

Supporting Information
for

Simultaneous Improvement of Dissolution Behavior and Oral Bioavailability of Antifungal Miconazole via Cocrystal and Salt Formation

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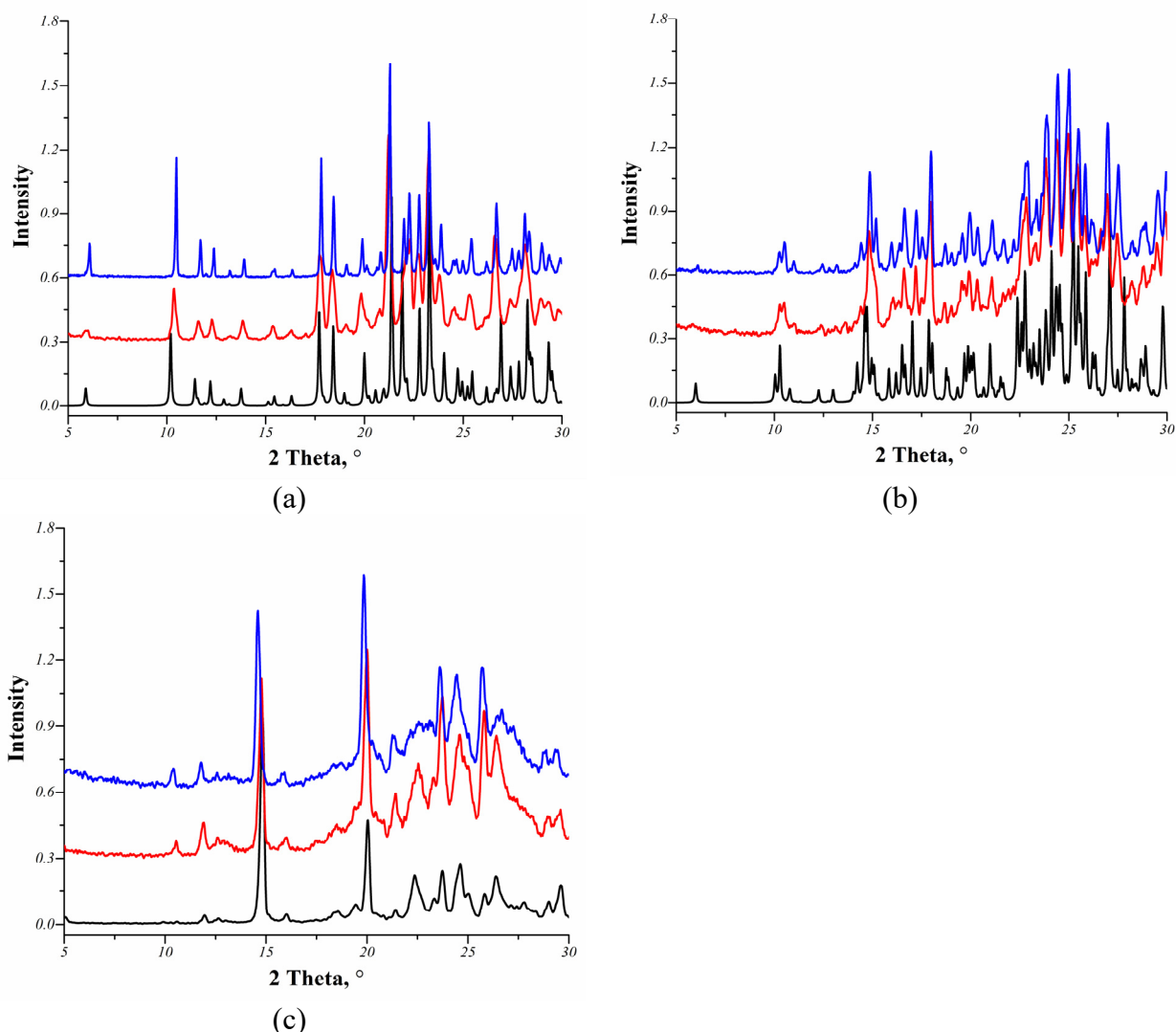


Figure S1. Overlay of the experimental PXRD patterns of the MCL multicomponent crystals prepared by LAG (red line) and slurry (blue line) and calculated PXRD (black line) from the X-ray crystal structure for: (a) [MCL+SucAc] (2:1), (b) [MCL+MlcAc] (1:1) and (c) [MCL+TartAc] (1:1).

