

Control of Crystal Size Distribution using Non-Isothermal Taylor Vortex Flow

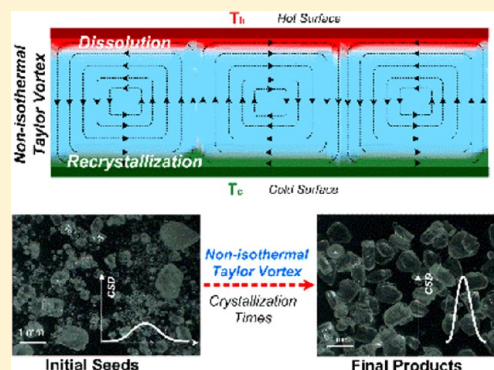
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S Supporting Information

ABSTRACT: Using a Couette-Taylor (CT) crystallizer, a non-isothermal technique was developed for effective control of the crystal size distribution (CSD) of the suspension. The proposed technique is based on the internal heating–cooling cycle in a non-isothermal CT crystallizer, consisting of a hot cylinder (T_h) and cold cylinder (T_c). Thus, an internal loop of fines destruction of the suspension in the heating boundary layer of the hot cylinder and recrystallization in the cooling boundary layer of the cold cylinder is formed by the periodic circulating flow of the Taylor vortex in the non-isothermal CT crystallizer. The efficiency of the heating–cooling cycle for improving the CSD depends on the non-isothermal mode and non-isothermal parameters. When the inner cylinder temperature is hot and the outer cylinder temperature is cold (Mode-I), this is more efficient for improving the mean crystal size and dispersity of the CSD than when the cylinder temperatures are reversed (Mode-II). In addition, the efficiency of the heating–cooling cycle is optimized using the temperature difference between hot and cold cylinders ($\Delta T = T_h - T_c$) and saturated bulk temperature. The Taylor vortex fluid motion is always found to enhance the internal cycle efficiency. Thus, the initially small crystal size and broad CSD of the seed suspension (230 μm of mean crystal size and 81% of coefficient of variation) are improved to a large crystal size and narrow CSD of the product suspension (1020 μm of mean crystal size and 31% of coefficient of variation) at a non-isothermality of 8.7 ± 0.1 °C, saturated bulk temperature of 24.0 °C, and rotation speed of 800 rpm. The variation of the cycle efficiency is explained in terms of the driving forces for heating dissolution and cooling recrystallization.



INTRODUCTION

Crystal size distribution (CSD) is one of important characteristics of crystals in industry, because the downstream processes such as filtration, drying, and washing of crystals are significantly affected by CSD.^{1,2} Also, the content uniformity, tablet strength, and productivity of the API (active pharmaceutical ingredient) in the formulation process depend directly on the CSD of pharmaceuticals.^{3,4} Thus, various attempts have already been performed to develop techniques, such as seeding technique, programmed cooling profile technique, and fines destruction technique, for controlling CSD in the crystallization.^{5–8}

In the seeding technique, the seed crystals were used to control the supersaturation within the metastable limit and prevent undesired nucleation for large crystal size and narrow CSD of product suspension in cooling crystallization.^{9,10} Due to its simplicity, the seeding technique was frequently used to control the CSD of the suspension in industry. However, this technique was sensitively dependent on many operating parameters, including seed purity, seed amount, seed size, seeding time, and cooling rate, as reported in previous studies.^{11–13} So, the operating parameters should be adjusted carefully and accurately to obtain the desired CSD in the

crystallization. In the programmed cooling technique proposed first by Mullin and Nývlt,¹⁴ the cooling rate was the most critical parameter for controlling CSD of the suspension in cooling crystallization. In the case of natural cooling, the cooling profile is fast during the early stage of crystallization in order to generate high nucleation and then slows down. Consequently, the supersaturation profile is broad and hardly controllable below the metastable limit during crystallization, resulting in a small crystal size and broad CSD in the product suspension. While a linear cooling profile somewhat relieves these problems with the natural cooling profile, it frequently fails to maintain the supersaturation within the metastable zone during crystallization. Thus, in the programmed cooling profile, the cooling rate during the early stage is set as low and then slowly increased to accelerate the crystal growth within the metastable zone. This technique is more effective for controlling uniform CSD when combined with the seeding technique, as demonstrated in the crystallization of potassium sulfate and ammonium sulfate.¹⁵ Furthermore, the inclusion of

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a dissolution strategy with the programmed cooling profile technique also improves the control of the CSD during crystallization.^{16,17} As a result, Takiyama et al. achieved a highly narrow and large CSD of potash alum (784 μm mean crystal size and 16% coefficient of variation (CV)) using this combined technique, as the fine crystals in the suspension were destroyed during the dissolution strategy of the temperature swing. In contrast, the broad CSD of potash alum (266 μm mean crystal size and 59% CV) was produced using the simple linear cooling profile technique.¹⁸

The fines destruction technique is frequently used for effective control of the CSD of the product suspension during the cooling crystallization process.^{19,20} Based on the use of an extra dissolver, the excess fine crystals in the suspension are completely dissolved, and the dissolved solution is then fed back into the crystallizer for recrystallization in the suspension. With this technique, a crystal classifier is also required to identify the fine crystals in the suspension for the dissolver. Thus, the cutoff threshold of fine crystals by the classifier is important for determining CSD of the suspension. A new batch crystallizer, called a wall wetter/double-deck jacket (WWDJ) crystallizer, for precise control of the CSD of the suspension was developed by Gu et al.²¹ This crystallizer is composed of two double-deck jackets, where the lower jacket deals with cooling crystallization and the upper jacket deals with crystal dissolution, and its working principle is based on the internal fines destruction process in the crystallizer. That is, the crystallization suspension in the lower deck is continuously sprinkled onto the hot wall of the upper deck using a wall wetter. The fine crystals are then destroyed on the hot wall of the upper deck, while the rest of the suspension runs down the wall and the dissolved solution flows back into the lower deck for recrystallization. Here, the jacket temperature of the upper deck was set above the saturated temperature of the suspension, while the jacket temperature of the lower deck is set below the saturation temperature. Thus, the temperature difference between double-deck jackets is crucial for determining the efficiency of the internal fines destruction–recrystallization process in the crystallizer. When using this crystallizer, it was demonstrated that the initial CSD (44% CV) of the seed suspension was improved to a 35% CV in the final product suspension in batch mode crystallization. Similarly, the temperature swing or temperature cycling technique also exploits the principle of internal dissolution–recrystallization for CSD control of the suspension in cooling crystallization.^{22,23} As shown in previous studies,^{24–27} successive alternate cycling of heating and cooling of the suspension gradually destroys the fine crystals and enhances the mean crystal size and dispersity of the CSD of the suspension. In addition, based on the fines destruction technique, an automated direct nucleation control approach was suggested to control the CSD of a suspension during batch cooling crystallization by Salemi et al.²⁸

This study presents a new technique using a non-isothermal Taylor vortex flow for the easy and effective control of the CSD during crystallization. The non-isothermal Taylor vortex fluid motion is generated in a non-isothermal Couette-Taylor (CT) crystallizer with two different cylinder temperatures for internal loop of heating dissolution and cooling recrystallization, respectively. It has already been demonstrated that a Taylor vortex flow is highly effective for promoting heat and mass transfers.^{29–31} Therefore, it is expected that a non-isothermal technique using a Taylor vortex flow will also be efficient for

controlling the CSD. In addition, the working mechanism of this technique is studied and the influential operating parameters investigated.

