ASSOCIATED CONTENT

Supporting Information

X-ray powder diffraction data

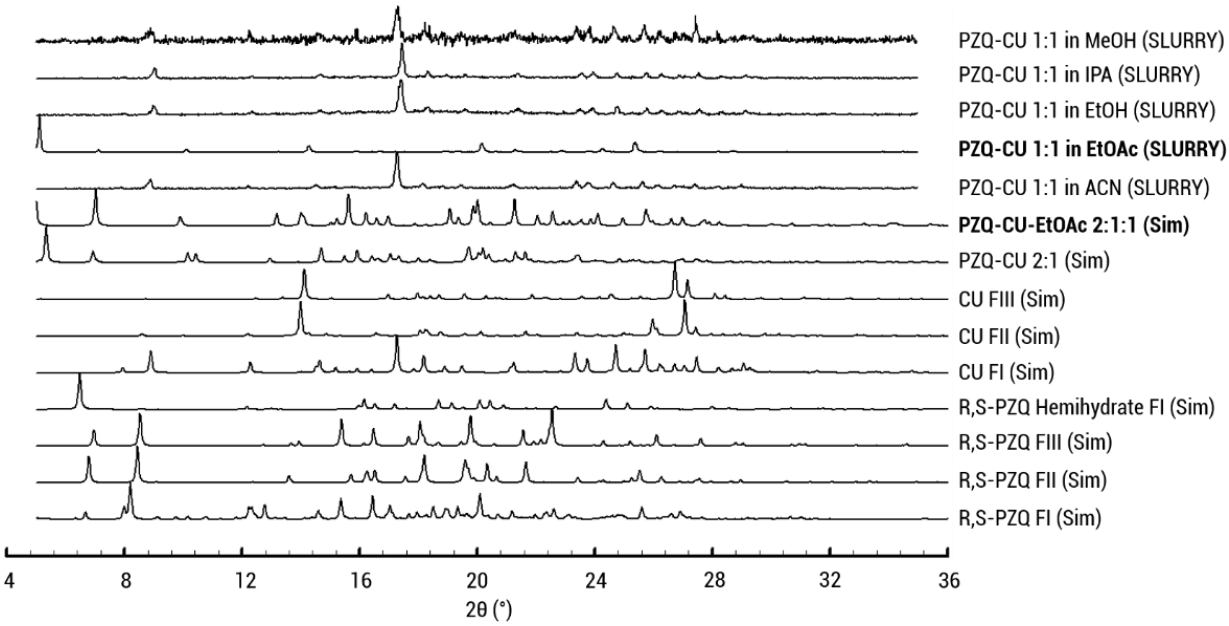

Figure S1. Normalized diffraction patterns. Simulated diffraction pattern of the known polymorphs (FI-III) and hemihydrate of the parent compounds racemic praziquantel and curcumin, praziquantel–curcumin cocrystal (PZQ-CU 2:1), and praziquantel–curcumin–ethyl acetate cocrystal solvate (PZQ-CU-EtOAc 2:1:1), and experimental patterns of the slurry sample powders obtained in acetonitrile (ACN), ethanol (EtOH), ethyl acetate (EtOAc), 2-propanol (IPA), and methanol (MeOH).

