

## Supporting Information

# Combining a Drug and a Nutraceutical: A New Cocrystal of Praziquantel and Curcumin

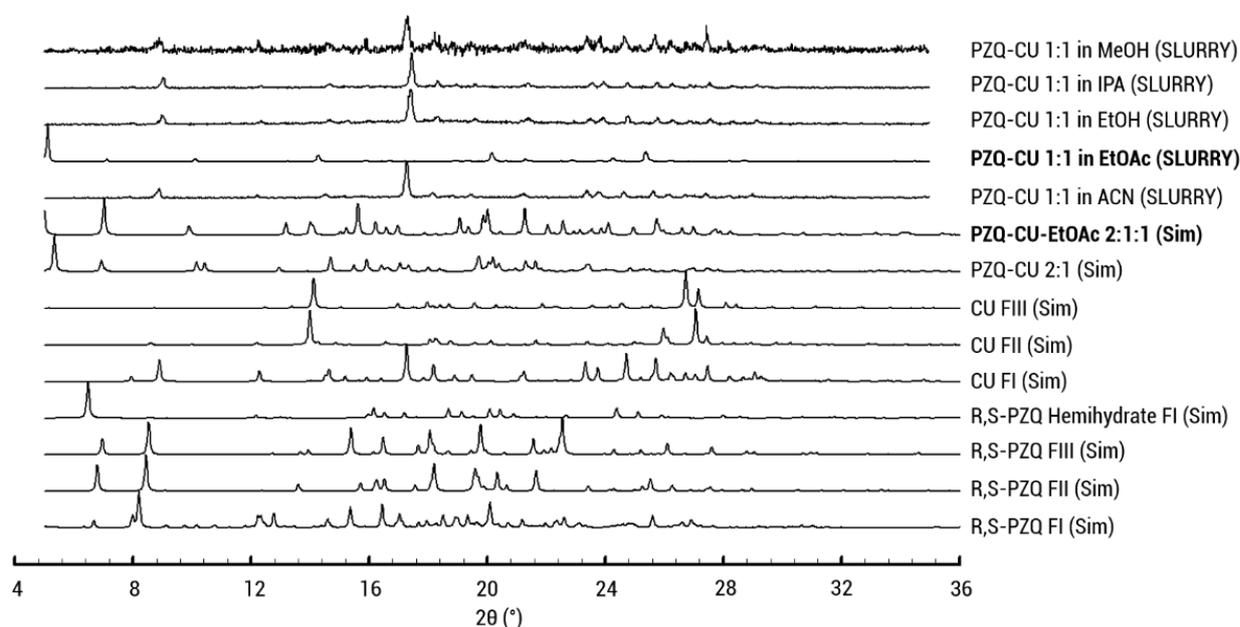
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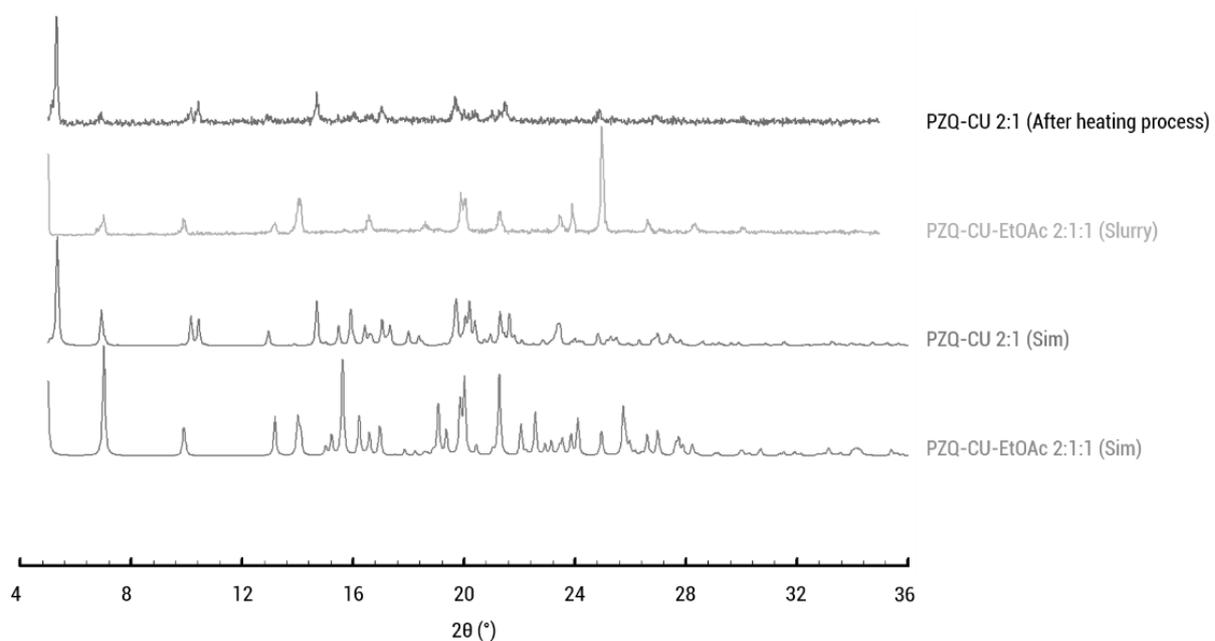
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### X-ray powder diffraction data



