Electronic Supplementary Material (ESI) for CrystEngComm.

Polymorphism and distinct physicochemical properties of the phloretin-nicotinamide cocrystal

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Supporting Information

(8 pages)

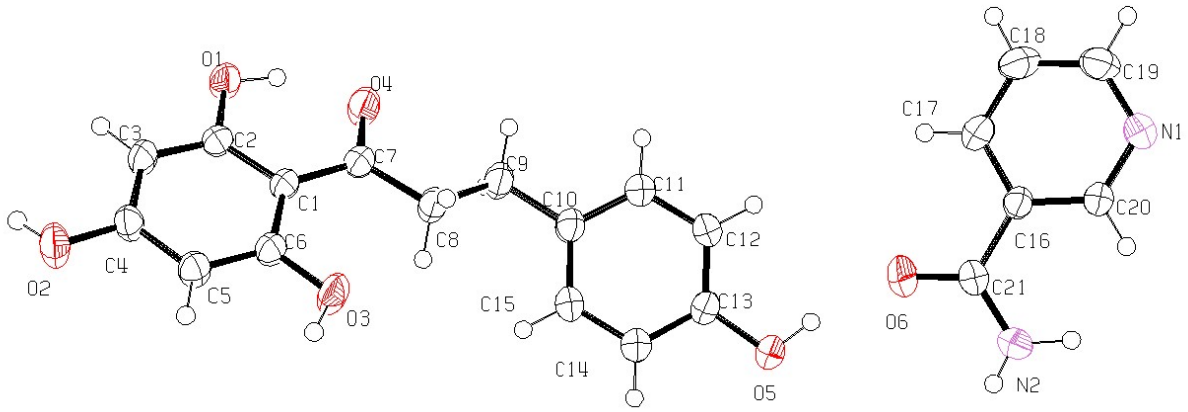


Figure S1. ORTEP plot of the crystal structure of PHL-NA cocrystal Form II. Thermal ellipsoids were drawn at 50 % probability.

