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Fabrication of composite particles through single pass using a coaxial tube reactor

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ABSTRACT

Composite particles were prepared by liquid–liquid interfacial crystallization in a coaxial tubular reactor. A microfluidic channel was utilized for controlling particle properties and fabricating composite particles via a single pass in a continuous flow process. Changes in flow patterns with Weber number were investigated by visualizing flow patterns in the reactor; four types of flow patterns were observed. Particle size distributions of sodium chloride (NaCl) in the reactor were optimized by controlling flow patterns. Crystal nucleation rates and growth rates were calculated using the Rosin–Rammler distribution, which is also used in conventional crystallizers. Indomethacin (IMC) crystals with a fibrous morphology were obtained in any of three flow patterns by ultrasonic irradiation of the tube reactor; however, precipitation of IMC did not occur without ultrasonic irradiation. Composite particles of NaCl and IMC were produced by ultrasonic irradiation in a dispersed flow. The process involving dispersed flow could be used to continuously fabricate composite particles in a single pass through the reactor.

1. Introduction

To prepare advanced functional materials consisting of fine particles, it is necessary to control interfacial structures in composite particles. Composite particles with fine interfacial structures could contribute to the development of materials with new functions; therefore, such particles have been recognized as drivers of innovative product development. Several methods are available for producing such composite materials [1,2]. Liquid-phase methods have often been used to produce composite particles, such as metal alloys for hydrogen storage. Methods involving water-in-oil microemulsions have been used to prepare battery materials and cosmetic products. Sol–gel processing has also been widely used for creating nanostructured materials with controlled porosities and shapes [3]. Sol–gel processing is an important approach to the fabrication of nanostructured materials in the form of bulk solids and surface coatings [4]. However, applications of these methods are limited because the syntheses of coated particles depend on differences in reaction rates between mixed precursors [5].

Microchannels have attracted attention for producing composite particles because there is the possibility for production in a single step [6]. Use of microchannels offers three advantages: large interfacial area per unit volume, residence time of the fluid can be controlled by changing the channel length, and operation at low Reynolds numbers [7]. Moreover, in a microchannel, molecular diffusion at a stable interface can be precisely performed. Fabrication of fine particles in confined microspaces would provide useful information about the precise control of particle properties such as particle size distributions [8,9]. In addition, flow patterns can be changed by controlling the flow rate in a microchannel. Some researchers have analyzed flow patterns and utilized them as reaction, mixing, and diffusion fields [10–15]. These many operational parameters could expand the possibility of controlling particle properties and preparing composite particles.

Some researchers have studied how flow behavior can be used for fluid control [16–18]. Wong et al. [19] succeeded in maintaining crystal characteristics at high qualities by controlling flow patterns in the confined space of a microchannel. Alvarez et al. [20] showed that an unconventional plug flow crystallizer was able to produce small crystals with a narrow size distribution by adding an

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Notation

Latin symbols

We	Weber number (–)
D_H	Hydraulic diameter (m)
U	Flow velocity (m/s)
Q	Flow rate (m^3/s)
A	Cross-sectional area (m^2)
a	Surface area of suspended crystals in crystallizer (mm^2)
l	Crystal size (mm)
$f(l)$	Particle size distribution based on numbers in products (/mm m^3)
$g(l)$	Particle size distribution based on numbers in channel (/mm m^3)
$F_{\nu'}$	Nucleation rate (/h m^3)
k_a	Surface shape factor (–)
k_v	Volume shape factor (–)
l^*	Particular crystal size corresponding to relative cumulative amount of crystal of 0.368id=6#on numerical basis (mm)
m	Gradient of Rosin–Rammler diagram (–)
P	Production rate (kg/h)
V	Volume of all crystals in crystallizer (m^3)
V'	Volume of the crystallizer (m^3)
x	Dimensionless size of l/l^* (–)
G	Free energy (J)
r	Crystal size (m)
G_v	Energy change per unit volume at the phase transition (J)
G_{US}	Energy of ultrasound per unit volume of medium (J)

Greek symbols

ρ	Density (kg/m^3)
θ	Retention time of a crystal whose size is l (h)
ε	Void fraction (–)
γ	Interfacial tension (N/m)

