

Charge-assisted Intermolecular Hydrogen Bond Formed in Coamorphous System is Important to Relieve the pH-dependent Solubility Behavior of Lurasidone Hydrochloride

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Legend of supplementary figures

- Fig. S1** Photomicrographs of surface-scraped species of amorphous LH tablet (a), APM (1:1) tablet (b) and CM (1:1) tablet (c) at the end of intrinsic dissolution test
- Fig. S2** Intrinsic dissolution rate ($\text{nmol}\cdot\text{ml}^{-1}\cdot\text{min}^{-1}$) for LH and REP from CM (1:1) in 0.2 M PBS 3.8 ($n = 6$)
- Fig. S3** Photomicrographs of collected solid samples at different time points (2, 10, 30 and 90 min) during supersaturated dissolution tests of (A) amorphous LH and (B) amorphous REP
- Fig. S4** XRPD and PLM of (A) amorphous LH and (B) amorphous REP after 2 days storage at 25 °C /0% RH
- Fig. S5** Photomicrograph of CM (1:1) after 90 days storage at 25 °C /60% RH
- Fig. S6** Chromatograms of (A) oxidation of crystalline LH, (B) oxidation of crystalline REP, freshly prepared and stored (C) amorphous LH, (D) amorphous REP, (E) CM (1:1) and (F) APM (1:1) under different conditions
- Fig. S7** Content of (A) LH and (B) REP in CMs after 90 days' storage at 25 °C/60% RH ($n = 3$)

Tables

- Table S1** ^{13}C NMR prediction results of LH and REP by ACD Labs
- Table S2** Impurity contents of freshly prepared and stored CM (1:1) and APM (1:1) under different conditions (mean value represented, $n = 3$)

Fig. S1

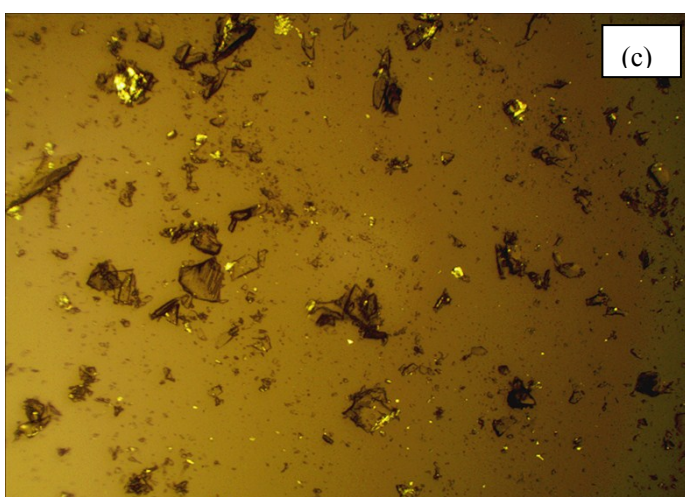
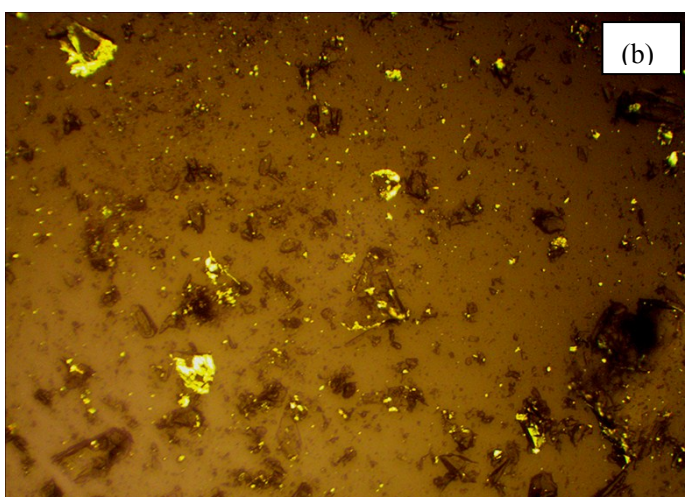
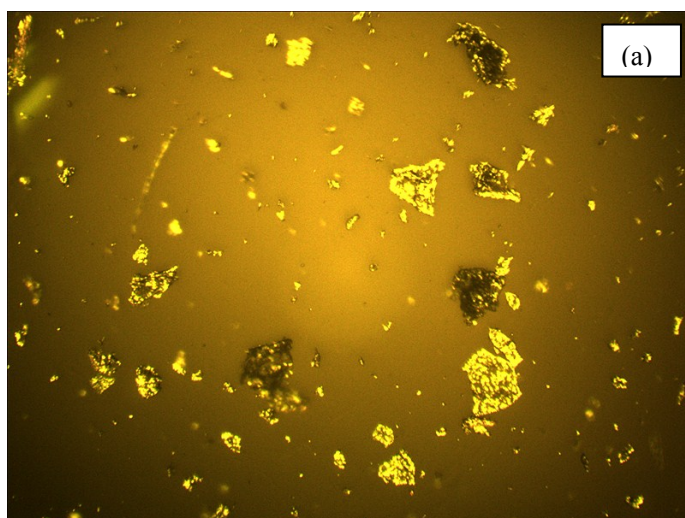


