generation to control physical and chemical properties [10,11]. Recently, crystallization and polymerization in oil-in-water and water-in-oil emulsions have been investigated as particle production techniques [12–14]. There are problems concerning the emulsion stability such as flocculation and coalescence [15,16].

To solve these problems, liquid–liquid interfacial crystallization was proposed as an advanced particle formation method in our previous studies [17,18]. Liquid–liquid interfacial crystallization is a production technique for precipitating solute particles at a liquid–liquid interface that is partially miscible. Interdiffusion between aqueous solutions and organic solvents occurs near the liquid–liquid interface according to the mutual solubility curve. In our previous studies, different types of asymmetric particles were obtained at liquid–liquid interfaces, and porous glycine particles were successfully produced by liquid–liquid interfacial crystallization [19], demonstrating that the particle growth rate depends on mutual diffusion between water and organic liquids. The morphology of particles can be controlled by preparing uniform spherical droplets using an inkjet nozzle. The inkjet technique has recently started drawing considerable attention for particle

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production in manufacturing [20,21]. The advantages of the inkjet technique include the ability to control the size of droplets without heating. The inkjet technique was used to produce polymer particles by Bohmer et al. [20] and metal particles by Kitsomboonloha et al. [21], where the particle size distribution and morphology were successfully controlled in both cases. These results are promising in terms of meeting the expectation that liquid–liquid interfacial processes are effective for producing composite materials since the precipitation field is limited to a uniform spherical interface.

In this study, the inkjet technique was applied to liquid–liquid interfacial crystallization. The batch process was compared with instillation to elucidate its effectiveness for controlling particle morphology. The effect of amino acid solution concentration and organic solvent type on particle properties in interfacial crystallization using an inkjet nozzle was also investigated.

2. Experimental

2.1. Materials

All reagents, including alanine (98%), glycine (99%), 1-butanol (99%) and 2-butanone (99%) were purchased from Nacalai Tesque (Japan). Alanine and glycine were used as solutes, and 1-butanol and 2-butanone were used as solvents for liquid–liquid crystallization. Alanine and glycine were used as received without further purification, and the solvents 1-butanol and 2-butanone were sufficiently dried over molecular sieve. All solutions prepared for the experiments were passed through a membrane filter with a pore size of 0.1 μm before commencing crystallization.

2.2. Preparation of amino acid particles by instillation crystallization using an inkjet nozzle

Alanine and glycine were selected as solutes for liquid–liquid crystallization using an inkjet nozzle. Alanine has no crystal polymorphs, but glycine has three: α, β and γ [22]. Alanine and glycine saturated solutions were prepared by stirring for 24 h at room temperature. The organic solvents 1-butanol and 2-butanone were used to create a liquid–liquid interface by placing them in contact with the aqueous solution. A schematic of the experimental apparatus used for instillation with an inkjet nozzle (Pulse Injector, Cluster Technology Co., Ltd., Japan) is shown in Fig. 1. In this system, droplets of the aqueous solution were discharged from the inkjet nozzle into an organic solvent (1-butanol or 2-butanone) which is slightly miscible with water [19]. Amino acids crystallized immediately within the droplets, which were present for approximately 300 s in the organic solvent. The suspension containing the droplets in the organic solvent was passed through a membrane filter with a pore size of 0.1 μm in a vacuum deaerator. The particles were collected and dried in a desiccator containing blue silica for 24 h after removing excess solution around particles.

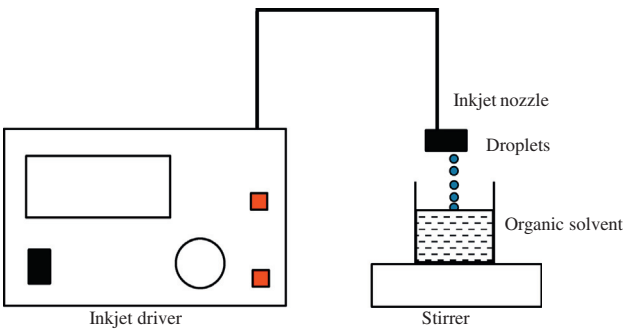

Fig. 1. Experimental apparatus for instillation process using an inkjet nozzle.

2.3. Preparation of amino acid particles by batch process

In the batch process, amino acid particles were prepared by mixing the amino acid solution with 1-butanol solvent under constant agitation. Alanine- or glycine-saturated solution (10 mL) was added to 10 mL of 1-butanol. The resulting suspension containing droplets of alanine or glycine solution in the organic solvent (1-butanol or 2-butanone) was stirred for 300 s. The suspension was filtered in the same way as in the instillation process.

2.4. Observation of droplets discharged from inkjet nozzle

Droplets were illuminated at intervals of 0.2 ms by a blue diode and observed with a light microscope (Moticam 1000, Shimadzu Rika Co., Ltd.). It was also possible to observe droplets continuously discharged from an inkjet nozzle. Droplet size was evaluated from micrographs by using image analysis software (WinROOF, Mitani Corp.)

2.5. Characterization of particle size and crystal structure of particles

The morphology of alanine and glycine particles was observed by scanning electron microscopy (SEM) (VE-7800, Keyence Corp.). Prior to examination, the samples were mounted onto metal stubs and sputter-coated with a thin layer of gold under vacuum (E-1045, Hitachi Co., Ltd.). The particle size was estimated by measuring the Martin diameter in SEM images by using image analysis software (WinROOF).

The crystal structure of alanine and glycine particles was investigated by X-ray powder diffraction (XRD) (RINT2000, Rigaku Corp.) using a Cu Kα source (r = 1.5406 Å). Phase identification was performed using a continuous scan of the 10–90° range of 2θ in 0.02° steps.

The inner structure of alanine and glycine particles was investigated by cutting particles (dispersed in graphite in advance) with an ion milling machine (E-3500, Hitachi). A cut was produced by milling at an acceleration voltage of 6 kV and a discharge voltage of 4 kV for 12 h, and the resulting cross section was observed by SEM.

3. Results and discussion

3.1. Relationship between droplet size and particle size

Fig. 2 shows the mean particle size of alanine plotted against the droplet size produced by instillation. The mean particle size is approximately 1.2-fold the droplet size in 1-butanol. Both

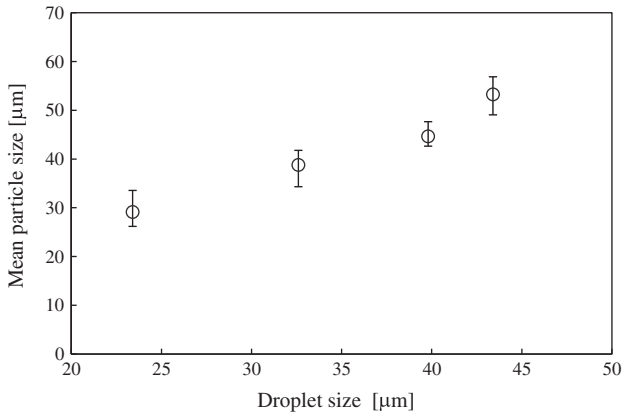

Fig. 2. Relationship between droplet size and mean particle size of alanine for instillation using an inkjet nozzle (alanine concentration: 0.80 mol/L).