

Crystallisation diagram for antisolvent crystallisation of lactose: Using Design of Experiments to investigate continuous mixing- induced supersaturation: Supporting Information

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Table SI.1 Complete Results of DoE1 runs for IPA and Acetone as Antisolvent.

Antisolvent	Antisolvent Mass Flow Fraction	Concentration of Lactose ($\text{g}_{\text{lac}}/\text{g}_{\text{H}_2\text{O}}$)	Total Mass Flow rate (g/min)	Solid State Index	Solid Yield (%)	Solid Yield (%) Error	D ₅₀ (μm)	D ₉₀ (μm)	Process Notes
IPA	0.9	0.144	25	0.315	80	6.3	9.48	17.99	Ran for 90 min. Medium fouling
Acetone	0.5	0.118	50	0.953	20	1.7	Glass	Glass	Ran for 90 min. Medium fouling
IPA	0.5	0.133	100	0.070	4.49	8.4	Glass	Glass	Ran for 90 min. No fouling
IPA	0.5	0.130	25	0.120	15	5.1	N/A	N/A	Ran for 90 min. Medium fouling
Acetone	0.75	0.132	25	0.056	45	2.3	14.49	28.83	Blocked at 45 min
Acetone	0.9	0.134	25	0.443	42	3.1	10.78	22.07	Ran for 90 min. Medium fouling
Acetone	0.9	0.214	25	0.754	80	2.3	9.16	20.87	Blocked at 70 min
Acetone	0.75	0.161	50	0.692	89	5.2	17.63	71.78	Blocked at 38 min
IPA	0.75	0.1589	50	0.558	57	5.3	24	40.9	Blocked at 48 min
IPA	0.75	0.1589	50	0.443	40	2.3	15.09	38.9	Blocked at 45 min
IPA	0.75	0.159	50	0.434	42	4.7	16.43	39.7	Blocked at 43 min
IPA	0.75	0.159	50	0.435	40	3.9	11.73	28.33	Blocked at 42 min
Acetone	0.50	0.161	25	0.833	8	2.3	12.63	43.72	Ran for 90 min. Little fouling
Acetone	0.6	0.161	50	0.362	63	4.2	20.45	50.19	Ran for 90 min. Heavy fouling
Acetone	0.5	0.132	25	0.125	6	1.2	N/A	N/A	Ran for 90 min. Little fouling
IPA	0.9	0.214	25	0.303	90	6.7	23.41	63.62	Ran for 90 min. Heavy fouling
Acetone	0.5	0.134	100	0.914	5	0.7	Glass	Glass	Ran for 90 min. No fouling
Acetone	0.6	0.217	25	0.487	68	2	13.78	34.46	Blockage at 87min
Acetone	0.6	0.131	100	0.884	32	2	19.32	42.87	Ran for 90 min. Heavy fouling
Acetone	0.6	0.217	100	0.307	73	3	13.52	33.37	Ran for 90min. Heavy fouling
IPA	0.5	0.134	25	0.123	18	3	Glass	Glass	Ran for 90 min. Little fouling
Acetone	0.5	0.214	25	0.840	15	5.3	21.62	72.42	Ran for 90min. Little fouling
IPA	0.5	0.214	25	0.851	11	4.2	26.38	85.85	Ran for 90min. Medium fouling
Acetone	0.5	0.137	100	0.911	25	2.8	11.74	24.7	Ran for 90min. Little fouling
IPA	0.9	0.1341	100	0.298	60	7.3	11.2	20.51	Ran for 90min. Heavy fouling
IPA	0.9	0.161	100	0.289	78	4.9	12.11	25.22	Ran for 90 min. Heavy fouling
Acetone	0.5	0.214	100	0.851	23	3.7	11.74	24.7	Ran for 90min. Medium fouling
IPA	0.5	0.214	100	0.861	11	4.6	22.71	56.7	Ran for 90min. Medium fouling
IPA	0.9	0.214	100	0.298	50	5.4	12.28	24.19	Blocked at 87 min
Acetone	0.6	0.131	25	0.877	9	3.5	18.91	39.93	Ran for 90min. Medium fouling