Fig. S2

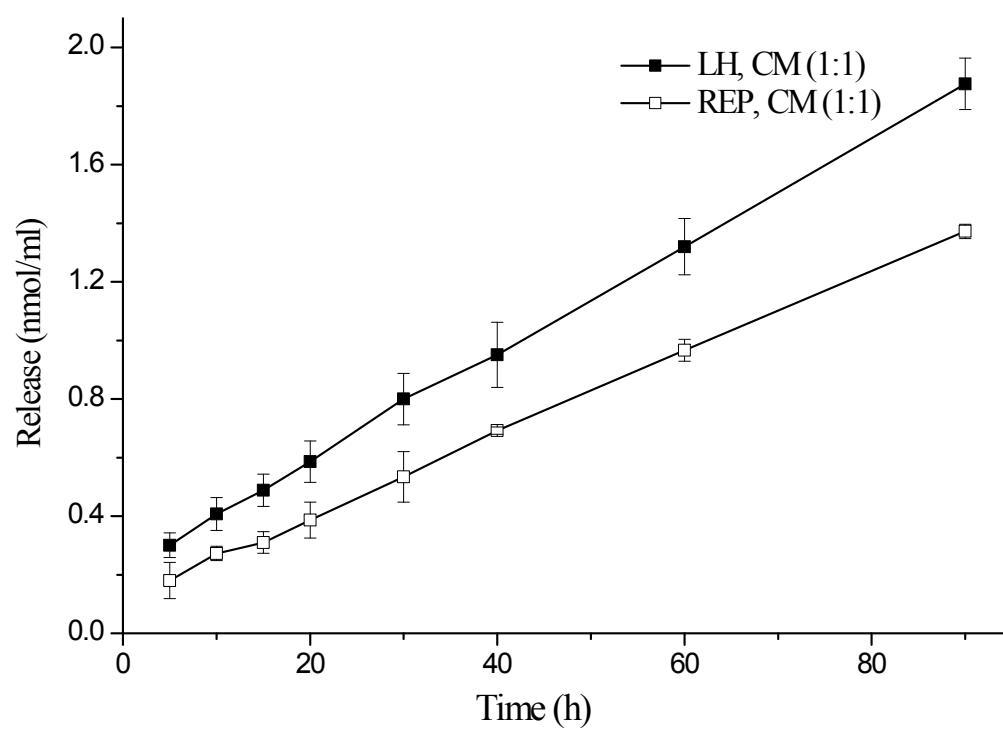
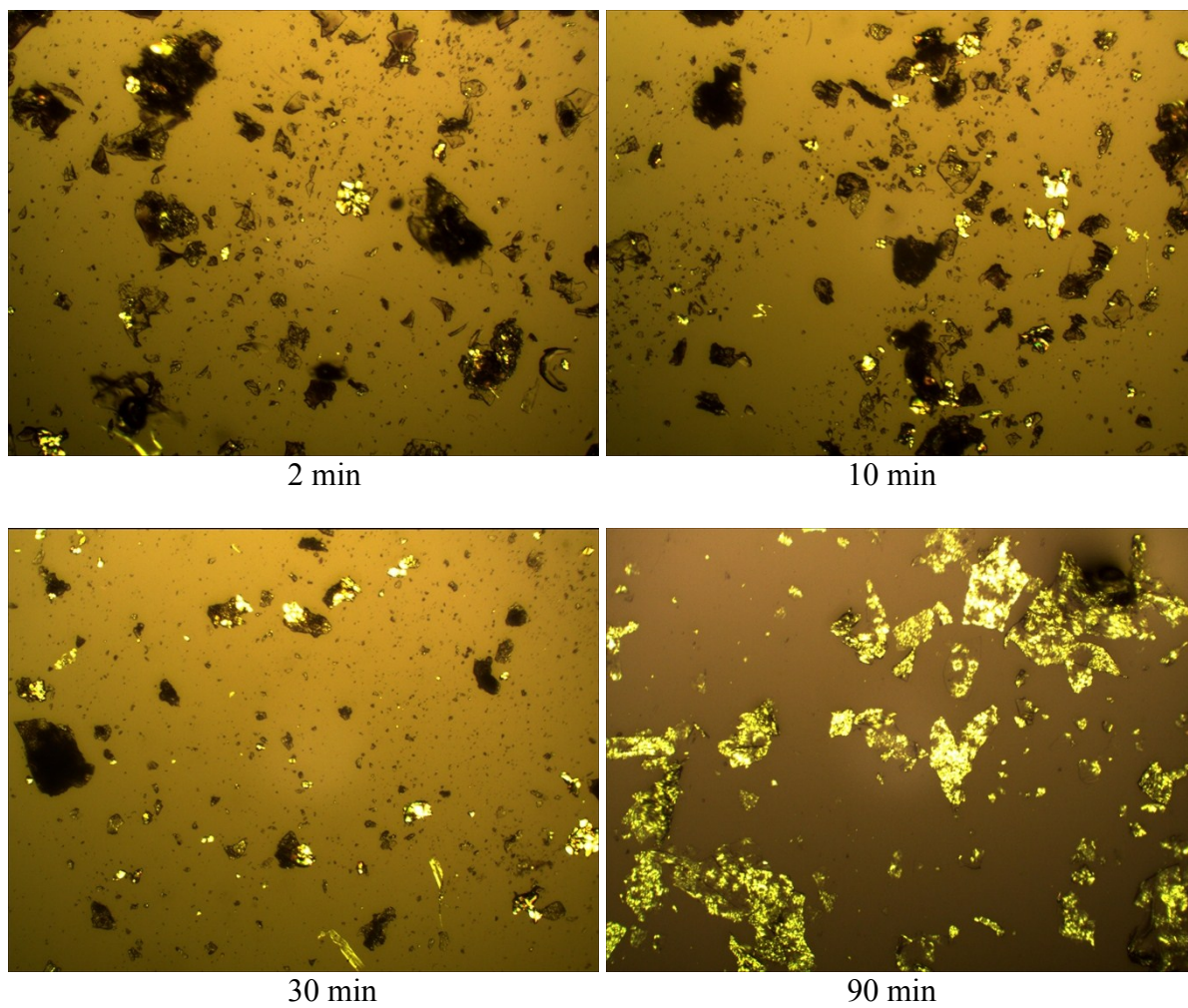
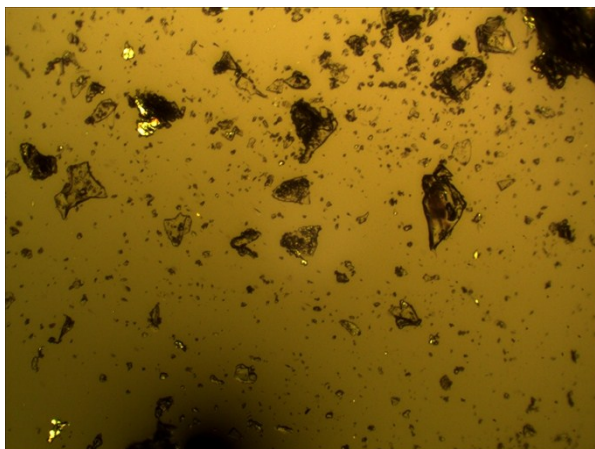


