

Supporting Information

**Chemical Stabilization Strategy for
Cymoxanil: Synthesis and
Characterization of Cocrystals with
Small Organic Acids**

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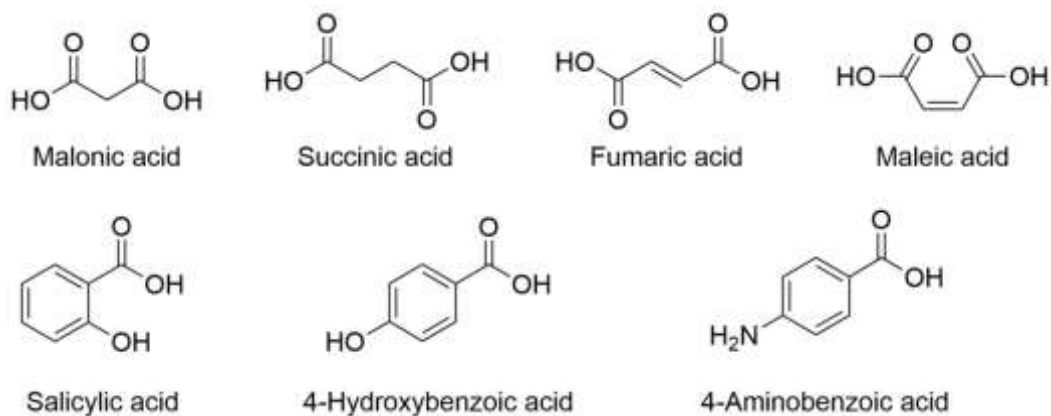


Fig. S1 The types of coformers used in screening experiments.

Table S1 Overview of screening experiments.

API	Coformer	Result
Cymoxanil	Malonic acid	×
Cymoxanil	Succinic acid	√√
Cymoxanil	Fumaric acid	√
Cymoxanil	Maleic acid	×
Cymoxanil	Salicylic acid	√√
Cymoxanil	4-Hydroxybenzoic acid	×
Cymoxanil	4-Aminobenzoic acid	×

□ represents a new potentially cocrystal determined by PXRD; □□ represents a new cocrystal determined by PXRD and its structure is determined by SCXRD; × represents no new cocrystal found by PXRD.

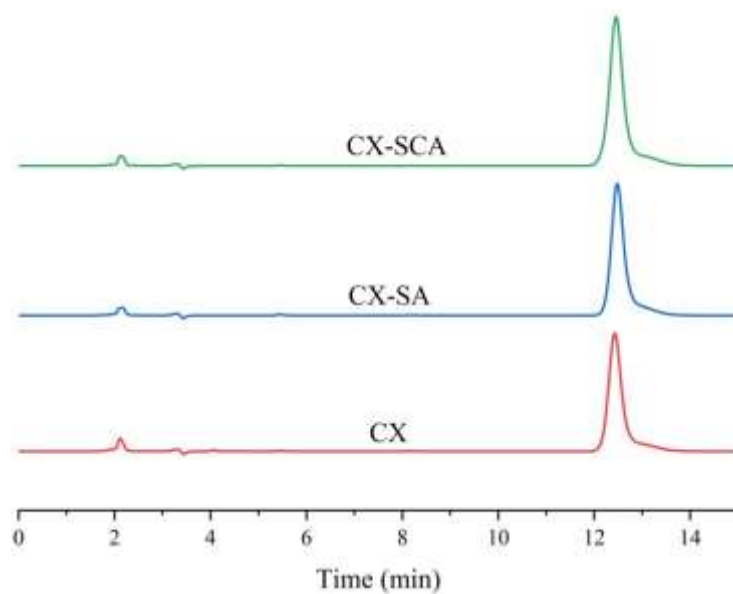


Fig. S2 Typical HPLC chromatograms of CX, CX-SA cocrystal and CX-SCA cocrystal.