EXPERIMENTAL SECTION

A Couette-Taylor (CT) crystallizer for a non-isothermal Taylor vortex flow was designed, as shown in Figure 1. In the CT crystallizer, the

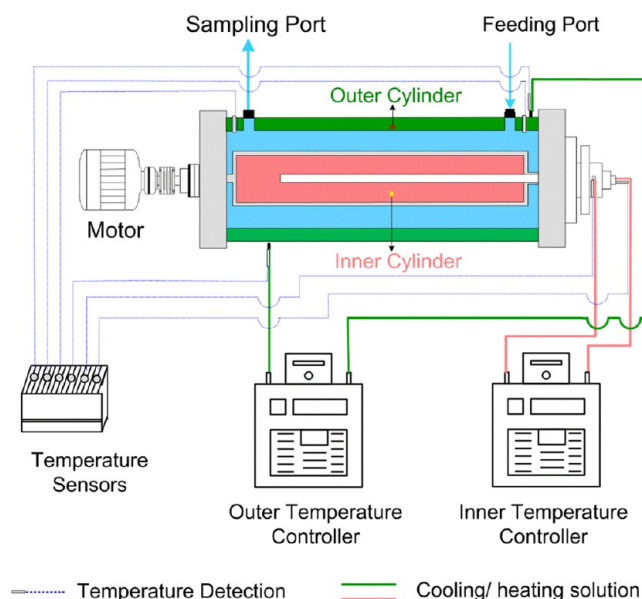


Figure 1. Experimental system for non-isothermal technique using Couette-Taylor crystallizer.

Taylor vortex fluid motion was induced in the gap between the inner and outer cylinders by rotation of the inner cylinder. Both CT crystallizer cylinders were equipped with thermal jackets to control the cylinder temperatures. When the temperature of both cylinders was the same, an isothermal Taylor vortex flow was formed. Meanwhile, a non-isothermal Taylor vortex flow was generated when the cylinder temperatures were different. Two non-isothermal Taylor vortex modes were considered. The first non-isothermal mode was generated using a hot temperature for the inner cylinder (T_{ih}) and cold temperature for the outer cylinder (T_{oc}), while the second mode was generated using a cold temperature for the inner cylinder (T_{ic}) and hot temperature for the outer cylinder (T_{oh}). It should be noted that the hot and cold cylinder temperatures in both modes were carefully adjusted to provide the same bulk temperature (T_b) in the gap of the CT crystallizer.

First, seed crystals of L-lysine were prepared by continuous cooling crystallization using an isothermal CT crystallizer. The L-lysine feed solution was prepared by dissolving 850 g/L of L-lysine in deionized water at a saturated temperature of 40 $^{\circ}\text{C}$, and the solution temperature was then increased to 50 $^{\circ}\text{C}$ for complete dissolution. Thereafter, the feed solution was cooled to 20 $^{\circ}\text{C}$ in the isothermal CT crystallizer to obtain seed crystals of L-lysine. Here, the rotation speed of the inner cylinder and mean residence time were fixed at 500 rpm and 15 min, respectively. These seed crystals were filtered and dried in a convection oven for use in the crystal size distribution (CSD) experiments with a non-isothermal CT crystallizer. The seed crystals were about 230 μm in average size and 81% of CV in crystal size distribution.

The CSD control was carried out using a non-isothermal CT crystallizer (Figure 1). Initially, the CT crystallizer in a non-isothermal mode was filled with a clear saturated solution at T_b and the inner cylinder rotated until the temperature profile in the CT crystallizer reached at steady state. The clear saturated solution was then quickly drained out of the CT crystallizer and a seed suspension saturated at the same T_b was quickly pumped into the CT crystallizer to modify the

CSD of the seed crystals in the non-isothermal Taylor vortex. In this experiment, the temperature difference between the hot and cold cylinders, $\Delta T = T_h - T_c$ was varied from 0 to 20.5 °C, the saturated bulk temperature (T_b) was changed from 20.0 to 30.0 °C at a constant temperature difference between the hot and cold cylinders (ΔT), and the rotation speed of the inner cylinder was adjusted from 200 to 900 rpm. During the experiment, the temperatures of the inner and outer cylinders and bulk solution at the axial position of the CT crystallizer were in situ monitored using the LabVIEW program (National Instruments). Intermittently, the product suspension was taken for analysis of the CSD, while a seed suspension was simultaneously injected to refill the CT crystallizer. The CSD of the product suspension was analyzed using Video Microscope (IT System, Somatech, USA) and software Size Measurement Xoj Binary Project (Xoj Inc., USA). For the measurement of crystal size distribution, over 500 crystals were analyzed using the microscopic images.

RESULTS AND DISCUSSION

Scheme of Heating–Cooling Cycle in Non-Isothermal Taylor vortex. The non-isothermal technique was based on

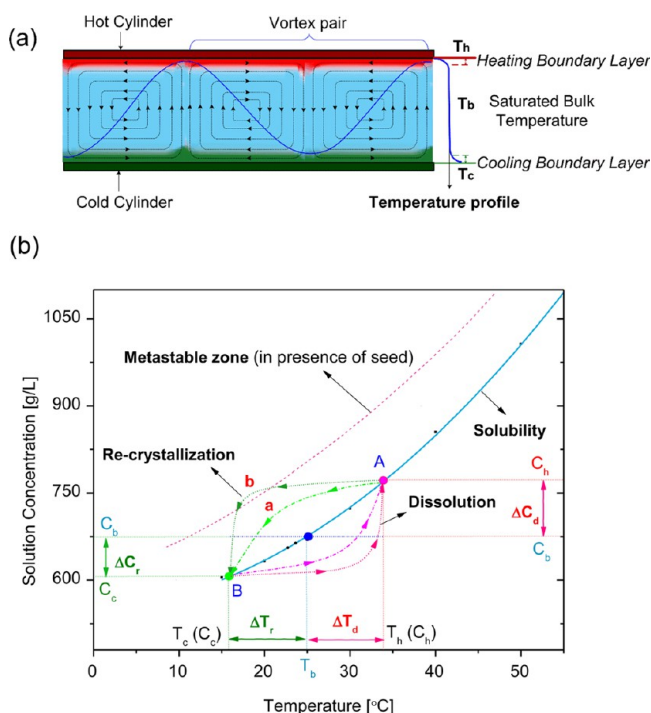


Figure 2. (a) Diagram of non-isothermal Taylor vortex in Couette-Taylor crystallizer and (b) scheme of internal heating–cooling cycle in non-isothermal Couette-Taylor crystallizer.

