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Determination and Data Correlation of Solubility of Sofosbuvir Polymorphs in Ethyl Acetate + Toluene and Methyl *tert*-Butyl Ether Binary Solvents at the Temperature Range from 268.15 to 308.15 K

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Table 1. Main data of peaks in PXRD patterns of sofosbuvir of form **A** and form **B**.

Form A		Form B	
2θ	I (Height)%	2θ	I (Height)%
6.02	6.6	8.08	81.3
8.12	40.5	10.36	52.1
10.32	37.2	12.40	100.0
10.74	6.5	13.44	19.7
12.12	14.2	16.20	18.2
12.60	43.2	16.80	52.8
13.62	11.8	17.20	50.0
14.04	10.2	17.96	13.3
15.84	3.6	18.66	24.0
16.76	17.0	19.36	91.7
19.00	12.3	20.00	95.3
19.72	30.1	20.82	89.3
20.04	24.3	21.98	11.7
20.76	100.0	23.28	24.5
21.72	10.6	23.62	17.6
		24.34	11.1
		24.94	19.6
		25.32	26.8
		27.14	29.3
		28.00	24.8
		28.58	12.6
		29.02	7.3
		29.60	9.6
		31.30	20.0

Table 2. Experimental (x_A) and calculated (x_A^{cal}) solubility data of form **A** in ethyl acetate + toluene binary solvents[a].

T/K	$10^4 x_A$	$10^4 x_A^{cal}$		
		Apelblat	**CNIBS/R-K**	**Jouyban-Acree**
x_B = 0.32				
268.15	1.23	1.19	1.23	1.06
273.15	1.42	1.45	1.42	1.32
278.15	1.77	1.75	1.77	1.64
283.15	2.05	2.11	2.05	2.01
288.15	2.59	2.53	2.59	2.46
293.15	2.91	3.02	2.91	2.99
298.15	3.66	3.58	3.66	3.60
303.15	4.28	4.24	4.28	4.32
308.15	4.95	4.99	4.95	5.16
x_B = 0.36				
268.15	1.25	1.21	1.24	1.22
273.15	1.50	1.51	1.49	1.51
278.15	1.90	1.87	1.90	1.85
283.15	2.21	2.29	2.21	2.25
288.15	2.76	2.78	2.76	2.72
293.15	3.31	3.34	3.31	3.28
298.15	4.04	3.99	4.04	3.93
303.15	4.79	4.73	4.79	4.68
308.15	5.51	5.56	5.51	5.55
x_B = 0.40				
268.15	1.35	1.41	1.36	1.51
273.15	1.70	1.72	1.71	1.84
278.15	2.21	2.10	2.21	2.22
283.15	2.48	2.55	2.48	2.68
288.15	3.11	3.09	3.11	3.21
293.15	3.86	3.74	3.86	3.83
298.15	4.41	4.50	4.41	4.55
303.15	5.33	5.41	5.33	5.38
308.15	6.55	6.49	6.55	6.34
x_B = 0.46				
268.15	2.03	2.08	2.03	2.23
273.15	2.55	2.55	2.55	2.66
278.15	3.11	3.10	3.11	3.16
283.15	3.79	3.73	3.79	3.74
288.15	4.48	4.45	4.48	4.42
293.15	5.26	5.25	5.26	5.19
298.15	6.12	6.16	6.12	6.08
303.15	7.07	7.16	7.07	7.10
308.15	8.33	8.27	8.33	8.27
x_B = 0.53				
268.15	3.18	3.25	3.18	3.13
273.15	3.74	3.74	3.74	3.66
278.15	4.34	4.32	4.34	4.26
283.15	5.10	4.98	5.10	4.96
288.15	5.76	5.74	5.76	5.75
293.15	6.57	6.62	6.57	6.65

298.15	7.55	7.64	7.55	7.68
303.15	8.82	8.81	8.82	8.85
308.15	10.2	10.16	10.20	10.18

[a] x_B^0 denotes the initial mole fraction of ethyl acetate in binary solvents. The standard uncertainty of temperature is 0.1 K; the relative standard uncertainty of the solubility measurement is 0.05; the relative uncertainty of initial mole fraction is 0.01.

Table 3. Experimental (x_A) and calculated (x_A^{cal}) solubility data of form **B** in ethyl acetate + toluene binary solvents[a].

