Supporting information

Multicomponent solid forms of antibiotic Cephalexin towards improved chemical stability

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Table S1. Hydrogen bond geometry (Å/°)

CPX binary solids	D–H···A	D-H/ Å	H···A/Å	D···A/Å	D-H···A/°	Symmetry code
CPX–SER	N2–H2···O4	0.86	2.24	2.9792(4)	144	x,y,-1+z
	N3–H3A···O1	0.89	1.73	2.5844(4)	159	1/2+x,1/2-y,-z
	N3–H3B···O5	0.89	2.08	2.8598(4)	145	1-x,1/2+y,3/2-z
	N3–H3C···O5	0.89	2.02	2.6942(4)	132	1-x,1/2+y,1/2-z
	N4–H4A···O6	0.89	1.92	2.6659(4)	141	1/2-x,-y,-1/2+z
	N4–H4B···O2	0.89	2.14	2.9803(4)	158	-
	N4–H4C···O2	0.89	2.03	2.8657(4)	156	x,y,1+z
	O7–H7···O3	0.82	2.31	2.9770(4)	140	x,y,1+z
	C1–H1···O3	0.98	2.49	3.1797(5)	128	x,y,1+z
	C5–H5···O3	0.98	2.54	3.2274(5)	127	x,y,1+z
	C10–H10···O4	0.98	2.25	3.1225(5)	148	x,y,-1+z
	C16–H16···O5	0.93	2.16	3.0851(4)	174	1-x,1/2+y,3/2-z
	C18–H18···O6	0.98	1.86	2.8106(4)	163	x,y,-1+z
CPX–DHB . H_2O	O2–H2···O5	0.89	1.70	2.5699(1)	167	2-x,-1/2+y,1-z
	N2–H2A···O9	0.83	2.32	3.1048(2)	156	1+x,y,z
	N3–H3A···O2	0.89	2.30	3.0520(2)	143	-1+x,y,z
	N3–H3B···O7	0.95	1.74	2.6720(1)	167	-
	N3–H3C···O5	0.89	2.55	3.1982(2)	130	-
	N3–H3C···O1	0.89	1.97	2.7153(1)	141	2-x,1/2+y,1-z
	O5–H5A···O3	0.81	2.14	2.8914(2)	155	-1+x,y,z
	O5–H5B···O6	0.93	1.77	2.6591(1)	159	-
	C1–H1···O9	0.98	2.36	3.2431(2)	149	1+x,-1+y,z
	C10–H10···O1	0.98	2.60	3.0112(2)	105	2-x,1/2+y,1-z

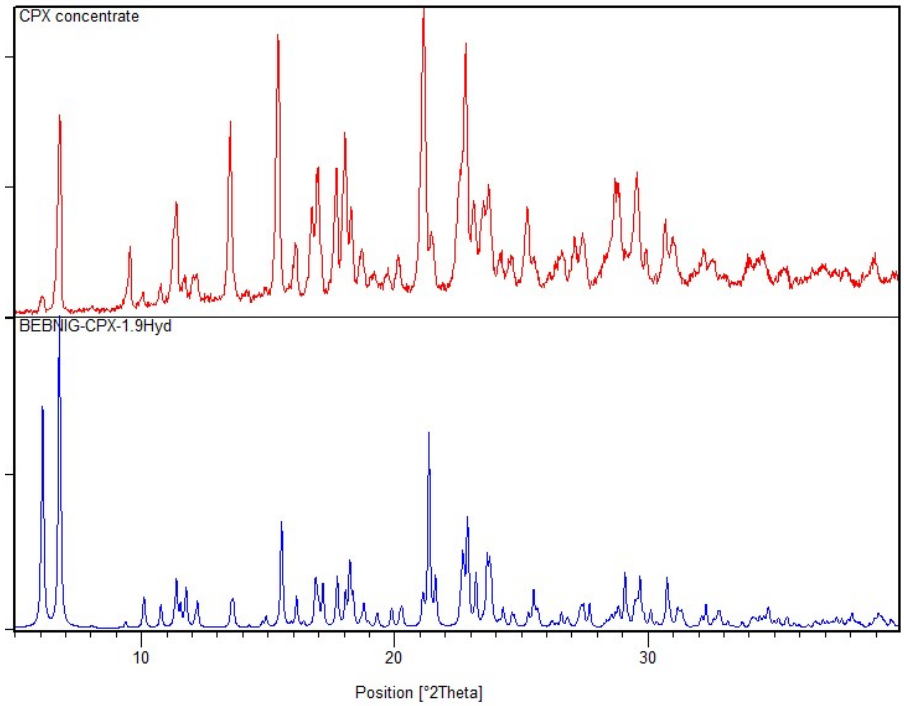


Fig. S1. PXRD comparison of CPX (extracted from commercialized tablets) with the calculated XRD pattern of CPX-1.9 hydrate from its crystal structure (CCDC refcode: BEBNIG). Peak to peak match confirms its bulk phase purity.