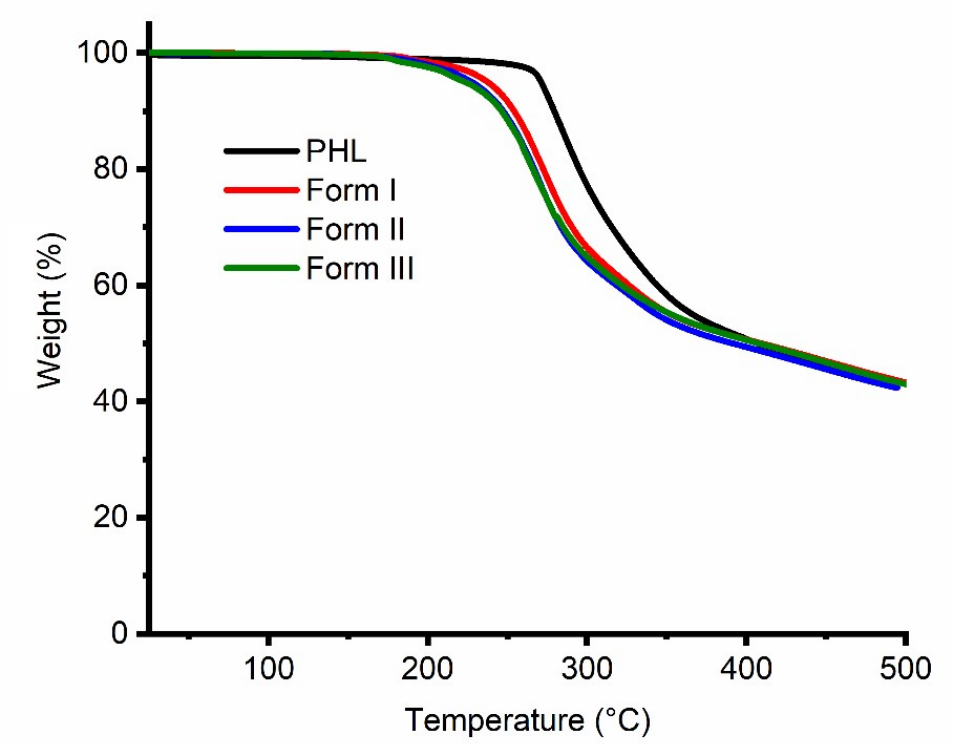


Figure S2. TGA plots of PHL and PHL-NA cocrystal polymorphs

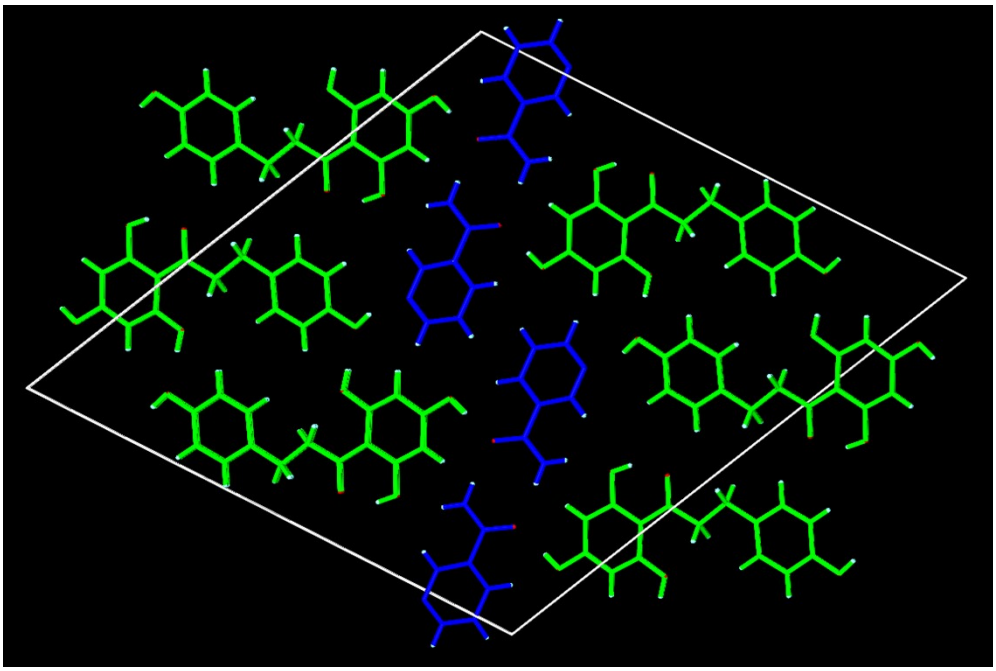


Figure S3. Crystal packing of PHL and NA in Form I showing perfect overlap of the molecules along the crystallographic *b*-axis. PHL molecules are shown green and NA molecules are shown blue stick model.

