

Supplementary Materials: Identification and Pharmaceutical Characterization of a New Itraconazole Terephthalic Acid Cocrystal

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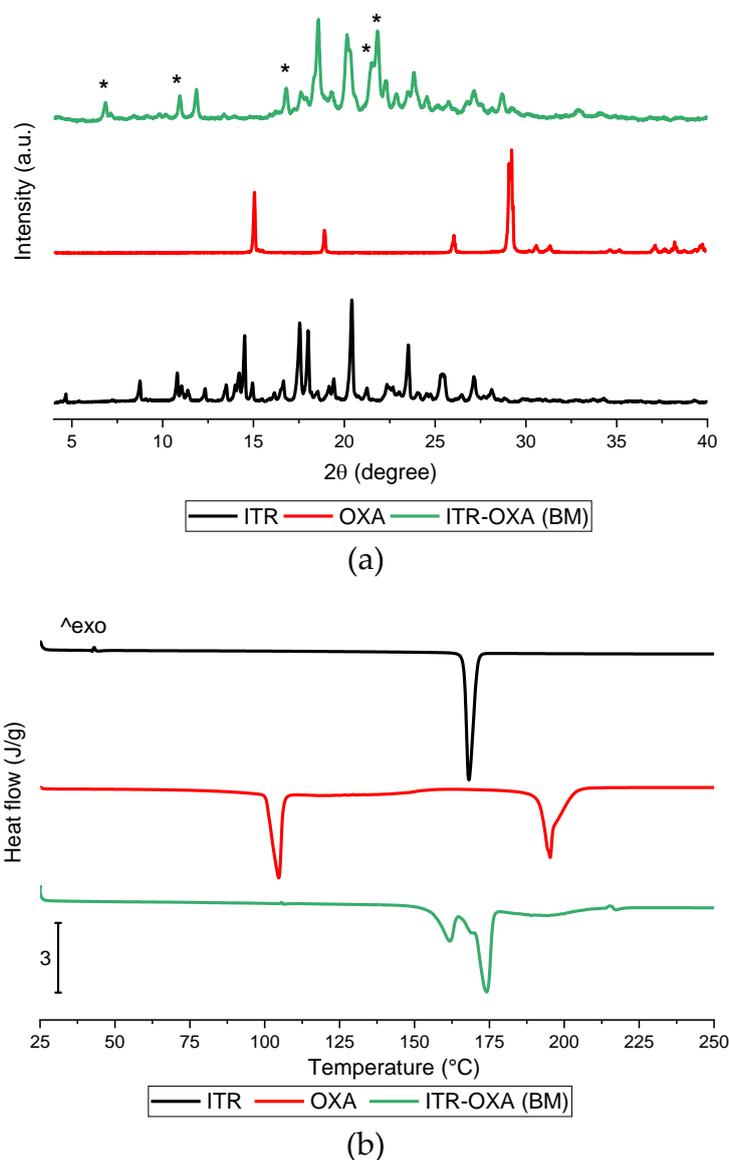


Figure S1. (a) PXRD patterns of itraconazole (ITR) and oxalic acid (OXA) starting material powders and ITR-OXA cocrystal produced by ball milling (BM). * indicate distinct peaks of the cocrystal. (b) DSC thermograms of ITR and OXA starting material powders and ITR-OXA cocrystal.