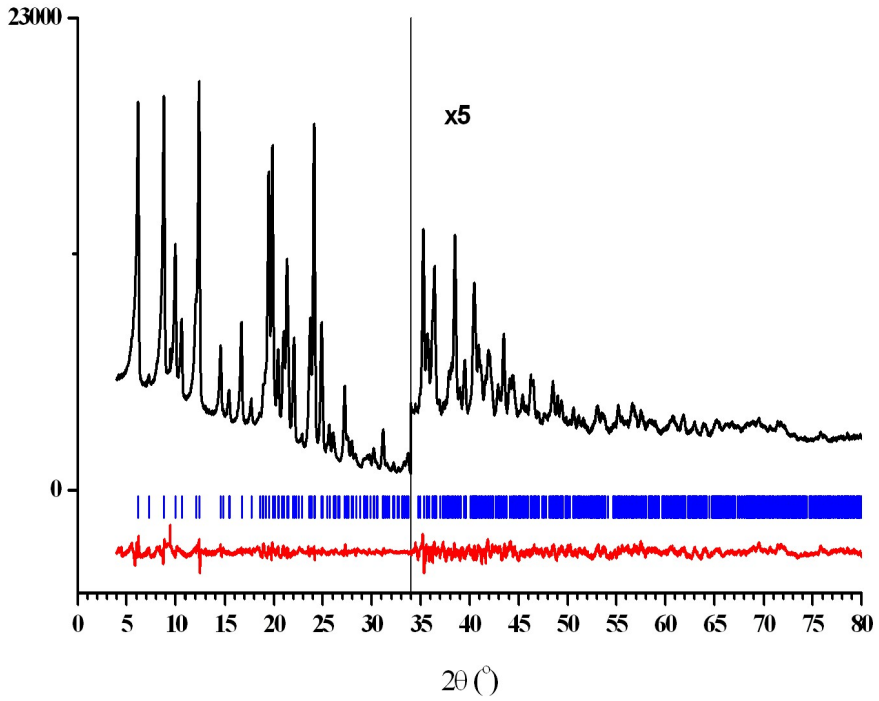


Fig. S2. The Rietveld plot after the final bond-restrained refinement for CPX–SER, showing the experimental and difference diffraction profiles as black (top) and red (bottom) curves, respectively. The vertical blue bars correspond to the calculated positions of the Bragg peaks.

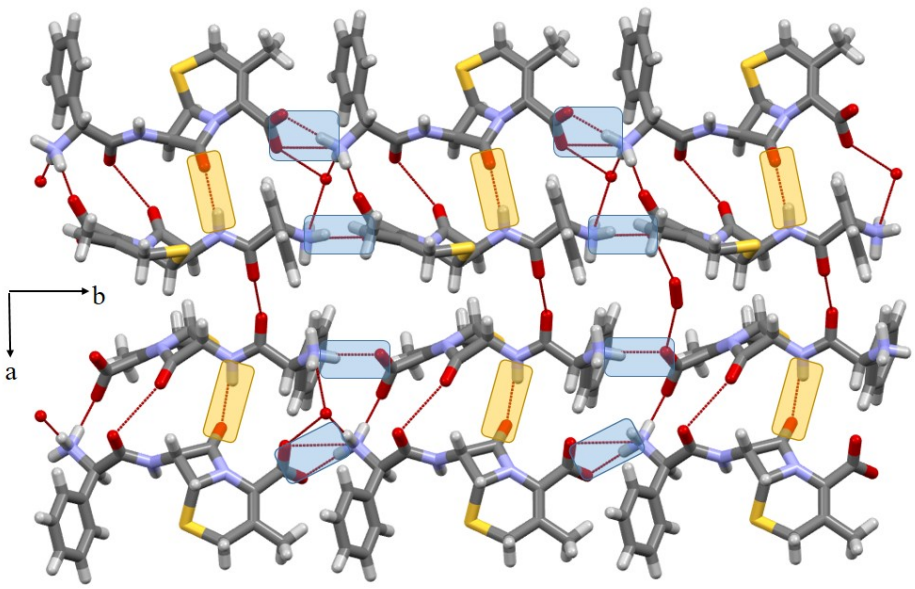


Fig. S3. CPX molecules form N^{+}–H···O^{-} hydrogen bonded 1D chain between carboxylate and ammonium ions along the *b* axis, whereas N–H···O hydrogen bond (amide NH/ and lactam CO) and O···O short contacts along the *a* axis resulted 2D sheet structure in CPX hydrate.