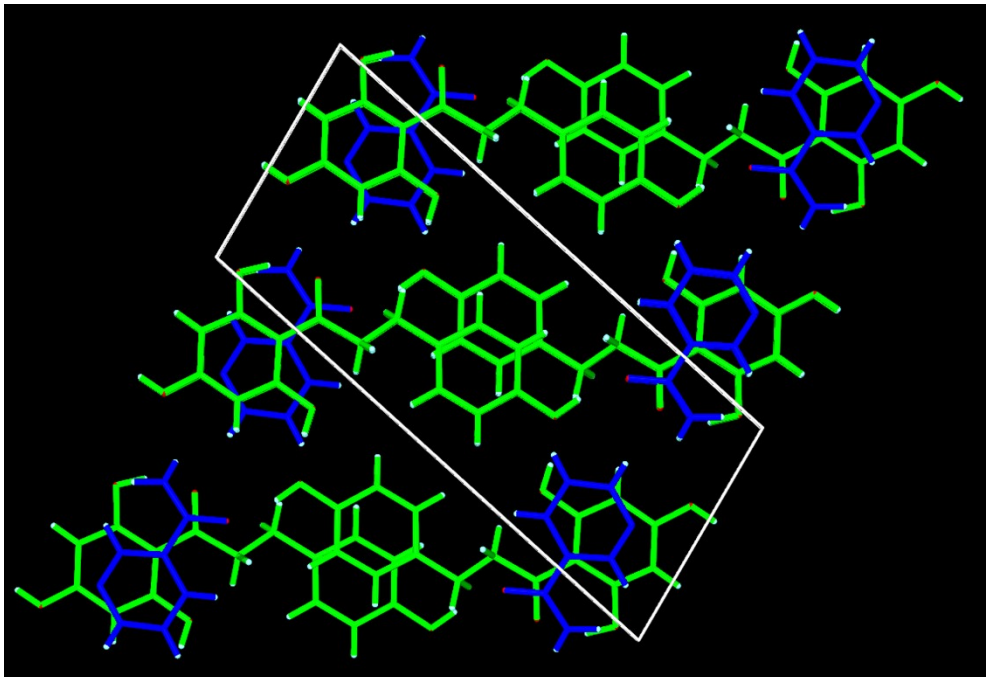


Figure S4. Crystal packing of PHL and NA in Form II showing an offset overlap of the molecules along the crystallographic *b*-axis. PHL molecules are shown green and NA molecules are shown blue stick model.

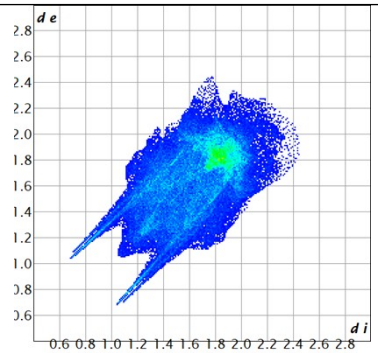
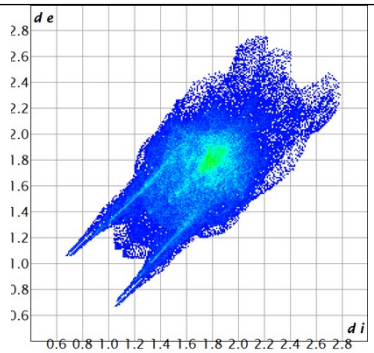
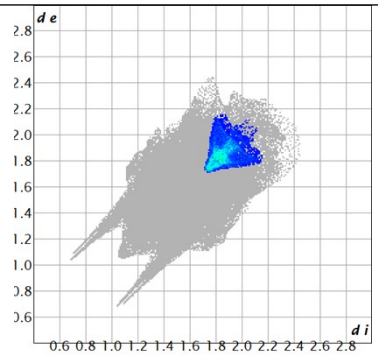
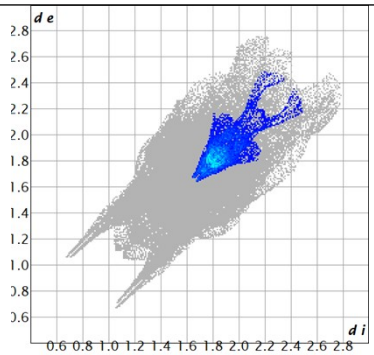
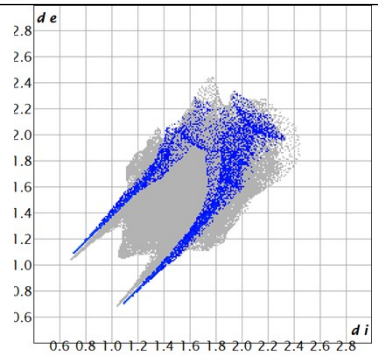
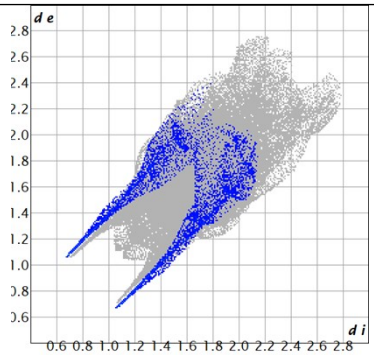
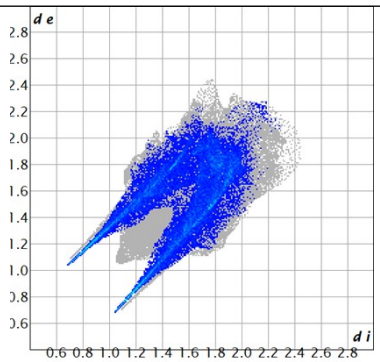
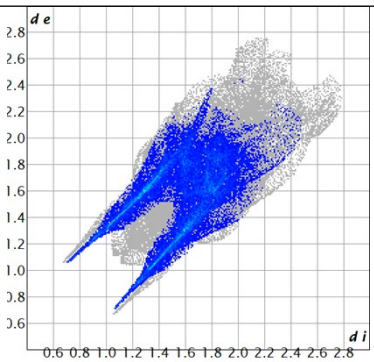
Crystal form	Form I	Form II
All		
C···C (π···π)		
N···H		
O···H		

