The Influence of Structurally-Related Impurities on the Crystal Nucleation of Curcumin

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Supplementary Information:

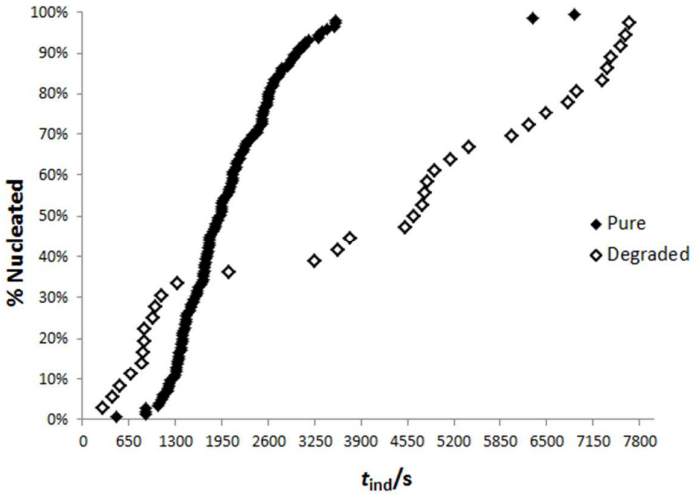

Figure S1. Induction time distribution of CUR showing a pure and a degraded sample at S = 3.81.

Figure S1, shows the difference in induction time distributions between a pure CUR sample and a CUR sample which has been degraded by light.

Table S1. Critical nucleus size and critical free energy values for pure and impure CUR systems versus supersaturation. Impurity concentrations are in mmol.dm^{-3}.

	ΔG_{crit} kJ/mol cluster^{-1}					r_c nm				
S C/C*	**4.90**	**4. 29**	**4.23**	**3.81**	**3.16**	**4.90**	**4.29**	**4.23**	**3.81**	**3.16**
Pure CUR	3.8	4.5	4.6	5.4	7.2	0.6	0.6	0.7	0.7	0.8
DMC 0.1	6.4	7.6		9.0	12.1	0.7	0.8		0.8	1.0
DMC 0.3	8.5	10.1		12.0	16.2	0.8	0.8		0.9	1.1
DMC 0.6	5.7	6.8		8.1	11.0	0.7	0.7		0.8	0.9
BDMC 0.1	7.3	8.7		10.3	14.0	0.7	0.8		0.9	1.0

BDMC 0.3	6.9	8.3		9.8	13.2	0.7	0.8	0.9	1.0
BDMC 0.6	5.8	6.9		8.2	11.1	0.7	0.7	0.8	0.9

Often the influence of the impurities on the solubility is neglected based on the argument that the impurity concentrations are low, and the influence is small. In the present work the solubility decreases by 7 % in the presence of impurities. If that is neglected there will be an error in the driving forces leading to altered values for the interfacial energy and the pre-exponential factors. It can be seen that the values do differ slightly in Table S2 and S3 when different solubilities are applied for the calculation of interfacial energy and pre-exponential factors using the cumulative exponential-based probability distribution function (eqn 2). The biggest influence is noticed for the pre-exponential values, as the values are a lot smaller when the influence of the impurities on the solubility of CUR is neglected, DMC 0.10 mmol.dm^{-3} pre-exponential value = 67 m^{-3} s^{-1} when solubility of CUR in the presence of impurities is ignored and DMC 0.10 mmol.dm^{-3} = 113 m^{-3} s^{-1} when solubility of CUR in the presence of impurities is not ignored. A slight decrease in the interfacial energy values is also observed when the influence of the impurities on the solubility of CUR is neglected, DMC 0.10 mmol.dm^{-3} interfacial energy value = 4.50 mJ.m^{-2}, in comparison to 4.70 mJ.m^{-2} when the solubility of CUR in the presence of impurities is not ignored.

Table S2. Solid-liquid Interfacial energy values (γ_{SL}) and pre-exponential factors (A) of the impure CUR systems at different impurity concentrations, all calculated according to nucleation rate (J) by the cumulative exponential-based probability distribution function. The solubility data used here ignore the influence of impurities on the solubility of CUR.

	***c*(impurity) / mmol.dm^{-3}**	**γ_{SL} (mJ.m^{-2})**	**A (m^{-3} s^{-1})**
DMC	0.10	4.50	67
	0.30	4.91	175
	0.60	4.17	30
BDMC	0.10	4.77	40
	0.30	5.54	193
	0.60	4.94	127

A similar trend is noticed in Table S3 as was seen also in Table S2, as the biggest effect is seen amongst the pre-exponential factor values. For DMC 0.10 mmol.dm^{-3}, the pre-exponential values change from 96 m^{-3}s^{-1} to 888 m^{-3}s^{-1} and for BDMC 0.10 mmol.dm^{-3}, the pre-exponential values change from 258 m^{-3} s^{-1} to 569 m^{-3}s^{-1}. A slight change is noticed for the interfacial energy values, DMC 0.10 mmol.dm^{-3} interfacial energy values change from 4.87 mJ.m^{-2} to 5.12 mJ.m^{-2} and for BDMC 0.10 mmol.dm^{-3} the interfacial energy values change from 5.09 mJ.m^{-2} to 5.36 mJ.m^{-2}.