Fig. S3

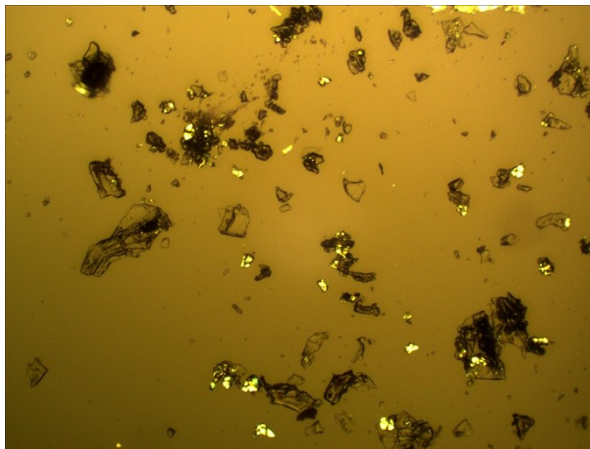
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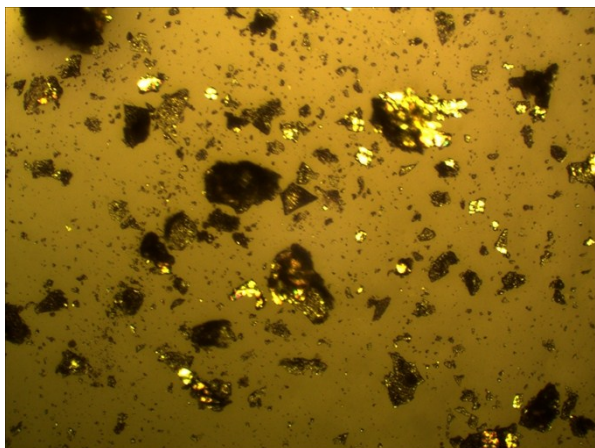
B



