AIDIC *Conference Series*, Vol. 9, 2009
Editor Sauro Pierucci
DOI: 10.3303/ACOS0909014

ISBN 978-88-95608-10-5 ISSN 2036-5969

PREFERENTIAL CRYSTALLIZATION INCLUDING FINES DISSOLUTION: HOW TO KILL TWO BIRDS WITH ONE STONE

Matthias Johannes Eicke[a], Andreas Seidel-Morgenstern[a,b], Martin Peter Elsner[a]

[a]Max Planck Institute for Dynamics of Complex Technical Systems, Magdeburg, Germany
[b]Otto von Guericke University, Magdeburg, Germany

Preferential crystallization (PC) is an alternative process to separate enantiomers from solution which is subcooled and seeded with crystals of the preferred species. An innovative improvement of two process concepts for PC is achieved by applying fines dissolution. It is shown in this contribution to be a potent means to improve the product quality and at the same time achieve a higher yield and productivity. D-/L-threonine dissolved in water was used as a model system for the experiments. During a simple batch it is possible to gain highly pure enantiomers up to a certain point after which the counter enantiomer nucleates from the solution and leads to a purity drop. Fines dissolution is shown to be an effective way to prolong the period of product formation while the purity is still above the required constraint. The second process variant uses two crystallizers seeded with opposite enantiomers which are connected via the liquid phase. Crystals can grow for a much longer time than in the case of the simple batch as the respective impurities crystallize separately in each vessel. In the case of coupled PC the use of fines destruction can be used effectively to influence the final shape and position of the size distribution due to the longer process duration.

1. INTRODUCTION

1.1 Motivation

The availability of enantiopure substances is becoming seemingly important especially in the pharmaceutical industries. Chiral drugs consist of enantiomers which can show different metabolic effects. Depending on the type of molecule it may be necessary to administer the racemate or one specific stereoisomer. The possibility to separate enantiomers is thus of great value and different techniques are being used. Preferential crystallization is a very straight forward process combining separation and production of a solid product without the use of resolving agents. Starting from a racemic solution which is seeded with homochiral crystals of the preferred type, one is faced with 50 % impurity (counter enantiomer) which initially leaves the liquid phase due to the mechanism of primary nucleation. It is thus first formed as minute particles, much smaller in size than the seeded species. Naturally, the process needs to be stopped at a certain point (t_{stop}) by a solid-liquid separation step to maintain a high product purity. If t_{stop} can be prolonged while maintaining the same purity, a higher mass of the preferred enantiomer will be gained. Fines dissolution seems to be a very promising improvement of PC as it will withdraw and dissolve small particles stemming from nucleation and thus will remove the counter enantiomer from the solid phase to a certain extent. As a consequence t_{stop} can be prolonged leading to a higher product mass at equal purity. At the same time one is also given a means to influence the crystal size distribution (CSD) of the product which was shown theoretically by Qamar et al. (2008). This effect is also exploited in industrial applications of continuous crystallization by what is commonly referred to as clear liquid overflow as described by Mersmann (2001). Although the change of the CSD will not be very pronounced during simple batch operation, the effect will be the main benefit of fines dissolution when applied to coupled batch crystallization. This mode does not suffer from impurities contaminating the product as much as the simple batch, as each species is crystallizing in its own vessel, while clear liquid phase is exchanged between both crystallizers. In this contribution PC used to separate the conglomerate forming system D-/L-threonine/H_2O is investigated with respect to the possibility to improve its performance by the application of fines dissolution.

Please cite this article as: Eicke M.J., Seidel-Morgenstern A. and Elsner M.P., (2009), Preferential crystallization including fines dissolution: how to kill two birds with one stone, AIDIC Conference Series, 09, 111-120 DOI: 10.3303/ACOS0909014

1.2 Principle of preferential crystallization

Preferential crystallization has been shown to be applicable for the conglomerate forming system D-/L-threonine/water (Profir (2000)) and has been studied in detail by Elsner et al. (2005) and Lorenz et al. (2006). Figure 1 illustrates the simplest case of the process in a ternary phase diagram as well as the corresponding temporal mass fractions in the liquid phase (Figure 1b). The initial racemic solution represented by point A is saturated at a temperature $T_{cryst}+\Delta T$. Further subcooling to a temperature T_{cryst} leads to a supersaturated solution with respect to both enantiomers. Within the temperature interval $[T_{cyst}, T_{cyst} + \Delta T^{(hom)}_{MZW,max}]$, known as the Ostwald-Miers region, a metastable solution is present which does not undergo spontaneous nucleation (Mersmann (2001)). The metastable zone width has been determined for the system D-/L-threonine/H_2O in the group of the authors as its knowledge is crucial for the successful operation of preferential crystallization.
If the supersaturated system at point A is subjected to solid racemate, the composition of the liquid phase will change along a straight line to point E, assuming that both species have identical growth rates and promote secondary nucleation of the same magnitude. A separation is only feasible if homochiral seeds of the preferred enantiomer (e.g. pure E_1) are introduced into the system at point A. In this case the liquid phase composition will initially tend towards point Z. At some point the unseeded species E_2 will appear in the solid phase due to primary nucleation which changes the direction of the trajectory towards the common equilibrium point E. Depending on the purity demands, the process has to be interrupted before the contamination of the solid phase with the unseeded counter enantiomer exceeds a certain threshold value (e.g. at point B). The mass as well as the mean particle size of highly pure product is therefore limited by kinetics and the challenge is to have the trajectory extend along the line AZ towards point Z as far as possible. Dissolution of small particles from primary nucleation will result in such an effect, i.e. the time of undisturbed growth of E_1 will be prolonged, shifting point B to the right on the time axis in Figure 1b.