Acetone Mass Flow Fraction	Concentration of Lactose (g_{lac}/g_{H_2O})	Total Mass Flow Rate (g/min)	Solid State Index	Induction Time (min)	Solid Yield (%)	Solid Yield (%)Error	D ₅₀ (μm)	D ₉₀ (μm)	Process Notes
0.4	0.213	100	0.832	30	11.57	1.89	13.52	33.37	Ran for 90 min. Little fouling
0.4	0.132	100	0.857	330	52.47	4.79	13.55	26.32	Ran for 90 min. Little fouling
0.4	0.169	50	0.875	70	52.56	3.46	19.63	43.57	Ran for 90 min. Little fouling
0.4	0.217	25	0.857	27	25.12	1.89	31.11	85.56	Ran for 90 min. No fouling
0.4	0.132	25	0.858	170	8.51	3.11	19.84	42.52	Ran for 90 min. Little fouling
0.5	0.215	100	0.876	0.5	20.05	0.5	11.74	24.7	Ran for 90 min. No fouling
0.5	0.131	100	0.912	0.5	31.06	0.5	22.67	51.97	Ran for 90 min. Medium fouling
0.5	0.132	50	0.851	25	9.78	2.31	16.72	33.45	Ran for 90 min. No fouling
0.5	0.164	50	0.849	9	21.56	2.09	38.91	58.91	Ran for 90 min. Heavy fouling
0.5	0.164	50	0.867	10	25.60	0.56	9.7	19.8	Ran for 90 min. Heavy fouling
0.5	0.163	50	0.843	10.5	23.30	4.48	25.18	68.51	Ran for 90 min. Heavy fouling
0.5	0.214	25	0.864	9	9.52	6	21.52	72.42	Ran for 90 min. Heavy fouling
0.5	0.113	25	0.854	75	8.29	3.5	20.73	36.09	Ran for 90 min. Heavy fouling
0.5	0.164	25	0.865	19	20.65	3	17.75	41.39	Ran for 90 min. Heavy fouling
0.6	0.218	100	0.831	0	74.30	3	13.52	33.37	Ran for 90 min. Heavy fouling
0.6	0.132	100	0.888	0	30.47	2	51.32	98.01	Ran for 90 min. Heavy fouling
0.6	0.164	100	0.909	0	24.44	3	N/A	N/A	Blocked at 75 min
0.6	0.164	100	0.377	0	37.41	4	19.05	68.99	Ran for 90 min. Heavy fouling
0.6	0.217	50	0.859	0	39.67	4.87	31.37	72.42	Blocked at 23 min
0.6	0.161	50	0.855	12	37.41	6	27.13	67.83	Ran for 90 min. Heavy fouling
0.6	0.218	25	0.488	3	68.99	2	13.78	34.46	Blocked at 87 min.
0.6	0.131	25	0.860	5	37.90	4	18.91	39.93	Ran for 90 min. Heavy fouling
0.6	0.132	25	0.849	6	23.48	2	18.91	39.93	Ran for 90 min. Heavy fouling
0.75	0.161	50	0.306	0	60.26	5	17.63	41.78	Blocked at 38 min.
0.75	0.132	25	0.488	0	53.74	4	14.49	28.83	Blocked at 42 min.
0.9	0.214	100	0.049	0	37.17	7	9.16	20.87	Ran for 90 min. Medium fouling
0.9	0.133	100	0.126	0	7.06	N/A	11.2	20.51	Blocked at 8 min. (Repeated)
0.9	0.134	50	0.153	0	75.31	8	10.78	22.07	Blocked at 35 min.
0.9	0.214	25	0.153	0	84.02	6	10.18	18.68	Blocked at 70 min.