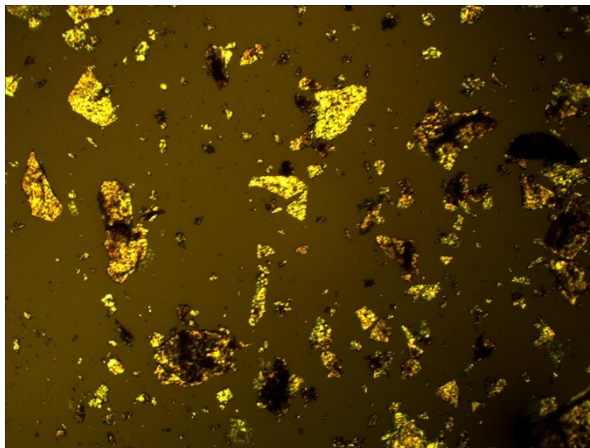
2 min



10 min



30 min



90 min

Fig. S4

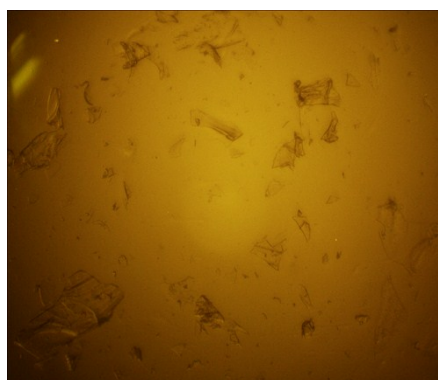
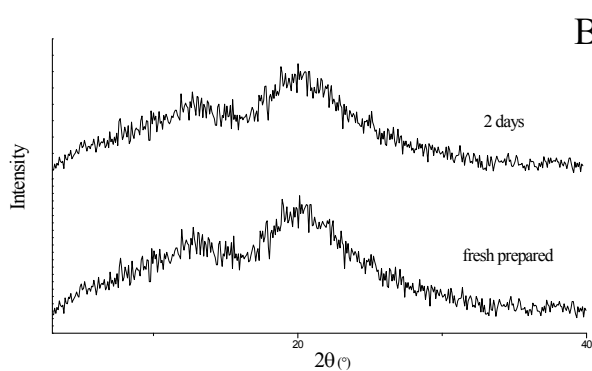
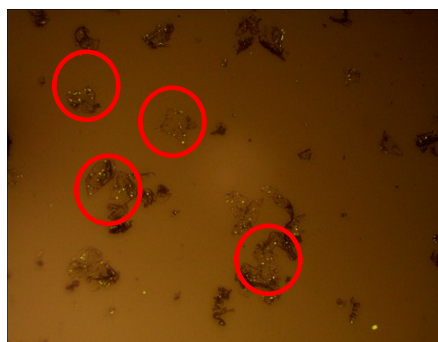
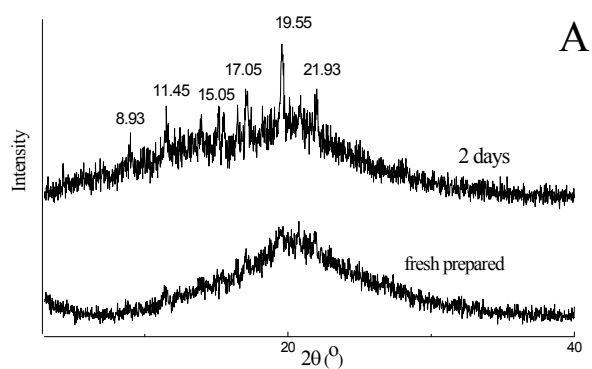


