crystals

MDPI

Furosemide/Non-steroidal anti-inflammatory drug-drug pharmaceutical solids: novel opportunities in drug formulation

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Figure S1. PXRD patterns of FUR–ETZ obtained by grinding the two components at different molar ratios. Blue dotted lines indicate characteristic FUR reflections. Orange dotted lines indicate characteristic ETZ reflections.

Figure S2. PXRD patterns of FUR–PRX obtained by grinding the two components at different molar ratios. Blue dotted lines indicate characteristic FUR reflections. Orange dotted lines indicate characteristic PRX reflections.

Figure S3. Le bail profile fit (red line) to the experimental PXRD data (blue line) of FUR-ETZ (a) and FUR-PRX (b). The profile fitting for both the cocrystals shows low discrepancy (grey line).

Figure S4. ORTEP representation showing the asymmetric unit of FUR—ETZ with atom numbering scheme (thermal ellipsoids are plotted with the 50% probability level).

Figure S5. ORTEP representation showing the asymmetric unit of FUR—PRX with atom numbering scheme (thermal ellipsoids are plotted with the 50% probability level).

Figure S6. TGA traces of FUR–ETZ (top) and FUR–PRX (bottom).

Figure S7. Solubility curve of FUR—ETZ in water PBS at pH 7.4.

Figure S8. Solubility curve of FUR—PRX in water PBS at pH 7.4.

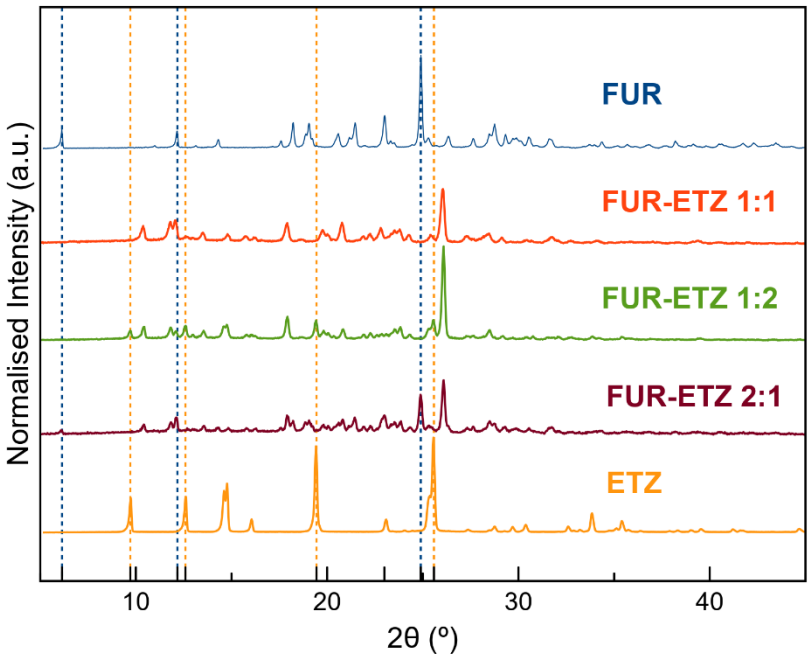
Figure S9. PXRD patterns of FUR–ETZ after the stability slurry assay (at 25 ºC, during 24 h, in water).

Figure S10. PXRD patterns of FUR–PRX after the stability slurry assay (at 25 ºC, during 24 h, in water).

Table S1. Hydrogen bonds for FUR—ETZ [Å and deg.].

Table S2. π,π-stacking interactions analysis of compound FUR—ETZ.

Table S3. Hydrogen bonds for FUR—PRX [Å and deg.].