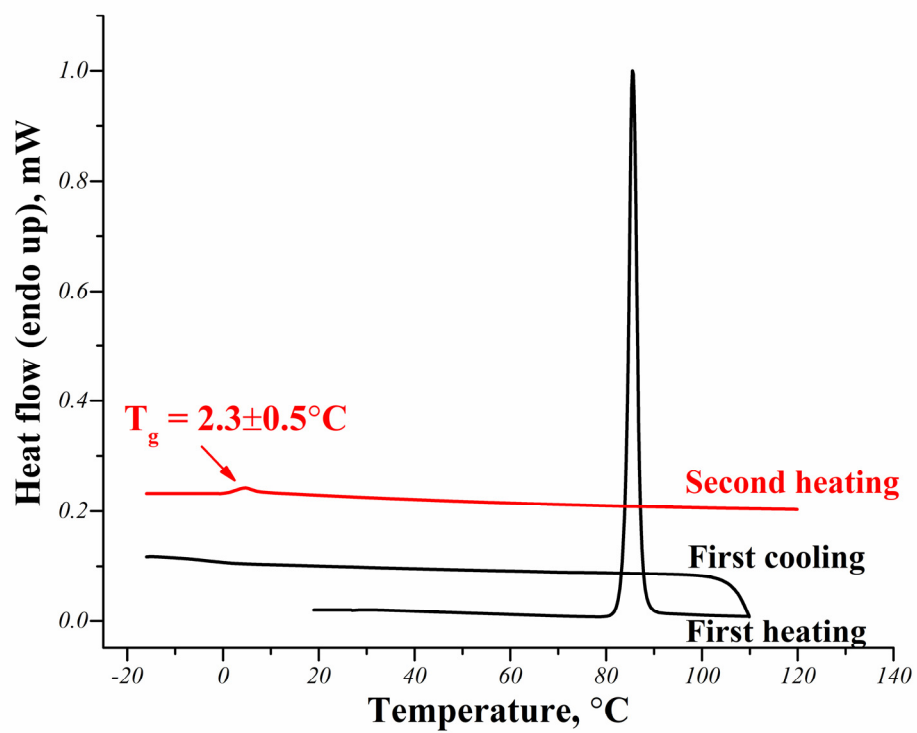


Figure S2. DSC profiles of MCL indicating its transformation from crystalline to the glassy state by cooling sample from the melt.

