Electronic Supplementary Material (ESI) for CrystEngComm.

Supplementary Information

Cocrystals of zonisamide: physicochemical characterization and sustained release solid forms

Srinivasulu Aitipamula,[a] Joseph Cadden,[a,b] Pui Shan Chow[a]*

[a]Crystallization and Formulation Science, Institute of Chemical and Engineering Sciences, A*STAR (Agency for Science Technology and Research), 1 Pesek Road, Jurong Island, Singapore, 627833. E-mail: srinivasulu_aitipamula@ices.a-star.edu.sg

[b]Chemistry, Faculty of Natural and Environmental Sciences, University of Southampton, University Road, Southampton, SO17 1BJ, UK.

(5 Pages)

1. List of coformers used in the cocrystal screening of zonisamide (ZNS)
2. Table of crystal structure data
3. Table of hydrogen bonds
4. TGA analysis of the cocrystals
5. PXRD analysis of samples remained after IDR experiments

1. List of coformers used in the cocrystal screening of ZNS

List of coformers used in the cocrystal screening of zonisamide. The coformers that resulted cocrystals were highlighted.

Methylparaben	3-Hydroxybenzoic acid
Ethylparaben	**5-Methyl-2-pyridone (HMP)**
Propylparaben	Citric acid
Piperazine	Piperine
Pyrogallol	Bisphenol A
Methyl gallate	Urea
Betaine monohydrate	2-Picolinic acid
Nicotinamide	Nicotinic acid
4,4'-Dipyridyl anhydrous	Isonicotinic acid
4-Aminobenzoic acid	2,5-Dihydroxybenzoic acid
EDTA	2-Picolinamide
L-(+)-Mandelic acid	Salicylamide
L-Proline (LP)	Salicylic acid
L-Tartaric acid	Pimelic acid
Acesulfame	Saccharin
Adipic acid	N-Acetyl-L-cysteine
Benzoic acid	Imidazole
Fumaric acid	Indole-3-acetic acid
Glutaric acid	Pamoic acid
Glycine	Orotic acid anhydrous
Isonicotinamide	4-Acetamidophenol
p-Coumaric acid	**Caffeine (CAF)**
Lactose	**Catechol (CTC)**
Maleic acid	Resorcinol
Malonic acid	Hydroquinone
4-Hydroxybenzoic acid	Succinic acid

2. Crystal structure parameters

Table S1 Crystal structure data for the cocrystals, ZNS-CAF and ZNS-HMP.

Compound reference	ZNS-CAF	ZNS-HMP
Chemical formula	$C_8H_8N_2O_3S•C_8H_{10}N_4O_2$	$C_8H_8N_2O_3S•C_6H_7NO$
Formula Mass	406.42	321.35
Crystal system	Monoclinic	Monoclinic
a/Å	9.59020(10)	14.1373(3)
b/Å	13.30840(10)	11.23707(18)
c/Å	14.24360(10)	9.45521(17)
α/°	90	90.00
β/°	91.8550(10)	106.2761(19)
γ/°	90	90.00
Unit cell volume/Å^3	1816.96(3)	1441.87(4)
Temperature/K	297	100
Space group	$P2_1/n$	$P2_1/c$
No. of formula units per unit cell, *Z*	4	4
Radiation type	Cu-Kα	Mo-Kα
No. of reflections measured	27367	23512
No. of independent reflections	3217	3301
R_{int}	0.0209	0.0251
Final R_1 values ($I > 2\sigma(I)$)	0.0504	0.0301
Final $wR(F^2)$ values ($I > 2\sigma(I)$)	0.1446	0.0775
Final R_1 values (all data)	0.0504	0.0324
Final $wR(F^2)$ values (all data)	0.1446	0.0790
Goodness of fit on F^2	1.041	1.056
CCDC number	1832355	1816488

3. Table of hydrogen bonds

Table S2. Neutron normalized intermolecular interactions in the crystal structure of ZNS-CAF and ZNS-HMP cocrystals.