the internal heating–cooling cycle in the non-isothermal Couette-Taylor crystallizer. As shown in Figure 2a, the scheme of the internal heating–cooling cycle was to exploit the simultaneous dissolution and recrystallization in the non-isothermal CT crystallizer. That is, the crystals in the non-isothermal CT crystallizer were periodically circulated between the hot and cold cylinders based on the Taylor vortex fluid motion. The dissolution of the suspension crystals occurred in the boundary layer on the hot cylinder (T_h), called the heating boundary layer, while the cooling recrystallization simultaneously occurred in the boundary layer on the cold cylinder (T_c), called the cooling boundary layer. Conceptually, as shown in Figure 2b, when the crystal suspension saturated at the bulk temperature (T_b) was circulated to the heating boundary layer (T_h) in the CT crystallizer, the corresponding solution

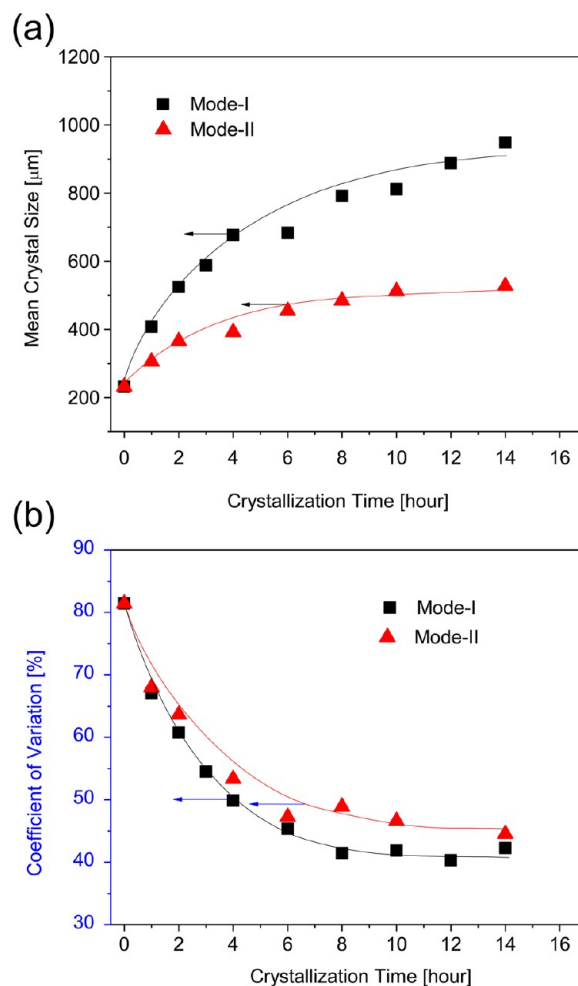


Figure 3. Influence of non-isothermal mode on CSD of suspension. (a) Change of mean crystal size with crystallization time; (b) change of CV with crystallization time. The crystallization conditions were fixed at saturated bulk temperature (T_b) of 24.0 °C, temperature difference (ΔT) of 8.7 ± 0.1 °C, rotation speed of the inner cylinder of 600 rpm, and seed amount of the suspension of 150 g/L.

concentration was increased from C_b to C_h by the dissolution of the crystals (point A). During this heating course, the crystal size in the suspension was reduced and the fine crystals were completely dissolved. Then, as the suspension was circulated back to the cooling boundary layer (T_c), the supersaturation was generated for recrystallization (point B). Here, when the supersaturation profile was within the metastable zone during the cooling course, as shown in profile “a”, the crystals in the suspension grew in the supersaturated solution without any nucleation. As such, this heating–cooling cycle in the non-isothermal CT crystallizer was effective in making the CSD of the suspension larger and narrower via fines destruction and crystal growth. However, when the supersaturation profile exceeded the metastable zone limit, as shown in profile “b”, nucleation occurred during the course of the recrystallization. As a result, this heating–cooling cycle made the CSD of the suspension smaller and broader. Thus, based on this concept, it was anticipated that the CSD of the suspension could be controlled by adjusting of the heating–cooling cycle in the non-isothermal CT crystallizer, including the temperature difference ($\Delta T = T_h - T_c$) between the hot (T_h) and cold (T_c) cylinders,

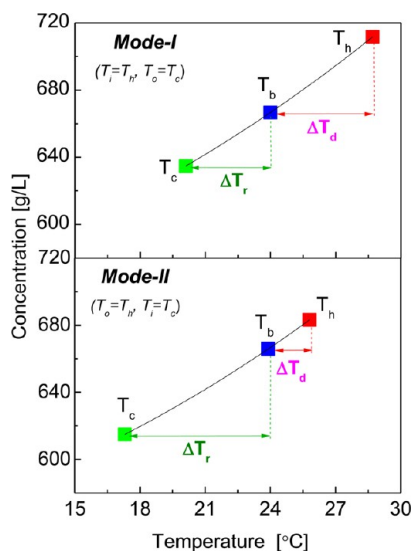


Figure 4. Temperature set of hot (T_h) and cold (T_c) cylinders for two non-isothermal modes of Mode-I and Mode-II with same saturated bulk temperature (T_b). The crystallization conditions were fixed at saturated bulk temperature (T_b) of 24.0 °C, temperature difference (ΔT) of 8.7 ± 0.1 °C, rotation speed of the inner cylinder of 600 rpm and seed amount of the suspension of 150 g/L.

Table 1. Temperature Sets of Hot and Cold Cylinders for Two Non-Isothermal Modes

mode	Mode-I ($T_i > T_o$)	Mode-II ($T_i < T_o$)
Temperature difference [°C]	8.7 ± 0.1	8.5 ± 0.1
Saturated bulk temperature [°C]	24.1 ± 0.1	24.0 ± 0.1
Temperature of inner cylinder [°C]	28.7 ± 0.2	17.3 ± 0.1
Temperature of outer cylinder [°C]	20.0 ± 0.1	25.8 ± 0.1
ΔT_d [°C]	4.6 ± 0.1	1.8 ± 0.1
ΔT_r [°C]	4.1 ± 0.1	6.7 ± 0.1
$\Delta T_d / \Delta T_r$	1.122	0.269

saturated bulk temperature (T_b), and Taylor vortex fluid motion (rotation speed of the inner cylinder).

