



Fabrication of composite particles by liquid–liquid interfacial crystallization using an ultrasonic spray nozzle



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ABSTRACT

The purpose of this study was to produce composite particles, consisting of core starch particles coated with glycine, by liquid–liquid interfacial crystallization with an ultrasonic spray nozzle and to investigate the effect of operating conditions on glycine particle morphology. We confirmed that ultrasonic irradiation could improve the coating efficiency of the core starch particles during the crystallization process. We also investigated the transformation between different polymorphs of glycine crystals that covered the starch surface. The coating efficiency of the fine glycine crystals on the starch particles was improved by using an ultrasonic spray nozzle rather than anti-solvent crystallization without an ultrasonic spray nozzle. The glycine crystals on the surface of starch particles transformed from unstable to stable forms according to the solution-mediated mechanism and Ostwald rule of stages. The interaction between the core particles and guest particles was found to be a key factor in producing the composite particles. The results indicate that this crystallization process using the ultrasonic spray nozzle is promising for efficiently producing composite particles.

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1. Introduction

Advanced functional materials used in various fields often require accurate control of particle properties. The advanced functionality of the particles, which constitute a basic unit of materials, can have an enormous effect on the performance of commercial products [1,2]. Composite structures and interfaces in particular could give new functions to materials, and technologies that produce such structures have been recognized as drivers of innovative product development. Particles are generally utilized as precursors for creating composite structures. There are several kinds of composite particles, such as organic–inorganic particles and organic matrix products. Organic–inorganic particles have recently garnered attention in photoelectronic materials and pharmaceutical products [3,4], while organic–organic composites are being investigated in biomaterial products.

Several methods are available for producing such composite materials [5,6]. Build-up processes have been used extensively for production of composite materials because these processes can control the properties of composite particles. Crystallization has been widely used as a process to simultaneously carry out separation and particle generation [7]. Recently, crystallizations using polymerization in oil-

in-water and water-in-oil emulsions have been developed as particle production technologies [8–11]. However, some problems remain concerning particle stability, such as flocculation and coalescence of the emulsions [12,13].

We have previously proposed crystallization at a liquid–liquid interface as a new crystallization method [14–16]. Liquid–liquid interfacial crystallization is a technique to precipitate solute particles at an interface of two liquids that are partially miscible. Inter-diffusion between aqueous solutions and organic solvents occurs near the liquid–liquid interface according to the mutual solubility curve. We successfully produced different types of asymmetric particles, porous glycine particles, and composite particles by using this crystallization technique [17–20]. The results of that work also provided evidence that the growth rate of particles near the liquid–liquid interface depends on mutual diffusion between water and organic solvents. Liquid–liquid interfacial crystallization is a promising method to apply to heat-sensitive proteins and drugs. Moreover, the control of crystal morphology is relatively easy using this technique because the change in the supersaturation ratio is slight due to the limited precipitation space at the liquid–liquid interface. We produced composite particles by applying this liquid–liquid interfacial crystallization technique [18,19]. Atomizing crystallization based on the principle of liquid–liquid interfacial crystallization was developed to produce organic/inorganic composite particles [18]. Further development of liquid–liquid interfacial crystallization is nevertheless needed to apply this method to a wide range of composite particles.

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Ultrasound has attracted attention from researchers in the crystallization field because it is promising for the development of micro-particulation processes for the production of composite materials. It is known that ultrasonic irradiation affects crystalline properties. Changes of crystal habit (i.e., the characteristic external shape of an individual crystal or group of crystals) and of crystal size distribution have been shown to occur when ultrasonic irradiation induces primary nucleation [21–23]. Kurotani et al. [21] studied the effect of ultrasonic irradiation on the primary nucleation behavior of amino acids in supersaturated solutions. Their results indicate that a weak ultrasonic irradiation could inhibit primary nucleation rates, whereas strong ultrasonic irradiation can enhance them. Measurements of crystal size for each irradiation and supersaturation condition showed that mean particle size is affected by ultrasonic irradiation and is highly correlated with the induction period. Hatkar and Gogate applied ultrasonic irradiation to anti-solvent crystallization of salicylic acid [24]. They demonstrated that the ultrasonic irradiation resulted in a low mean crystal size and a narrow size distribution. Stelzer et al. have already applied ultrasonic crystallization as a monitoring technique for process analytical technology [25]. Controlling the conditions of supersaturation and ultrasonic irradiation should allow production of the desired crystal size of the final product.