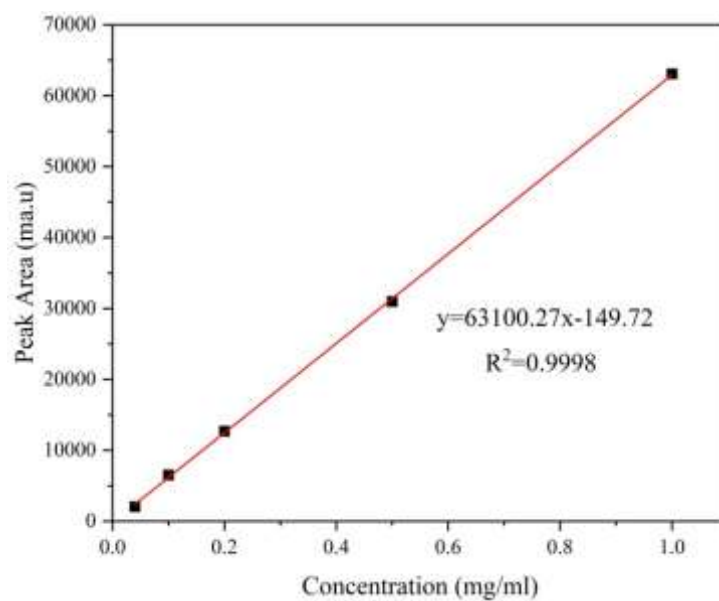


Fig. S3 Standard curve of CX content (concentration-peak area) determined by HPLC.

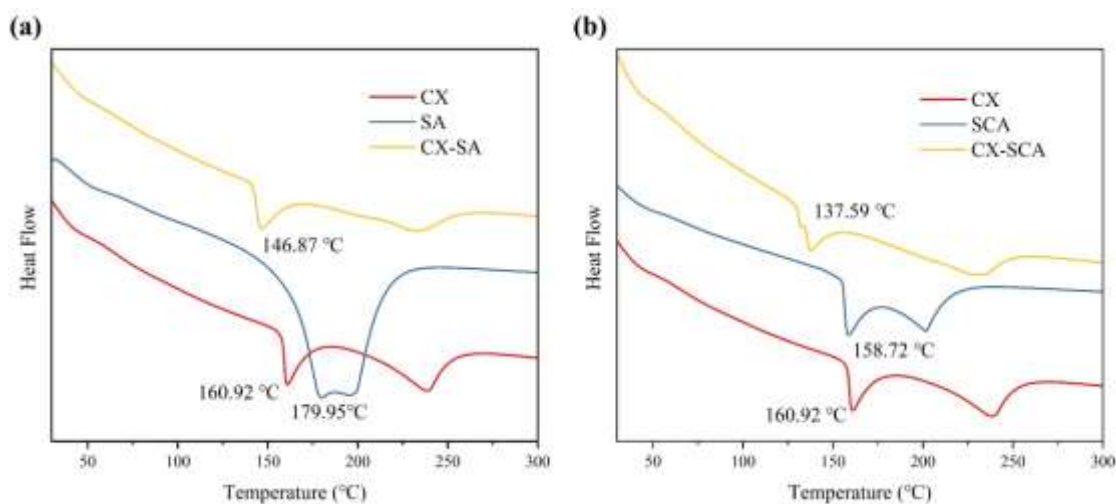


Fig. S4 DSC curves of the raw materials and cocrystals. (a) DSC curves of the CX-SA cocrystal compared to CX and SA. (b) DSC curves of the CX-SCA cocrystal compared with CX and SCA.