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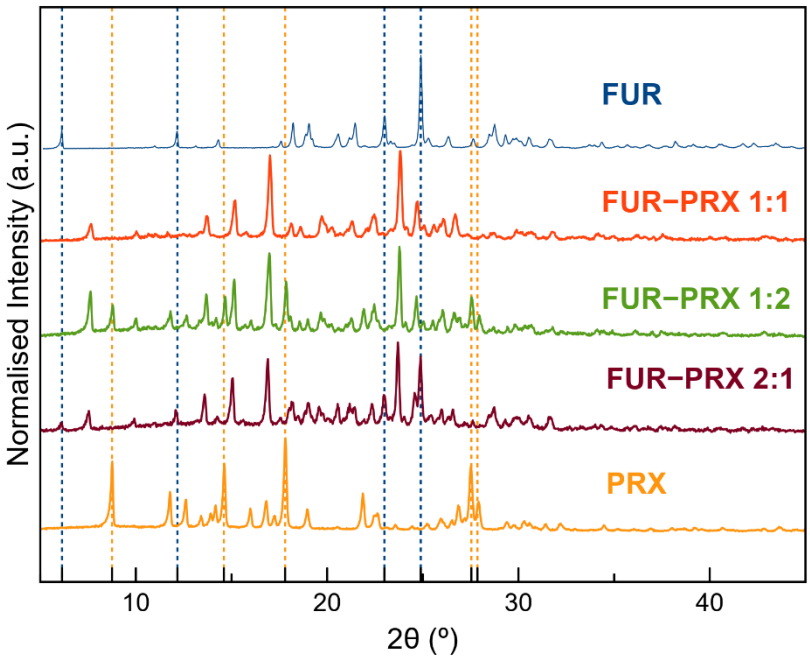
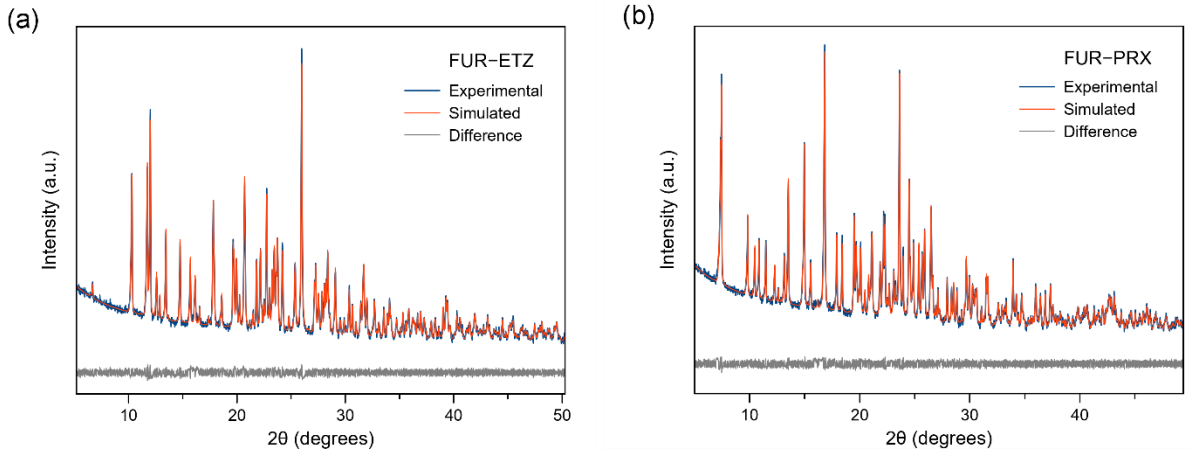


Figure S2. PXRD patterns of FUR–PRX obtained by grinding the two components at different molar ratios. Blue dotted lines indicate characteristic FUR reflections. Orange dotted lines indicate characteristic PRX reflections.



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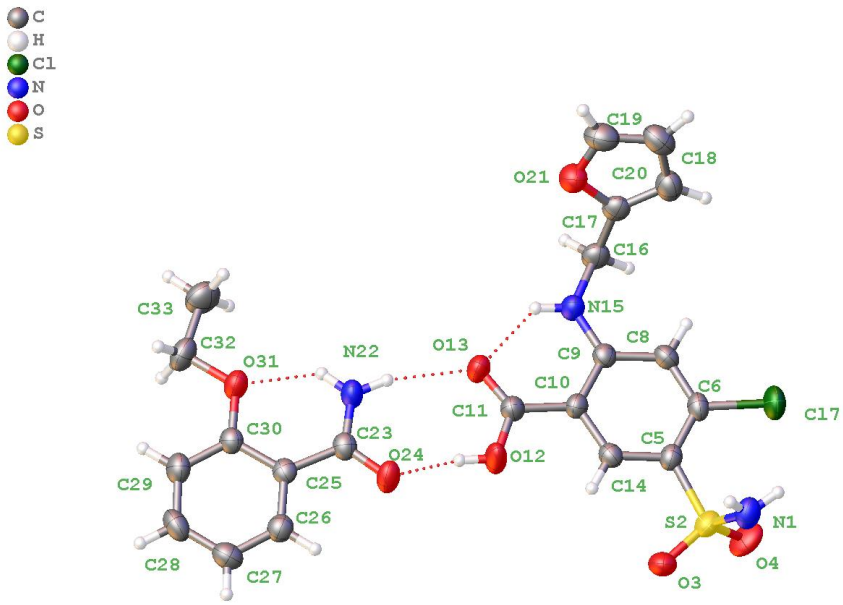


Figure S4. ORTEP representation showing the asymmetric unit of FUR—ETZ with atom numbering scheme (thermal ellipsoids are plotted with the 50% probability level).