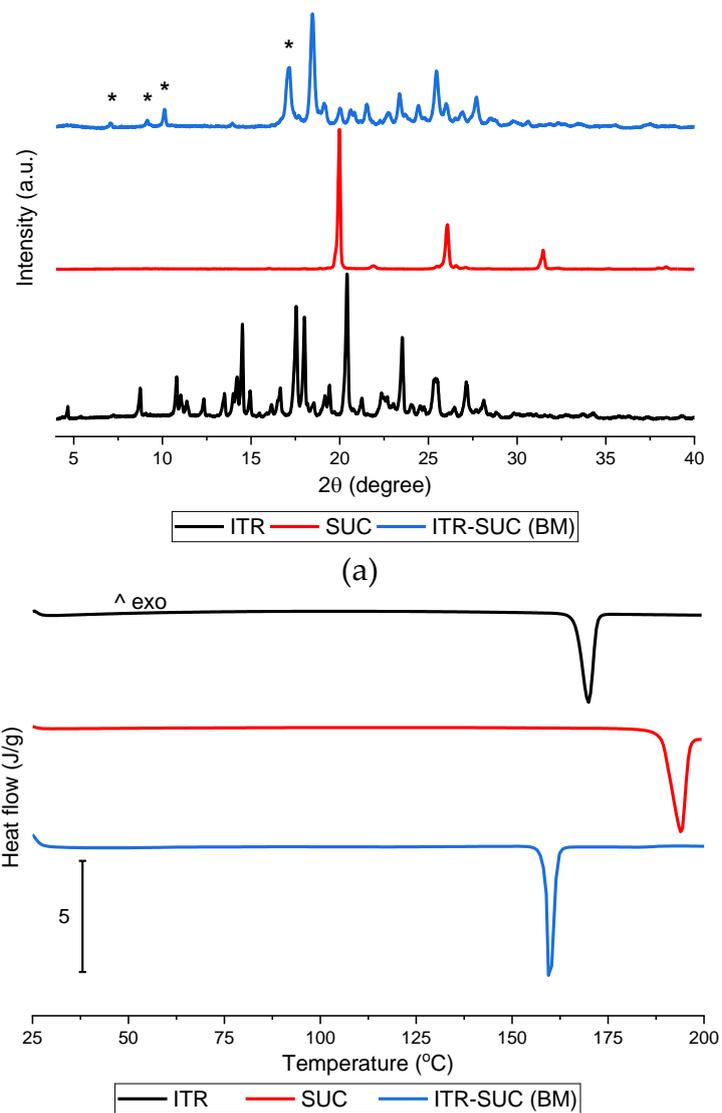


Figure S2. (a) PXRD patterns of itraconazole (ITR) and succinic acid (SUC) starting material powders and ITR-SUC cocrystal produced by ball milling (BM). * indicate distinct peaks of the cocrystal. (b) DSC thermograms of ITR and SUC starting material powders and ITR-SUC cocrystal.

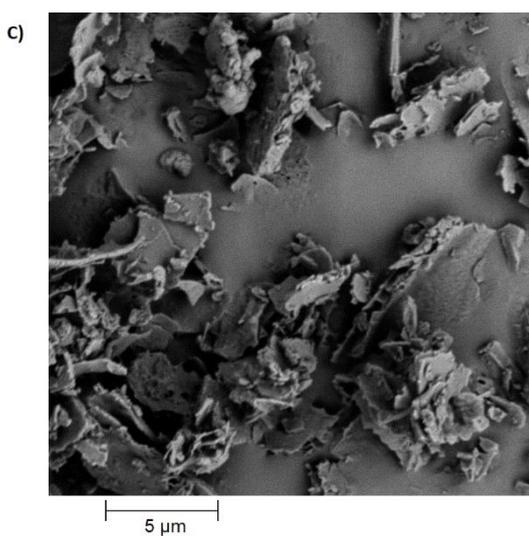
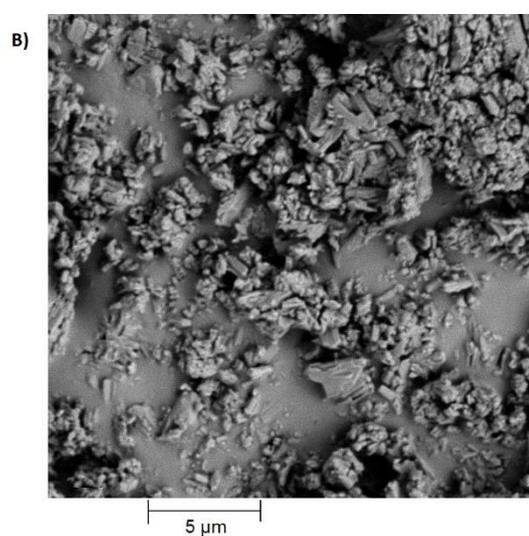
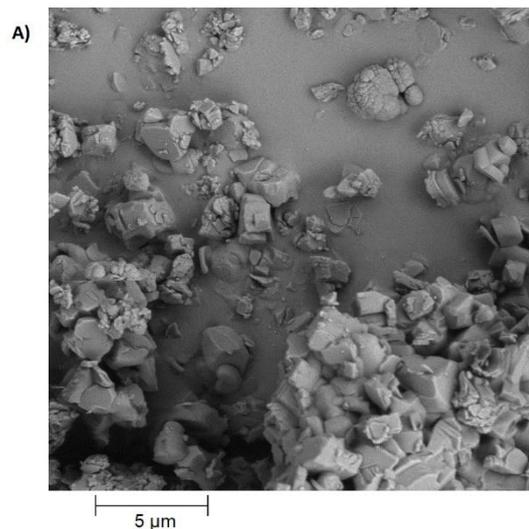
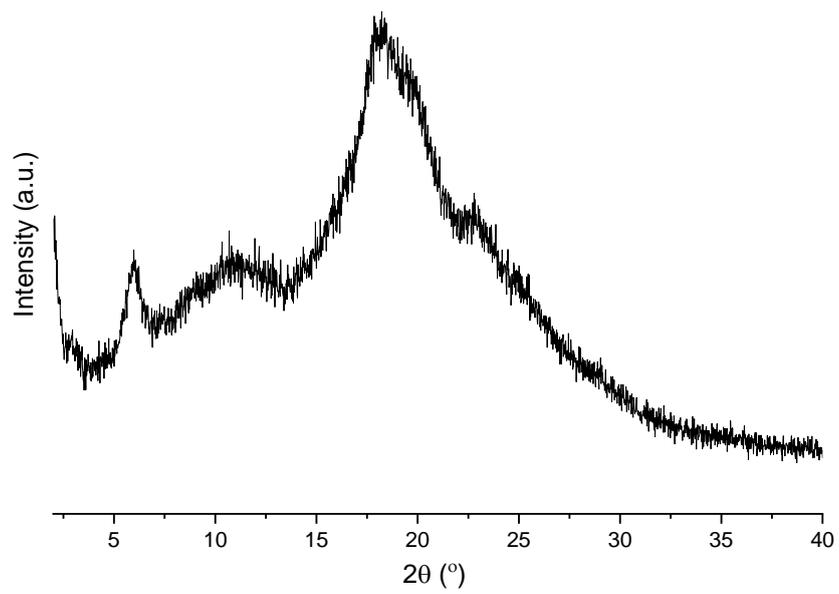
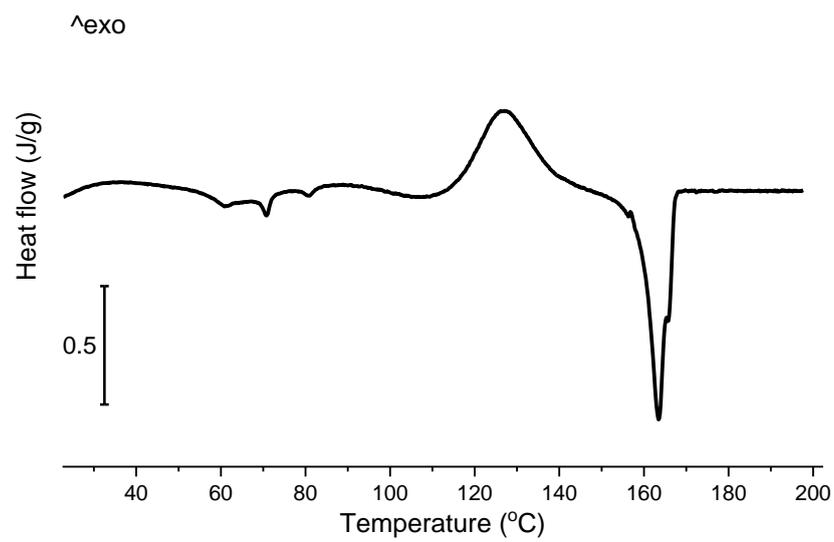