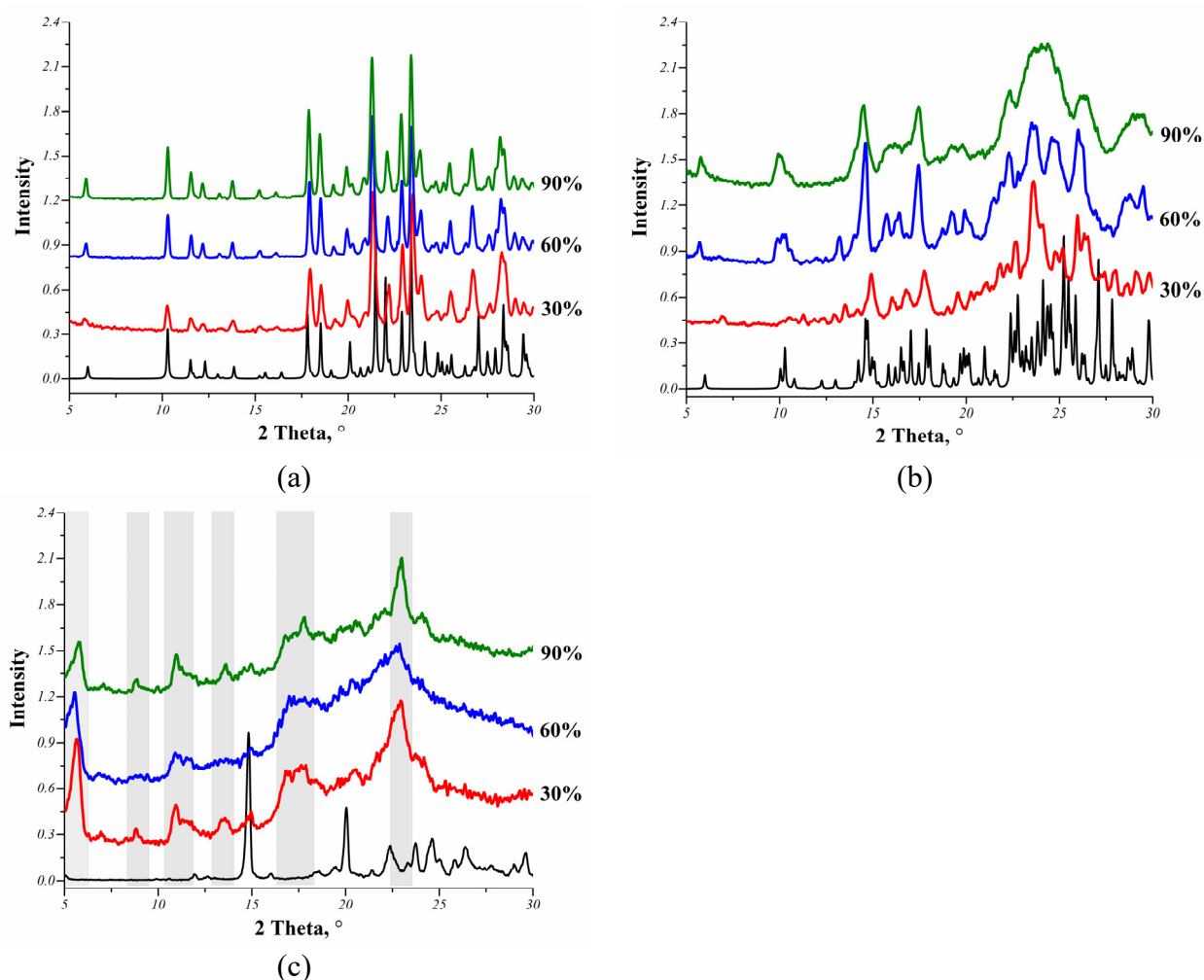


Figure S3. Overlay of the experimental PXRD patterns of the freeze-dried powders of (a) [MCL+SucAc] cocrystal (2:1), (b) [MCL+MlcAc] salt (1:1) and (c) [MCL+TartAc] salt (1:1) obtained from TBA/H₂O mixtures with different TBA content. The numbers show the percentage of TBA in the TBA/H₂O mixture. The black patterns correspond to the calculated PXRD of the MCL multicomponent crystals. Grey stripes highlight some unique peaks different from the peaks of the crystalline [MCL+TartAc] salt.