**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 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 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 <sub>63</sub> H <sub>76</sub> N <sub>4</sub> O <sub>12</sub>	C <sub>59</sub> H <sub>68</sub> N <sub>4</sub> O <sub>10</sub>
Formula weight	1081.27	993.17
Temperature (K)	150(2)	297(2)
Wavelength (Å)	0.71073	0.71073
Crystal system	Monoclinic	Monoclinic
Space group	<i>C2/c</i>	<i>P2<sub>1</sub>/n</i>
Unit cell dimensions (Å, °)	a = 37.992(3) b = 5.9769(5) c = 26.8477(15) β = 110.218(7)	a = 27.330(4) b = 5.8708(7) c = 35.486(7) β = 111.06(2)
Volume Å <sup>3</sup>	5720.8(7)	5313.5(17)
Z	4	4
Density (calc.) mg.m <sup>-3</sup>	1.255	1.242
Absorption coeff. mm <sup>-1</sup>	0.087	0.085
F (000)	2312	2120
Crystal size mm <sup>3</sup>	0.35 x 0.06 x 0.02	0.35 x 0.06 x 0.02
θ range for data collection (°)	3.234 to 25.514	3.147 to 17.230
Reflections collected	14153	10776
Independent reflections	5310 [R(int) = 0.0341]	3128 [R(int) = 0.1496]
Completeness to θ	99.3 % (q=25.242°)	97.5 % (θ = 17.230°)
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.00000 and 0.40329	1.00000 and 0.74717
Refinement method	Full-matrix least-squares on F <sup>2</sup>	
Data / restraints / parameters	5310 / 204 / 514	3128 / 635 / 660
Goodness-of-fit on F <sup>2</sup>	1.054	1.099
Final R indices [I > 2σ <sub>I</sub> ]	R <sub>1</sub> = 0.0514, wR <sub>2</sub> = 0.1295	R <sub>1</sub> = 0.1265, wR <sub>2</sub> = 0.2385
R indices (all data)	R <sub>1</sub> = 0.0749, wR <sub>2</sub> = 0.1404	R <sub>1</sub> = 0.2128, wR <sub>2</sub> = 0.2791
Δρ max, min (e.Å <sup>-3</sup> )	0.173 and -0.142	0.375 and -0.277