Table SI.2: Complete Results of DoE2 Run for Acetone as Antisolvent

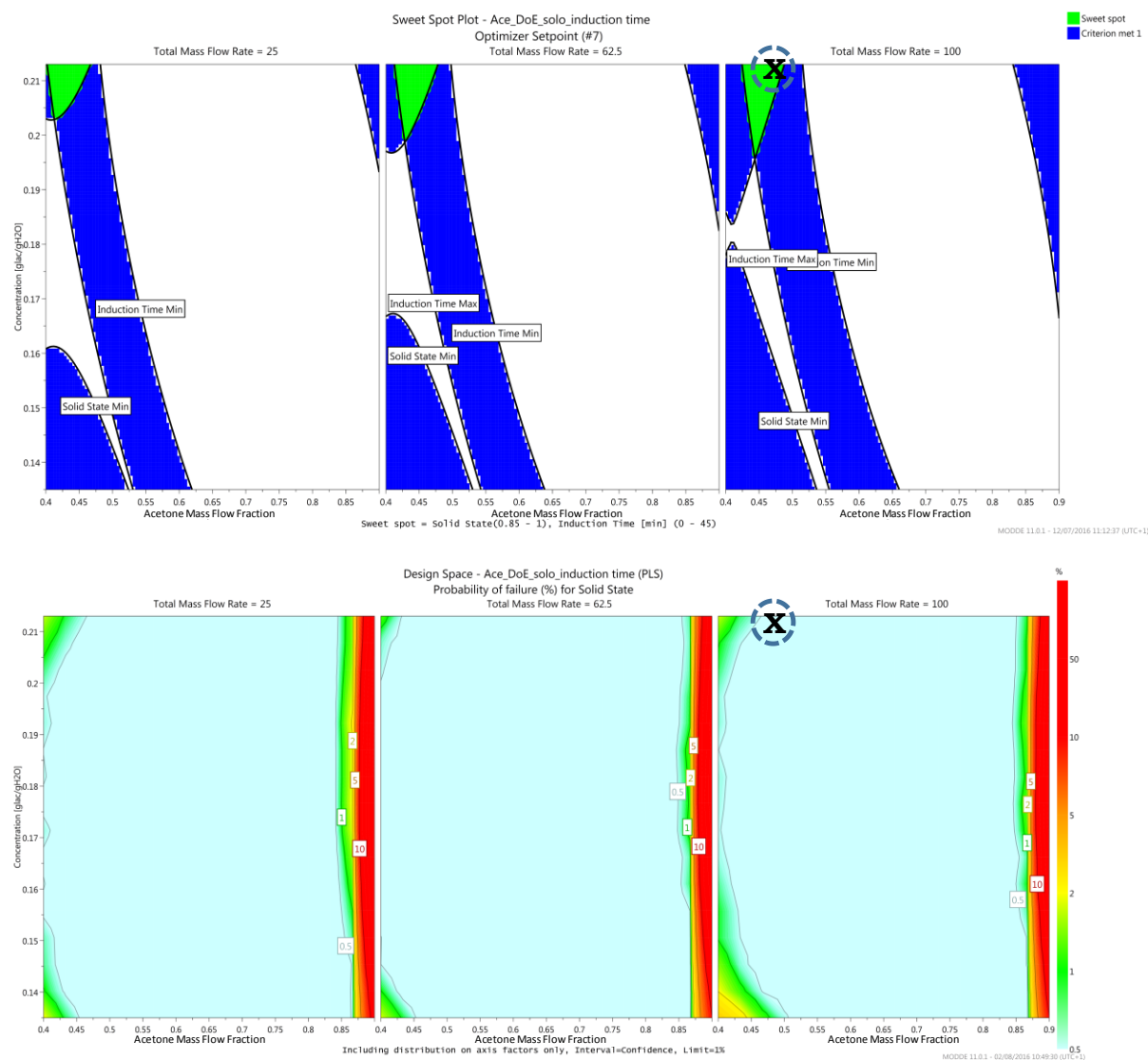


Figure S1 Sweet Spot (Top) and Probability of failure (Bottom) Diagrams for the Crystallisation of α -Lactose Monohydrate

