

Electronic Supplementary Information (ESI)

Synthon-driven polymorphism in the favipiravir-theophylline cocrystal

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Table S1. Summary of experiments performed for reproducing FAV-THP form II.

Sl. No.	FAV-THP	Method	Solvent	Result
1.	1:1	Solvent evaporation (SE)	Ethanol	Form I
2.	1:1		Methanol	
3.	1:1		Isopropyl alcohol (IPA)	
4.	1:1		1-Butanol	
5.	1:1		N,N-dimethylacetamide (NNDMA)	
6.	1:1		2-butanol	
7.	1:1		Nitromethane	
8.	1:1		Ethylacetoacetate	Phase separation
9.	1:1		Isopropyl acetate	Form I
10.	1:1		Tetrahydrofuran (THF)	Phase separation
11.	1:1		Butane-2-one	Form I
12.	1:1		Acetonitrile (ACN)	
13.	1:1		1,4-dioxane	
14.	1:1		Dimethylsulfoxide (DMSO)	
15.	1:1		DCM, nitromethane	
16.	1:1		Chloroform, THF	
17.	1:1		IPA, 1-butanol	
18.	1:1		Methanol, ethanol	
19.	1:1		Acetone, THF	
20.	1:1		Ethanol, ethylacetoacetate	
21.	1:1		Chloroform, nitromethane	
22.	1:1		2-butanol, ethylacetate	
23.	1:1		Butane-2-ol, IPA	
24.	1:1		Nitromethane, THF	
25.	1:1		Acetic acid, nitromethane	
26.	1:1		Methanol, IPA	
27.	1:1		Acetic acid, IPA	
28.	1:1		Acetone, ethanol	
29.	1:1		Chloroform, acetic acid	
30.	1:1		THF, butane-2-one	
31.	1:1		Acetic acid, methanol, ethanol	
32.	1:1		Methanol, NNDMA, nitromethane	
33.	1:1		Dimethylformamide (DMF), IPA, ethanol	
34.	1:1		1,4-dioxane, 1-propanol, ethanol	

35.	1:1		Isopropylacetate, ethylacetate, methanol	
36.	1:1		ACN, methanol, IPA	
37.	1:1		DMSO, methanol, 1-propanol	
38.	1:1		Methanol, ACN, ethanol	
39.	1:1		Nitromethane, methanol, 1-propanol	
40.	1:1		Chloroform, DMF, DMSO	
41.	1:1		Methanol, DMSO, DMF	
42.	1:1		Chloroform, methanol, nitromethane	
43.	1:1		DMSO, ethanol, methanol	
44.	1:1		Chloroform, DMF, ethanol	
45.	1:1		Methanol, ACN, 1-propanol	
46.	1:2		2-butanol	
47.	1:2		Methanol/2-butanol	
48.	1:2		2-butanol	
49.	1:2		Ethanol	
50.	2:1		IPA	
51.	1:2		Ethanol/IPA	
52.	1:3		Methanol	
53.	3:1		Methanol	
54.	4:1		IPA/methanol	Form I
55.	1:4		IPA/ methanol	
56.	1:1		Methanol, SPAN-20 (5%)	
57.	1:1		Methanol, hydroxypropyl cellulose (5%)	
58.	1:1		Methanol, TWEEN-80 (5%)	
59.	1:1		Ethanol, lactose monohydrate (2%)	
60.	1:1		Methanol/ ethanol (1:1), SPAN-80 (10%)	
61.	1:1	Anti-solvent crystallization	IPA, hexane	Physical mixture
62.	1:1		Methanol, heptanes	Form I
63.	1:1	Vapor diffusion	Acetone, hexane	Physical mixture
64.	1:1		ACN, hexane	Form I
65.	1:1		ACN, heptane	
66.	1:1		Methanol, hexane	
67.	1:1		Methanol, heptane	
68.	1:1		IPA, hexane	
69.	1:1		Methanol, hexane	
70.	1:1		Acetone, hexane	
71.	1:1		Methanol, THF	