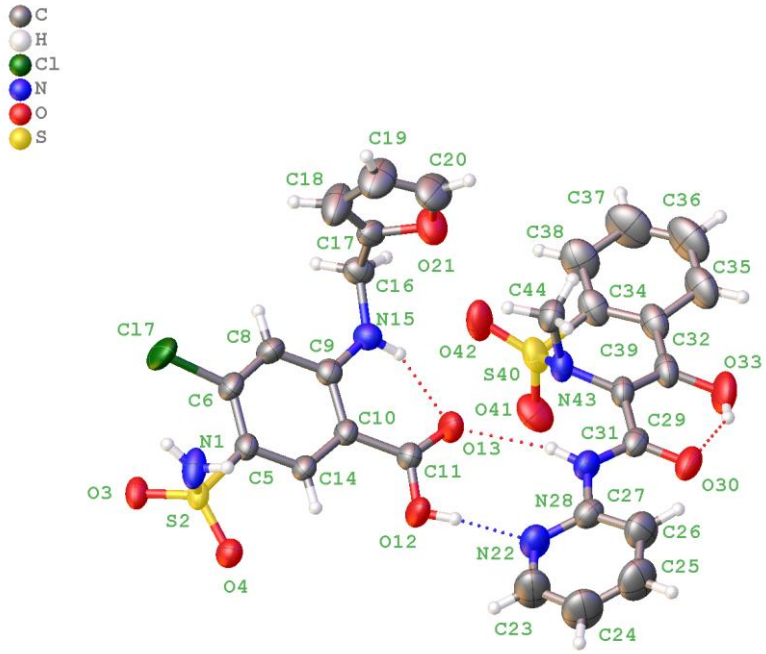


Figure S5. ORTEP representation showing the asymmetric unit of FUR—PRX with atom numbering scheme (thermal ellipsoids are plotted with the 50% probability level).