Figure S5. 2D Hirshfeld fingerprint plots for PHL-NA cocrystal polymorphs I and II showing Notice the significant differences in the blue spikes corresponding to observed differences in their hydrogen bonding synthons and π···π interactions in the crystal structures.

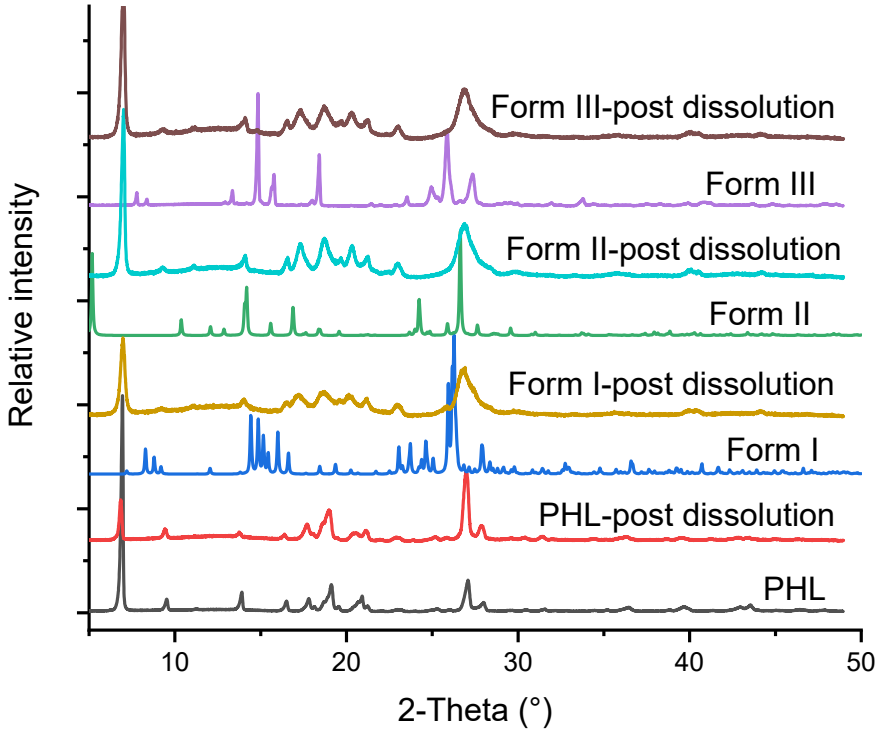


Figure S6. PXRD patterns of the cocrystal polymorphs post solubility-dissolution experiments. Notice that all the polymorphs dissociate and convert to PHL.

