crystals

Supplementary Materials: Enhancement of Crystallization Process of the Organic Pharmaceutical Molecules through High Pressure

Yaoguang Feng [1], Hongxun Hao [1,2], Yiqing Chen [1], Na Wang [1,2], Ting Wang [1,2] and Xin Huang [1,2]*

Table S1. Mole fraction solubility of RBV (Form I) at 0.1 MPa and 12.0 MPa.

T/K	10^3x			
	Dimethylformamide		Dimethylacetamide	
	p = 0.1 MPa	*p* = 12.0 MPa	*p* = 0.1 MPa	*p*=12.0MPa
283.15	38.4	37.9	63.6	62.3
288.15	39.3	38.6	65.7	64.2
293.15	41.2	40.3	70.0	68.7
298.15	44.4	43.2	74.3	73.1
303.15	47.8	46.3	79.9	77.8
308.15	51.4	50.1	84.6	82.8
313.15	56.8	54.6	89.0	86.0
318.15	61.9	59.3	94.5	90.9
323.15	66.4	63.7	98.6	94.3

Table S2. Mole fraction solubility of RBV (Form I and Form II) in water at 0.1 MPa and 12.0 MPa.

T/K	10^3x			
	Form I		Form II	
	p = 0.1 MPa	*p* = 12.0 MPa	*p* = 0.1 MPa	*p* = 12.0 MPa
283.15	5.08	4.19	5.43	4.56
288.15	5.97	5.01	6.25	5.49
293.15	7.38	6.63	7.93	7.10
298.15	9.97	9.02	10.9	9.49
303.15	13.6	11.6	14.4	11.9
308.15	17.6	15.3	18.5	16.0
313.15	23.8	20.4	25.1	21.3
318.15	30.7	28.2	32.6	29.2
323.15	38.5	36.4	41.4	37.2

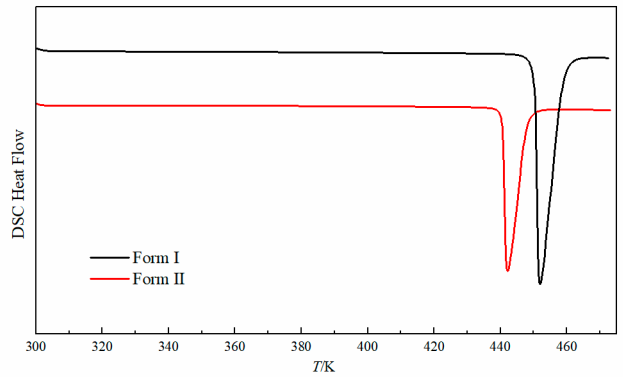

Figure S1. The DSC plots of the RBV raw material (Form I and Form II).

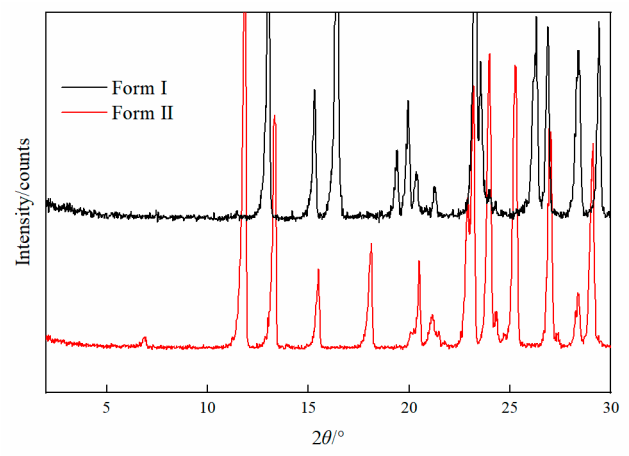

Figure S2. The PXRD patterns of the RBV raw material (Form I and Form II).