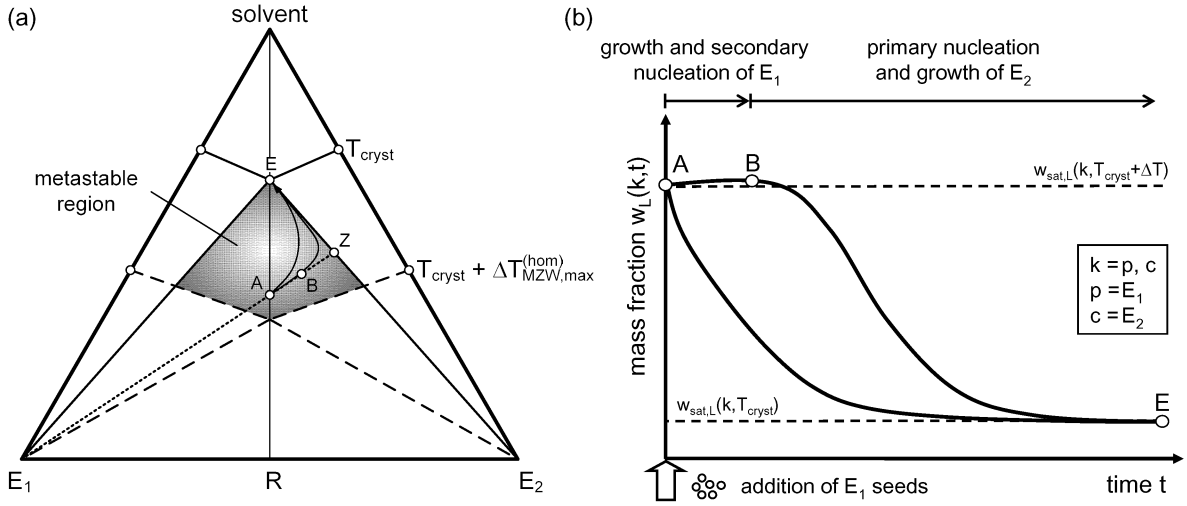

Figure 1: Principle of preferential crystallization for conglomerate forming systems.

1.3 Coupled batch preferential crystallization

The simple batch operation used to explain the principle of preferential crystallization in the previous chapter, suffers from a decreasing driving force for crystal growth (and nucleation) due to the depletion of supersaturation. As a consequence the productivity will eventually be reduced to values at which it is no longer feasible to maintain operation. Additionally one is faced with the even more pronounced restraint of having to stop the process at an early stage. Both effects can be overcome by coupled batch preferential crystallization. This concept has been scrutinized theoretically by Elsner et al. (2007) and was shown to be a feasible approach by experimental studies presented in Elsner et al. (2009). As suggested in Figure 2 particle free liquid is constantly exchanged between two vessels which are seeded with opposite enantiomers (e.g., E1 in vessel 1, E_2 in vessel 2).

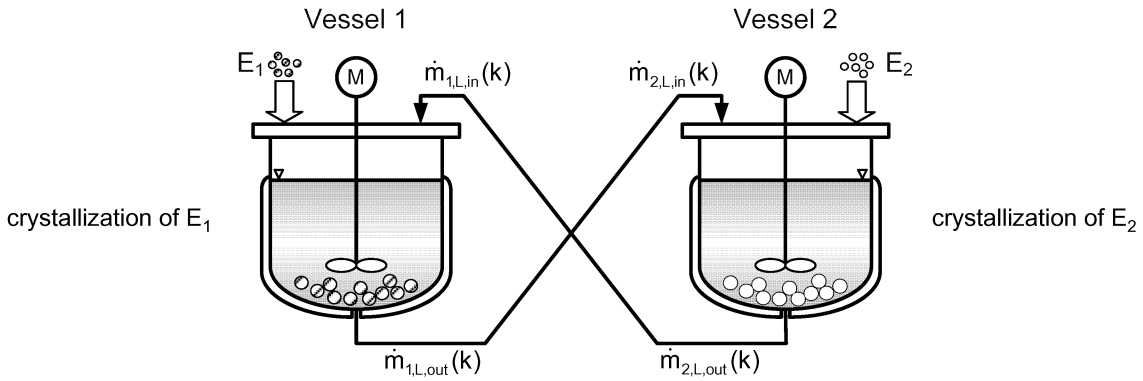

Figure 2: Principle of coupled batch preferential crystallization. Both vessels are connected via the liquid phase and seeded with E_1 (vessel 1) and E_2 (vessel 2).