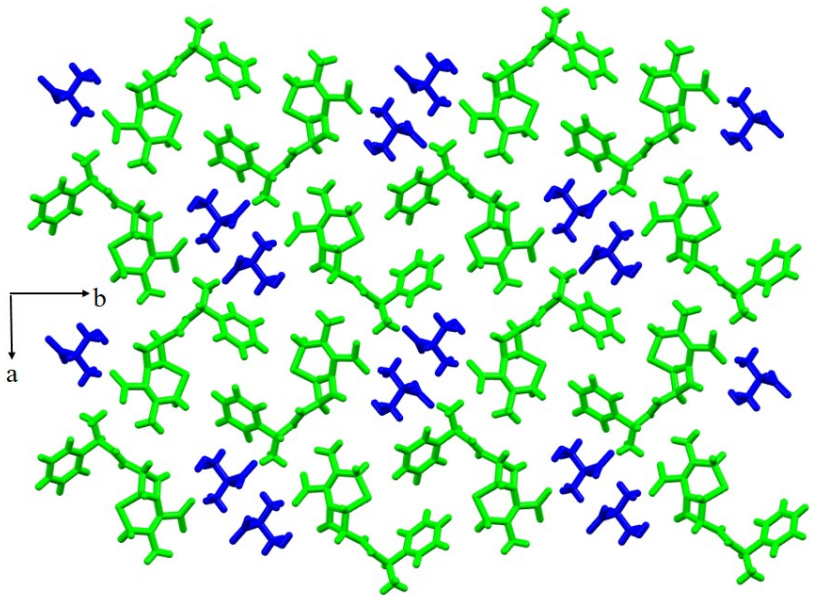
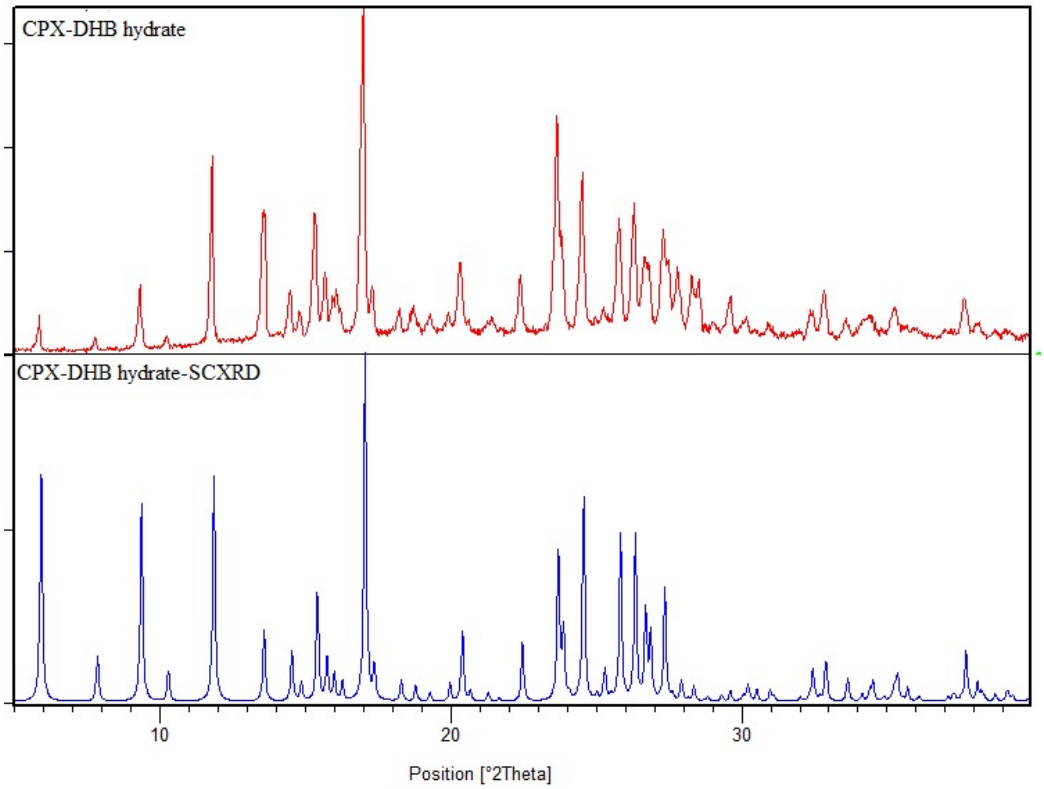
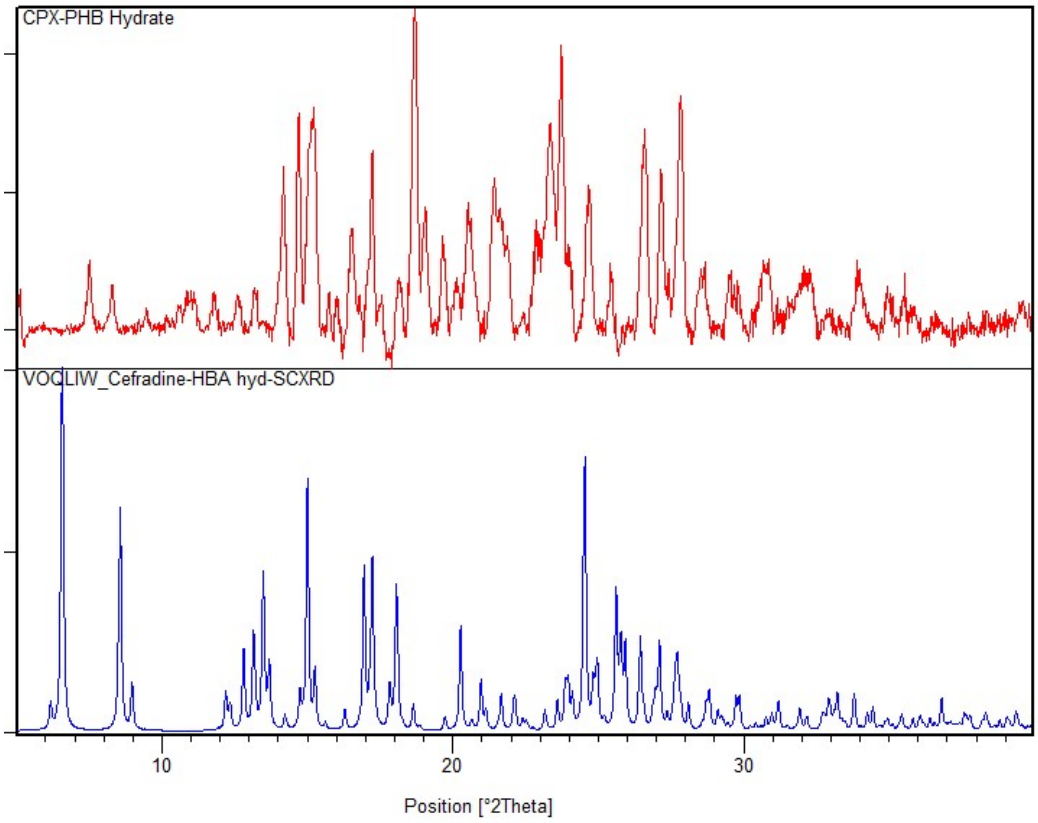