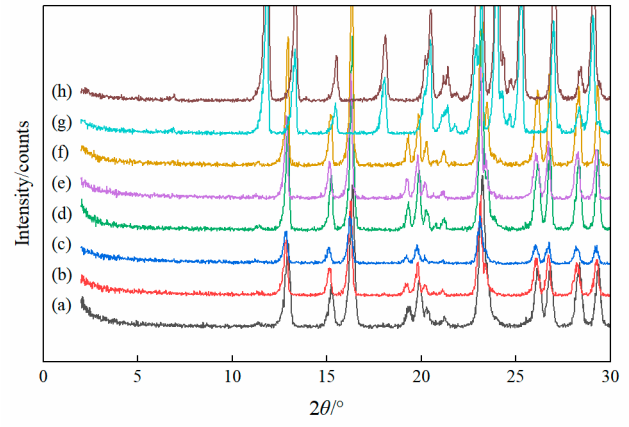

Figure S3. The PXRD patterns of residual solid in solubility experiment: (**a**–**c**) Form I in DMF, DMA, and water at 0.1 MPa, (**d**–**f**) Form I in DMF, DMA, and water at 12.0 MPa, (**g**) Form II in water at 0.1 MPa, (h) Form II in water at 12.0 MPa.

Table S3. The induction time and coefficient of variation of cooling crystallization of RBV in water at different pressures.

	S	Experimental t_{ind}/min			Average	c_v/%
T = 283.15 K p = 0.1 MPa	1.909	1057	1045	1016	1039	1.66
	2.011	879	842	830	850	2.45
	2.113	687	662	642	664	2.77
	2.215	470	462	431	454	3.70
	2.316	261	247	238	249	3.81
	2.418	141	133	129	134	3.71
T = 283.15 K p = 5.0 MPa	1.909	760	744	730	745	1.65
	2.011	573	564	550	562	1.68
	2.113	496	472	485	484	2.03
	2.215	366	358	342	355	2.81
	2.316	176	169	192	179	5.38
	2.418	105	115	119	113	5.21
T = 283.15 K p = 10.0 MPa	1.909	620	644	607	624	2.46
	2.011	499	474	484	486	2.12
	2.113	409	396	414	406	1.87
	2.215	287	276	305	289	4.13
	2.316	153	147	173	158	7.05
	2.418	101	91	87	93	6.33
T = 293.15 K p = 0.1 MPa	1.914	955	970	931	952	1.69
	2.016	736	701	721	719	1.99
	2.119	537	519	508	521	2.29
	2.221	287	293	309	296	3.13
	2.324	205	192	215	204	4.62
	2.427	148	153	139	147	3.95
T = 293.15 K p = 5.0 MPa	1.914	717	696	683	699	2.00
	2.016	519	492	484	498	3.00
	2.119	401	381	395	392	2.14
	2.221	181	176	165	174	3.84
	2.324	119	129	135	128	5.17
	2.427	84	87	95	89	5.24
T = 293.15 K p = 10.0 MPa	1.914	551	566	541	553	1.86
	2.016	417	401	406	408	1.64
	2.119	312	323	299	311	3.15
	2.221	128	117	111	119	5.93
	2.324	91	82	79	84	6.07
	2.427	59	67	64	63	5.21
T = 303.15 K p = 0.1 MPa	1.718	842	827	814	828	1.38
	1.821	515	499	487	500	2.29
	1.925	274	282	261	272	3.18
	2.030	226	234	237	232	2.00
	2.134	186	173	176	178	3.12
T = 303.15 K p = 5.0 MPa	1.718	604	624	600	609	1.72
	1.821	353	343	329	342	2.88
	1.925	203	216	236	218	6.22
	2.030	168	172	183	174	3.64
	2.134	126	117	130	124	4.37
T = 303.15 K p = 10.0 MPa	1.718	515	523	495	511	2.30
	1.821	231	237	254	241	4.05
	1.925	158	161	175	165	4.50
	2.030	131	134	141	135	3.10
	2.134	101	109	98	103	4.52