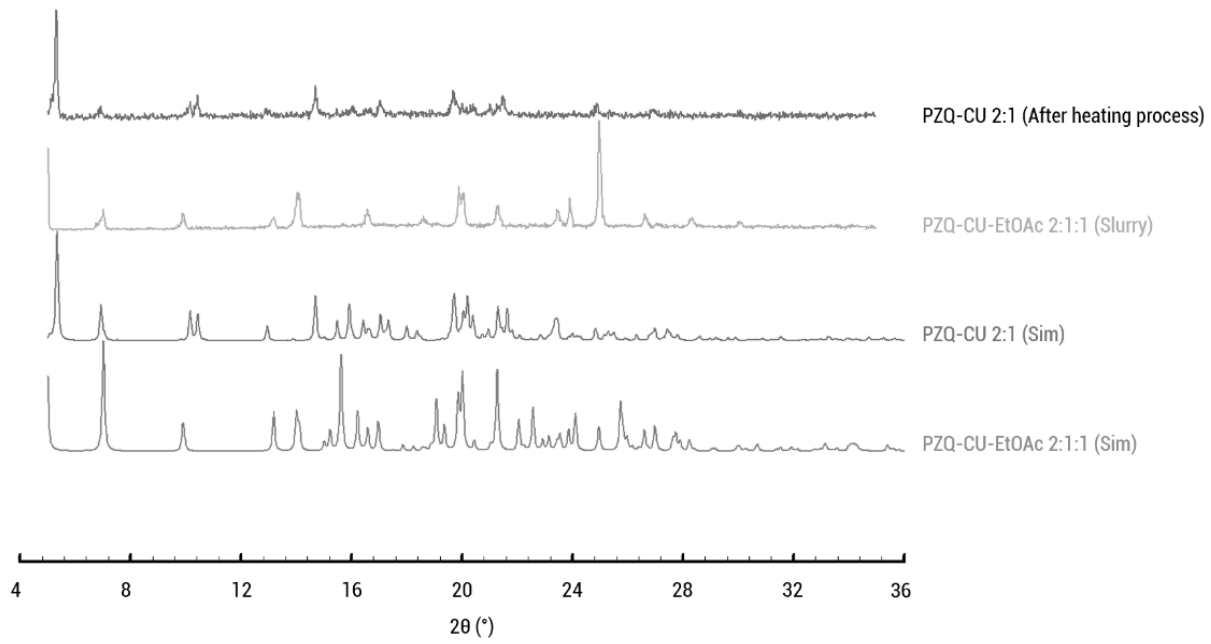

Figure S2. Normalized diffraction patterns. Simulated diffraction pattern of the praziquantel–curcumin cocrystal (PZQ-CU 2:1) and the praziquantel–curcumin–ethyl acetate cocrystal solvate (PZQ-CU-EtOAc 2:1:1), and the experimental patterns of the powders obtained after slurry in ethyl acetate and heating treatment (by DSC).

Single crystal X-ray diffraction data

Table S1. Crystal data and structure refinement for PZQ–CU–EtOAc (2:1:1) and the desolvated PZQ-CU (2:1) cocrystal.

Identification code	PZQ-CU-EtOAc (2:1:1)	PZQ-CU (2:1)
Empirical formula	$C_{63}H_{76}N_4O_{12}$	$C_{59}H_{68}N_4O_{10}$
Formula weight	1081.27	993.17
Temperature (K)	150.0(2)	297(2)
Wavelength (Å)	0.71073	0.71073
Crystal system	Monoclinic	Monoclinic
Space group	*C2/c*	$P2_1/n$
Unit cell dimensions (Å, °)	a = 37.570(2)	a = 27.330(4)
	b = 5.9187(3)	b = 5.8708(7)
	c = 26.6434(17)	c = 35.486(7)
	β= 110.574(7)	β = 111.06(2)
Volume $Å^3$	5546.6(6)	5313.5(17)
Z	4	4
Density (calc.) $mg.m^{-3}$	1.295	1.242
Absorption coeff. mm^{-1}	0.089	0.085
F (000)	2312	2120
Crystal size mm^3	0.50x 0.03 x 0.02	0.35 x 0.06 x 0.02
θ range for data collection (°)	3.267 to 25.242	3.147 to 17.230
Reflections collected	16301	10776
Independent reflections	4976 [R(int) = 0.0924]	3128 [R(int) = 0.1496]
Completeness to θ	99.4 % (θ=25.242°)	97.5 % (θ = 17.230°)
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.00 and 0.88	1.00 and 0.75
Refinement method	Full-matrix least-squares on F^2	
Data/restraints/parameters	4976 / 204 / 511	3128 / 635 / 660
Goodness-of-fit on F^2	1.102	1.099
Final R indices [$I > 2\sigma_I$]	R1 = 0.0785, wR2 = 0.1791	R_1 = 0.1265, wR_2 = 0.2385
R indices (all data)	R1 = 0.1129, wR2 = 0.1981	R_1 = 0.2128, wR_2 = 0.2791
Δρ max., min. ($e.Å^{-3}$)	0.455, -0.308	0.375 and -0.277

Table S2. Crystal data and structure refinement for the PZQ–CU–EtOAc (2:1:1) cocrystal at room temperature.