Fig. S4. Molecular packing of CPX–SER cocrystal viewed down the c axis represent host (CPX, green trace)-guest (SER, blue trace) assembly.

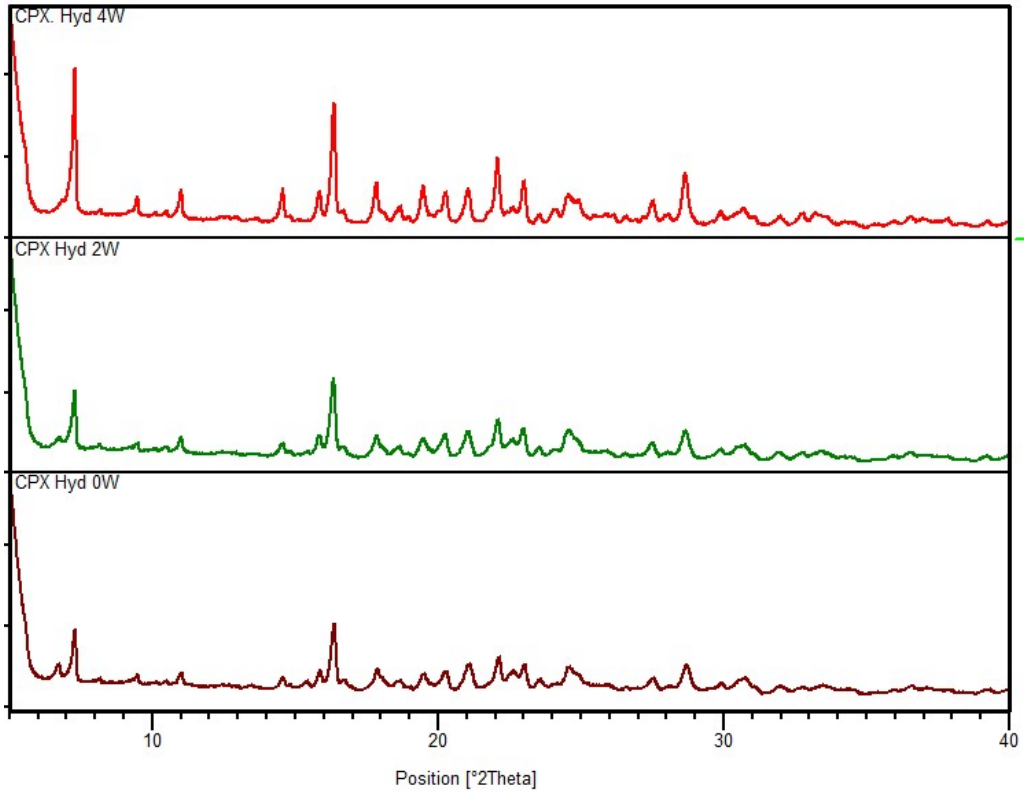


(a)



(b)