The reduction of supersaturation of the unseeded enantiomer in one vessel is then due to growth of its seeds in the other crystallizer. At the same time the concentration of the seeded preferred enantiomer is raised leading to faster growth because of a higher driving force. Under favorable conditions this prevents the respective counter enantiomer to undergo primary nucleation until thermodynamic equilibrium has been reached. It is then not necessary to stop the process prematurely and product of very high purity will always be obtained. Introducing fines dissolution to this concept further pushes the process into a safer regime with respect to contamination of the preferred species and at the same time results in solid product of greater mean particle size.
The remainder of this contribution is organized as follows. In the following section the experimental setup, protocol of operation and the materials used are explained. The section results and discussion will first look at the effects of fines dissolution on the simple batch process and in the second part at the impact on coupled preferential crystallization. Conclusions and further possibilities shall be considered in the last section.

2. EXPERIMENTS

2.1 Experimental setup and materials

Simple batch and coupled PC experiments where conducted using D- and L-threonine (Sigma, D-threonine, L-threonine, purity > 98 %) dissolved in water (HPLC grade). All results were obtained using stirred jacketed glass vessels with a total working volume of 450 ml. Identical equipment and periphery geometry was used twice for coupled PC experiments including the second vessel. The temperature was measured by Pt-100 resistance thermometers and controlled by two separate thermostats (Julabo, FS 18). Online measurement of the optical rotation angle and solution density was done with polarimeters (POLARmonitor, IBZ Messtechnik, Hannover, cell length: 5 cm) and density meters (Mettler Toledo DE40). Both signals allow for later reconstruction of the masses. Particle free solution withdrawn from the vessels via HPLC filters (Dionex GmbH, external diameter: 9.8 mm, pore size: 0.45 µm) was circulated through two identical thermostated analytics bypasses by peristaltic pumps (Heidolph PD 5201, SP Quick.). All analytics paths were kept at a temperature of 46 °C, well above the solubility temperature. Fines dissolution was done using tailored filters (pore size d_{pore} = 650 µm) submerged into the liquid phase and connected to each of the two fines dissolution paths (heating path, length: 1.2 m, inner diameter: 3.2 mm; recooling path, length: 3 m, inner diameter: 3.2 mm) which were thermostated at 60 °C (fines dissolution path) and 25 °C (recooling path) respectively. The volumetric flow rate through the fines destruction path was set to 50 ml/min and the pump (Heidolph PD 5201, SP Quick) was started after water was added to the vessels during the preparation of each experiment. A schematic representation of the process setup and the involved mass flows for one vessel is depicted in Figure 3.
The solution was prepared with D- and L-threonine dissolved in water according to solubility data determined by Sapoundjiev et al. (2006). Quantitative dissolution was guaranteed by setting the crystallizer temperature to 50 °C. Subsequently the solution was cooled to the saturation temperature followed by further subcooling to the crystallization temperature T_{cryst} at a constant rate (14 K/h).

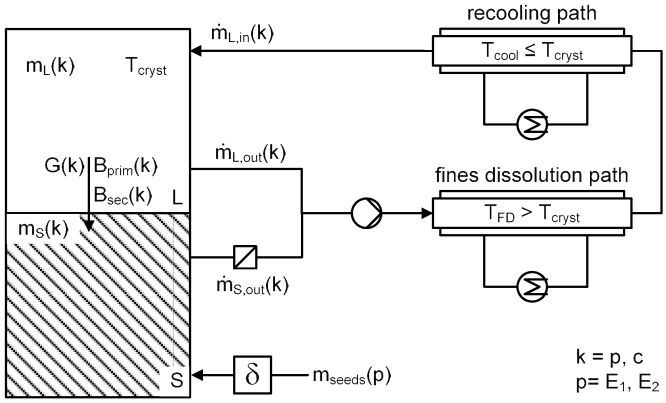

Figure 3: Schematic representation of the crystallization process including the fines destruction path for one vessel.