In the present work, we fabricated organic–organic composite particles using an ultrasonic spray nozzle based on the fundamental principle of liquid–liquid interfacial crystallization. We selected starch and glycine particles as model substances to confirm the potential of crystallization resulting from use of an ultrasonic spray nozzle. Starch was selected since it is often used as an excipient for pharmaceutical products and glycine was selected as a model drug. The ultrasonic method is compared to the more commonly used anti-solvent crystallization technique without an ultrasonic spray nozzle. The coating efficiency of composite particles prepared by ultrasonic crystallization was compared with that of anti-solvent crystallization. Also, the effect of an ultrasonic spray nozzle on glycine polymorphism was investigated since the polymorphism affects the properties of composite particles. In previous studies, the crystal shape and growth rate were controlled by the concentration of NaCl and the contact time of the two solvents at the liquid–liquid interface [14,16]. Controlling crystallization temperature is of particular importance because the temperature of the solution affects the solubility, nucleation, and crystal growth of the substance [26]. In the case of glycine, the temperature could moreover influence whether its α , β , or γ polymorph is produced [27]. The mechanism of the transformation between these different forms of glycine crystals on the surface of starch is discussed. Ultrasound-induced crystallization at the liquid–liquid interface is expected to produce composite particles efficiently.

2. Experimental procedure

2.1. Materials

Starch (100%) was purchased from Mylan Inc. (Cecil, PA) and used as a core particle since this starch is practically insoluble in water. The mean particle size of this starch is 10.92 μm . Glycine (99%) was purchased from Nacalai Tesque Inc. (Kyoto, Japan), and used as the solute. Glycine was used as a model substance to investigate the transformation between the different polymorphic forms [27–29]. The organic solvents 1-butanol (99%) and ethanol (99%) were purchased from Nacalai Tesque. 1-Butanol was used for liquid–liquid interfacial crystallization because it is an appropriate solvent for this technique [14,15] according to its mutual solubility curve with water. Ethanol was used for anti-solvent crystallization.

2.2. Anti-solvent crystallization without ultrasonic spray nozzle

For anti-solvent crystallization, a saturated glycine aqueous solution was prepared by stirring glycine in distilled water for 24 h at 293 K. Starch particles (3 wt.%) were added into the saturated glycine solution. After that, the saturated glycine solution containing suspended starch was dropped from the nozzle into ethanol or 1-butanol, where 1-butanol has been used for liquid–liquid interfacial crystallization [14]. The solution droplets exited the nozzle, flowed into the ethanol or 1-butanol, and solidified for the crystallization. The suspension was passed through a filter with a pore size of 0.1 μm before commencing crystallization. The anti-solvent crystallization without an ultrasonic spray nozzle was compared to ultrasonic atomizing crystallization. The contact time was kept for 7 min.

2.3. Liquid–liquid interfacial crystallization using ultrasonic spray nozzle

Fig. 1 shows a schematic of the experimental apparatus used for crystallization with the ultrasonic spray nozzle (130K50ST, Sonaer Ultrasonics, Farmingdale, NY). In this procedure, droplets of aqueous solution are discharged from the ultrasonic spray nozzle into organic solvents that are slightly miscible with water. The organic solvent used in the present study was 1-butanol. Ultrasonic atomizing crystallization was controlled by vibrating the spray nozzle with an ultrasonic oscillator (Digital Ultrasonic Generator, Sonaer Ultrasonics). A custom-built fluid dispenser (TIC Co., Ltd., Tokyo, Japan) was operated at a flow rate of 4.34 mL/min. The ultrasound frequency was maintained at a constant 130 kHz. Starch particles (3 wt %) were dispersed in

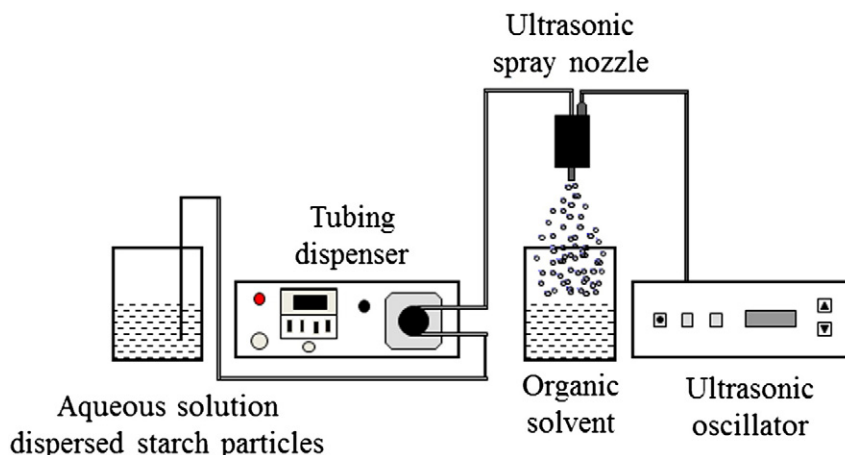


Fig. 1. Schematic diagram of the experimental ultrasonic spray nozzle apparatus used for the liquid–liquid interfacial crystallization.

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