Figure S3. Scanning electron micrographs of (a) ITR-SUC cocrystal and (b) ITR-OXA cocrystal produced by ball mill; (c) freeze dried ITR.



(a)



(b)

Figure S4. (a) PXRD pattern of freeze dried itraconazole (ITR FD) (b) DSC thermogram of of freeze dried itraconazole (ITR FD).

Table S1. Crystal data and structure refinement for ITR-TER cocrystal.

CCDC No.	2015894	
Empirical formula	C ₃₉ H ₄₁ Cl ₂ N ₈ O ₆	
Formula weight (Da)	788.70	
Temperature of measurement (K)	100 ± 2	
Wavelength (Å)	1.54178	
Crystal system	Triclinic	
Space group	P $\bar{1}$	
Unit cell dimensions (Å, °)	a = 10.3910 ± 6	α = 81.310 ± 5
	b = 14.3714 ± 10	β = 81.019 ± 6
	c = 25.418 ± 2	γ = 89.951 ± 4
Volume (Å ³)	3705.2 ± 5	
Z	4	
Calculated density (mg/m ³)	1.414	
Absorption coefficient (mm ⁻¹)	2.075	
F(000)	1652	
Crystal size (mm ³)	0.15 × 0.14 × 0.03	
Theta range for data collection (°)	1.780 to 66.203	
Index ranges	-12 ≤ h ≤ 12, -15 ≤ k ≤ 16, -29 ≤ l ≤ 14	
Reflections collected	12852	
Independent reflections	12852 [R(int) = 0.1182]	
Completeness to theta = 66.203°	97.5 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.752586 and 0.547278	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	12852 / 435 / 1076	
Goodness-of-fit on F ²	1.093	
Final R indices [I > 2σ (I)]	R1 = 0.1069, wR2 = 0.2616	
R indices (all data)	R1 = 0.1188, wR2 = 0.2689	
Largest diff. peak and hole	0.703 and -1.004 e.Å ⁻³	

Table S2. Hydrogen bonds for ITR-TER cocrystal [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
C(10)-H(10)...O(50)	0.95	2.53	3.144(11)	123
C(63)-H(63)...O(103)	0.95	2.48	3.122(11)	125
O(48)-H(48)...N(9)	0.84	1.81	2.645(10)	171
O(101)-H(101)...N(62)	0.84	1.81	2.632(10)	167