72.	1:1			Ethanol, DCM
73.	1:1			Ethanol, THF
74.	1:1			Acetic acid, hexane
75.	1:1			NNDMA, heptane
76.	1:1			1-butanol, hexane
77.	1:1			Nitromethane, cyclohexane
78.	1:1			1-butanol, heptane
79.	1:1			NNDMA, benzene
80.	1:1	Rotary evaporation	60 °C, 70rpm	1-butanol
81.	1:1		55 °C, 70 rpm	DCM, methanol
82.	1:1		60 °C, 70rpm	IPA
83.	1:1		60 °C, 70rpm	methanol
84.	1:1		60 °C, 70rpm	ethanol
85.	1:1		60 °C, 70rpm	Ethanol, 1-propanol
86.	1:1		60 °C, 70rpm	IPA-methanol
87.	1:1		50 °C, 50 rpm	1-propanol, ethanol
88.	1:1		50 °C, 80 rpm	1-propanol, ethanol
89.	1:1		50 °C, 100 rpm	1-propanol, ethanol
90.	1:1		50 °C, 150 rpm	1-propanol, ethanol
91.	1:1	Reflux, 100 °C, 2 hours		ethanol
92.	1:1	Cooling crystallization		Ethylacetoacetatae
93.	1:1			Acetone
94.	1:1			IPA
95.	1:1	Rapid solvent evaporation under vacuum (speed vac.)	60 °C	IPA
96.	1:1			Ethanol
97.	1:1			ACN
98.	1:1			Methanol
99.	1:1			Ethanol, methanol
100.	1:1			Methanol, ACN
101.	1:1			IPA, ethanol
102.	1:1			IPA, methanol

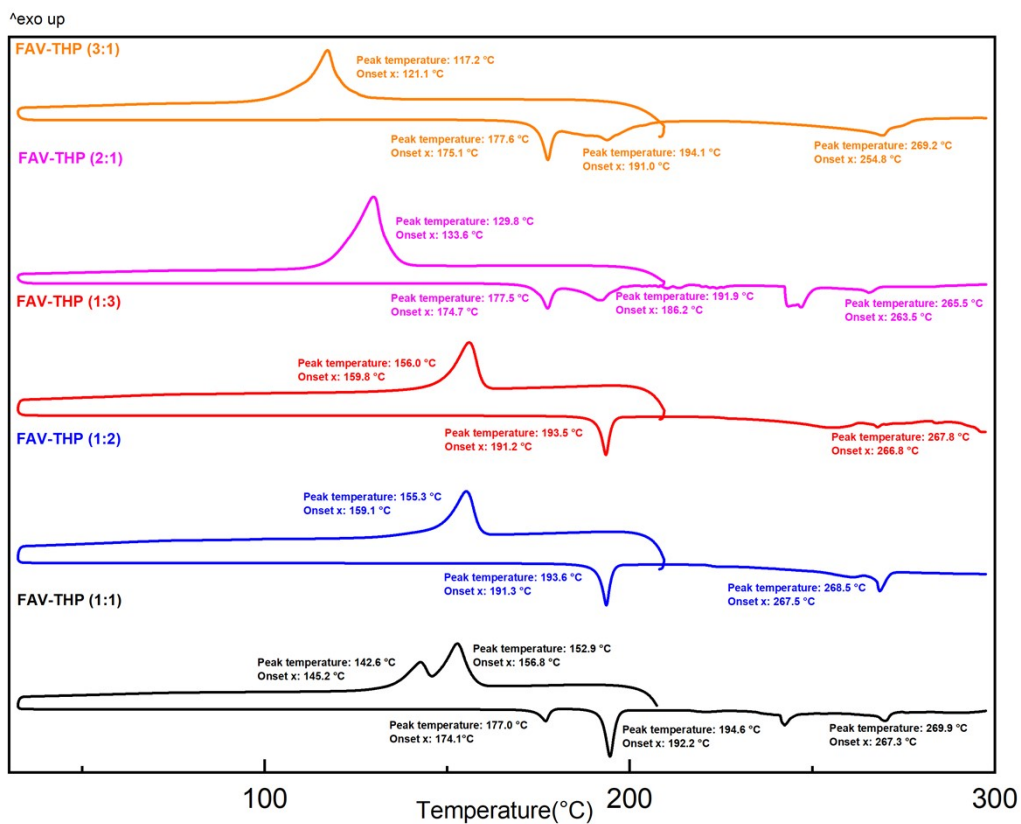


Figure S1. DSC overlays of cooling and second heating cycle of varying compositions of FAV and THP.