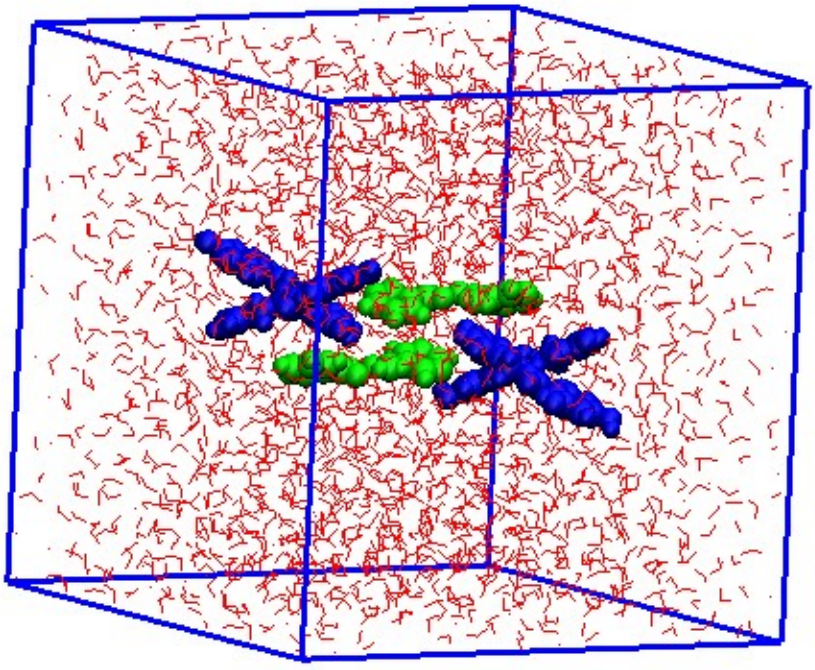


Figure S7. A schematic representation of the simulation system. Color code: PHL-blue; NA-green; water-red.