Fig. S5. a) Overlay of PXRD (red trace) of CPX–DHB salt hydrate with its calculated X-ray patterns (blue trace) from crystal structure confirms the bulk phase purity. b) Overlay of PXRD pattern of CPX–PHB hydrate with the simulated XRD pattern of VOQLIW indicated partial match that suggested possibility of multiple phases may be present in the sample.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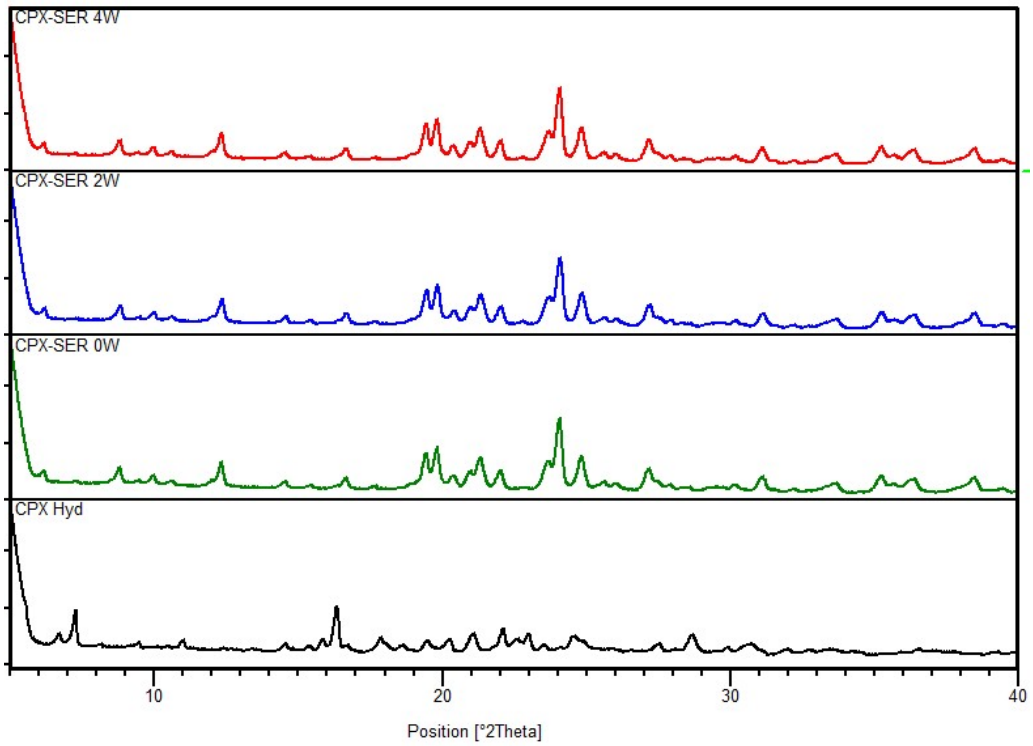
CPX Hyd 2W
CPX Hyd 0W
10
20
30
40
Position [°2Theta]

(a)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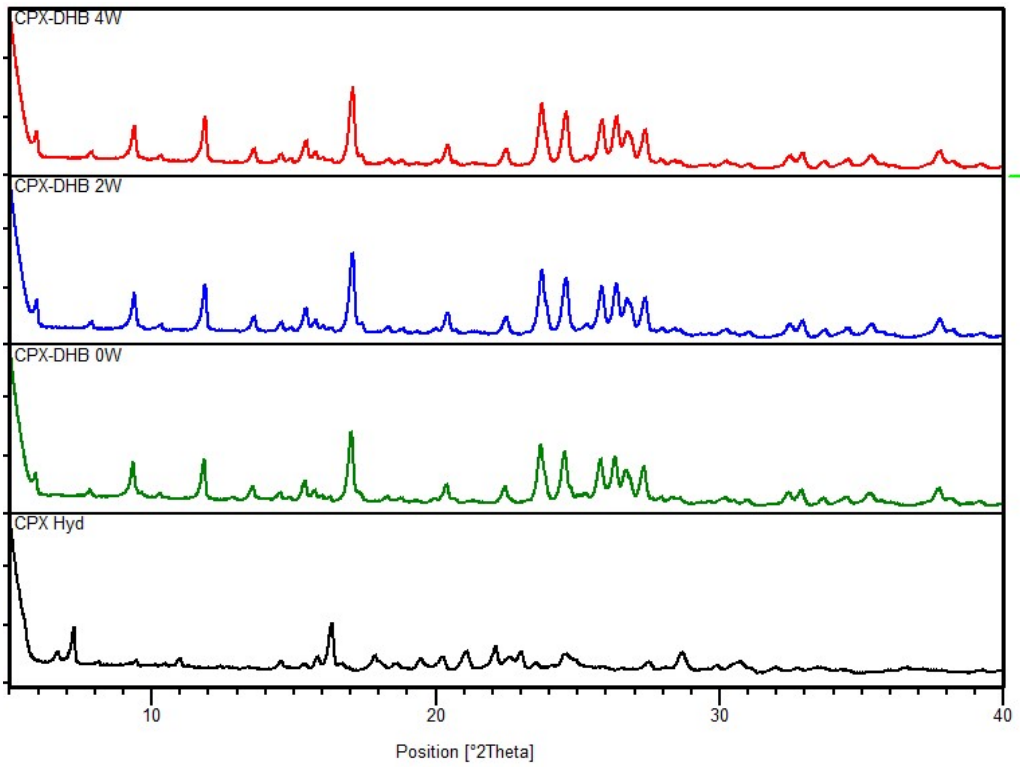
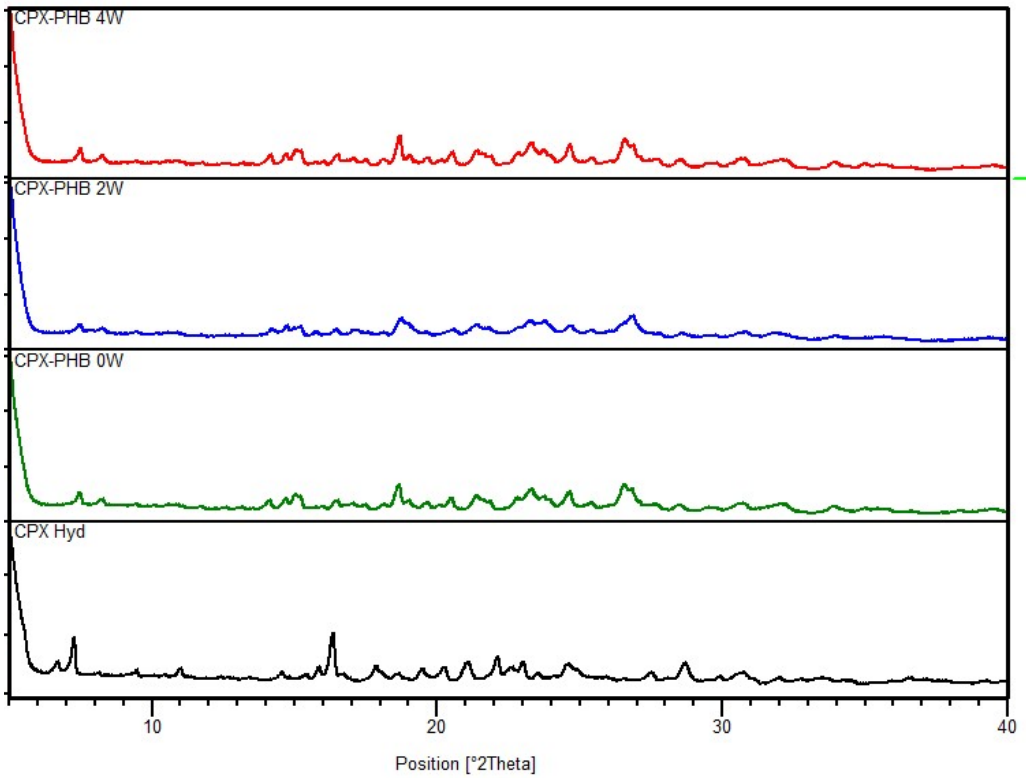
CPX-SER 2W
CPX-SER 0W
CPX Hyd
10
20
30
40
Position [°2Theta]