Fig. S5

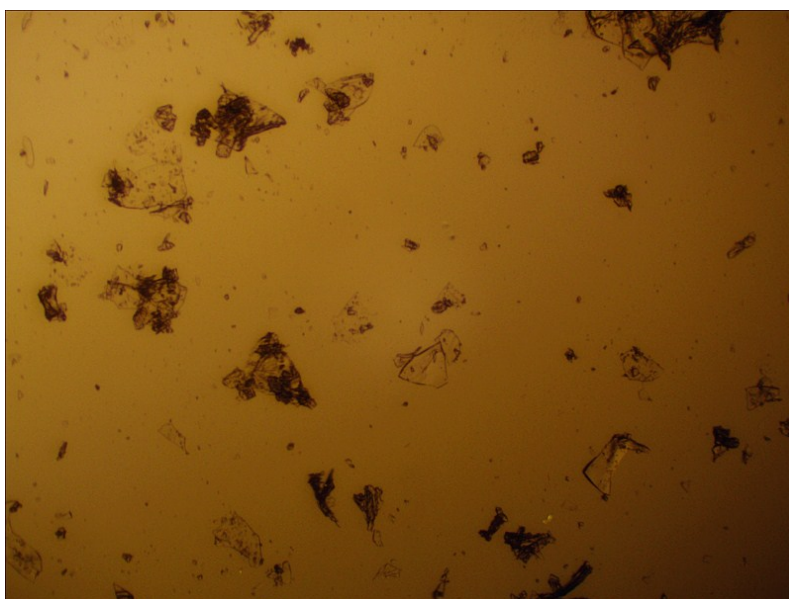
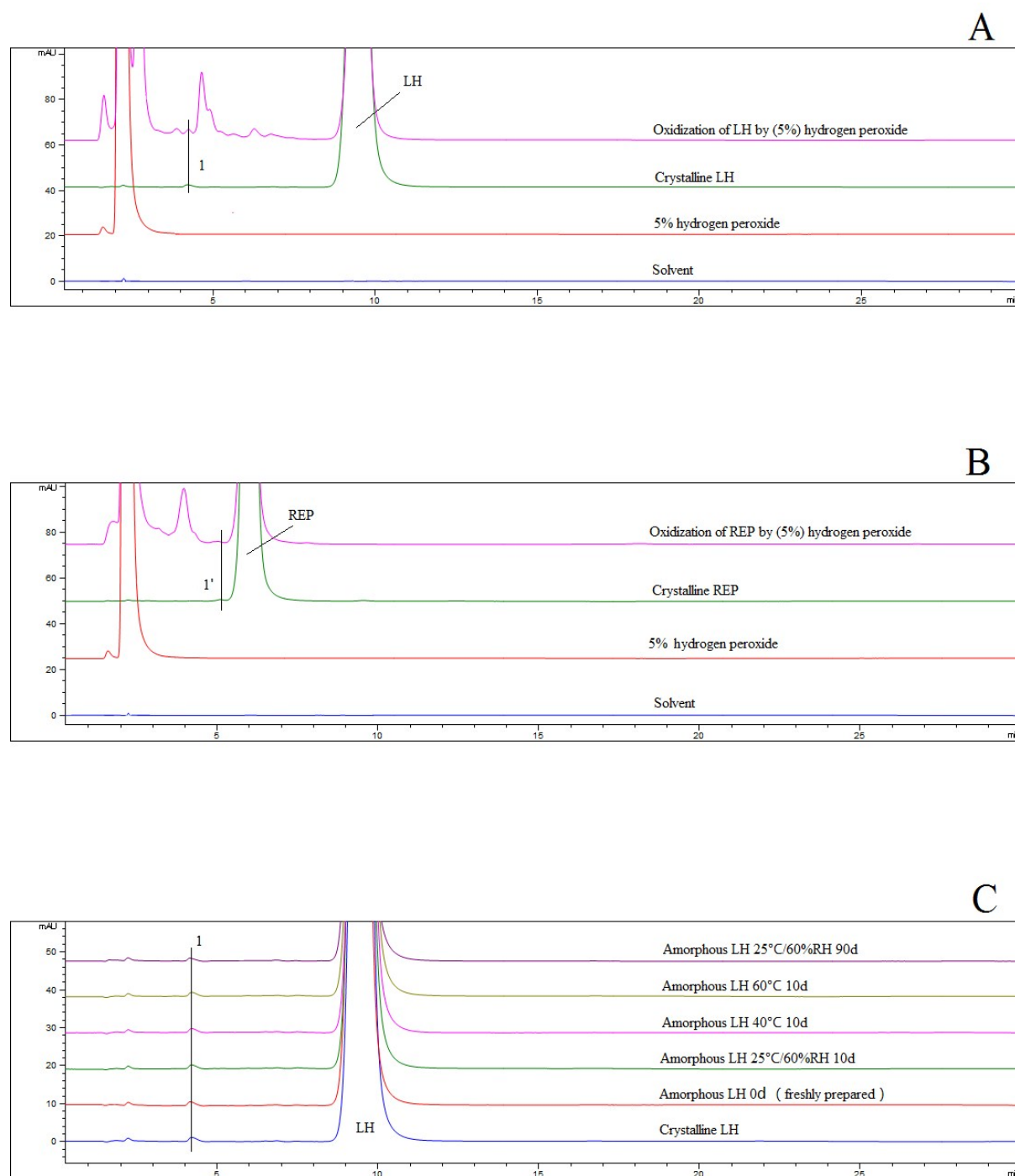
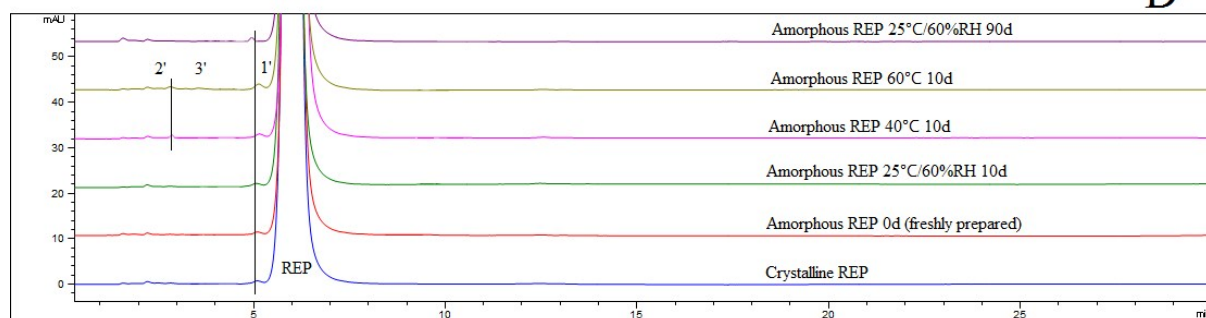


