

Supporting Information

Design of spherical crystallization for drugs based on thermal-induced liquid-liquid phase separation: case studies of water-insoluble drugs

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Comparison of the solid-liquid equilibrium (SLE) data and liquid-liquid equilibrium (LLE) data of the Ibuprofen/water with the data in literature¹:

Table S1. Comparison of the experimental SLE and LLE data in this work with the data reported in the literature ^a.

SLE data (w_{RS})			SLE data (w_{RS}) in literature		
40°C	5.18×10^{-5}		40°C	$(5.95 \sim 6.41) \times 10^{-5}$	
50°C	6.24×10^{-5}		52°C	$(11.28 \sim 13.32) \times 10^{-5}$	
60°C	7.20×10^{-5}		62°C	$(17.45 \sim 20.41) \times 10^{-5}$	
LLE data	w_{RS}^1	w_{RS}^2	LLE data in literature	w_{RS}^1	w_{RS}^2
80°C	2.31×10^{-4}	0.976	75°C	$(3.68 \sim 3.86) \times 10^{-4}$	0.98~0.9806
85°C	7.22×10^{-4}	0.938	82°C	$(4.22 \sim 4.68) \times 10^{-4}$	0.974~0.976

a. w_{RS} is the mass fraction of the racemic mixture of ibuprofen in the ibuprofen/water system; w_{RS}^1 is the mass fraction of ibuprofen in the solvent-rich phase and w_{RS}^2 , in the solute-rich phase.

It can be seen from the **Table S1** that relatively large deviation exists in the two sets of SLE data. It may result from the difference between HPLC device and the HPLC method. In addition, the difference between the raw materials of the RS-ibuprofen and the exceedingly low solubility of ibuprofen in water may also have an effect on the determined values and the deviation.



Figure S1. Geometry of the stirrer used in the experiments.

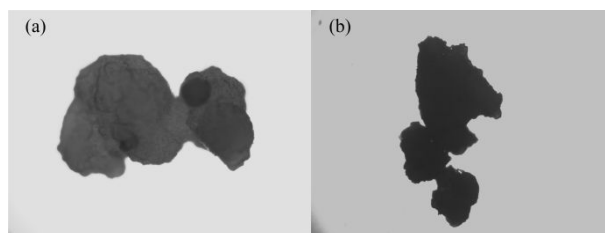
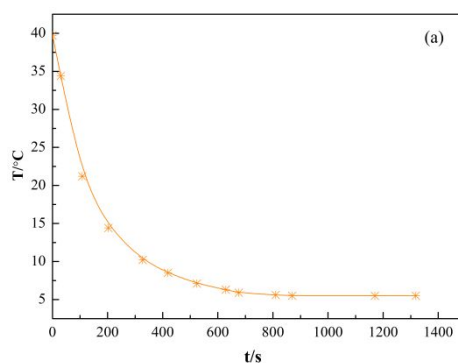


Figure S2. Secondary agglomerates of the (a) L-menthol and (b) Ibuprofen without the use of SDS.



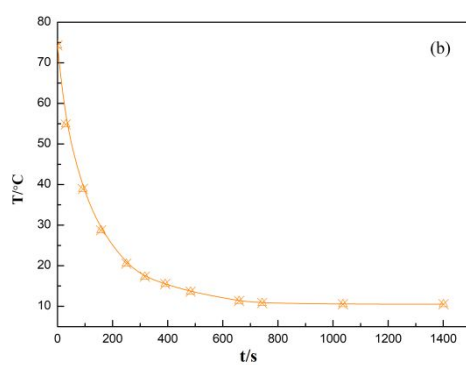


Figure S3. Temperature history of the spherical crystallization process: (a). L-menthol; (b). Ibuprofen

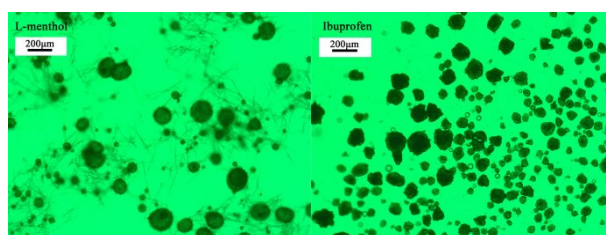


Figure S4. The products of L-menthol and ibuprofen when adding the SDS right starting the process

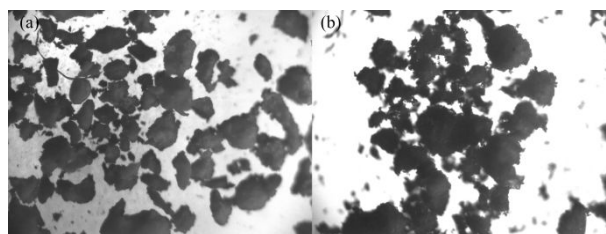


Figure S5. The products of (a) L-menthol and (b) ibuprofen under the condition of LLPS in the mixture of ethanol/water.

REFERENCE

- (1) Codan L.; Casillo S.; Babler M. U.; Mazzotti M., Phase Diagram of a Chiral Substance Exhibiting Oiling Out. 2. Racemic Compound Forming Ibuprofen in Water, *Crystal Growth Design*, **2012**, 12, 5298–5310.