Cocrystal	D–H···A[a]	H···A/Å	D···A/Å	D–H···A/°	Symmetry code
ZNS-CAF	N2–H2B···O4	1.91	2.9047(1)	167	-
	N2–H2A···N5	2.02	2.9598(1)	155	3/2-x,-1/2+y,3/2-z
	C2–H2···O2	2.63	3.3390(1)	122	-1+x,y,z
	C3–H3···O4	2.45	3.4058(1)	146	1/2-x,1/2+y,3/2-z
	C8–H8A···O2	2.49	3.4627(3)	149	2-x,1-y,1-z
	C15–H15B···O3	2.44	3.4236(1)	151	-
	C15–H15C···O4	2.64	3.5293(1)	139	1-x,1-y,2-z
	C16–H16A···O4	2.56	3.1679(1)	115	-
ZNS-HMP	N2–H2A···O1	2.01	3.022(1)	176	x,3/2-y,-1/2+z
	N2–H2B···O4	1.83	2.828(1)	169	-
	N3–H3A···O4	1.78	2.784(1)	174	1-x,2-y,1-z
	C3–H3···O2	2.64	3.359(2)	123	-x,1/2+y,-1/2-z
	C8–H8A···O2	2.93	3.329(2)	102	x,3/2-y,1/2+z
	C8–H8B···O2	2.79	3.329(2)	111	x,3/2-y,1/2+z

[a]D = Donor, A = Acceptor.

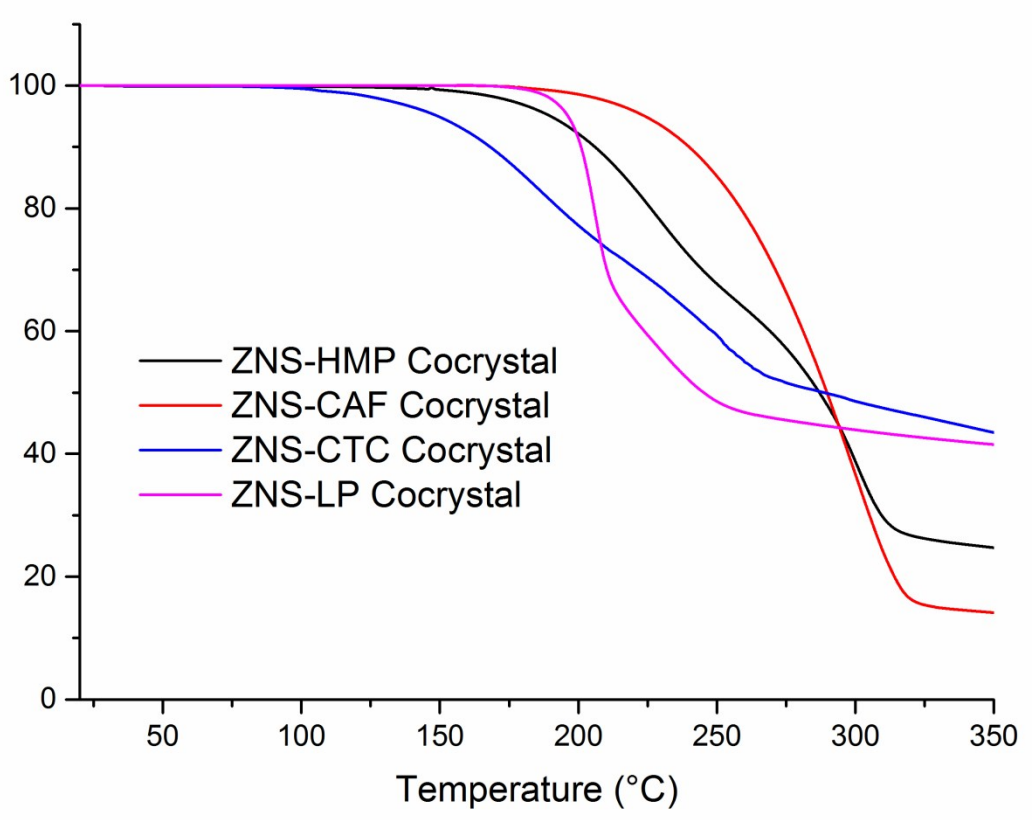

Figure S1. TGA thermograms of ZNS cocrystals.