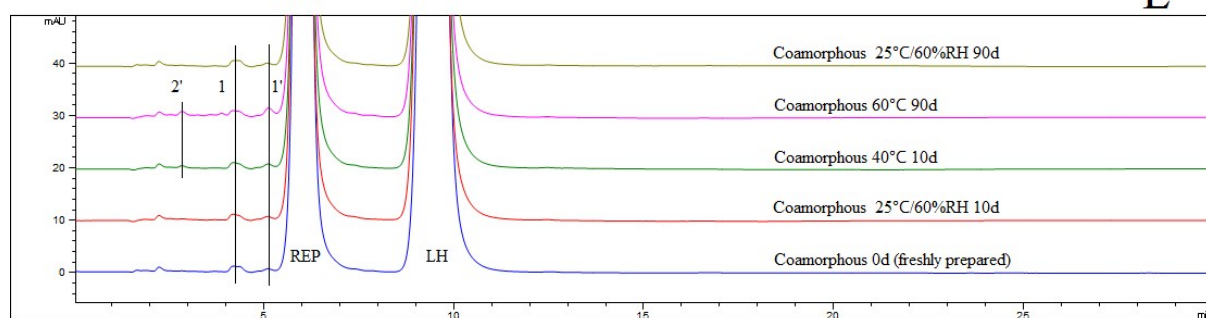
Fig. S6



D



E



F

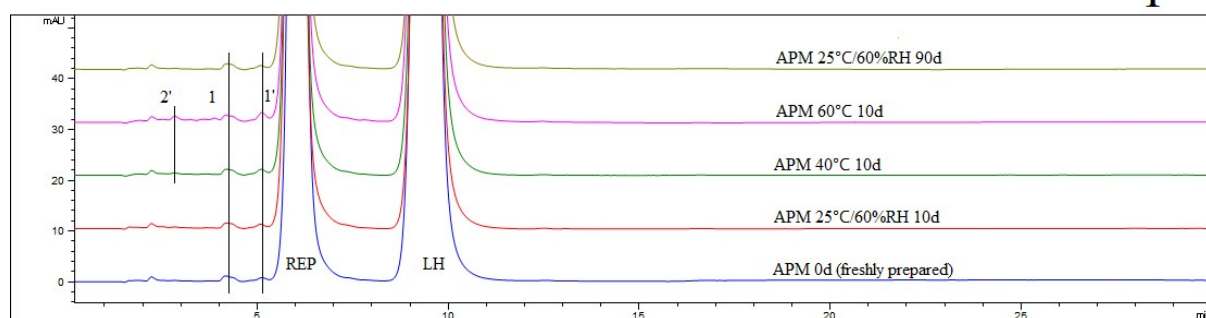


Fig. S7

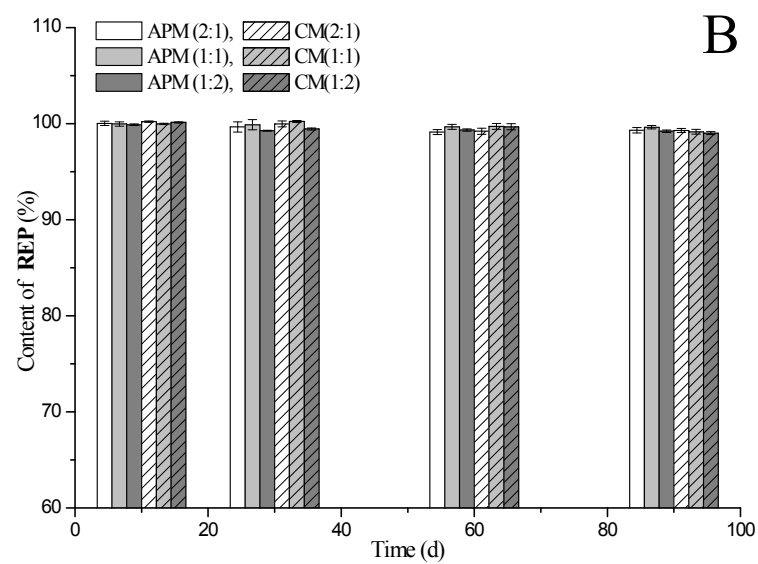