Identification code	PZQ-CU-EtOAc (2:1:1)
Empirical formula	$C_{63}\ H_{76}\ N_4\ O_{12}$
Formula weight	1081.27
Temperature (K)	297(2)
Wavelength (Å)	0.71073
Crystal system	Monoclinic
Space group	*C*2/*c*
Unit cell dimensions (Å, °)	a = 37.992(3)
	b = 5.9769(5)
	c = 26.8477(15)
	β= 110.218(7)
Volume ($Å^3$)	5720.8(7)
Z	4
Density (calculated) (g/cm^3)	1.255
Absorption coefficient (mm^{-1})	0.087
F (000)	2312
Crystal size (mm^3)	0.35x 0.06 x 0.02
Theta range for data collection (°)	3.234 to 25.514
Reflections collected	14153
Independent reflections	5310 [R(int) = 0.0341]
Completeness to θ = 25.242° (%)	99.3
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1.00 and 0.40
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	5310 / 204 / 511
Goodness-of-fit on F^2	1.059
Final R indices [$I > 2\sigma_I$]	R1 = 0.0515, wR2 = 0.1300
R indices (all data)	R1 = 0.0750, wR2 = 0.1409
Δρ max., min. ($e.Å^{-3}$)	0.171, -0.142

Table S3. Hydrogen bonds in the praziquantel–curcumin–ethyl acetate (2:1:1) cocrystal solvate and the desolvated praziquantel–curcumin (2:1) cocrystal.

				Interatomic Distances (Å)			Angles (°)
Descriptors	**Donors**	**H···**	**Acceptors**	**D-H**	**H···A**	**D···A**	**D-H···A**
	Praziquantel–curcumin–ethyl acetate (2:1:1) cocrystal solvate (150K)						
$D_1^1(2)$ *b*	O12	H12	O23	0.93(4)	1.73(4)	2.651(5)	171(4)
	Praziquantel–curcumin–ethyl acetate (2:1:1) cocrystal solvate (RT)						
$D_1^1(2)$ *b*	O12	H12	O23	0.89(3)	1.79(3)	2.673(7)	175(3)
	Desolvated praziquantel–curcumin (2:1) cocrystal						
$D_1^1(2)$ *b*	O12	H12	O23	0.82	1.81	2.634(18)	178
$D_1^1(2)$ *b*	O12’	H12’	O23B	0.82	1.82	2.640(18)	179

CCDC 2309015-2309017 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/structures.