(b)



(c)



(d)

Fig. S6. PXRD comparison of a) CPX Hyd, b) CPX–SER, c) CPX–DHB, and d) CPX–PHB upto 4 weeks in 35±5 ^{O}C and 75±5% relative humidity that confirmed the physical stability of all the multicomponent solids as CPX hydrate.

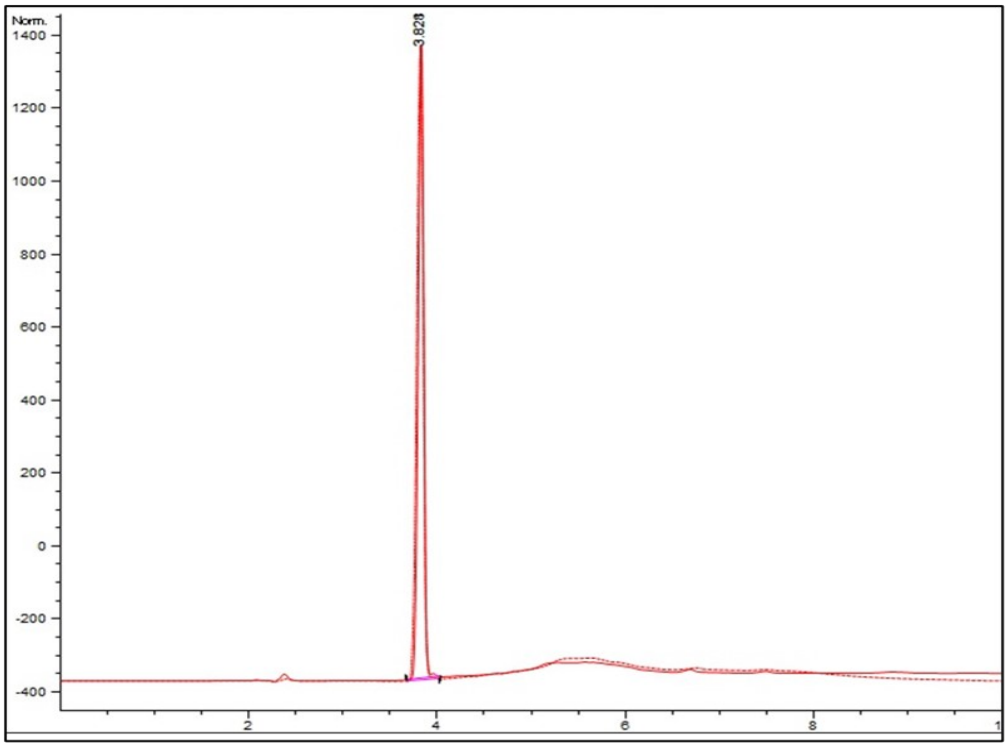
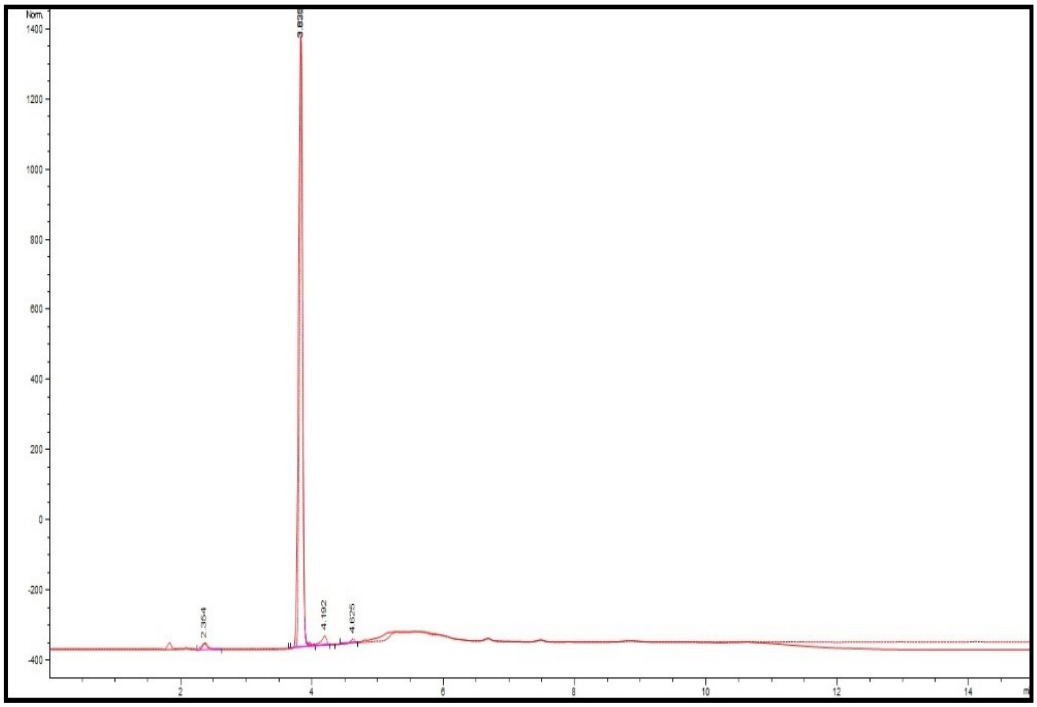
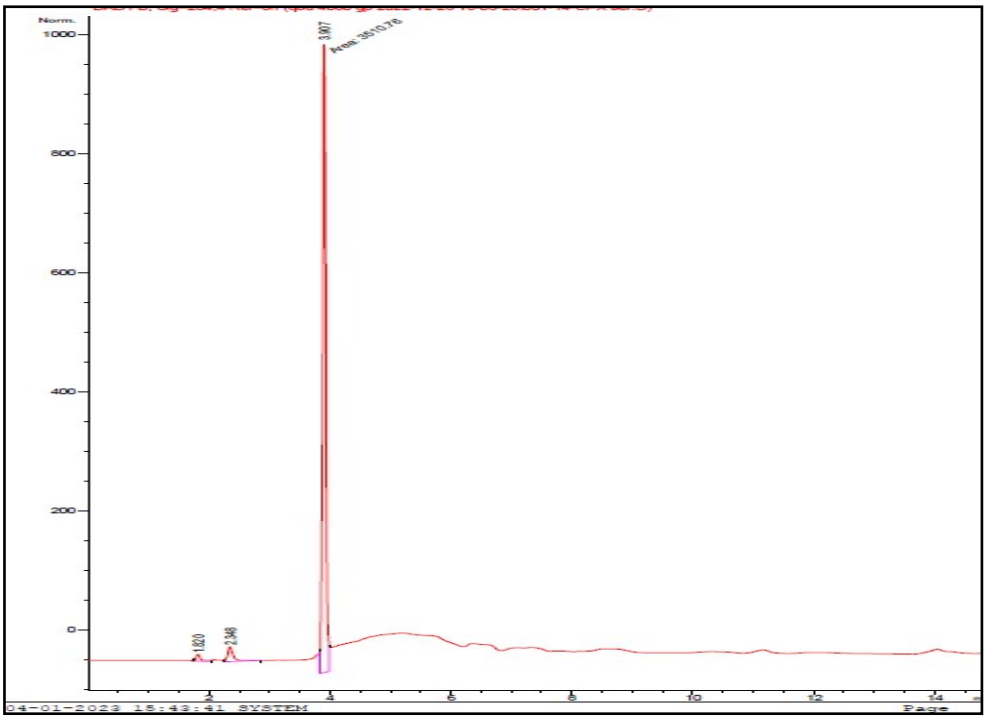