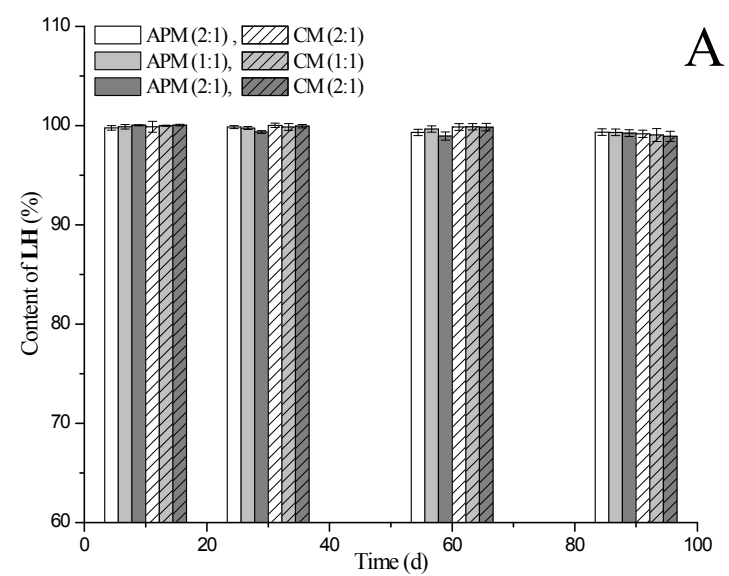
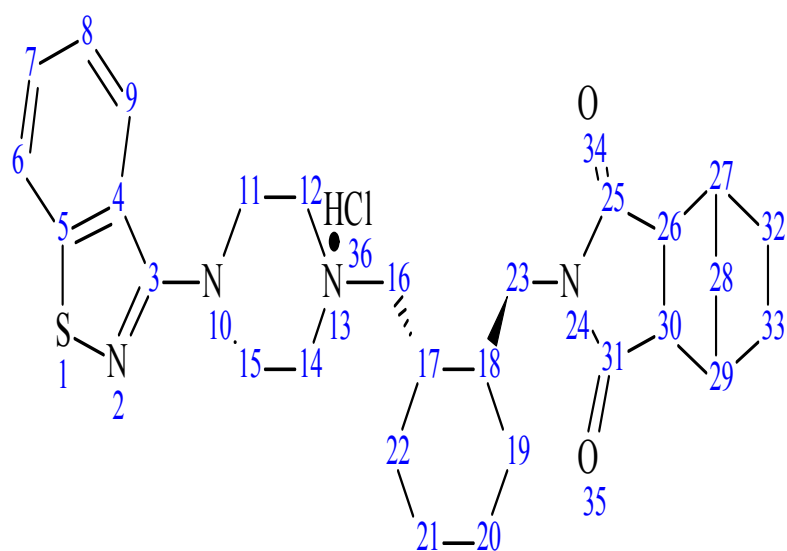
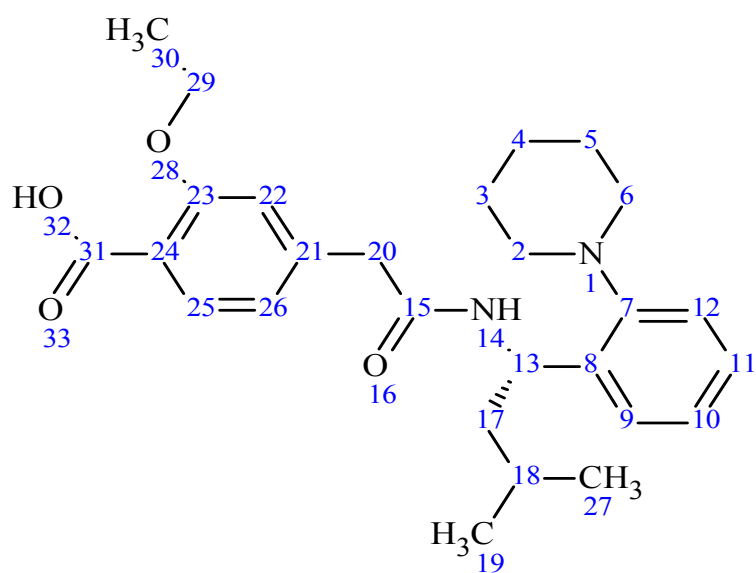