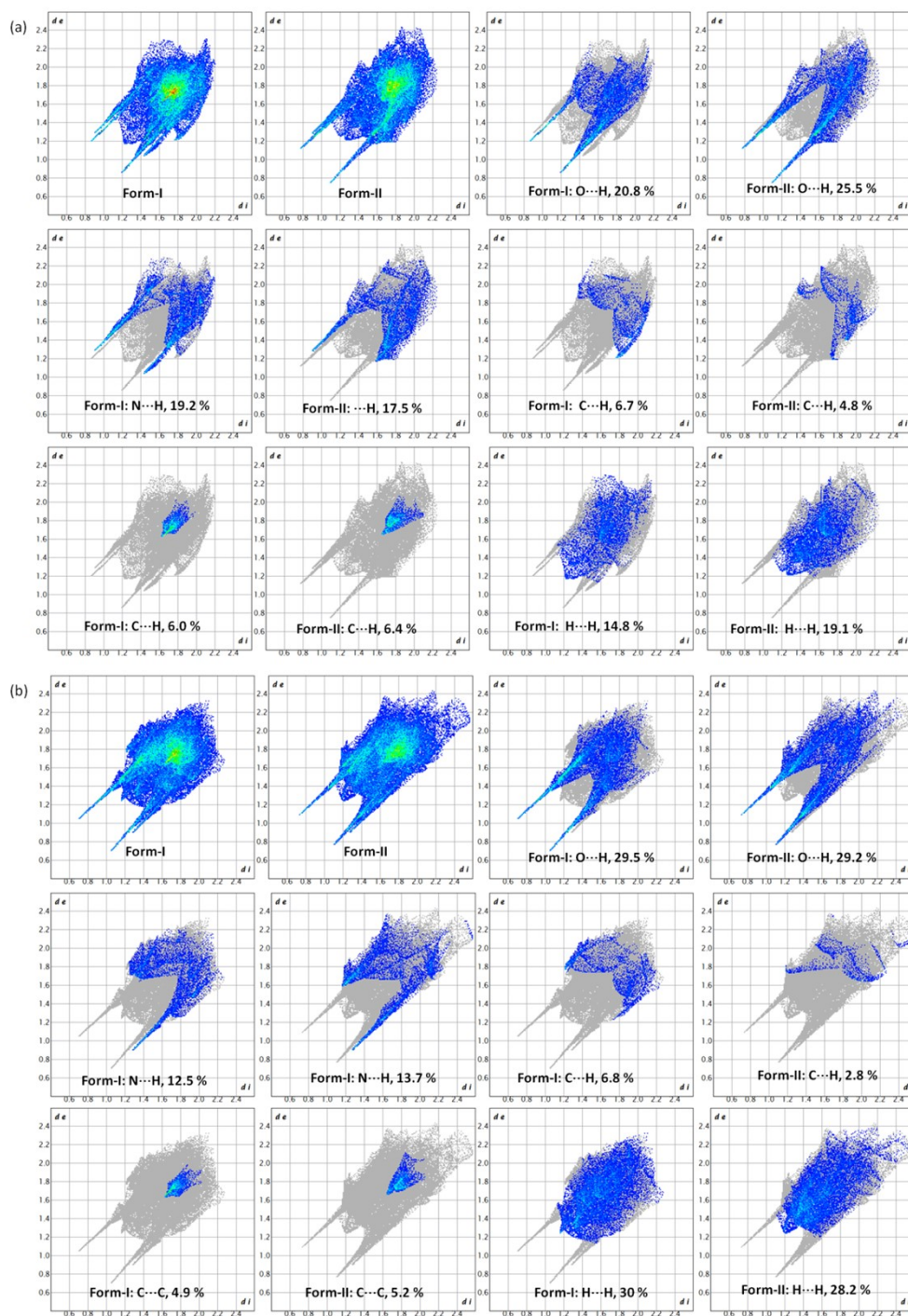


Figure S2. Fingerprint plot analysis of (a) favipiravir, (b) theophylline in FAV-THP cocrystal forms I and II. The fingerprint plot quantifies the percentage of O...H, N...H, C...H, C...C and H...H contacts.