Subscripts

w	Water phase
o	Organic phase
c	Crystal
max	Maximum
av	Average

antisolvent at multiple points along the crystallizer. Li et al. [21] succeeded in synthesizing composite particles using a fluidized bed reactor. Wang et al. prepared ZnO nanoparticles using $ZnSO_4$ and NH_4HCO_3 aqueous solutions in a microreactor [22]. Recent studies report that preparation and synthesis of composite particles have been performed using a microreactor [23–25]. Specifically, a tube reactor using liquid–liquid interfacial crystallization may provide confined spaces for preparing composite particles without heat transfer and in a single pass.

Liquid–liquid interfacial crystallization is a new crystallization method that we proposed in previous papers [26–28]. In this technique, solute particles are precipitated from solutions at an interface between two partially miscible liquids. Solute or solvent ions mutually diffuse in the vicinity of the liquid–liquid interface based on their mutual solubility curve. Use of this technique has led to the successful creation of varieties of asymmetric particles, porous particles, and composite particles [29–32]. Our results reveal that particle properties near the liquid–liquid interface correlate with inter-diffusion between aqueous solutions and organic solvents. Specially, interfacial crystallization is an innovative method that can be applied to heat-sensitive materials because precipitation of substances from solutions takes place without any heat treatment. In addition, control of particle properties is relatively easier using this technique because changes in the supersaturation ratio is slight due to the limited space for precipitation near the liquid–liquid interface. We hypothesize that efficient liquid–liquid interfacial crystallization can be used to fabricate composite particles in a single pass by using confined spaces in a microfluidic process.

In this study, we examined mechanisms for precipitating particles and fabrication of composite particles based on liquid–liquid interfacial crystallization in a coaxial tubular reactor. Sodium chloride (NaCl) and indomethacin (IMC) particles were selected as model substances to confirm the potential for using crystallization in a tubular reactor. In our previous papers, we used NaCl for liquid–liquid interfacial crystallization [26–28]; here we selected IMC as a representative drug having poor water solubility [33]. This technology involving a tube reactor holds the promise of producing composite particles in one step, although in later applications, composite particles of NaCl with IMC may not be the target product. Flow patterns in the tube reactor were observed for creating a confined field for crystallization. Control of NaCl and IMC particles was carried out using the liquid–liquid interface between an aqueous solution and 2-butanone. Nucleation and crystal growth rates of NaCl particles in the tube reactor were studied by applying our previous continuous crystallizer in steady-state operations [34]. Fabrication of composite particles by a single pass through a tube reactor was achieved.

2. Experimental procedure

2.1. Materials and methods

NaCl (purity, 99.0%) and the organic solvent 2-butanone (purity, 99.0%) were purchased from Nacalai Tesque Inc. (Kyoto, Japan). IMC (purity, 98.0%) was purchased from Wako Pure Chemical Industries, Ltd. (Osaka, Japan). NaCl and IMC were used as received without further purification, and 2-butanone was sufficiently dried over a molecular sieve. Before commencing crystallization, all solutions prepared for the experiments were passed through a membrane filter with a pore size of 0.1 μm.

An aqueous NaCl solution was prepared by stirring for 24 h at room temperature. The concentration of the NaCl solution was 6.160 mol/L. The organic solvent was chosen to be 2-butanone because a large number of crystals can be obtained from 2-butanone over a short time [30]. A liquid–liquid interface was created by contacting 2-butanone with the aqueous NaCl solution according to the mutual solubility curve of 2-butanone with water (Fig. 1S). The physical properties of the solvents are shown in Table 1.

In the present crystallization, composite particles precipitate at a liquid–liquid interface by individually supplying two different solutes: one from the aqueous solution, the other from the 2-butanone solution. The solution of IMC dissolved in 2-butanone was kept at equilibrium by letting it stand for one week after

Table 1
Physical properties of the used solvent.

	Water	2-Butanone
Density ρ [kg/m^3]	998.2	780.7
Viscosity μ [mPa × s]	1.002	0.441
Interfacial tension σ [mN/m]	72.75	24.6

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