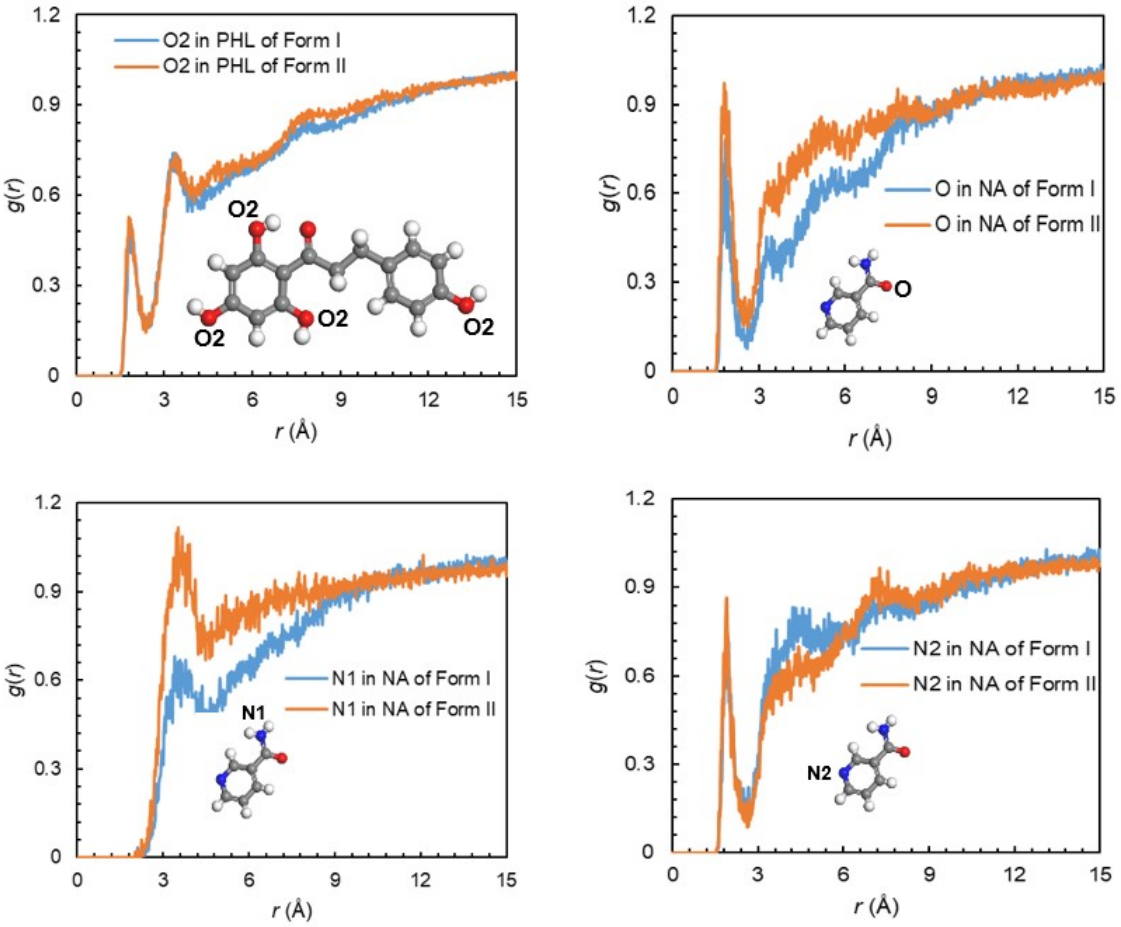


Figure S8. The g(r)'s of the hydrogen atom of water around the O2 atom of PHL and the O, N1, and N2 atoms of NA in Form I and Form II, respectively. Notice that pronounced peaks are observed at distances *r* ~1.92 Å, 1.82 Å, and 1.90 Å for the O2, O and N2 atoms, respectively, indicating interactions in both Forms I and II between water and these atom sites. The peeks are slightly higher in Form II compared to Form I. Interestingly, observable difference can be seen around the N1 atom, but this interaction is at a longer distance *r* ~3.64, compared to the rest of the three atoms. Therefore, it can be concluded that the Form II owns marginally higher interaction with water compared to Form I, particularly, corresponding to above interaction sites.

Table S1. Crystal data and structure refinement for PHL-NA cocrystal Form II.

Empirical formula	$C_{21}H_{20}N_2O_6$
Formula weight	396.39
Temperature/K	293(2)
Crystal system	monoclinic
Space group	$P2_1$
a/Å	7.51190(10)
b/Å	7.5163(2)
c/Å	17.4195(3)
α/°	90
β/°	101.945(2)
γ/°	90
Volume/Å^3	962.24(3)
Z	2
ρ_{calc}g/cm^3	1.368
μ/mm^{-1}	0.846
F(000)	416.0
Crystal size/mm^3	0.224 × 0.123 × 0.074
Radiation	Cu-Kα (λ = 1.54184)
2Θ range for data collection/°	5.186 to 144.776
Index ranges	$-9 \leq h \leq 9$, $-7 \leq k \leq 8$, $-21 \leq l \leq 21$
Reflections collected	9930
Independent reflections	3334 [R_{int} = 0.0371, R_{sigma} = 0.0298]
Data/restraints/parameters	3334/1/286
Goodness-of-fit on F^2	1.052
Final R indexes [I>=2σ (I)]	R_1 = 0.0438, wR_2 = 0.1075
Final R indexes [all data]	R_1 = 0.0449, wR_2 = 0.1091
Largest diff. peak/hole / e Å^{-3}	0.22/-0.34
Flack parameter	-0.03(12)

Table S2. Neutron normalized intermolecular interactions in the crystal structure of Form II of PHL-NA cocrystal.

Crystal form	D–H···A	H···A/Å	D···A/Å	D–H···A/°	Symmetry code
Form II	O1−H1···O4	1.58	2.4822(1)	150	Intramolecular
	O2−H2···N1	1.73	2.6948(1)	166	2+x,y,1+z
	N2−H2A···O2	2.15	3.0075(1)	142	2-x,-1/2+y,1-z
	N2−H2B···O1	2.08	3.0324(1)	157	-1+x,y,-1+z
	O3−H3···O5	1.77	2.7201(1)	162	2-x,1/2+y,1-z
	O5−H5···O6	1.72	2.6817(1)	165	x,y,z
	C8−H8A···O3	2.31	2.7249(1)	100	Intramolecular
	C19−H19···O4	2.34	3.4186(1)	171	-x,1/2+y,1-z
	C20−H20···O1	2.32	3.3965(1)	171	-1+x,y,-1+z

Interactions between aromatic rings			
Centroid···Centroid	Distance/Å	Dihedral angle (°)	Beta
Cg2···Cg2^{i}	4.1082(1)	23	12.9, 35.2
Cg1···Cg3^{i}	3.9037(1)	4	27.4, 31.6
Cg1···Cg3^{ii}	3.8919(1)	4	26.6, 27.7

Cg1: C1-C2-C3-C4-C5-C6, Cg2: C10-C11-C12-C13-C14-C15, Cg3: N1-C19-C18-C17-C16-C20
i) 1-x,-1/2+y,1-z, ii) 1-x,1/2+y,1-z