T/K	$10^4 x_A$	$10^4 x_A^{cal}$		
		Apelblat	**CNIBS/R-K**	**Jouyban-Acree**
x_B = 0.32				
268.15	1.72	1.70	1.72	1.55
273.15	1.97	1.96	1.97	1.84
278.15	2.20	2.27	2.20	2.17
283.15	2.64	2.62	2.64	2.55
288.15	3.08	3.03	3.06	2.99
293.15	3.46	3.52	3.44	3.49
298.15	4.10	4.07	4.05	4.06
303.15	4.74	4.73	4.70	4.71
308.15	5.47	5.48	5.44	5.45
x_B = 0.36				
268.15	2.00	1.98	2.00	2.09
273.15	2.33	2.35	2.33	2.51
278.15	2.77	2.79	2.78	3.01
283.15	3.35	3.32	3.35	3.58
288.15	3.97	3.97	4.01	4.25
293.15	4.78	4.76	4.83	5.03
298.15	5.66	5.72	5.77	5.92
303.15	6.95	6.89	7.04	6.93
308.15	8.30	8.32	8.37	8.10
x_B = 0.40				
268.15	2.35	2.32	2.35	2.42
273.15	2.81	2.85	2.81	2.96
278.15	3.50	3.49	3.49	3.60
283.15	4.15	4.25	4.15	4.36
288.15	5.34	5.17	5.31	5.25
293.15	6.23	6.27	6.19	6.30
298.15	7.56	7.58	7.47	7.51
303.15	9.13	9.15	9.05	8.92
308.15	11.02	11.00	10.96	10.55
x_B = 0.46				
268.15	3.21	3.28	3.21	2.78
273.15	3.96	3.99	3.96	3.49
278.15	4.78	4.83	4.78	4.37

283.15	6.01	5.82	6.01	5.42
288.15	7.12	6.99	7.13	6.69
293.15	8.25	8.36	8.26	8.20
298.15	9.88	9.96	9.91	10.00
303.15	11.77	11.82	11.79	12.13
308.15	14.05	13.98	14.07	14.63
x_B = 0.53				
268.15	4.35	4.55	4.35	4.74
273.15	5.89	5.95	5.89	6.12
278.15	7.78	7.69	7.78	7.84
283.15	9.70	9.85	9.70	9.96
288.15	12.93	12.49	12.93	12.56
293.15	15.89	15.71	15.89	15.72
298.15	19.51	19.60	19.51	19.56
303.15	23.67	24.25	23.67	24.17
308.15	30.11	29.79	30.11	29.68

[a] x_B^0 denotes the initial mole fraction of ethyl acetate in binary solvents. The standard uncertainty of temperature is 0.1 K; the relative standard uncertainty of the solubility measurement is 0.05; the relative uncertainty of initial mole fraction is 0.01.

Table 4. Experimental (x_A) and calculated (x_A^{cal}) solubility data of form **A** in MTBE + toluene binary solvents[a].

***T*/K**	**$10^4 x_A$**	**$10^4 x_A^{cal}$**		
		Apelblat	**CNIBS/R-K**	**Jouyban-Acree**
x_B = 0.40				
268.15	2.15	2.14	2.15	1.80
273.15	2.35	2.36	2.35	2.06
278.15	2.61	2.60	2.61	2.36
283.15	2.87	2.87	2.87	2.69
288.15	3.12	3.16	3.12	3.05
293.15	3.48	3.48	3.48	3.45
298.15	3.89	3.83	3.89	3.89
303.15	4.18	4.20	4.18	4.37
308.15	4.61	4.62	4.61	4.89
x_B = 0.46				
268.15	2.27	2.32	2.27	2.25
273.15	2.66	2.64	2.66	2.59
278.15	3.04	3.00	3.04	2.96
283.15	3.36	3.39	3.36	3.37
288.15	3.89	3.82	3.89	3.83
293.15	4.33	4.29	4.33	4.33
298.15	4.72	4.80	4.72	4.88
303.15	5.30	5.35	5.30	5.49
308.15	6.00	5.95	6.00	6.15
x_B = 0.53				

268.15	2.54	2.54	2.54	2.82
273.15	3.06	3.03	3.06	3.24
278.15	3.54	3.56	3.54	3.71
283.15	4.17	4.16	4.17	4.23
288.15	4.77	4.82	4.77	4.81
293.15	5.51	5.53	5.51	5.45
298.15	6.42	6.30	6.42	6.16
303.15	7.06	7.13	7.06	6.93
308.15	8.03	8.02	8.03	7.78
x_B = 0.63				
268.15	3.13	3.24	3.13	3.45
273.15	3.81	3.77	3.81	3.98
278.15	4.43	4.37	4.43	4.57
283.15	5.18	5.06	5.18	5.23
288.15	5.83	5.83	5.83	5.96
293.15	6.56	6.71	6.56	6.78
298.15	7.70	7.71	7.70	7.69
303.15	8.86	8.83	8.86	8.69
308.15	10.1	10.09	10.10	9.80
x_B = 0.77				
268.15	4.23	4.38	4.23	4.20
273.15	5.07	5.02	5.07	4.86
278.15	5.78	5.74	5.78	5.62
283.15	6.72	6.56	6.72	6.47
288.15	7.57	7.48	7.57	7.42
293.15	8.38	8.51	8.38	8.50
298.15	9.59	9.66	9.59	9.70
303.15	10.83	10.95	10.83	11.05
308.15	12.50	12.38	12.50	12.55