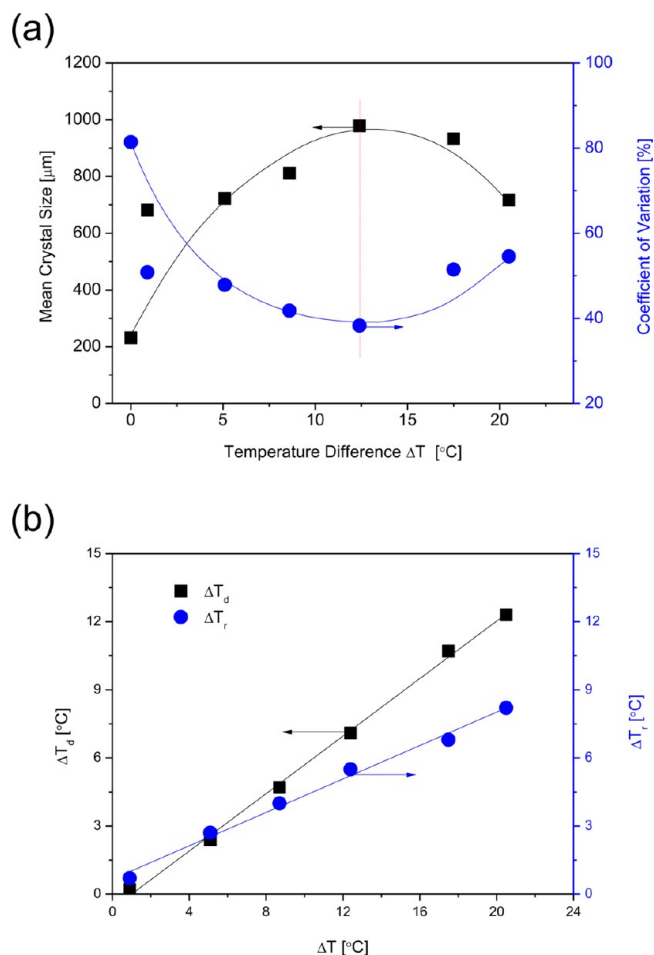


Figure 6. (a) Influence of temperature difference (ΔT) on mean crystal size and CV of product suspension; (b) variation of ΔT_h and ΔT_c with non-isothermality. The experiments were run in Mode-I. The other crystallization conditions were fixed at saturated bulk temperature (T_b) of 24.0 °C, rotation speed of the inner cylinder of 600 rpm, and seed amount in the suspension of 150 g/L.

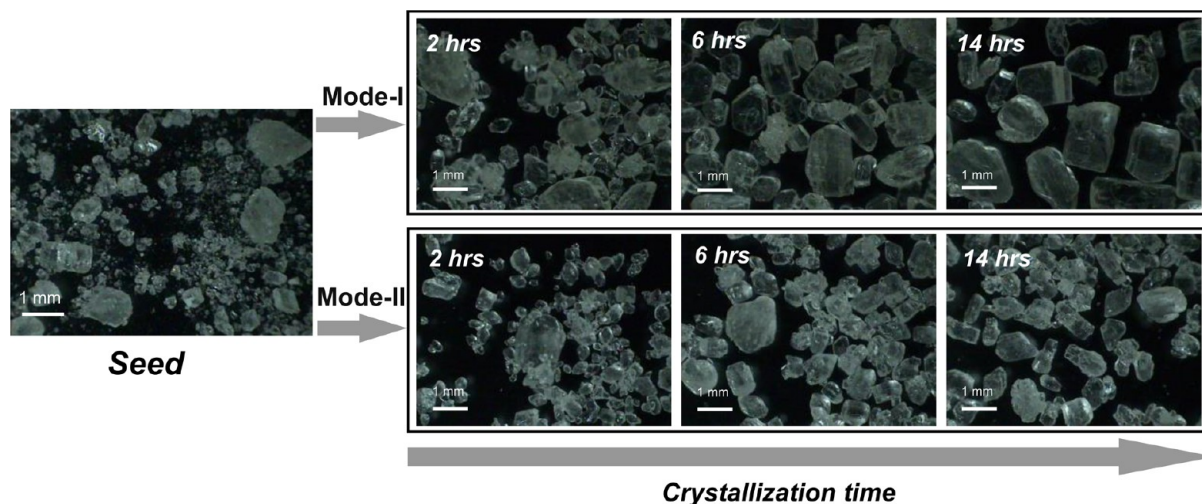


Figure 5. Microscopic images of crystals obtained in Mode-I and Mode-II with crystallization time. The crystallization conditions were fixed at saturated bulk temperature (T_b) of 24.0 °C temperature difference (ΔT) of 8.7 ± 0.1 °C, rotation speed of the inner cylinder of 600 rpm, and seed concentration of the suspension of 150 g/L.

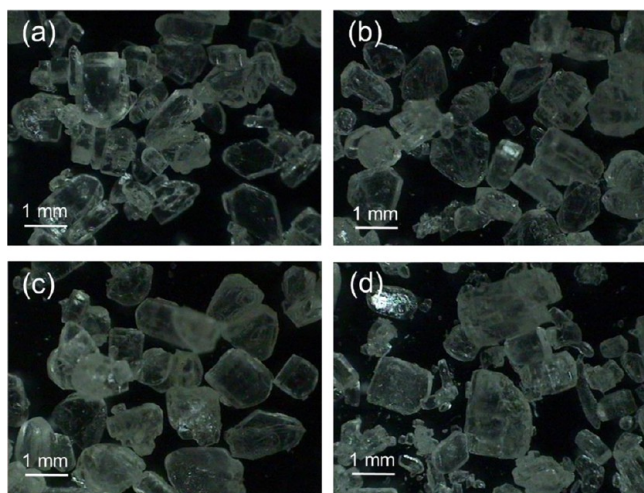


Figure 7. Microscopic images of crystals obtained in various temperature difference (ΔT). (a) $\Delta T = 0.9$ °C, (b) $\Delta T = 5.1$ °C, (c) $\Delta T = 12.5$ °C, and (d) $\Delta T = 20.5$ °C. All experiments were run in Mode-I. The other crystallization conditions were fixed at saturated bulk temperature (T_b) of 24.0 °C, rotation speed of the inner cylinder of 600 rpm, and seed concentration of the suspension of 150 g/L.

First, the influence of the non-isothermal mode of the CT crystallizer on the CSD was investigated at a fixed the temperature difference ($\Delta T = T_h - T_c = 8.7 \pm 0.1$ °C), bulk solution temperature ($T_b = 24.0$ °C), and rotation speed of the inner cylinder (600 rpm), as shown in Figure 3. Here, Mode-I means that the inner cylinder (T_i) was heated and the outer cylinder (T_o) was cooled ($T_i > T_o$), while the reverse case ($T_i < T_o$) was called Mode-II. The characteristic length and dispersity of the CSD of the product suspension were represented by the mean crystal size and coefficient of variation (CV), respectively. In both modes, the mean crystal size increased and the CV decreased with the crystallization time due to the dissolution and recrystallization of the crystal suspension during the heating–cooling cycles in the non-isothermal CT crystallizer. As a result, the initial seed crystals of 231.4 μm grew to 1000 μm , and the CV dropped from 81.4% to about 40%. Interestingly, the mean crystal size (1000 μm) of the product suspension in Mode-I was always much larger than that (500 μm) in Mode-II. Also, the CSD of the product suspension in Mode-I was about 10% narrower than that in Mode-II.