Table S3. Solid-liquid Interfacial energy values (γ_{SL}) and pre-exponential factors (A) of the impure CUR systems at different impurity concentrations, all calculated according to median induction times by the CNT method. Solubility values used in calculating interfacial energy values and pre-exponential factors here with asterisk (*) ignore the influence of the impurities on the solubility of CUR* and values calculated without asterisk apply the influence of impurities on the solubility of CUR.

	***c*(impurity) / mmol.dm^{-3}**	**γ_{SL}* (mJ.m^{-2})**	**A* (m^{-3} s^{-1})**	**γ_{SL} (mJ.m^{-2})**	**A (m^{-3} s^{-1})**
DMC	0.10	4.87	96	5.12	888
	0.30	5.37	65	5.64	317
	0.60	4.71	127	4.95	1348
BDMC	0.10	5.09	258	5.36	569
	0.30	5.02	147	5.27	667
	0.60	4.73	79	4.97	1102

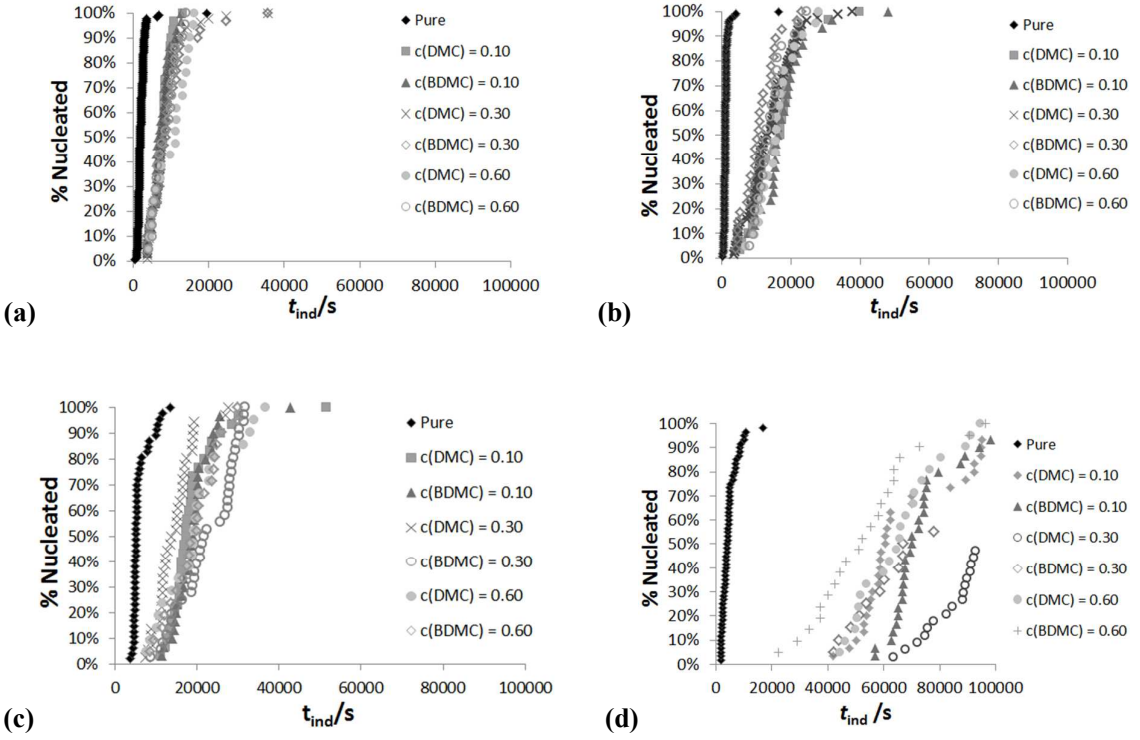

Figure S2. Plots of CUR with different *c* (imp) = mmol.dm^{-3}; **(a)** S=4.90, **(b)** S=4.29, **(c)** S = 3.81, **(d)** S=3.16. Plots show the % nucleated and induction times (s).

When the impurities are grouped together and plotted at different supersaturations of CUR, the influence of varying concentrations of impurities can clearly be observed (Figure S2). No clear trend can be seen at the different supersaturations of CUR, but a clear influence of the impurities can be noticed. At S = 4.90, (a) BDMC and DMC at 0.30 mmol.dm^{-3} showed the biggest effect by delaying the induction time of CUR. At CUR S = 4.29, (b) BDMC and DMC at 0.10 mmol.dm^{-3} delayed the induction time of CUR the most. At CUR S = 3.81, (c) DMC and BDMC at 0.10 mmol.dm^{-3} had the biggest effect on the induction time of CUR. At CUR S = 3.16, (d) DMC 0.30 mmol.dm^{-3} had the biggest effect on the induction time of CUR. Therefore, the results do show that the impurities have an effect by delaying the onset of nucleation by prolonging the induction time of CUR. However, no trend has been observed with regards to the nucleation of CUR with different concentrations of impurities applied to the CUR system and no clear difference has been observed between the DMC and BDMC impurities themselves on the nucleation of CUR.