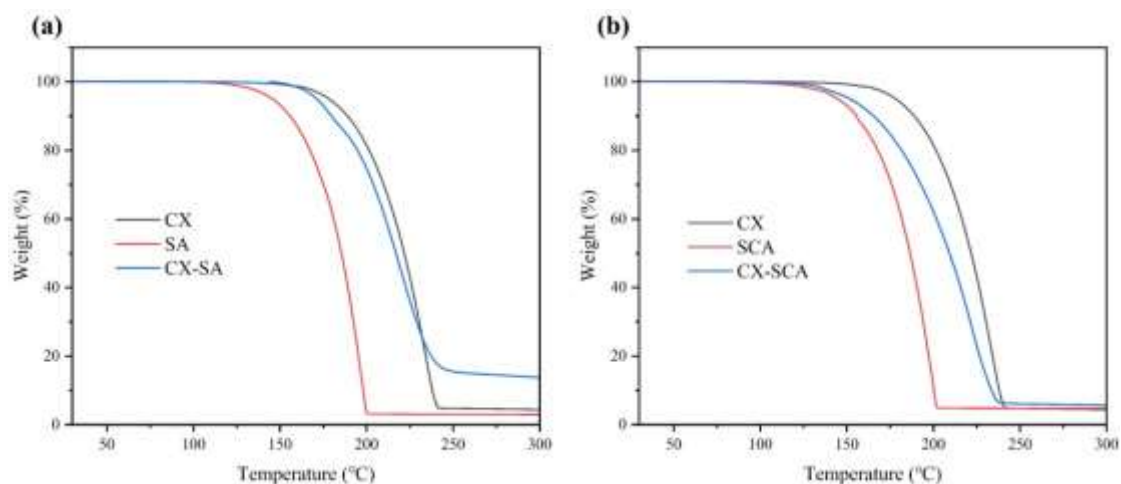


Fig. S5 TGA curves of the raw materials and cocrystals. (a) TGA curves of the CXSA cocrystal compared to CX and SA. (b) TGA curves of the CX-SCA cocrystal compared with CX and SCA.

Table S2 Hydrogen bonds of CX-SA and CX-SCA cocrystals

D-H...A	d(D...H) (Å)	d(H...A) (Å)	d(D...A) (Å)	∠D-H...A (deg)	symmetry code
CX-SA					
N3-H3...O4	0.86	2.26	3.083(2)	160	x, y, z
Intra N3-H3...N1	0.86	2.35	2.715(3)	106	
Intra N4-H4...O2	0.86	2.03	2.696(2)	134	
O5-H5O...O3	0.82	1.80	2.616(2) CX-SCA	173	x, y, z
N3-H3...O5	0.86	2.17	3.000(3)	163	-1+x, y, z
Intra N3-H3...N1	0.86	2.36	2.738(3)	107	
Intra N4-H4...O2	0.86	2.02	2.677(4)	132	
N4-H4...N2	0.86	2.60	3.321(5)	142	3-x,1-y,1-z
O4-H4A...O3	0.82	1.75	2.561(4)	172	-1+x, y, z
Intra O6-H6...O5	0.82	1.87	2.590(3)	145	

Table S3 Residual percentages of CX content in stability experiments.

	Sample	1	2	3	Average	Error
pH=5.8	CX	72.91	72.31	72.32	72.51	0.34
	CX-SA	77.85	81.47	89.21	82.84	5.80
	CX+SA	88.50	92.43	90.72	90.55	1.97
	CX-SCA	96.69	92.51	90.61	93.27	3.11
	CX+SCA	92.11	96.45	91.82	93.46	2.59
Pure water	CX	62.85	58.13	53.51	58.16	4.67
	CX-SA	79.56	88.95	89.61	86.04	5.62
	CX+SA	85.58	92.59	90.67	89.61	3.62
	CX-SCA	91.75	93.86	89.24	91.62	2.32
	CX+SCA	91.30	94.73	91.10	92.38	2.04
pH=8.0	CX	0.60	0.49	0.45	0.51	0.08
	CX-SA	88.69	90.06	89.57	89.44	0.69
	CX+SA	89.69	88.09	89.93	89.24	1.00
	CX-SCA	96.70	92.94	88.53	92.73	4.09
	CX+SCA	89.50	91.03	90.24	90.26	0.77