Proton nuclear magnetic resonance (^{1}H NMR) data

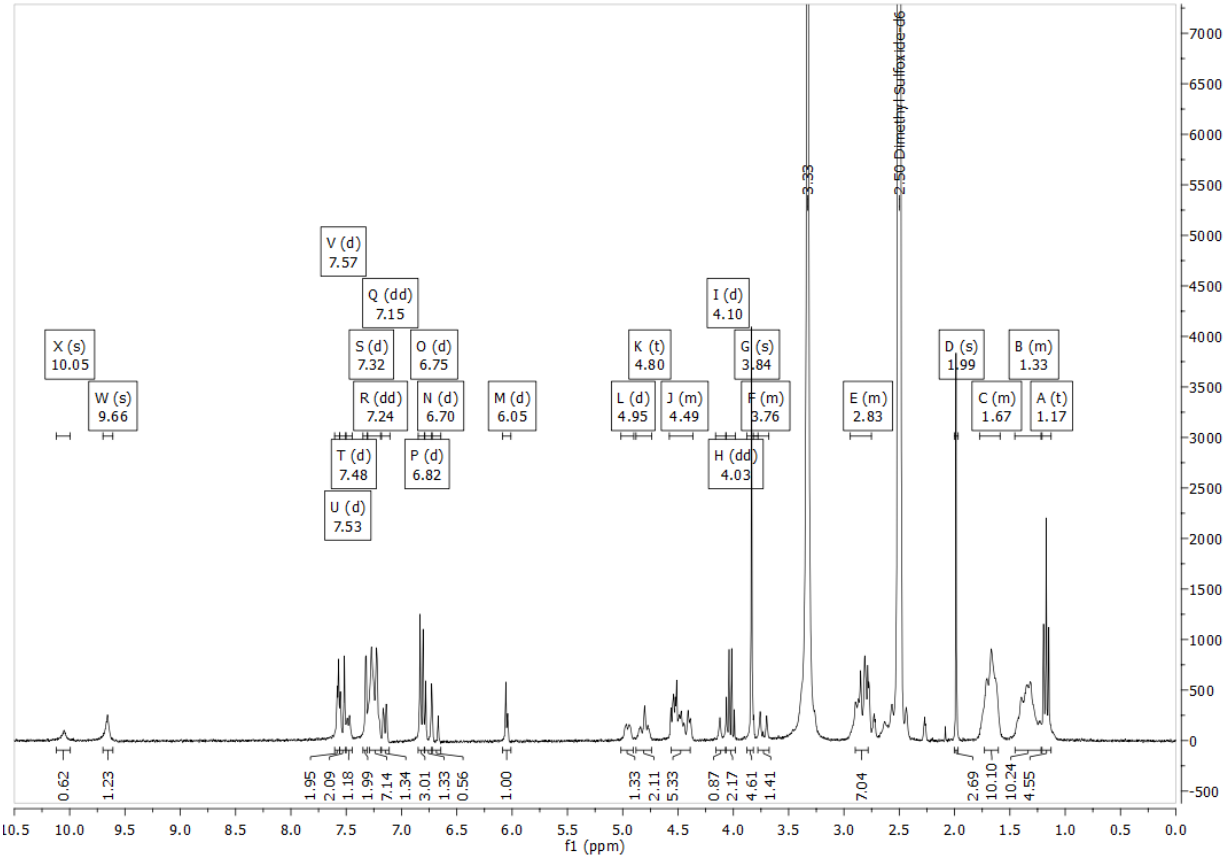

Figure S3. Proton NMR spectrum of the praziquantel–curcumin–ethyl acetate 2:1:1 cocrystal solvate obtained from the slurry experiment. The protons are colored in a shade of gray to match the corresponding products. ^{1}H NMR (300 MHz, DMSO-d^6) δ 10.05 (s, 1H), 9.66 (s, 1H), 7.57 (d, J = 3.5 Hz, 2H), 7.53 (d, J = 11.0 Hz, 2H), 7.48 (d, J = 5.9 Hz, 1H), 7.32 (d, J = 1.5 Hz, 2H), 7.24 (dd, J = 14.7, 5.9 Hz, 7H), 7.15 (dd, J = 8.2, 1.7 Hz, 1H), 6.82 (d, J = 8.2 Hz, 3H), 6.75 (d, J = 15.9 Hz, 1H), 6.70 (d, J = 15.9 Hz, 1H), 6.05 (d, J = 5.1 Hz, 1H), 4.95 (d, J = 7.0 Hz, 1H), 4.80 (t, J = 9.7 Hz, 2H), 4.60 – 4.35 (m, 5H), 4.13 (d, J = 3.6 Hz, 1H), 4.03 (dd, J = 14.3, 7.1 Hz, 2H), 3.84 (s, 5H), 3.82 – 3.67 (m, 1H), 2.95 – 2.70 (m, 7H), 1.99 (s, 3H), 1.77 – 1.59 (m, 10H), 1.46 – 1.22 (m, 10H), 1.17 (t, J = 7.1 Hz, 5H). δ 3.33 residual water peak. δ 2.50 DMSO-d^6 peak.