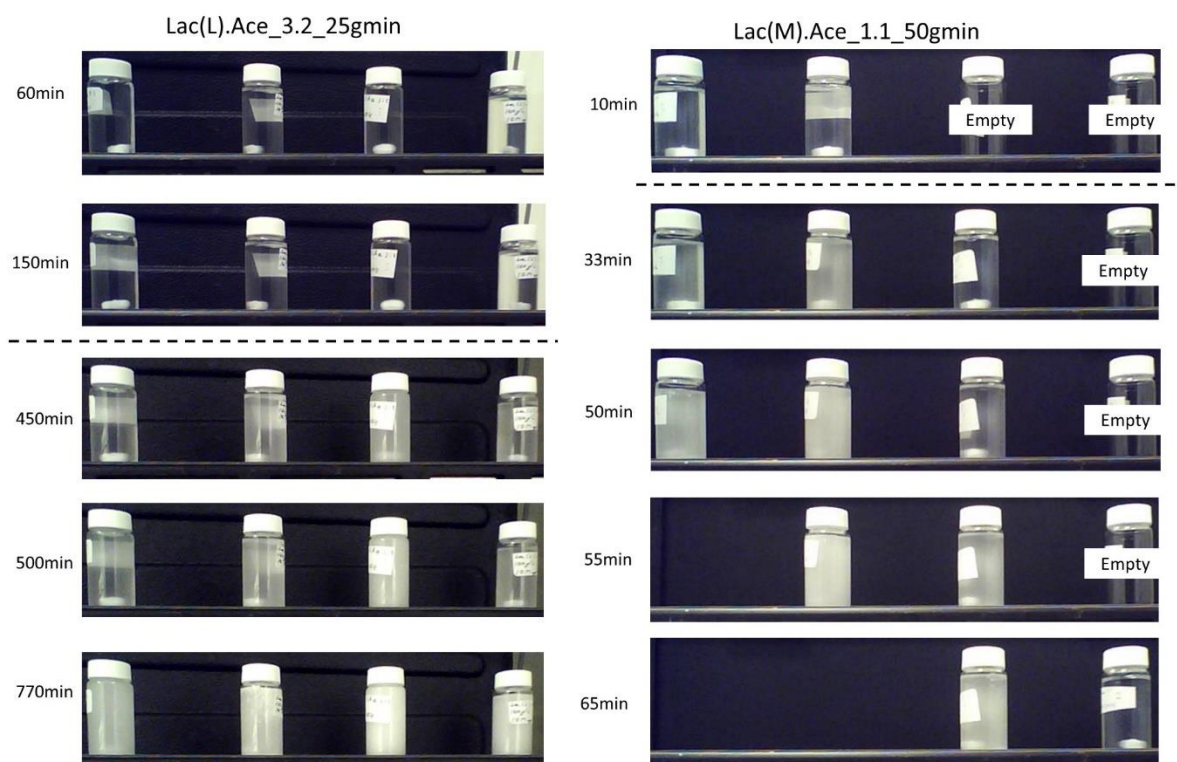


Figure S2 Turbidity Change of Samples over Time

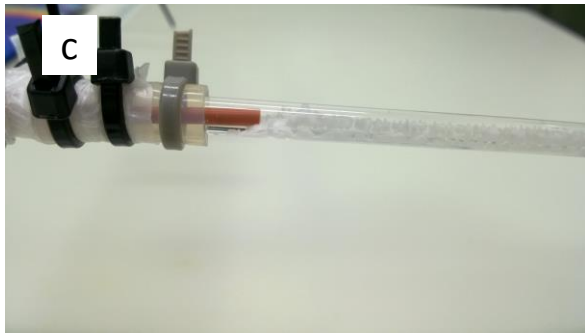


Figure S3 Example of systems with little fouling (a), medium fouling (b), heavy fouling (c), and blocked systems (d)