This result can be explained in terms of the driving forces for dissolution and recrystallization in the heating–cooling cycle in the non-isothermal CT crystallizer. That is, the temperature difference between the hot cylinder (T_h) and the bulk solution (T_b) is considered as the driving force for the dissolution ($\Delta T_d = T_h - T_b$) in the heating boundary layer and the temperature difference between the saturated bulk solution (T_b) and the cold cylinder (T_c) is considered as the driving force for the recrystallization ($\Delta T_r = T_b - T_c$) in the cooling boundary layer. Then, these driving forces directly determined the efficiency of the heating–cooling cycle for CSD control and significantly changed according to the non-isothermal mode, as shown in Figure 4 and Table 1. Thus, in Mode-I ($T_i > T_o$), the hot inner cylinder temperature (T_i) and cold outer cylinder temperature (T_o) were set at 28.7 and 20.0 °C, respectively, to maintain a saturated bulk temperature of 24.0 °C. In this case, the driving force for dissolution (ΔT_d) and the driving force for recrystallization (ΔT_r) were 4.6 and 4.1 °C, respectively. Thus, it can be surmised that the fines destruction in the

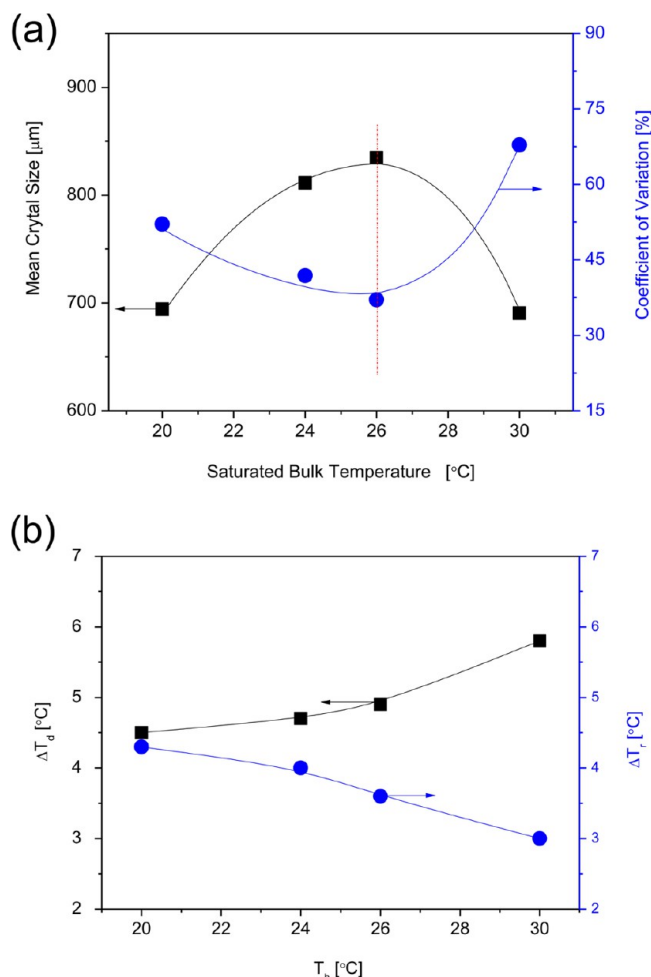


Figure 8. (a) Influence of saturated bulk temperature on mean crystal size and CV of product suspension; (b) variation of ΔT_h and ΔT_c with saturated bulk temperature. The experiments were run in Mode-I. The other crystallization conditions were fixed at temperature difference (ΔT) of 8.7 ± 0.1 °C, rotation speed of the inner cylinder of 600 rpm, and seed amount of the suspension of 150 g/L.

heating boundary layer was well balanced with the crystal growth in the cooling boundary layer without nucleation, resulting in an effective improvement of the CSD by the internal heating–cooling cycles in the non-isothermal CT crystallizer. Meanwhile, in the Mode-II, the temperatures of the cylinders were set at 25.8 °C for the hot outer cylinder temperature (T_o) and 17.3 °C for the cold inner cylinder temperature (T_i) in order to satisfy the same saturated bulk temperature of 24.0 °C. Thus, the driving force for the dissolution ($\Delta T_d = 1.8$ °C) was so small relative to the driving force for the recrystallization ($\Delta T_r = 6.7$ °C). As a result, the fines destruction was insufficient to improve the CSD based on the internal heating–cooling cycles in the non-isothermal CT crystallizer. Therefore, the mean crystal size in Mode-II was always smaller and the distribution always broader when compared with those in Mode-I. Furthermore, according to Kataoka et al.³² and Poncet et al.,³³ the toroidal Taylor vortex motion in the boundary layer of the rotating inner cylinder was more effective in promoting heat and mass transfers than the motion in the boundary layer of the stationary outer cylinder. Thus, Mode-I with well-balanced driving force for dissolution–growth was even more effective for fines destruction than

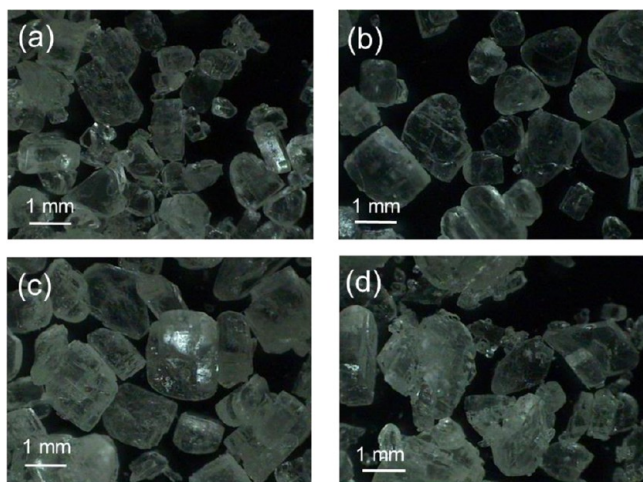


Figure 9. Microscopic images of crystals obtained in various saturated bulk temperature (T_b). (a) $T_b = 20.0$ °C, (b) $T_b = 24.0$ °C, (c) $T_b = 26.0$ °C, and (d) $T_b = 30.0$ °C. Experiments were run in Mode-I, and other crystallization conditions were fixed at temperature difference (ΔT) of 8.7 ± 0.1 °C, rotation speed of the inner cylinder of 600 rpm, and seed amount of the suspension of 150 g/L.

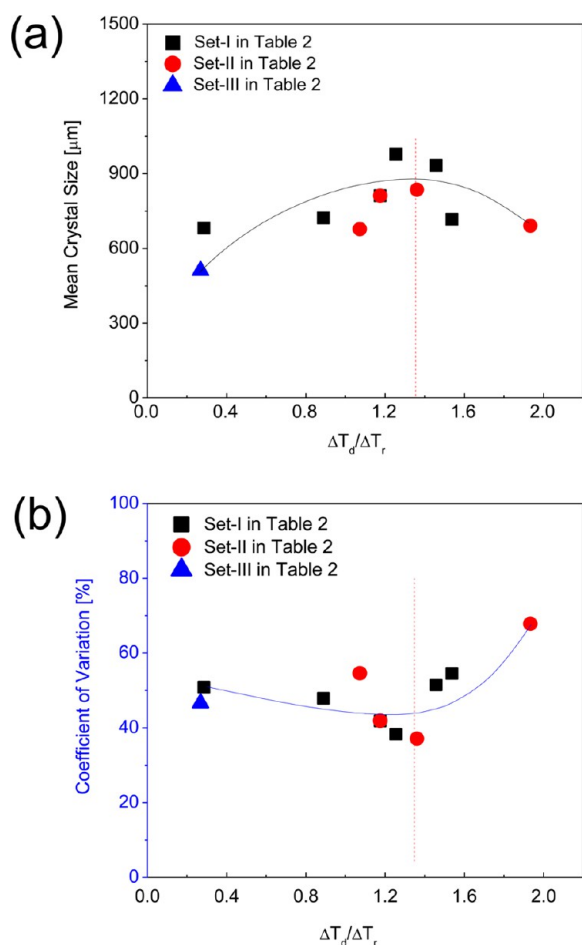


Figure 10. Correlation of (a) mean crystal size and (b) CV of product suspension with ratio of driving forces for dissolution and recrystallization ($\Delta T_d/\Delta T_r$).