Once the solution reached the crystallization temperature, homochiral seeds (sieve fraction 150-200 µm) were added to induce the process. In case of the coupled process, exchange of liquid phase was started at a rate of 40 ml/min using two peristaltic pumps (Heidolph PD 5201, SP Quick) after water was added to the vessels. To guarantee particle free exchange the liquid phase was separated from the solid phase by HPLC filters (Dionex GmbH, external diameter: 9.8 mm, pore size: 0.45 µm). Additionally the tubes connecting both vessels were thermostated at 46 °C. At the end of each experiment the solid phase was separated from the solution by filtration and washed with 10 ml of ice-cold water and 10 ml of ice-cold ethanol. Further analysis of the solid phase included measurement of the length of the needle-like crystals using images taken with a stereomicroscope (Zeiss, Stemi 2000-C). Product purity was measured using chrial HPLC (Agilent Technologies 1200 Series, column: CHIROBIOTIC T length 250 x 4.6 mm, mobile phase: 70 % H_2O / 30 % EtOH). The experimental conditions for simple batch and coupled batch are summarized in Tables 1 and 2. In order to compensate for the loss of volume due to the fines dissolution path the total mass was increased by 40 g. This was done to maintain a constant initial suspension density as well as to guarantee identical fluid dynamics which have significant effects on secondary nucleation.

Table 1: Experimental conditions for simple batch preferential crystallization

	No fines dissolution	With fines dissolution	Unit
Mass of water	359.19	391.12	g
Mass of L-Thr	45.405	49.441	g
Mass of D-Thr	45.405	49.441	g
Mass of seeds (L-Thr)	1	1	g
Saturation temperature	34	34	°C
Cooling rate	-14	-14	K/h
Crystallization temperature	30	30	°C
Stirrer speed	300	300	1/min
Fines dissolution flow rate	0	50	ml/min
Fines dissolution temperature	-	60	°C
Recooling path temperature	-	25	°C

Table 2: Experimental conditions for coupled batch preferential crystallization

	No fines dissolution		With fines dissolution		Unit
	Vessel 1	Vessel 2	Vessel 1	Vessel 2	
Mass of water	359.19	359.19	391.12	391.12	g
Mass of L-Thr	45.405	45.405	49.441	49.441	g
Mass of D-Thr	45.405	45.405	49.441	49.441	g
Mass of seeds (L-Thr)	0.5	0	0.5	0	g
Mass of seeds (D-Thr)	0	0.5	0	0.5	g
Saturation temperature	34	34	34	34	°C
Exchange flow rate	40	40	40	40	ml/min
Cooling rate	-14	-14	-14	-14	K/h
Crystallization temperature	30	30	30	30	°C
Stirrer speed	250	250	250	250	1/min
Fines dissolution flow rate	0	0	50	50	ml/min
Fines dissolution temperature	-	-	60	60	°C
Recooling path temperature	-	-	25	25	°C

2.2 Process evaluation

In order to compare the different modes of operation, a productivity Pr was used according to Elsner et al. (2005). It is defined as,

$$\mathrm{Pr}(p,t_{stop}) = \frac{m_S(p,t_{stop}) - m_{seeds}(p)}{(t_{stop} + t_{dead}) \cdot 0.5 \cdot m_{rac}}, \tag{1}$$

and relates the mass of solid preferred enantiomer $m_S(p,t_{stop})$ less the mass of seeds $m_{seeds}(p)$ to half the mass of invested racemate m_{rac} and the total process duration including the time needed for preparation and cleaning t_{dead} which was estimated to be 200 minutes.
Additionally the performance of each process was judged by the final product purity Pu_S,

$$Pu_S(p,t_{stop}) = \frac{m_S(p,t_{stop})}{m_S(p,t_{stop}) + m_S(c,t_{stop})}, \tag{2}$$

which is simply the ratio of the mass of preferred enantiomer and the total solid phase mass which includes possible traces of the counter enantiomer.

3. RESULTS AND DISCUSSION

3.1 Simple batch

The impact of fines dissolution on preferential crystallization of L-threonine from a racemic solution was first investigated for the case of an isothermal simple batch. Since the successful separation of L-threonine from the racemic mixture relies heavily on the point at which primary nucleation of the counter enantiomer starts, preliminary experiments up to thermodynamic equilibrium between solid and liquid phase were performed to determine the maximum process duration before a significant drop in purity occurred. Two cases were considered. Enantioseparation without fines dissolution (F_{FD} = 0 ml/min) and in the second case with a volumetric flow rate of 50 ml/min. Figure 4 compares the temporal change of the solid product purity. Regarding the onset of the purity decrease it can be clearly seen, that the process without fines dissolution proceeds faster as expected. Hence, under the chosen conditions it has to be stopped after 1.2 h in order to maintain a purity above 98 % which was arbitrarily selected as the threshold value. In the case where fines destruction was applied, a prolongation up to 2 h could be achieved. Since the purity trajectories were calculated based on the optical rotation and density measurement, fluctuations of the values in the initial phase of the process occur since concentration changes are of small magnitude in this region. Therefore only a rough estimation of the actual purity can be made from these processes. The accuracy of these estimates was thus verified from further experiments providing actual values from HPLC analyses of the solid phase.