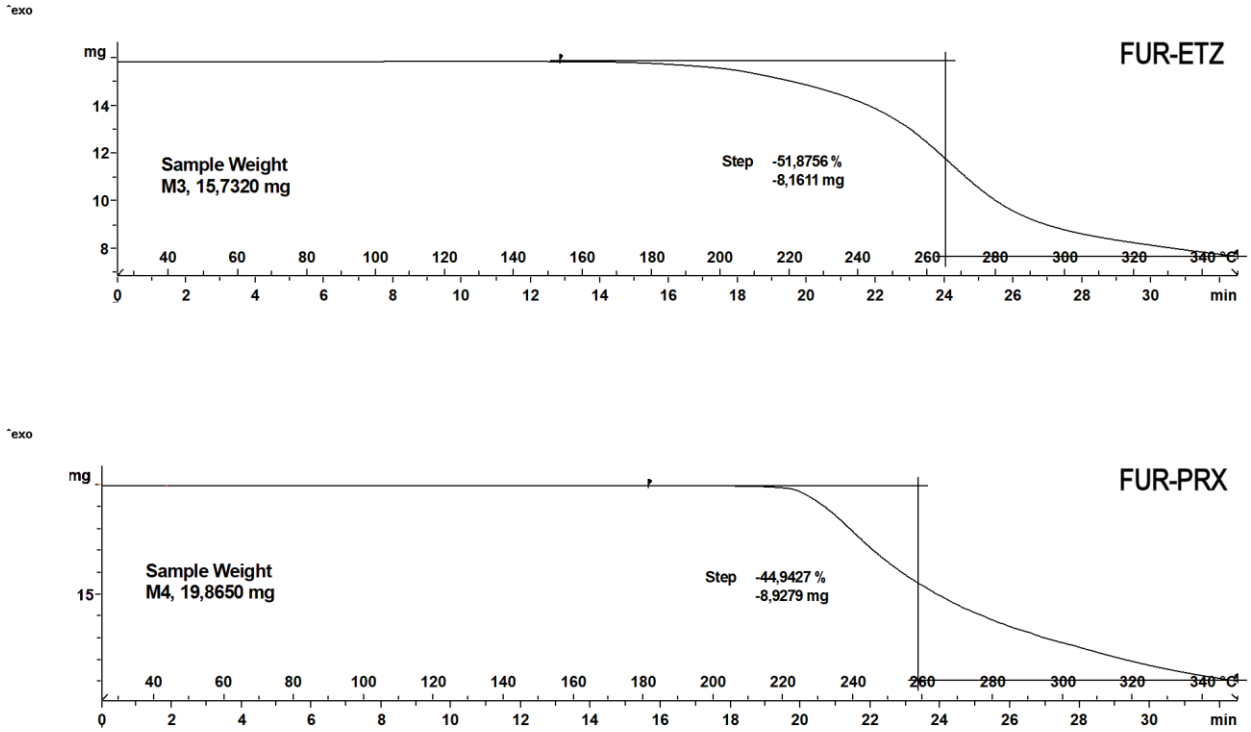


Figure S6. TGA traces of FUR–ETZ (top) and FUR–PRX (bottom).

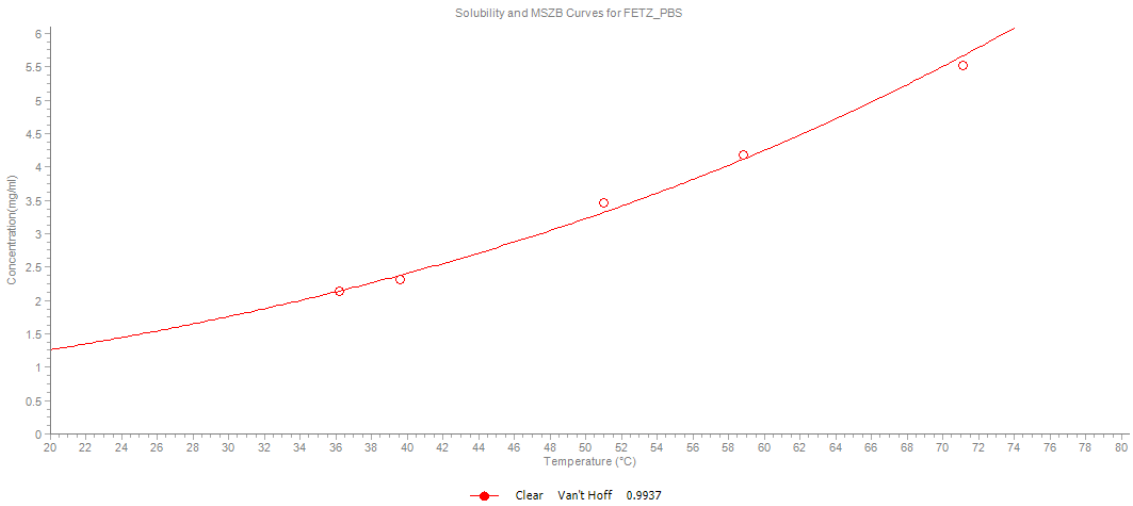


Figure S7. Solubility curve of FUR—ETZ in water PBS at pH 7.4.

