

Supporting information for

Mesoscale clusters in multicomponent systems: The effect of solution preparation and pre-treatment on primary nucleation of a carbamazepine-saccharin cocrystal

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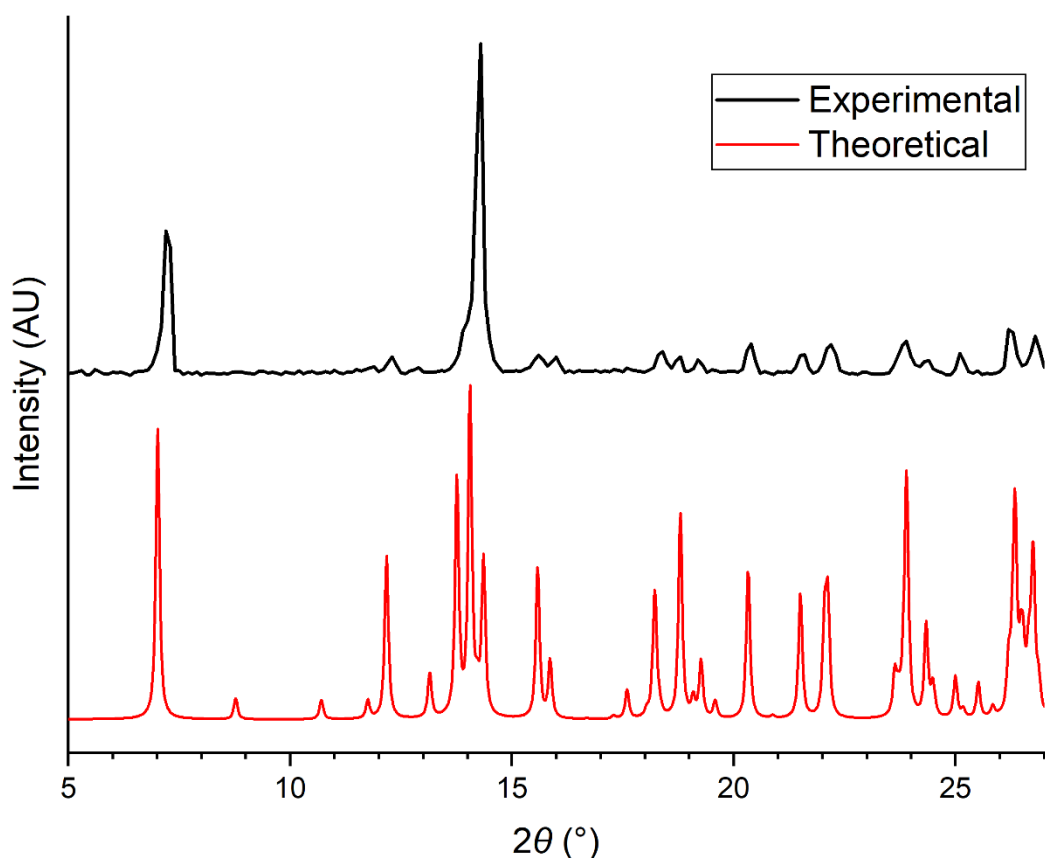


Figure S1. XRPD pattern obtained for the 1:1 CBZ-SAC cocrystal (top, black), with corresponding theoretical pattern of Form I (bottom, red; Fleischman et al., 2003).

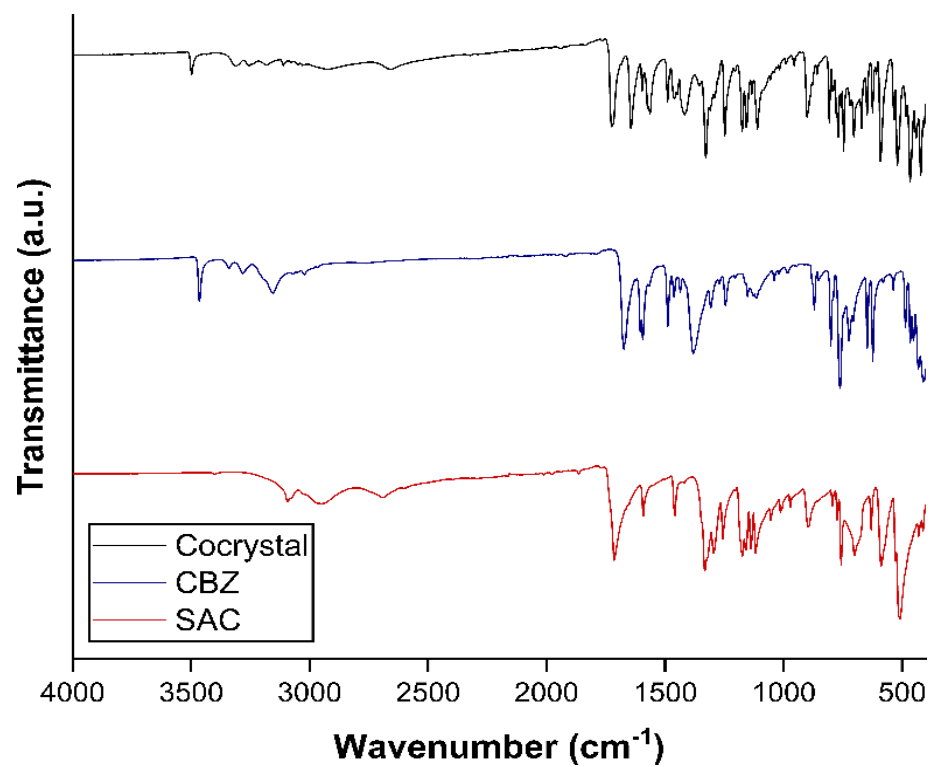


Figure S2. FTIR spectra of the three solid phases; cocystal Form I (top, black), carbamazepine Form III (middle, blue) and saccharin (bottom, red).