[a] x_B^0 denotes the initial mole fraction of ethyl acetate in binary solvents. The standard uncertainty of temperature is 0.1 K; the relative standard uncertainty of the solubility measurement is 0.05; the relative uncertainty of initial mole fraction is 0.01.

Table 5. Experimental (x_A) and calculated (x_A^{cal}) solubility data of form **B** in MTBE + toluene binary solvents[a].

***T*/K**	**$10^4 x_A$**	**$10^4 x_A^{cal}$**		
		Apelblat	**CNIBS/R-K**	**Jouyban-Acree**
x_B = 0.40				
268.15	2.4	2.49	2.40	2.34
273.15	3.01	2.95	3.01	2.81
278.15	3.52	3.48	3.52	3.36
283.15	4.16	4.08	4.16	3.99
288.15	4.74	4.77	4.74	4.72
293.15	5.43	5.56	5.43	5.54
298.15	6.52	6.46	6.52	6.49

303.15	7.48	7.47	7.48	7.56
308.15	8.62	8.62	8.62	8.78
x_B = 0.46				
268.15	2.75	2.76	2.75	2.90
273.15	3.41	3.40	3.41	3.48
278.15	4.12	4.12	4.12	4.14
283.15	4.89	4.95	4.89	4.91
288.15	5.93	5.88	5.93	5.80
293.15	7.02	6.93	7.02	6.82
298.15	8.04	8.08	8.04	7.98
303.15	9.24	9.34	9.24	9.31
308.15	10.77	10.71	10.77	10.81
x_B = 0.53				
268.15	3.26	3.31	3.26	3.37
273.15	3.96	3.96	3.96	4.04
278.15	4.74	4.72	4.74	4.81
283.15	5.53	5.61	5.53	5.71
288.15	6.89	6.65	6.89	6.74
293.15	7.85	7.86	7.85	7.93
298.15	9.14	9.27	9.14	9.30
303.15	10.85	10.91	10.85	10.86
308.15	12.88	12.81	12.88	12.65
x_B = 0.63				
268.15	3.88	3.80	3.88	3.91
273.15	4.66	4.60	4.66	4.68
278.15	5.51	5.54	5.51	5.58
283.15	6.4	6.62	6.40	6.63
288.15	7.93	7.87	7.93	7.86
293.15	9.27	9.31	9.27	9.27
298.15	11.04	10.9 5	11.04	10.90
303.15	12.93	12.82	12.93	12.78
308.15	14.84	14.94	14.84	14.94
x_B = 0.77				
268.15	4.65	4.74	4.65	4.62
273.15	5.65	5.63	5.65	5.54
278.15	6.85	6.67	6.85	6.62
283.15	7.65	7.91	7.65	7.89
288.15	9.67	9.36	9.67	9.37
293.15	11.05	11.07	11.05	11.11
298.15	12.81	13.09	12.81	13.14
303.15	15.6	15.45	15.60	15.49
308.15	18.22	18.23	18.22	18.22

[a] x_B^0 denotes the initial mole fraction of ethyl acetate in binary solvents. The standard uncertainty of temperature is 0.1 K; the relative standard uncertainty of the solubility measurement is 0.05; the relative uncertainty of initial mole fraction is 0.01.