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

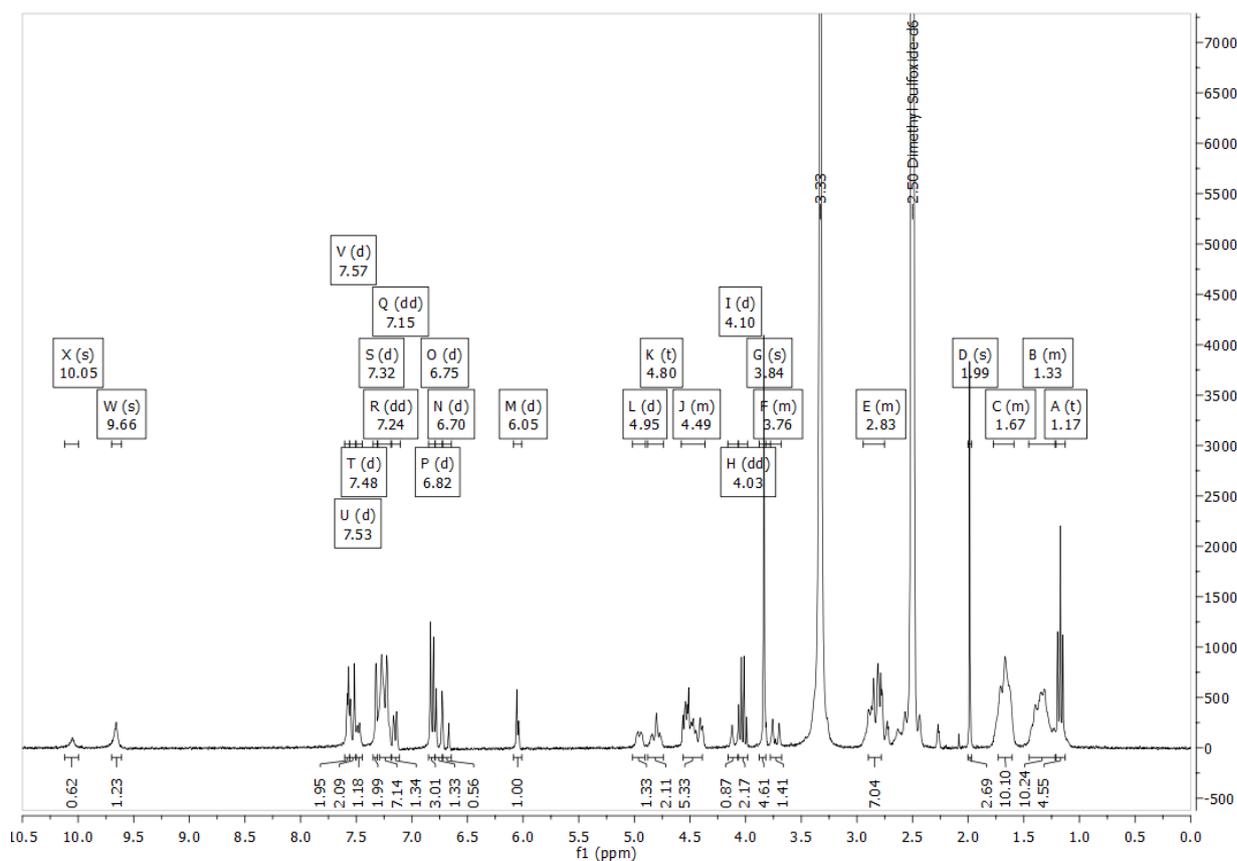
Identification code	PZQ-CU-EtOAc (2:1:1)
Empirical formula	C <sub>63</sub> H <sub>76</sub> N <sub>4</sub> O <sub>12</sub>
Formula weight	1081.27
Temperature (K)	150(2)
Wavelength (Å)	0.71073
Crystal system	Monoclinic
Space group	C2/c
Unit cell dimensions (Å, °)	a = 37.992(3) b = 5.9769(5) c = 26.8477(15) β = 110.218(7)
Volume (Å <sup>3</sup> )	5720.8(7)
Z	4
Density (calculated) (g/cm <sup>3</sup> )	1.255
Absorption coefficient (mm <sup>-1</sup> )	0.087
F (000)	2312
Crystal size (mm <sup>3</sup> )	0.35 x 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	1.00000 and 0.40329
Refinement method	Full-matrix least-squares on F <sup>2</sup>
Data / restraints / parameters	5310 / 204 / 514
Goodness-of-fit on F <sup>2</sup>	1.054
Final R indices [I > 2σ <sub>I</sub> ]	R <sub>1</sub> = 0.0514, wR <sub>2</sub> = 0.1295
R indices (all data)	R <sub>1</sub> = 0.0749, wR <sub>2</sub> = 0.1404
Δρ max, min (e.Å <sup>-3</sup> )	0.173 and -0.142