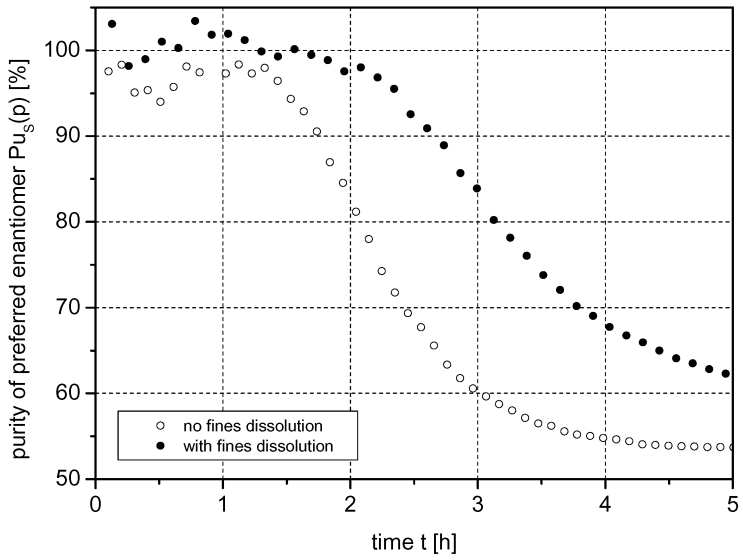

Figure 4: Preliminary investigation to determine the time of a significant purity decrease.

Table 3 summarizes the results for product mass, purity and productivity for the above processes. All values were calculated based on the measurement signals and the definitions given in the previous section. As was expected a higher mass of the preferred enantiomer can be produced while keeping the contamination within the set bounds when small particles are constantly dissolved. The increase in product mass evaluates to approximately 25 % but since the process duration is longer the productivity is raised only marginally.

Table 3: Comparison of calculated data determined from simple batch PC with and without fines dissolution.

Experiment	Process interruption t_{stop} [h]	Product mass $m_S(p,t_{stop})$ [g]	Purity $Pu_S(p,t_{stop})$ [%]	Productivity $Pr(p,t_{stop})$ [g/(g h)]
No fines dissolution	1.2	4.11	98.4	$1.5 \cdot 10^{-2}$
With fines dissolution	2.0	5.16	98.0	$1.6 \cdot 10^{-2}$

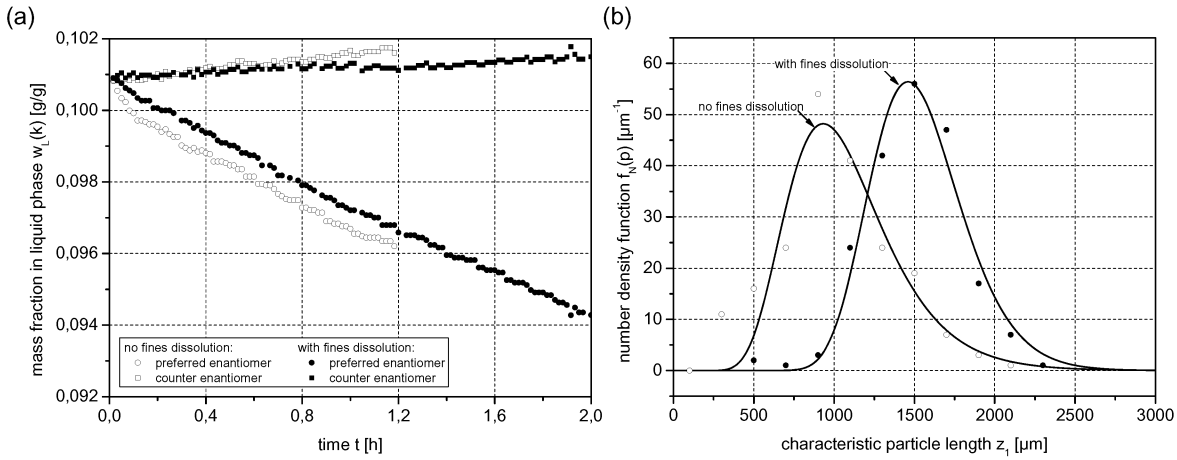

Figure 5: Comparison of mass fraction trajectories (a) and final crystal size distributions (b) of two isothermal simple batch experiments with and without fines dissolution.

Both experiments where repeated following the same protocol but with an interruption of the processes after the points in time that had been previously determined. Figure 5a shows the trajectories of the mass fractions in the liquid phase for both process variants. Seed crystals were added at t = 0 h which marks the beginning of the separation. For the duration of the experiments the concentration of L-threonine in the liquid phase decreases while D-threonine remains dissolved. The extension of the process duration allows more preferred enantiomer to leave the liquid phase which is also reflected in the CSDs depicted in Figure 5b, that have been fitted assuming a log normal distribution. The mean of the characteristic particle length is increased from 1030 µm to 1513 µm which is accompanied by a reduction of the coefficient of variation (cv) from 0.33 to 0.19 an indication that small particles were effectively dissolved. The latter observation is also supported by the absence of a small population of crystals in the lower size range (< 500 µm) when fines are removed. These are likely to stem from secondary nucleation. The L-threonine seeds had a mean length of 523 µm and a cv of 0.41.