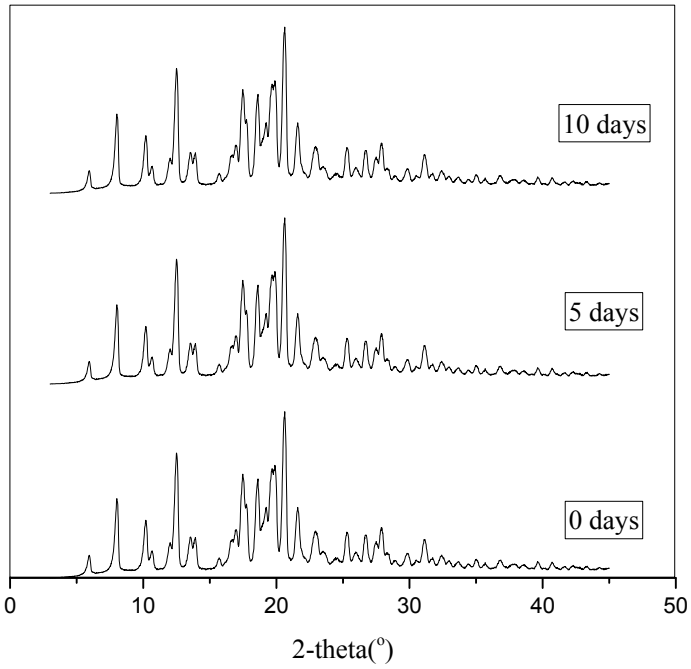

Figure 1. PXRD patterns of sofosbuvir of form **A** over high temperature stability testing.

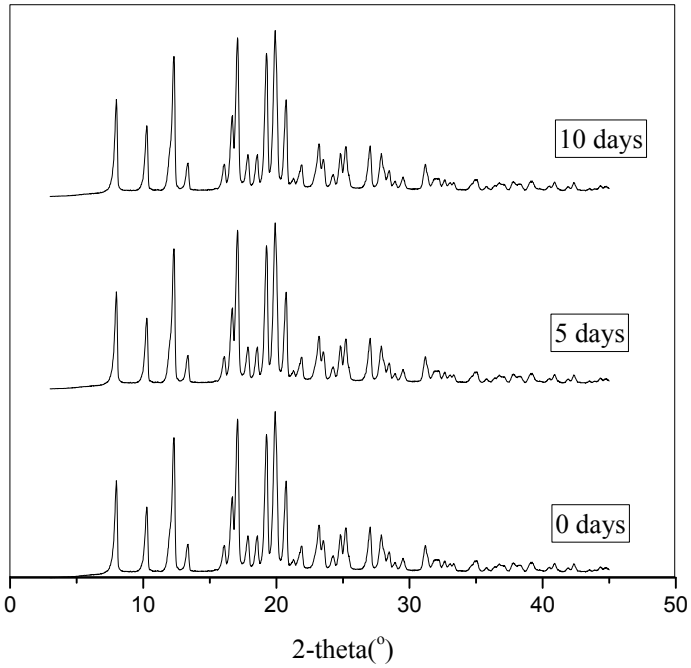

Figure 2. PXRD patterns of sofosbuvir of form **B** over high temperature stability testing.

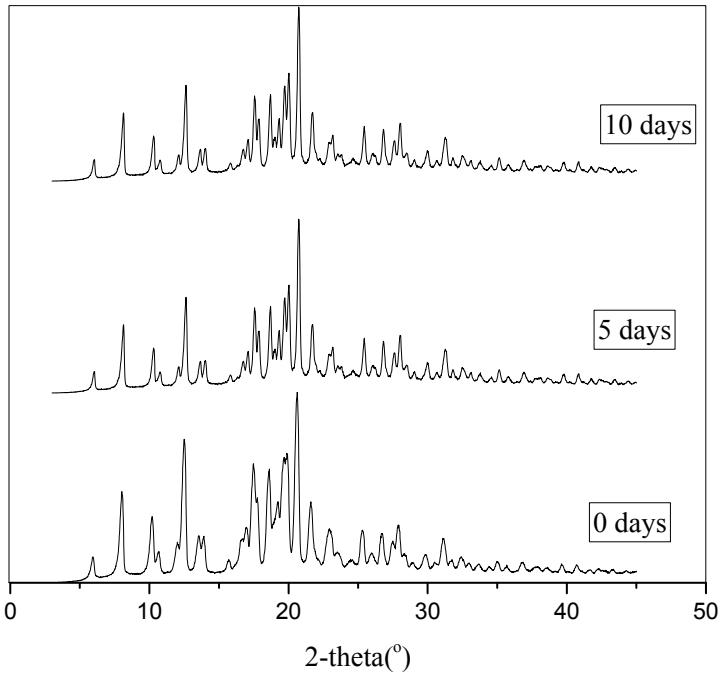

Figure 3. PXRD patterns of sofosbuvir of form **A** over high humidity stability testing.