Mode-II. This influence of the non-isothermal modes on the crystal size and distribution was visually confirmed by the microscopic images, as shown in Figure 5. The crystals obtained

using Mode-I were large and uniform when compared with those produced using Mode-II. It should be noted that the temperature asymmetry of Mode-I and Mode-II (Figure 4) might be due to complicated heat transfer behavior in solid–liquid suspension in the non-isothermal Couette–Taylor crystallizer having asymmetric heat flux rate and area on inner and outer cylinders.

Effect of Non-Isothermal Taylor Vortex Flow. When using Mode-I, the influence of the temperature difference between hot and cold cylinders ($\Delta T = T_h - T_c$) on the CSD was investigated, as shown in Figure 6. The mean crystal size was increased until the temperature difference (ΔT) reached to 12.5 °C, and then decreased when further increasing the temperature difference (ΔT) above 12.5 °C. Meanwhile, the CV was minimized at temperature difference (ΔT) of 12.5 °C (Figure 6a). Here, it should be mentioned that the samples used to analyze the CSD of the suspension were always taken at crystallization time of 10 h, as the CSD of the product suspension in the non-isothermal CT crystallizer did not vary significantly with a longer crystallization time of more than 10 h.

The variation of the CSD of the suspension according to the temperature difference (ΔT) was due to changes of the driving forces for dissolution (ΔT_d) and recrystallization (ΔT_r), as shown Figure 6b and Supporting Information Figure S1. When increasing the temperature difference (ΔT), the driving forces for dissolution and recrystallization both increased. Thus, the fines destruction in the heating boundary layer and crystal growth in the cooling boundary layer were facilitated, thereby effectively improving the CSD by increasing the mean crystal size and decreasing the CV of the product suspension. However, above the optimum temperature difference (ΔT) of 12.5 °C, the driving forces for dissolution and recrystallization were so high that the supersaturation in the cooling boundary layer exceeded the metastable zone limit. Plus, the high driving force for dissolution caused excessive fines destruction in the heating boundary layer, significantly reducing the crystal population and specific crystal surface area in the suspension. The crystal growth in this suspension was insufficient to instantaneously consume the supersaturation, which was generated in the cooling boundary layer, as mentioned in previous studies.^{6,11,34} Thus, the supersaturation level in the cooling boundary layer increased over the metastable zone limit, resulting in crystal nucleation.^{28,35} Consequently, the mean crystal size was reduced and the crystal size distribution broadened when increasing the temperature difference (ΔT) above the optimum point. This effect of the temperature difference (ΔT) on the CSD was also clearly displayed in the photo images of the crystals (Figure 7). When increasing the temperature difference (ΔT) up to 12.5 °C, the crystal size became larger and uniform. However, at high temperature difference (ΔT) of 20.5 °C, the crystal size was broadened and tiny crystals appeared, indicating the occurrence of crystal nucleation in the heating–cooling cycle in the non-isothermal CT crystallizer.

The influence of the saturated bulk temperature (T_b) on the CSD of the product suspension in the non-isothermal CT crystallizer was investigated at a fixed temperature difference ($\Delta T = 8.7 \pm 0.1$ °C) and rotation speed of the inner cylinder (600 rpm), as shown in Figure 8. At points of the mean crystal size and CV, the CSD of the product suspension was optimized at 26.0 °C of the saturated bulk temperature (Figure 8a), which was similar to the variation of the CSD according to the

Table 2. Driving Forces for Dissolution (ΔT_d) and Recrystallization (ΔT_r) at Various Non-Isothermal Conditions

classification	mode	conditions						
		T_b	T_h	T_c	ΔT	ΔT_d	ΔT_r	$\Delta T_d/\Delta T_r$
		± 0.1 [$^{\circ}\text{C}$]	± 0.1 [$^{\circ}\text{C}$]	± 0.1 [$^{\circ}\text{C}$]	± 0.1 [$^{\circ}\text{C}$]	± 0.1 [$^{\circ}\text{C}$]	± 0.1 [$^{\circ}\text{C}$]	
Set-I	Mode-I	24.0	24.2	23.3	0.9	0.2	0.7	0.29
	Mode-I	23.9	26.3	21.2	5.1	2.4	2.7	0.89
	Mode-I	24.1	28.7	20.0	8.7	4.6	4.1	1.12
	Mode-I	24.2	31.3	18.7	12.4	7.1	5.5	1.25
	Mode-I	24.4	35.1	17.6	17.5	10.7	6.8	1.46
	Mode-I	24.3	36.6	16.1	20.5	12.3	8.2	1.54
Set-II	Mode-I	20.2	24.7	16.2	8.5	4.5	4.0	1.07
	Mode-I	24.1	28.7	20.0	8.7	4.6	4.1	1.12
	Mode-I	26.3	31.2	22.7	8.5	4.9	3.6	1.36
	Mode-I	30.2	36.0	27.2	8.8	5.8	3.0	1.93
Set-III	Mode-II	24.0	25.8	17.3	8.5	1.8	6.7	0.27

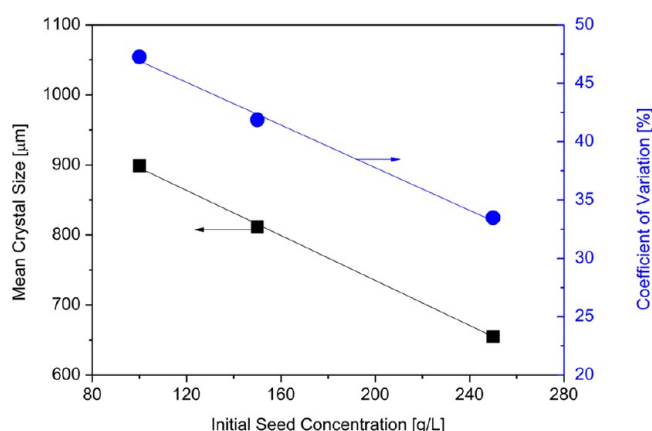


Figure 11. Influence of initial seed amount on mean crystal size and CV of product suspension. Experiments were run in Mode-I. The other crystallization conditions were fixed at saturated bulk temperature (T_b) of 24.0 $^{\circ}\text{C}$, temperature difference (ΔT) of 8.7 ± 0.1 $^{\circ}\text{C}$, and rotation speed of the inner cylinder of 600 rpm.

temperature difference (ΔT) in Figure 4a. However, the variation of the driving forces for dissolution and recrystallization according to the saturated bulk temperature was different, as shown in Figure 8b. When increasing the saturated bulk temperature, the driving force for dissolution increased, whereas the driving force for recrystallization was reduced (Supporting Information Figure S2).