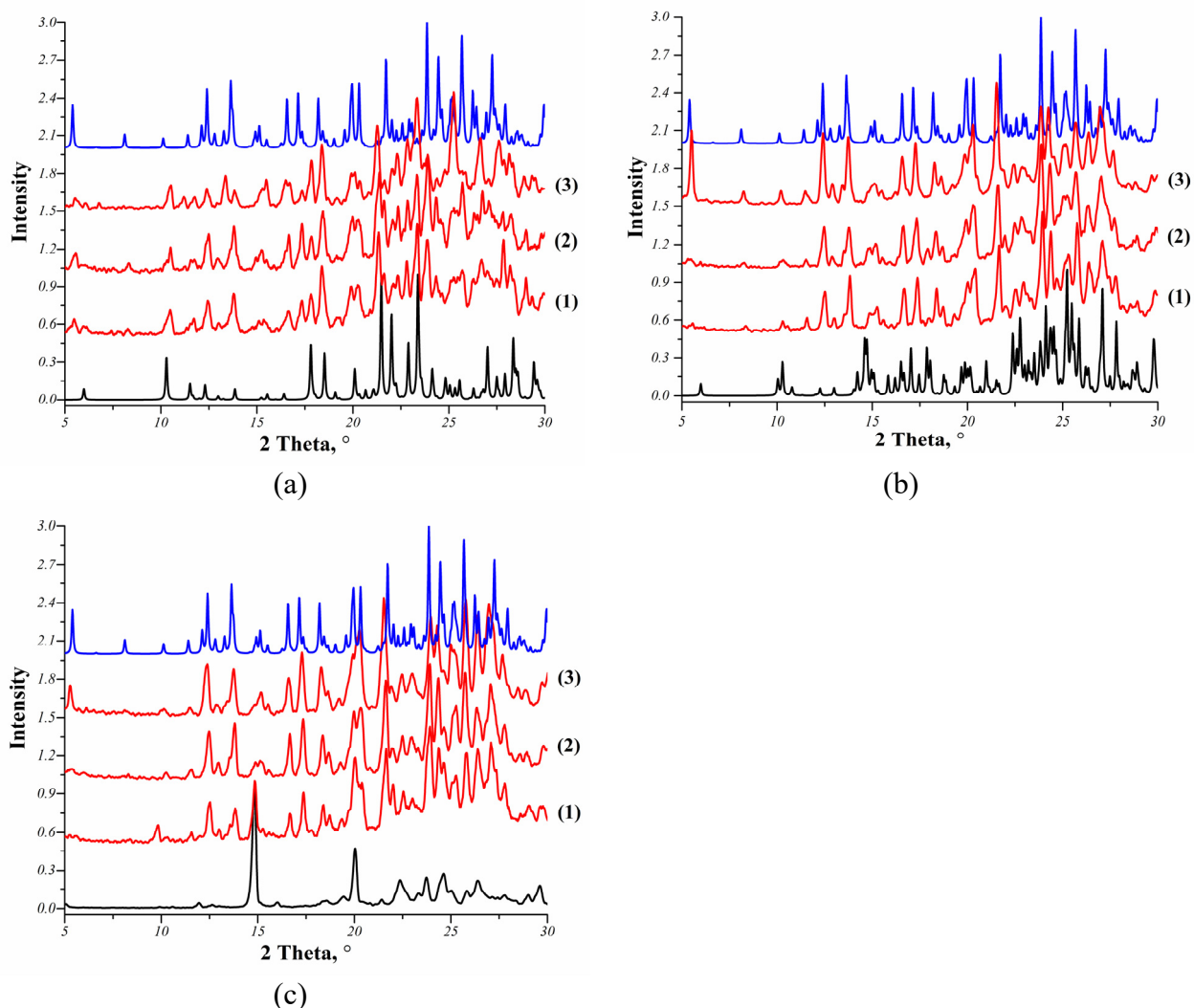


Figure S4. Results of PXR D analysis of the residual materials collected at the end of the dissolution experiments: (a) [MCL+SucAc] cocystal (2:1), (b) [MCL+MlcAc] salt (1:1) and (c) [MCL+TartAc] salt (1:1). Key: black line – calculated PXR D of the MCL cocystal/salt, blue line - calculated PXR D of the MCL hemihydrate. Red lines correspond to solid phases of the MCL multicomponent crystals prepared by LAG (1), slurring (2) or freeze-drying (3) after dissolution experiments.

Table S1. Crystallinity percentage of the freeze-dried powders of the MCL multicomponent crystals calculated on basis of PXRD analysis

	Crystallinity percentage of the freeze-dried powders, % ^a		
	TBA/H ₂ O 30:70	TBA/H ₂ O 60:40	TBA/H ₂ O 90:10
[MCL+SucAc] (2:1)	89.9	89.7	89.1
[MCL+MlcAc] (1:1)	84.3	82.0	79.4
[MCL+TartAc] (1:1)	60.6	46.0	50.1

^a The crystallinity was calculated from the ratio of the area of all crystalline peaks to the total area

Table S2. Thermophysical data of the MCL multicomponent crystals prepared by the multiple methods

MCL multicomponent crystal	Preparation method	T_{fus}^{onset} , °C		ΔH_{fus}^T , J·g ⁻¹	
		literature*	this work	literature*	this work
[MCL+SucAc] (2:1)	LAG	119.7±0.2	117.6±0.2	82.2±0.5	77.4±0.5
	slurry		119.5±0.2		82.5±0.5
	freeze-drying		117.7±0.2		85.6±0.5
[MCL+MlcAc] (1:1)	LAG	140.3±0.2	135.9±0.2	-	-
	slurry		140.5±0.2		-
	freeze-drying		136.8±0.2		-
[MCL+TartAc] (1:1)	LAG	171.4±0.2	170.6±0.2	164.4±0.5	163.6±0.5
	slurry		171.5±0.2		164.5±0.5
	freeze-drying		155.8±0.2		86.0±0.5

* Drozd, K. V; Manin, A.N.; Voronin, A.P.; Boycov, D.E.; Churakov, A. V; Perlovich, G.L. A combined experimental and theoretical study of miconazole salts and cocrystals: crystal structures, DFT computations, formation thermodynamics and solubility improvement. Phys. Chem. Chem. Phys. 2021, 23, 12456–12470