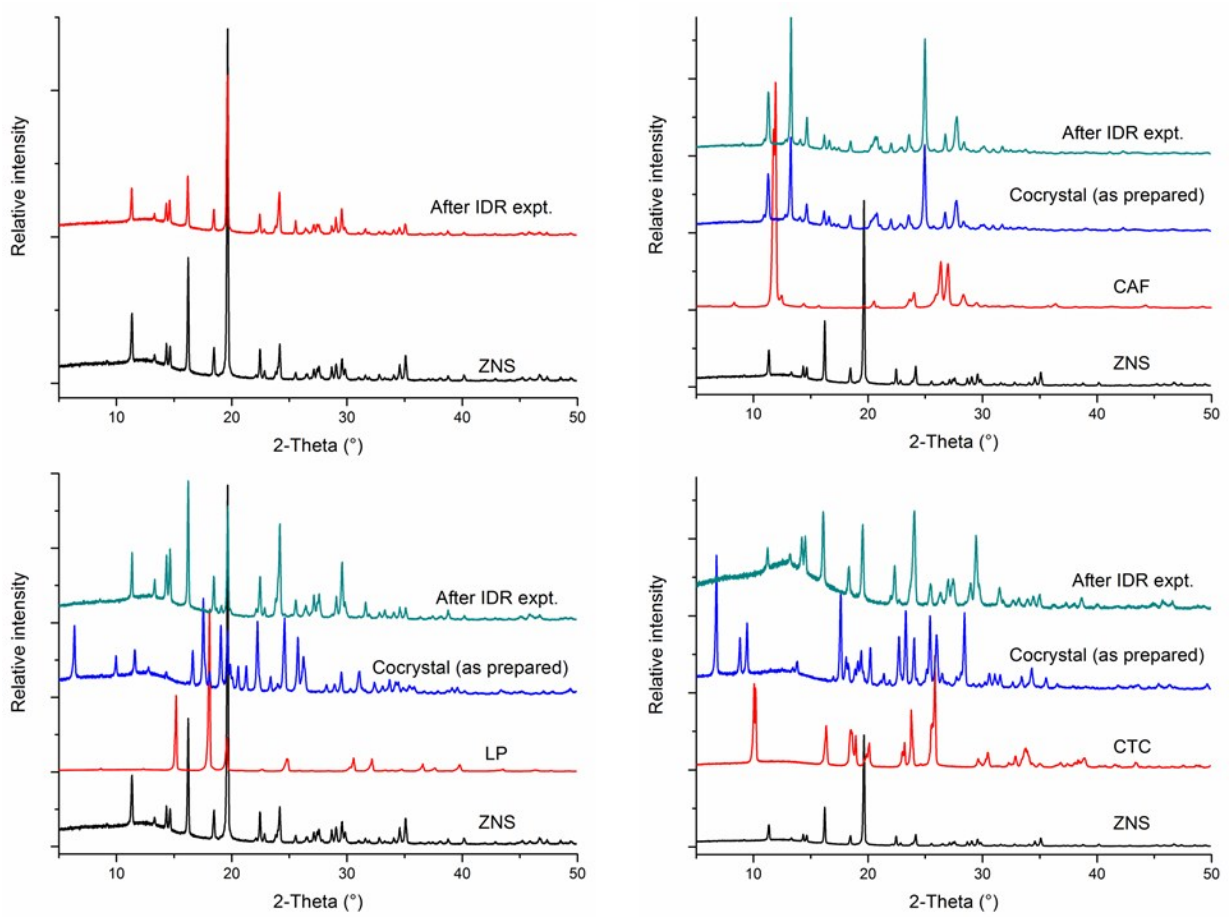

Figure S2. Comparison of the PXRD pattern of the samples remained after the IDR experiments with the respective reference PXRD patterns.