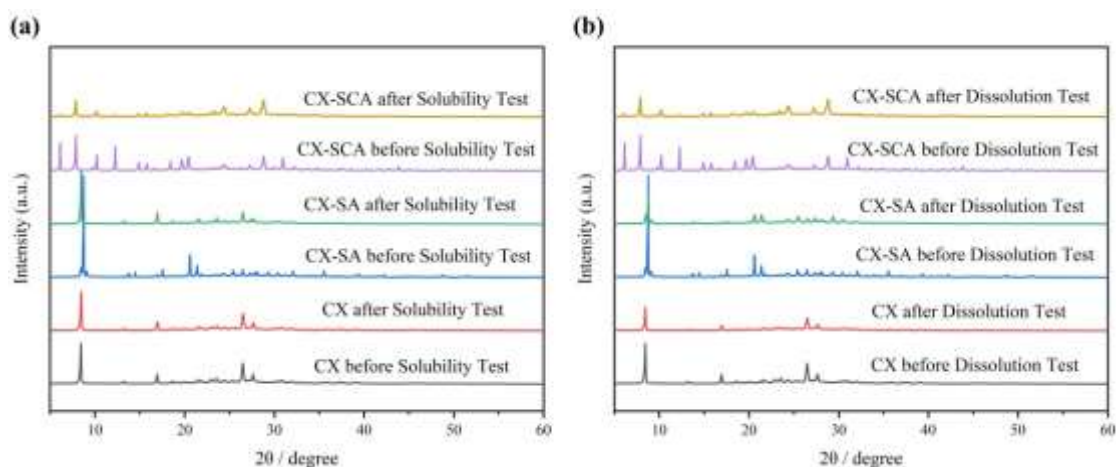


Fig. S6 (a) PXRD patterns of CX and two cocrystals before and after solubility test. (b) PXRD patterns of CX and two cocrystals before and after dissolution test.

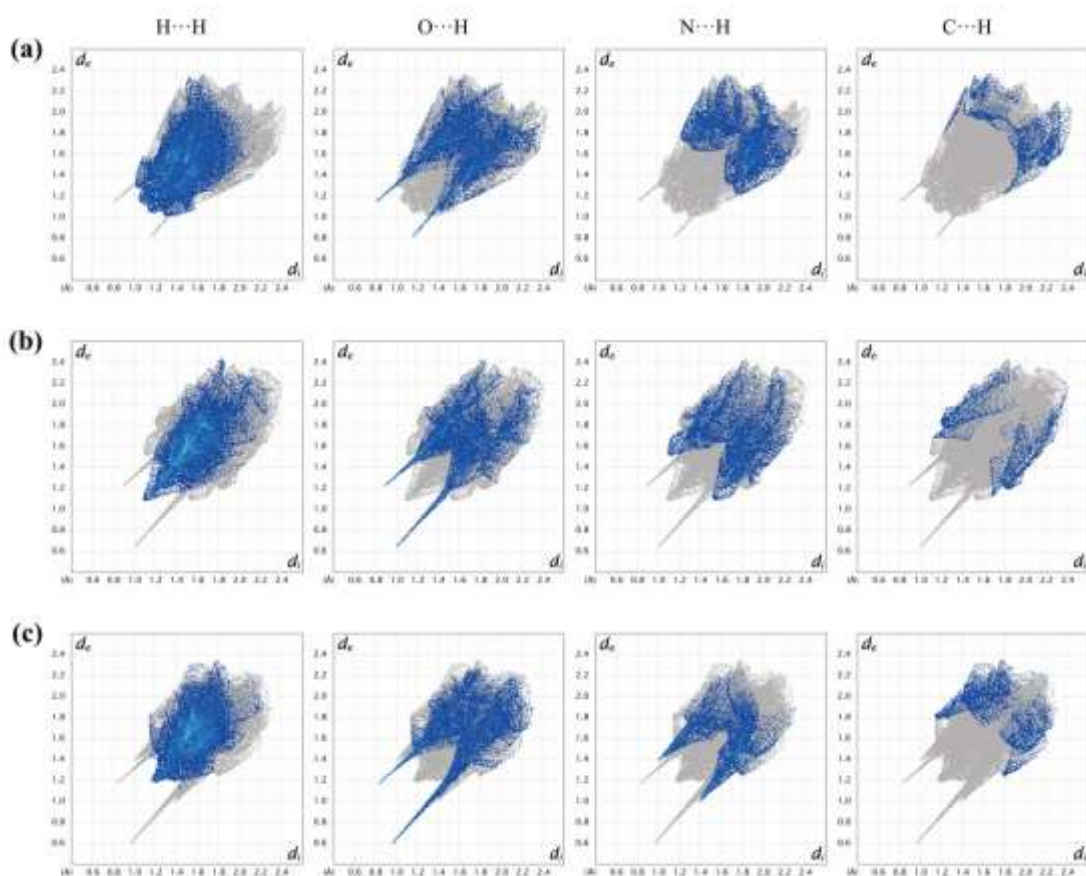


Fig. S7 Detailed two-dimensional fingerprint plots (a) CX. (b) CX-SA cocrystal. (c) CX-SCA cocrystal.