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

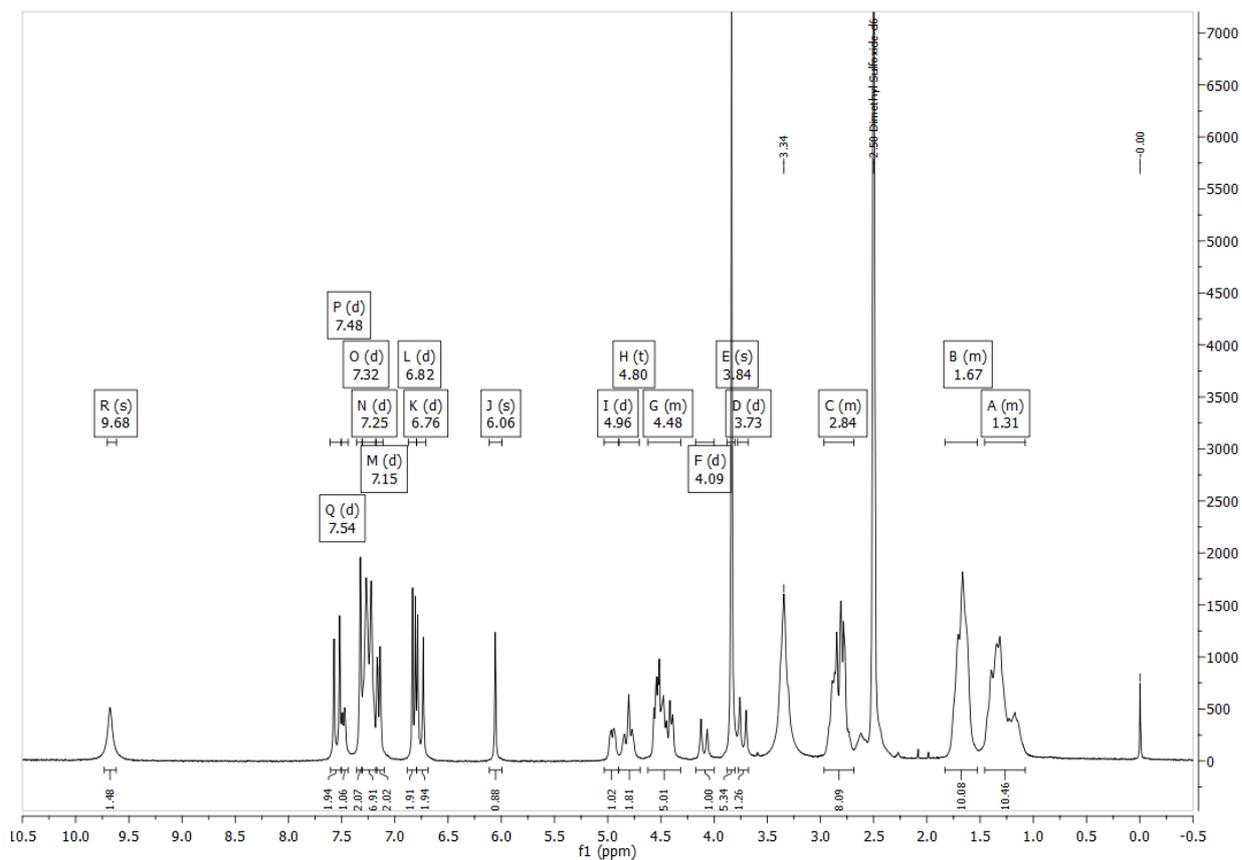
Descriptors	Donors	H $\cdots$	Acceptors	Interatomic Distances (Å)			Angles (°)
				D-H	H $\cdots$ A	D $\cdots$ A	D-H $\cdots$ A
	praziquantel-curcumin-ethyl acetate (2:1:1) cocrystal solvate (150K)						
D <sub>1</sub> <sup>1</sup> (2) <i>b</i>	O12	H12	O23	0.93(4)	1.73(4)	2.651(5)	171(4)
	praziquantel-curcumin-ethyl acetate (2:1:1) cocrystal solvate (RT)						
D <sub>1</sub> <sup>1</sup> (2) <i>b</i>	O12	H12	O23	0.89(3)	1.79(3)	2.673(7)	175(3)
	desolvated praziquantel-curcumin (2:1) cocrystal						
D <sub>1</sub> <sup>1</sup> (2) <i>b</i>	O12	H12	O23	0.82	1.81	2.634(18)	178
D <sub>1</sub> <sup>1</sup> (2) <i>b</i>	O12'	H12'	O23B	0.82	1.82	2.640(18)	179

CCDC 2309015-2309017 contain 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](http://www.ccdc.cam.ac.uk/structures).

## Proton nuclear magnetic resonance ( $^1\text{H}$ NMR) data



**Figure S3.** Proton NMR spectrum of praziquantel-curcumin-ethyl acetate 2:1:1 cocrystal solvate obtained from slurry experiment.  $^1\text{H}$  NMR (300 MHz,  $\text{DMSO-d}_6$ )  $\delta$  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).  $\delta$  3.33 residual water peak.  $\delta$  2.50 DMSO- $\text{d}_6$  peak.



**Figure S4.** Proton NMR spectrum of praziquantel-curcumin 2:1 cocrystal obtained from slurry experiment.  $^1\text{H}$  NMR (300 MHz,  $\text{DMSO-d}_6$ )  $\delta$  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).  $\delta$  3.34 residual water peak.  $\delta$  2.50  $\text{DMSO-d}_6$  peak.