As reported in previous study of the external fines destruction technique, the amount of fines destruction in the dissolver is critical to control the CSD in the crystallizer.²⁸ For example, excess destruction of fine crystals in the dissolver can over-reduce the specific crystal surface area of the suspension,

resulting in highly concentrated solution being fed back to the crystallizer. Thus, it then increases the supersaturation in the cooling crystallizer due to a shortage of crystal surface area to suppress the superaturation, resulting in spontaneous nucleation. Consequently, the suspension has a small and broad CSD. Similarly, with the temperature swing technique, excess dissolution of crystals in the heating cycle causes a significant reduction of the specific crystal surface area of the suspension and brings a significant increase of supersaturation in the cooling cycle for nucleation.^{11,18} Therefore, it can be inferred from Figure 8 that the modification of the CSD according to the saturated bulk temperature in the non-isothermal CT crystallizer was predominantly controlled by crystal dissolution in the heating boundary layer. That is, the efficiency of the heating-cooling cycle in the non-isothermal CT crystallizer was enhanced when increasing the saturated bulk temperature, as this promoted fines destruction in the heating boundary layer, thereby contributing to crystal growth without nucleation when the heated solution was circulated back to the cooling boundary layer. However, a further increase in the saturated bulk temperature above 26.0 $^{\circ}\text{C}$ caused the excessive fines destruction in the heating boundary layer, generating a high solution concentration. This then resulted in nucleation when the heated solution flowed back to the cooling boundary layer, producing a small size and broad CSD for the suspension. This explanation is consistent with the photo images shown in Figure 9. The crystal size became larger and more uniform as increasing the saturated bulk temperature up to 26.0 $^{\circ}\text{C}$ (Figure 9a–c). However, many newly generated crystals appeared at a high saturated bulk temperature of 30.0 $^{\circ}\text{C}$ (Figure 9d).

As shown in the above experimental results (Figures 3, 6, and 8), the driving forces for dissolution and recrystallization in the

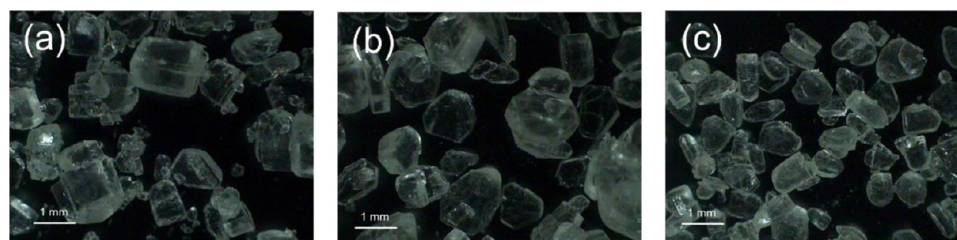


Figure 12. Microscopic images of crystals obtained in various initial seed amount: (a) 100 g/L, (b) 150 g/L, (c) 250 g/L. The experiments were run in Mode-I. The other crystallization conditions were fixed at saturated bulk temperature (T_b) of 24.0 $^{\circ}\text{C}$, temperature difference (ΔT) of 8.7 ± 0.1 $^{\circ}\text{C}$, and rotation speed of the inner cylinder of 600 rpm.

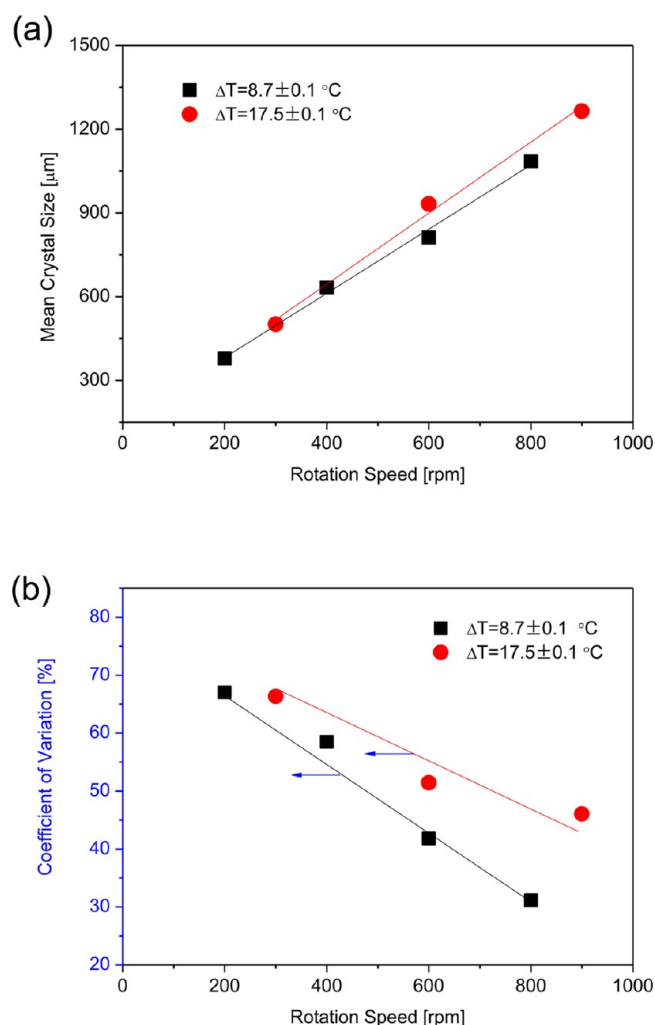


Figure 13. Influence of rotation speed of inner cylinder on (a) mean crystal size and (b) CV of product suspension. Experiments were run in Mode-I. The crystallization conditions were fixed at saturated bulk temperature (T_b) of 24.0 °C and seed amount of the suspension of 150 g/L.

internal heating–cooling cycle were the most critical factors determining the modification of the CSD of the suspension in the non-isothermal CT crystallizer. Thus, the ratio between the two driving forces ($\Delta T_d/\Delta T_r$) was introduced to predict the efficiency of the heating–cooling cycle for improving the CSD of the suspension, as shown in Figure 10 and Table 2. The efficiency of the heating–cooling cycle was enhanced when increasing the ratio of the driving forces ($\Delta T_d/\Delta T_r$) within the range of $\Delta T_d/\Delta T_r < 1.35$. In this case, the mean crystal size increased and the CV of the CSD was reduced. However, the efficiency of the heating–cooling cycle was reduced when increasing the driving force ratio beyond the range of $\Delta T_d/\Delta T_r > 1.35$, due to excessive dissolution of crystals in the heating boundary layer. Thus, the mean crystal size was reduced and the CV of the CSD increased. This optimum ratio of the driving forces (about 1.35) matched well with the optimum non-isothermal conditions in the CT crystallizer. Therefore, the driving force ratios at the optimum non-isothermality (12.5 °C) and optimum saturated bulk temperature (26.0 °C) were about 1.25 and 1.35, respectively.