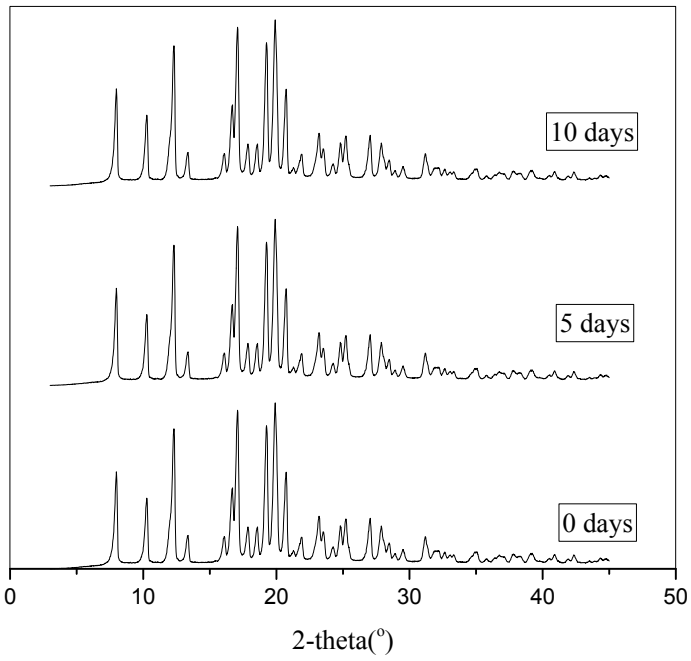

Figure 4. PXRD patterns of sofosbuvir of form **B** over high humidity stability testing.

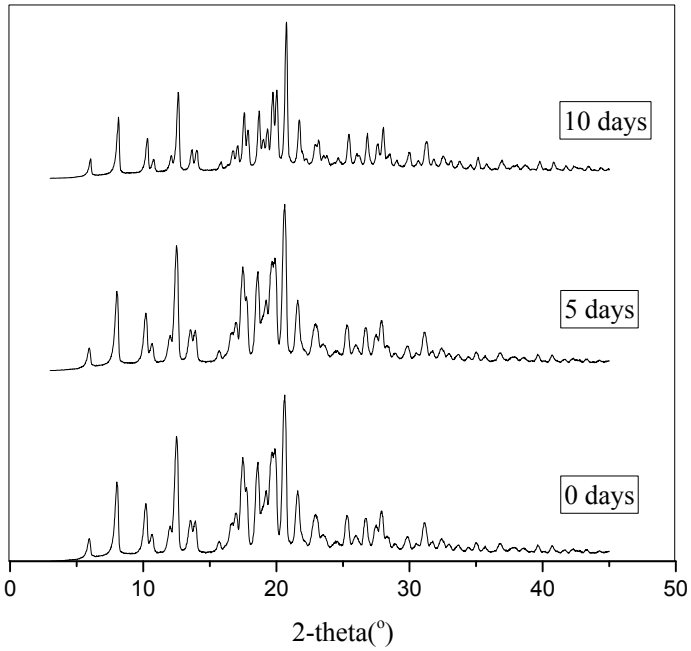

Figure 5. PXRD patterns of sofosbuvir of form **A** over strong light exposure stability testing.

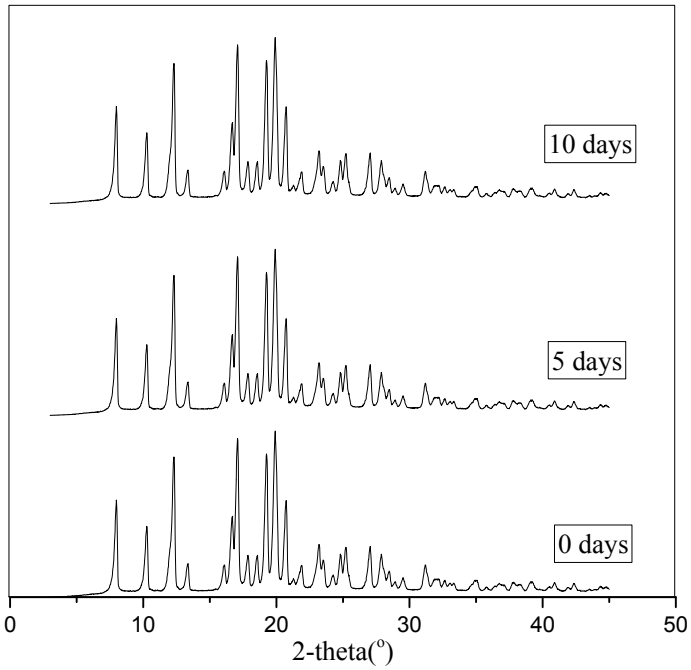

Figure 6. PXRD patterns of sofosbuvir of form **B** over strong light exposure stability testing.