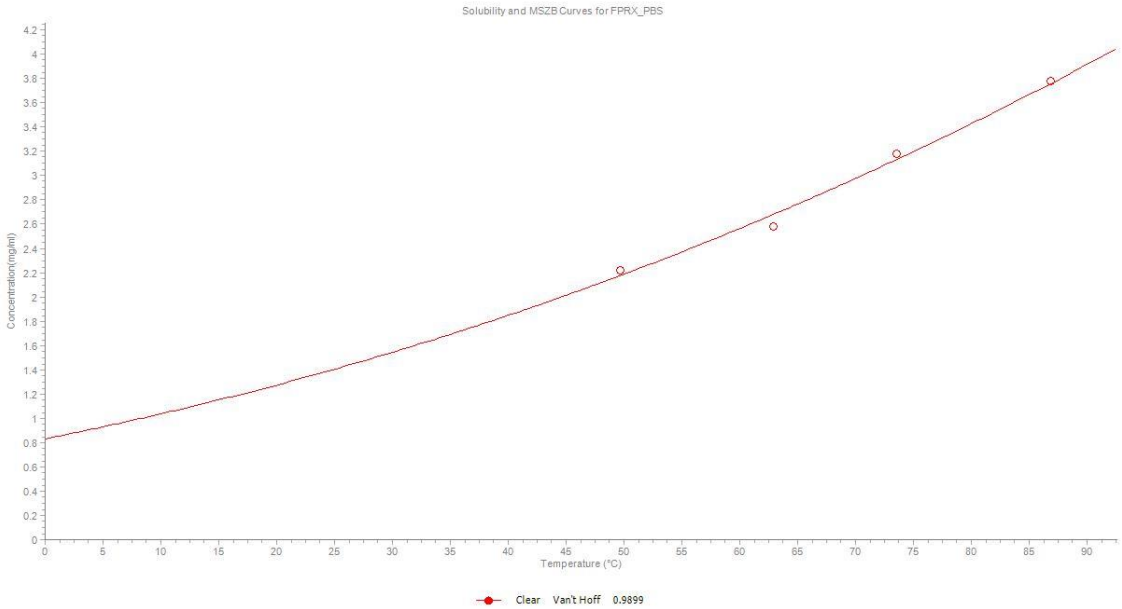


Figure S8. Solubility curve of FUR—PRX in water PBS at pH 7.4.

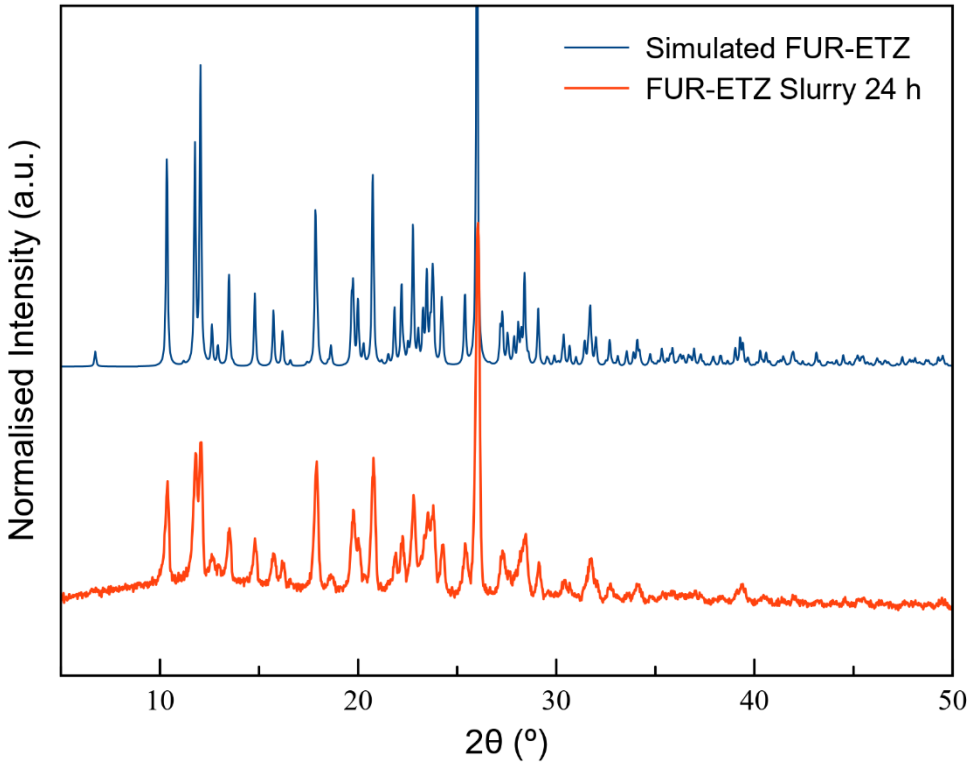


Figure S9. PXRD patterns of FUR–ETZ after the stability slurry assay (at 25 ºC, during 24 h, in water).

