

S1. Data related to solubility of paracetamol, metacetamol and acetanilide in 3-methyl-1-butanol

S1.1 Gravimetric method

Solubility of paracetamol in 3-methyl-1-butanol with the presence of impurities (metacetamol and acetanilide) obtained by equilibration and gravimetric analysis.

		25 °C	40 °C	55 °C
With the Presence of Metacetamol	1% mol	56.7 ± 0.13	86.9 ± 0.93	118.45 ± 3.75
	2% mol	56.98 ± 0.14	85.29 ± 1.82	126.18 ± 2.66
	4% mol	59.94 ± 5.23	85.7 ± 1.8	115.47 ± 15.9
With the Presence of Acetanilide	1% mol	53.18 ± 5.98	80.46 ± 0.45	105.38 ± 3.66
	2% mol	56.96 ± 0.66	82.83 ± 0.76	102.0 ± 3.43
	4% mol	55.34 ± 1.72	85.94 ± 3.5	112.67 ± 2.92

S1.2 Dissolution temperature detection method using Crystalline-Technobis Crystallization systems

S1.2.1 Solubility data of acetanilide

Concentration (mg/g)	80	100	110	130	140	150	160	170	180	200
Diss. T (Sample 1)	7.3	12	14.7	19.7	21.2	23.1	25.1	27.6	29	32.6
Diss. T (Sample 2)	8.4	12.1	14.2	19.1	21.2		25.7	27.9	29.2	31.6
Diss. T (Sample 3)		12.4	14.1	19			25		28.4	31.8
Diss. T (Sample 4)										32.5
Average Diss. T (°C)	7.85	12.17	14.33	19.27	21.2	23.1	25.27	27.75	28.87	32.13
STDEV	0.777	0.070	0.353	0.424			0.424	0.212	0.141	0.707

S1.2.2 Solubility data of metacetamol

Concentration (mg/g)	50	70	90	110	130
Diss.T (°C) (Sample 1)	12.5	23.7	33.5	40.8	49
Diss.T (°C) (Sample 2)	12	23.3	33.9	41	48.5
Diss.T (°C) (Sample 3)	12.5	24	33.5	41.9	
Diss.T (°C) (Sample 4)	12.3	23.3			
Average Dissolution T (°C)	12.33	23.58	33.63	41.23	48.75
STDEV	0.236	0.340	0.231	0.586	0.353

S2. Comparison of the mean PSD of paracetamol nucleated and grown in the presence of structurally similar impurities (this work) with the PSD of some organic materials obtained from sonocrystallisation from literature.

Compounds	Ultrasonic Power (mW/cm ² or W/m ³)	Frequency (kHz)	Insonication Time and crystallisation Mode	Particle Size Distribution (µm)	References
Paracetamol	0.19 (mW/cm ²)	35 ± 3	3 h during cooling crystallization (from 3 methyl 1-butanol)	85–105	This study
	1.29 (mW/cm ²)	35 ± 3	3hours during cooling crystallization (from 3 methyl 1-butanol)	40–55	This study
	13.3 (W/m ³)	22–44	180 s (Antisolvent crystallization)	32–40	Bhangu S. K. et al. [86]
	26.6 (W/m ³)	22–44	180 s (Antisolvent crystallization)	20–25	Bhangu S. K. et al. [86]
	40 (w/m ³)	30	Continuous insonication (when cooling from 30 °C–12 °C in 22.5 min; crystallisation occurs at 28 °C)	D ₁₀ ~20, D ₅₀ ~47	Gielen,B. et al. [85]
Lactose	133.3 (W/m ³)	24	Particle Breakage experiment	Volume based distribution: (D ₅₀ reduced from 65 µm to 35 µm after 180 min)	Jordens, J. [84]
	10–30 (W/m ³)		10 min addition (Antisolvent cryst.)	30–40	Kougoulos E. et al. [42]
	10–30 (W/m ³)	20	60–120 min addition	10–15	Kougoulos E. et al. [42]
Adipic acid	96 (W/m ³)		2.5–10 min insonication	15–30	Van de Graaf, J. et al.
		20	Residence time < 1 s (Continuous Sonocrystallisation in Droplet-based microfluidics)	15	Rossi D. et al [64]
A drug compound (GSK)	1.24–6.22 W/cm ²	20	Antisolvent crystallisation	5–50	Dennehy, R. D. [87]
Compound A	100–200 W for 10 g of material	20	Particle size reduction in the crystal slurry post-crystallization, initial particle size of 100–200 µm were reduced to particles smaller than 20 µm	20	Kim S. et al. [41]