The influence of the seed amount on the CSD of the product suspension in the non-isothermal CT crystallizer was examined, as shown in Figure 11. When increasing the seed amount, the mean crystal size and CV of the CSD in the product suspension were both reduced. In this experiment, the temperature difference (ΔT) and saturated bulk temperature were fixed at 8.7 ± 0.1 and 24.0 °C, respectively. At the fixed non-isothermal conditions, more crystals were dissolved by heating–dissolution in the low-seeded suspension than in the high-seeded suspension. This resulted in a more significant reduction of the specific crystal surface area in the low-seeded suspension when compared to the high-seeded suspension. Thus, there are insufficient crystals in the low-seeded suspension to instantaneously consume the supersaturation for the crystal growth during the cooling–recrystallization, resulting in a high supersaturation level in solution. This high supersaturation then promoted crystal growth and also induced nucleation, resulting in a large mean crystal size and high CV for the CSD with the 100 g/L seed amount. However, the crystal population in the high-seeded suspension was high enough to control the supersaturation within the metastable limit, suppressing any nucleation during the cooling–crystallization. As a result, small

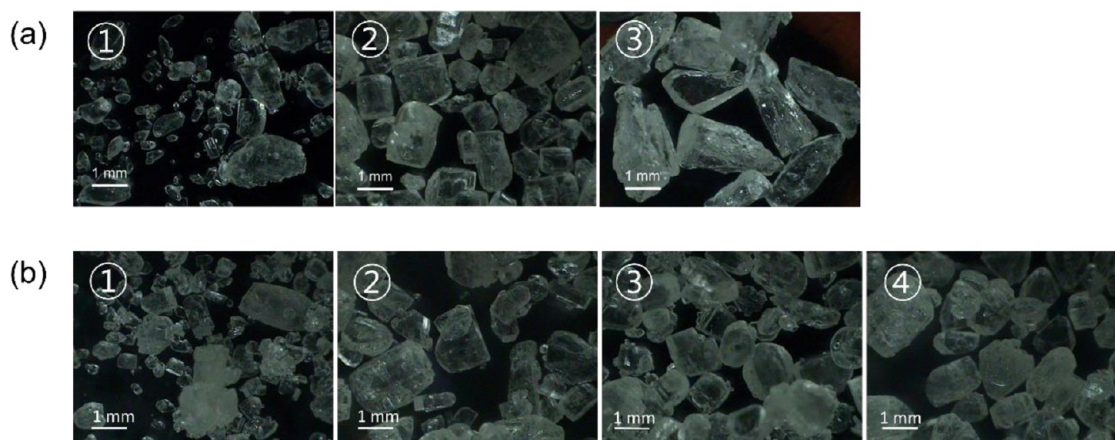


Figure 14. Microscopic images of crystals obtained in various rotation speed of inner cylinder at (a) temperature difference (ΔT) = 17.5 ± 0.1 °C [① 300 rpm, ② 600 rpm, and ③ 900 rpm], and (b) temperature difference (ΔT) = 8.7 ± 0.1 °C [① 200 rpm, ② 400 rpm, ③ 600 rpm, and ④ 800 rpm]. Experiments were run in Mode-I. The crystallization conditions were fixed at saturated bulk temperature (T_b) of 24.0 °C and seed concentration of suspension of 150 g/L.

and uniform crystals were produced in the product suspension, as shown with the 250 g/L seed amount. The influence of the seed amount on the CSD was also confirmed in the photo images (Figure 12). The tiny crystals in the product suspension with the 100 g/L seed amount suggested the occurrence of nucleation in the heating-cooling cycle (Figure 12a), whereas the small and uniform crystals produced with the 250 g/L seed amount indicated low crystal growth without nucleation (Figure 12c).

The internal heating-cooling cycle in the non-isothermal CT crystallizer was driven by the Taylor vortex fluid motion. Thus, the influence of the Taylor vortex flow on the CSD of the product suspension was investigated, as shown in Figure 13. It was already demonstrated that a Taylor vortex flow is an effective fluid motion for heat and mass transfers.^{32,33,36,37} Therefore, in the present study, the efficiency of the heating-cooling cycle for CSD control was promoted when increasing the rotation speed of the inner cylinder, thereby increasing the mean crystal size (Figure 13a) and decreasing the CV of the CSD (Figure 13b) in the product suspension. In particular, with a non-isothermality of 17.5 °C, the mass transfer for crystal growth in the cooling boundary layer at a rotation speed of 900 rpm might be high enough to maintain the supersaturation level within the metastable limit, suppressing any nucleation during the cooling course. Thus, almost no tiny crystals were found in the product suspension (Figure 14a3).

CONCLUSION

A non-isothermal technique in a CT crystallizer was successfully demonstrated for controlling the CSD of the product suspension. For this technique, a non-isothermal Taylor vortex flow was generated by setting different temperatures for the rotating inner and stationary outer cylinders of the CT crystallizer. One cylinder temperature (T_h) was set above the saturated bulk temperature (T_b) of the suspension for heating dissolution of the crystals, while the other cylinder temperature (T_c) was set below the saturated bulk temperature for cooling recrystallization. As a result, the CSD of the suspension was spontaneously modified by the internal heating-cooling cycles driven by the Taylor vortex fluid motion in the non-isothermal CT crystallizer. That is, fine crystals destruction occurred in the heating boundary layer, followed by crystal growth in the cooling boundary layer in the non-isothermal CT crystallizer. With repeated cycles, the crystal size in the suspension became large and uniform.

With regard to the mean crystal size and CV of the CSD, the efficiency of the internal temperature cycle for dissolution and recrystallization depended most significantly on the non-isothermal modes and non-isothermal parameters of the CT crystallizer. When using two non-isothermal modes, the mode with a hot inner cylinder and cold outer cylinder ($T_i > T_o$), called Mode-I, was more efficient for improving the CSD than the other mode with a cold inner cylinder and hot outer cylinder ($T_o > T_i$), called Mode-II. Among the non-isothermal parameters, the temperature difference between the inner and outer cylinders, saturated bulk temperature, and rotation speed of the inner cylinder were most influential on the CSD of the product suspension based on the efficiency of the heating-cooling cycle in the non-isothermal CT crystallizer. The efficiency of the heating-cooling cycle was described in terms of the driving forces for dissolution ($\Delta T_d = T_h - T_b$) and recrystallization ($\Delta T_r = T_b - T_c$) and was predicted well by the ratio between the two driving forces. That is, the efficiency

of the heating-cooling cycle was enhanced when increasing the temperature difference between the inner and outer cylinders and saturated bulk temperature below the driving force ratio of 1.35. However, above this driving ratio of 1.35, a further increase of the temperature difference between the inner and outer cylinders and saturated bulk temperature reduced the cycle efficiency due to the induction of nucleation. In conclusion, the non-isothermal technique using a CT crystallizer was simple and effective for improving the CSD of the suspension, making it highly applicable to various practical cooling crystallization processes.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.cgd.5b00431.

Figure S1. Temperature sets of hot (T_h) and cold (T_c) cylinders for various temperature difference (ΔT) at same saturated bulk temperature (T_b) of 24.0 °C in Mode-I. Figure S2. Temperature sets of hot (T_h) and cold (T_c) cylinders for variation of saturated bulk temperature (T_b) at fixed temperature difference (ΔT) of 8.7 ± 0.1 °C in Mode-I. (PDF)

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Notes

The authors declare no competing financial interest.

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