A summary of the experimental data is given in Table 4. Under the conditions chosen (see Table 1) it was possible to increase the product mass by almost 27 % and at the same time raise the productivity of the process by approximately 18 %. Judging from the purity data both processes could have been allowed a slightly longer running time with the given constraint of 98 %. Differences between the calculated (Table 3) and the weighed masses (Table 4) are due to the processing of the product since a quantitative collection of the solid phase is difficult to realize in practice. Because the operating conditions concerning fines dissolution were chosen empirically, it can be conjectured that this process variant of simple batch preferential crystallization has even more potential with respect to product yield and productivity. This gives rise to improvement and possibly creates an optimization problem. In the following section the results obtained using two coupled crystallizers shall be set in contrast with the previous findings.

Table 4: Comparison of experimentally determined data from simple batch PC of L-threonine with and without fines dissolution before the nucleation of the counter enantiomer.

Experiment	Process interruption t_{stop} [h]	Product mass $m_S(p,t_{stop})$ [g]	Purity $Pu_S(p,t_{stop})$ [%]	Productivity $Pr(p,t_{stop})$ [g/(g h)]
No fines dissolution	1.2	2.77	99.5	$8.1 \cdot 10^{-3}$
With fines dissolution	2.0	3.54	98.7	$9.6 \cdot 10^{-3}$

3.2 Coupled batch

Coupled preferential crystallization is an interesting improvement of crystallization for conglomerate forming systems. Particularly if one is interested in both enantiomers it is a very attractive alternative to the simple batch mode but it also has great advantages for the production of only one species. Figure 6 compares a conventional coupled process (a) to one with fines dissolution (b). In both cases Tank 1 was seeded with L-threonine and Tank 2 with D-threonine (compare Figure 2) both obtained from the same sieve fraction. Due to the exchange of liquid phase it has an almost racemic composition during the entire process. This indicates that crystallization of the respective preferred enantiomers in each vessel progresses at almost equal rates. However, it is not proof because a racemic composition can also be the consequence of equally fast contamination with the counter enantiomer. It is therefore mandatory to analyze the purity of the solid phase. Key results of the coupled PC experiments are summarized in Table 5.

Table 5: Comparison of experimentally determined data from coupled batch PC of D- and L-threonine with and without fines dissolution.

Experiment	Process interruption t_{stop} [h]	Product mass $m_S(p,t_{stop})$ [g]	Purity $Pu_S(p,t_{stop})$ [%]	Productivity $Pr(p,t_{stop})$ [g/(g h)]
No fines dissolution				
L-Thr (Tank 1)	19	11.4	98.3	$1.1 \cdot 10^{-2}$
D-Thr (Tank 2)	19	10.7	98.2	$1.0 \cdot 10^{-2}$
With fines dissolution				
L-Thr (Tank 1)	19	11.4	97.4	$9.9 \cdot 10^{-3}$
D-Thr (Tank 2)	19	9.4	98.8	$8.1 \cdot 10^{-3}$

The application of fines dissolution does not lead to an increase of the product mass as both coupled processes were stopped close to thermodynamic equilibrium after 19 h. Although the dissolution of small particles reduces the rate at which crystallization progresses, the duration was sufficiently long to allow the process to reach the beginning of steady state as well. Deviations of the product masses of L- and D-threonine are due to periodic replacement of the exchange path filters once blockage occurred. Solids adhering to the filters were discarded which resulted in an unequal loss of the respective preferred enantiomers since blocking proceeded at different rates. The purity analyses show that only minor contaminations of the solid phase by the respective counter enantiomers occurred. This is a direct consequence of the exchange of particle free solution and confirms the advantage of coupled PC as opposed to simple batch operation which was already shown by Elsner et al. (2008).