Table S1

Carbon Number	LH			REP		
	nH	Shift Value (PPM)	Error	nH	Shift Value (PPM)	Error
2	-	-	-	2	53.02	3.24
3	0	162.28	7.64	2	26.17	1.36
4	0	124.51	7.83	2	23.75	1.18
5	0	146.71	6.87	2	26.17	1.36
6	1	118.36	3.83	2	53.02	3.24
7	1	126.04	3.83	0	150.12	4.37
8	1	127.32	3.83	0	127.91	6.65
9	1	124.19	3.83	1	128.49	3.83
10	-	-	-	1	122.61	3.83
11	2	47.98	4.23	1	126.71	3.83
12	2	53.05	4.52	1	115.51	5.17
13	-	-	-	1	48.79	3.86
14	2	53.05	4.52	-	-	-
15	2	47.98	4.23	0	171.21	3.65
16	2	60.39	4.48	-	-	-
17	1	36.63	5.91	2	42.82	3.65
18	1	38.63	5.86	1	25.05	3.13
19	2	29.74	4.07	3	22.66	2.67
20	2	25.01	3.8	2	43.38	2.02
21	2	25.8	3.8	0	138.76	8.36
22	2	30.21	4.07	1	113.68	5.23
23	2	40.42	3.11	0	158.45	3.83
24	-	-	-	0	118.36	3.83
25	0	177.13	2.97	1	132.33	3.83
26	1	47.15	5.91	1	120.17	4.49
27	1	42.01	7	3	22.66	2.67
28	2	38.88	4.66	-	-	-
29	1	42.01	7	2	65.21	1.50
30	1	47.15	5.91	3	14.76	0.35
31	0	177.13	2.97	0	166.14	1.66
32	2	25.48	3.08	-	-	-
33	2	25.48	3.08	-	-	-



LH



REP

Table S2

Impurity content (%)	Crystal		CM (1:1)					APM (1:1)				
	LH	REP	Freshly prepared	^a 25 °C 90 d	^a 25 °C 10 d	^b 40 °C 10 d	^c 60 °C 10 d	Freshly prepared	^a 25 °C 90 d	^a 25 °C 10 d	^b 40 °C 10 d	^c 60 °C 10 d
Peak 1	0.0889	–	0.0923	0.0935	0.0899	0.0955	0.0938	0.0912	0.0934	0.0937	0.0969	0.1044
Peak 1'	–	0.0790	0.0854	0.0943	0.0930	0.1279	0.1800	0.0869	0.0931	0.0908	0.1333	0.1852
Peak 2'	–	–	–	–	–	0.0292	0.0673	–	–	–	0.0319	0.0691
Total amount	0.0889	0.0790	0.1777	0.1878	0.1829	0.2526	0.3411	0.1781	0.1865	0.1845	0.2621	0.3587

^a: Long-term storage condition, 25 °C/60% RH; ^b: 40 °C in oven; ^c: 60 °C in oven.