Table S1. Summary of all nucleation experiments with pre-treatment conditions, number of repeats (N) and mean induction time (in min) based on regression by eqn (4) with 95% confidence intervals.

	<i>Pre-treatment conditions</i>					
Solid phase	T (K)	filtration	stirring	duration	N	median $t_{ind} \pm 95\%$ CI (min)
separate	310	no	yes	60 min	15	431 $\pm$ 44
cocrystal	310	no	yes	60 min	15	85 $\pm$ 11
separate	310	no	no	60 min	15	326 $\pm$ 40
cocrystal	310	no	no	60 min	15	92 $\pm$ 11
separate	310	yes	yes	60 min	20	640 $\pm$ 44
separate	310	yes	no	60 min	15	321 $\pm$ 49
cocrystal	310	yes	no	60 min	15	321 $\pm$ 108
separate	305	no	yes	60 min	20	91.3 $\pm$ 6.3
cocrystal	305	no	yes	60 min	40	53.8 $\pm$ 2.5
separate	305	yes	yes	60 min	20	240 $\pm$ 27
cocrystal	305	yes	yes	60 min	20	84.9 $\pm$ 7.9
separate	310	yes	no	17 h	30	2055*
cocrystal	310	yes	no	17 h	30	1321 $\pm$ 149
separate	305	no	yes	17 h	20	187.9 $\pm$ 19
cocrystal	305	no	yes	17 h	20	52.1 $\pm$ 4.8
cocrystal	305	Yes	yes	17 h	20	357 $\pm$ 65
separate	305	yes	yes	17 h	20	186 $\pm$ 69
separate	305	yes	no	17 h	15	264 $\pm$ 40
cocrystal	305	yes	no	17 h	15	142 $\pm$ 103

Table S2. Parameters of eqn (4) and goodness of fit (reduced χ^2) for all nucleation experiments.

	<i>Pre-treatment conditions</i>						
Solid phase	T (K)	filtration	stirring	duration	$10^3 (A \text{ (min}^{-1}) \pm \text{SE})$	$t_g \text{ (min)} \pm \text{SE}$	$10^3 \chi^2_{red}$
separate	310	no	yes	60 min	1.5702 $\pm$ 0.106	-10.5 $\pm$ 21.7	2.38
cocrystal	310	no	yes	60 min	11.2037 $\pm$ 1.42	23.3 $\pm$ 5.93	8.43
separate	310	no	no	60 min	3.3505 $\pm$ 0.403	119.5 $\pm$ 20.3	10.33
cocrystal	310	no	no	60 min	10.6220 $\pm$ 1.16	26.7 $\pm$ 5.69	8.10
separate	310	yes	yes	60 min	1.2130 $\pm$ 0.064	68.2 $\pm$ 21.5	1.95
separate	310	yes	no	60 min	1.7674 $\pm$ 0.164	-71.1 $\pm$ 24.4	3.02
cocrystal	310	yes	no	60 min	1.3990 $\pm$ 0.226	-174.7 $\pm$ 53.4	7.61
separate	305	no	yes	60 min	7.8745 $\pm$ 0.439	3.3 $\pm$ 3.35	1.74
cocrystal	305	no	yes	60 min	13.3380 $\pm$ 0.512	1.8 $\pm$ 1.31	1.66
separate	305	yes	yes	60 min	3.2580 $\pm$ 0.295	27.5 $\pm$ 12.7	4.08
cocrystal	305	yes	yes	60 min	11.7704 $\pm$ 1.18	26.0 $\pm$ 3.88	4.64
separate	310	yes	no	17 h	0.3508 $\pm$ 0.020	79.2 $\pm$ 45.2	0.63
cocrystal	310	yes	no	17 h	0.5113 $\pm$ 0.042	-34.5 $\pm$ 60.3	3.15
separate	305	no	yes	17 h	3.0010 $\pm$ 0.184	-43.1 $\pm$ 9.46	1.96
cocrystal	305	no	yes	17 h	13.3781 $\pm$ 0.874	0.27 $\pm$ 2.34	2.57
cocrystal	305	Yes	yes	17 h	1.9235 $\pm$ 0.214	-3.2 $\pm$ 24.8	7.57
separate	305	yes	yes	17 h	3.6324 $\pm$ 0.776	-5.3 $\pm$ 18.9	22.08
separate	305	yes	no	17 h	2.4824 $\pm$ 0.253	-15.1 $\pm$ 19.2	3.83
cocrystal	305	yes	no	17 h	3.6434 $\pm$ 1.299	-47.9 $\pm$ 39.3	17.87

References:

Fleischman, S. G.; Kuduva, S. S.; McMahon, J. A.; Moulton, B.; Bailey Walsh, R. D.; Rodríguez-Hornedo, N.; Zaworotko, M. J. Crystal Engineering of the Composition of Pharmaceutical Phases: Multiple-Component Crystalline Solids Involving Carbamazepine. *Cryst. Growth Des.* 2003, **3**, 909.