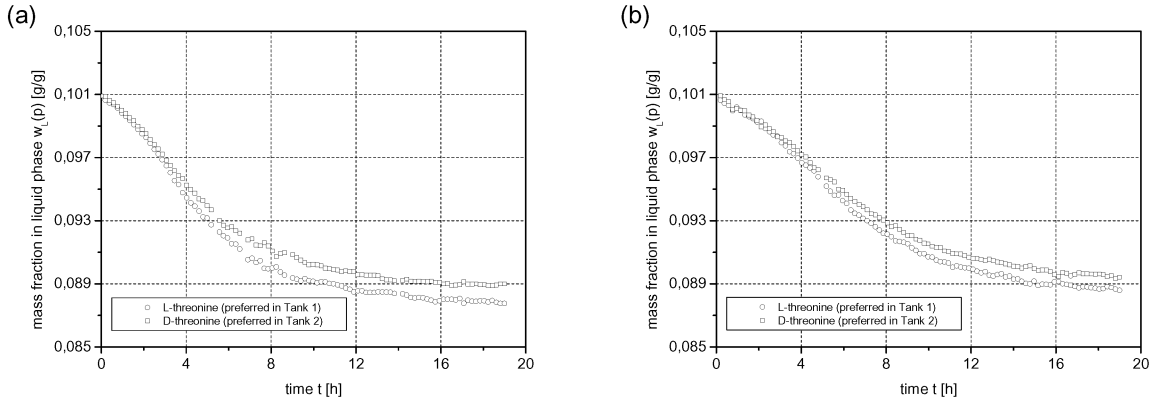

Figure 6: Comparison of mass fraction trajectories of two isothermal coupled batch experiments without (a) and with (b) fines dissolution.

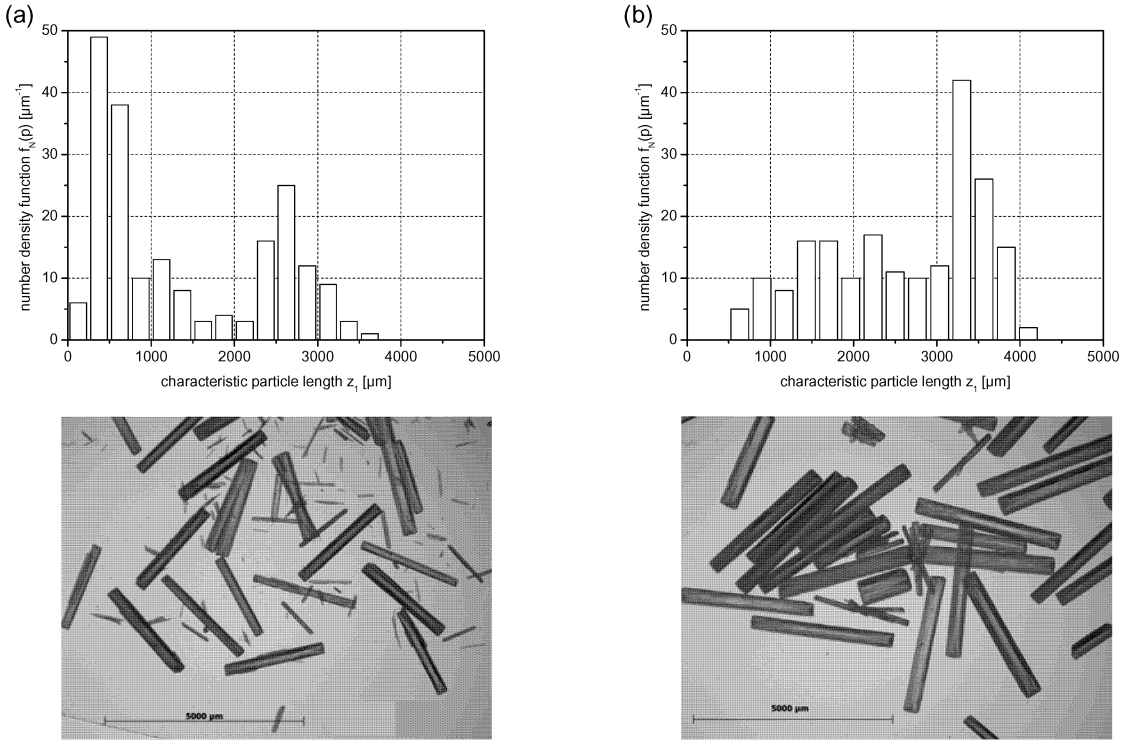

Figure 7: Crystal size distributions and appearance of L-threonine crystals at the end of each coupled process.

Comparison of purity and productivity for both coupled processes shows that they are not influenced considerably by the usage of fines dissolution. However, the crystal size distribution of the preferred enantiomer undergoes a noticeable change. Figure 7 compares the final CSDs of L-threonine derived from both processes as well as representative photographs of two control samples. A distinct bimodal distribution is generated with populations of crystals in the size ranges around 500 µm and 2600 µm for the case that fines are not dissolved (Figure 7a). This is reflected by the sample picture which shows quite a number of smaller particles among those of larger size. Fines dissolution results in an almost complete removal of crystals in the lower size range. Simultaneously it leads to a pronounced increase of a population between 3000 and 4000 µm under the given process conditions. The major effect of dissolving fines during coupled PC is thus the shaping of the crystal size distribution which has interesting implications for subsequent processing steps of the product that require specific qualities of the solids.