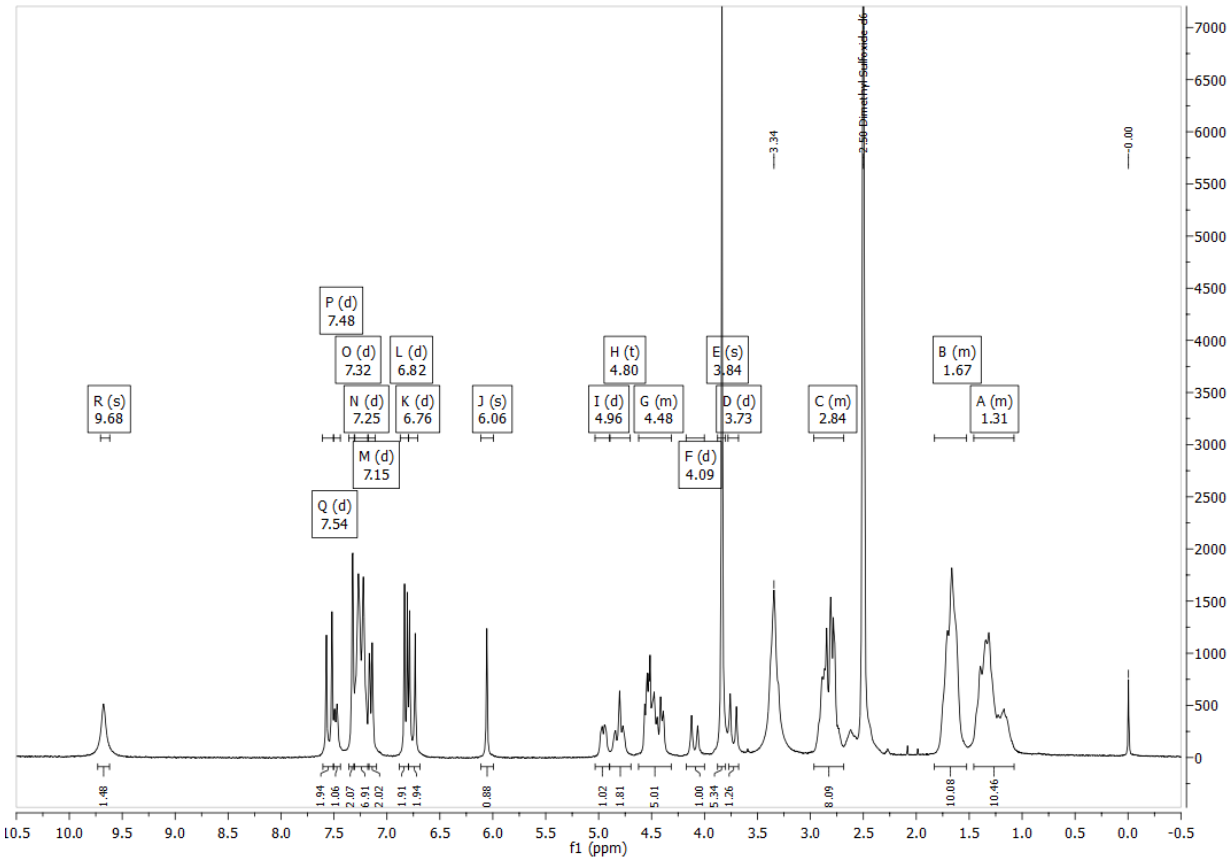

Figure S4. Proton NMR spectrum of the praziquantel–curcumin 2:1 cocrystal obtained from the slurry experiment. The protons are colored in a shade of gray to match the corresponding products. ^{1}H NMR (300 MHz, DMSO-d^{6}) δ 9.68 (s, 1H), 7.54 (d, *J* = 15.8 Hz, 2H), 7.48 (d, *J* = 6.8 Hz, 1H), 7.32 (d, *J* = 1.0 Hz, 2H), 7.25 (d, *J* = 13.8, 7H), 7.15 (d, *J* = 8.2, 2H), 6.82 (d, *J* = 8.2 Hz, 2H), 6.76 (d, *J* = 15.8 Hz, 2H), 6.06 (s, 1H), 4.96 (d, *J* = 6.7 Hz, 1H), 4.80 (t, *J* = 10.5 Hz, 2H), 4.62 – 4.31 (m, 5H), 4.09 (d, *J* = 17.4 Hz, 1H), 3.84 (s, 5H), 3.73 (d, J = 17.7 Hz, 1H), 2.92 – 2.75 (m, 8H), 1.83 – 1.52 (m, 10H), 1.46 – 1.08 (m, 10H). δ 3.34 residual water peak. δ 2.50 DMSO-d^{6} peak.