Fig. S7. HPLC overlay of CPX standard and CPX Sample used for cocrystallization



(a)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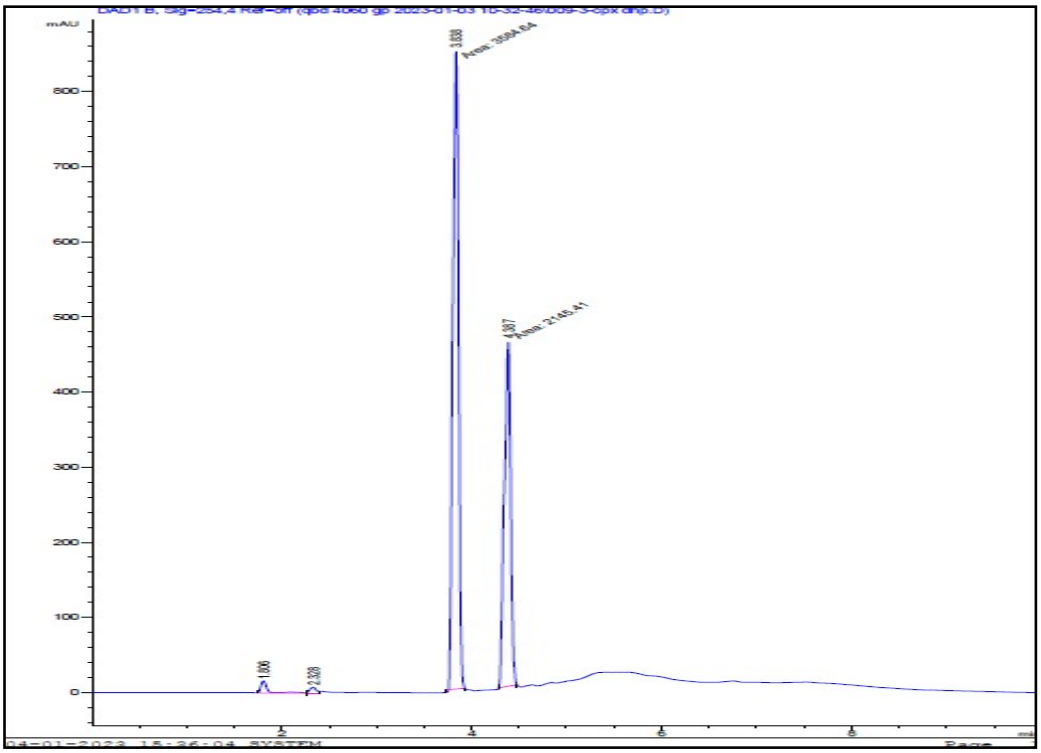
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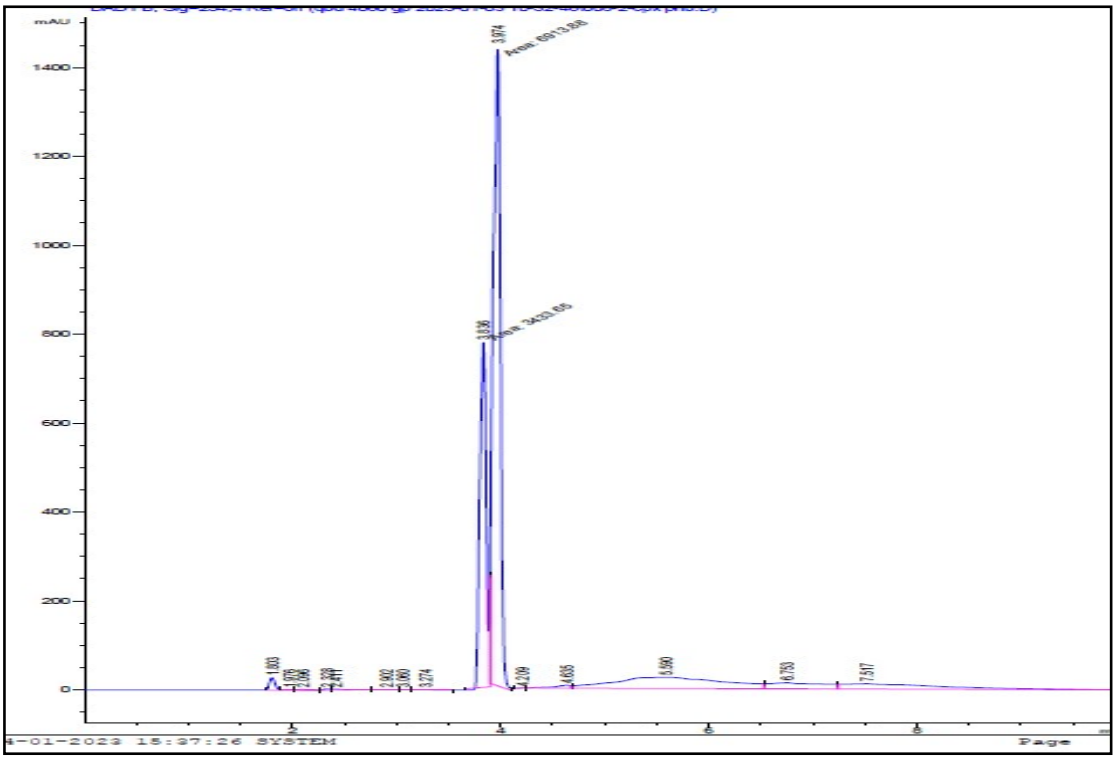
(c)



(d)

Fig. S8. HPLC chromatogram of a) CPX, b) CPX–SER, c) CPX–DHB and d) CPX–HBA following acid hydrolysis.