A comparison of simple and coupled batch preferential crystallization shows that it was possible to increase the final mass of L-threonine by 311 % (no fines dissolution) and 222 % (with fines dissolution) with respect to the simple batch while no significant changes in productivity occurred. Compared to the simple batch product purity is slightly lower, which is likely to be the result of the washing protocol. In each case (simple and coupled batch) the same amounts of water and ethanol were used. Since the mass of product gained during coupled PC is much higher, the amounts of rinsing agents did probably not suffice to entirely remove the racemic solution adhering to the crystals. Concerning the productivity it is necessary to emphasize the differences of seed mass and stirrer speed. Each vessel during coupled PC was seeded with half the mass of seeds used in the simple batch experiments. As a consequence crystallization is slower because of the smaller available total surface area. Additionally, the reduction of the stirrer speed by 50 min^{-1} leads to a reduced rate of secondary nucleation. It is therefore feasible to assume that a further increase in productivity can be achieved when these process parameters are altered. The results presented show that fines dissolution can be successfully applied to preferential crystallization. It has a high potential to increase the mass of highly pure product for the simple batch case and increase the size of crystals to some extent. Coupled batch PC benefits from fines dissolution in terms of the strong effects on the final size distribution. The results also suggest the possibility to use more radical subcooling which usually results in a higher possibility of nucleation which in turn can be reduced by fines destruction.

4. CONCLUSIONS

In this contribution first experimental results to investigate the effects of fines dissolution on preferential crystallization are presented. The process to separate enantiomers from a racemic mixture of the conglomerate forming system D-/L-threonine/H_2O was carried out using two different modes of operation. First a simple batch approach using one vessel seeded with homochiral crystals was investigated with and without the use of fines dissolution. The same procedure was then used to investigate coupled preferential crystallization. In this case two crystallizers are connected via the liquid phase and seeded with opposite enantiomers. It is clear from the presented results that the second process layout leads to much higher product masses and can be operated until thermodynamic equilibrium without a loss of purity. Both processes benefit from fines dissolution but in different ways. For the case of the simple batch process nucleation of the counter enantiomer can be delayed which is of great importance for the performance of this type of preferential crystallization. Simulation results presented in Figure 8 suggest that the drop in purity can be delayed much further by an increase of the volumetric fines dissolution rate. This is however limited by experimental constraints as an increase of the rate requires a redesign of the dissolution path to guarantee sufficient heat exchange.

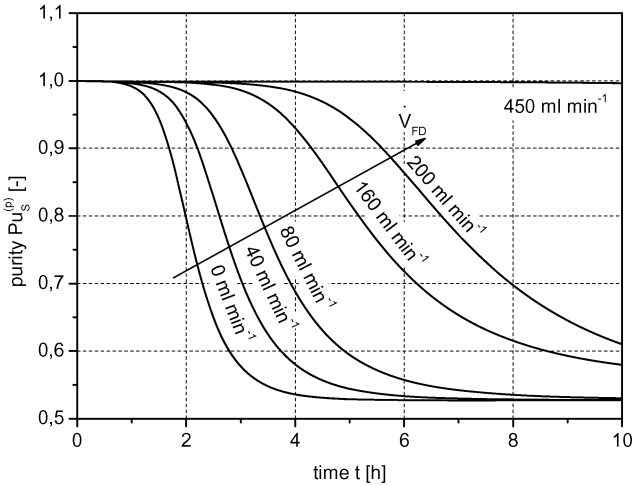

Figure 8: Simulation results for simple batch PC suggest a delay of the purity drop with increasing fines dissolution rate.

The predominant effect of fines destruction on coupled PC lies in the reshaping of the final CSD which shows almost a complete absence of particles resulting from secondary nucleation. Fines dissolution could be shown to be a potent means to influence the performance of both processes. Besides shaping of the CSD it was found to be suitable lever to enhance the productivity at a high purity level. It gives rise to further improvement and optimization and could thus evolve into a standard procedure when separating enantiomers by preferential crystallization.

5. REFERENCES

Elsner MP, Fernández Menéndez D, Alonso Muslera E, Seidel-Morgenstern A (2005). *Chirality*, 17, 183-195.
Elsner MP, Ziomek G, Seidel-Morgenstern A (2007). *Chem. Eng. Sci.*, 62, 4760-4769.
Elsner MP, Ziomek G, Seidel-Morgenstern A (2009). *AIChE Journal*, 55, 3, 640-649
Lorenz H, Perlberg A, Sapoundjiev D, Elsner MP, Seidel-Morgenstern A (2006). *Chem. Eng. Proc.*, 45, 863-873.
Mersmann A (2001). New York Marcel Dekker, Inc.
Profir VM, Matsuoka M (2000). *Colloids and Surf A: Physicochemical and Engineering Aspects*, 164, 315-324.
Qamar S, Ashfaq A, Angelov I, Elsner MP, Warnecke G, Seidel-Morgenstern A (2008). *Chem. Eng. Sci.*, 63, 1342-1352.
Sapoundjiev D, Lorenz H, Seidel-Morgenstern A (2006). *J. Chem. Eng. Data*, 51, 5, 1562-1566