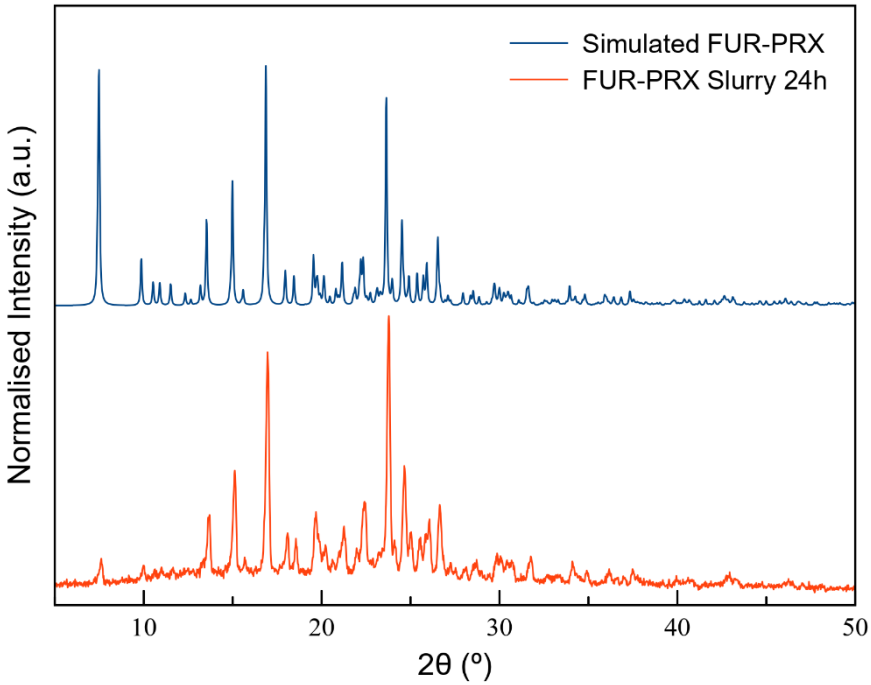


Figure S10. PXRD patterns of FUR–PRX after the stability slurry assay (at 25 ºC, during 24 h, in water).

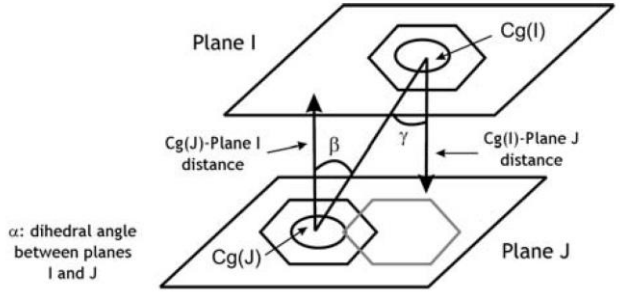
Table S1. Hydrogen bonds for FUR—ETZ [Å and deg.].

D-H...A	d(D-H)	d(H···A)	d(D···A)	<(DHA)
N(1)-H(1A)···O(24)[#1]	0.80(3)	2.20(3)	2.981(4)	167(4)
N(1)-H(1B)···O(21)[#2]	0.85(3)	2.42(3)	3.131(4)	142(3)
O(12)-H(12)···O(24)	0.84	1.71	2.535(3)	168.7
N(15)-H(15)···O(13)	0.86	2.01	2.692(3)	135.0
N(22)-H(22A)···O(13)	0.86	2.12	2.965(3)	165.5
N(22)-H(22B)···O(31)	0.86	1.97	2.636(3)	132.9

Symmetry transformations used to generate equivalent atoms:

#1 -x+1,y+1/2,-z+1/2 #2 x,y+1,z

Table S2. π,π-stacking interactions analysis of compound FUR—ETZ.



5-Membered Ring (1) O21 --> C17 --> C18 --> C19 --> C20 -->
6-Membered Ring (2) C5 --> C6 --> C8 --> C9 --> C10 --> C14 -->
6-Membered Ring (3) C25 --> C26 --> C27 --> C28 --> C29 --> C30 -->

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Analysis of Short Ring-Interactions with Cg-Cg Distances < 6.0 Ang., Alpha < 20.000 Deg. and Beta < 60.0 Deg.

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Cg(I)	Res(I)	Cg(J)	[ARU(J)]	Cg-Cg	Transformed J-Plane P, Q, R, S	Alpha	Beta	Gamma	CgI_Perp	CgJ_Perp	Slippage
Cg1	[1] ->	Cg1	[3566.01]	3.658(2)	-0.7413-0.6703-0.0345 -1.2138	0.0(2)	16.9	16.9	3.4994(14)	3.4994(14)	1.065
Cg2	[1] ->	Cg3	[2655.02]	3.7262(17)	-0.6158-0.0151-0.7878 -8.6970	5.78(14)	14.5	20.0	3.5023(11)	3.6077(12)	0.932
Cg3	[2] ->	Cg2	[2645.01]	3.7262(17)	-0.5400 0.0565-0.8398 -8.4158	5.78(14)	20.0	14.5	3.6076(12)	3.5023(11)	1.272

[3566] = -X,1-Y,1-Z
[1555] = X,Y,Z
[2655] = 1-X,1/2+Y,1/2-Z
[2645] = 1-X,-1/2+Y,1/2-Z

Table S3. Hydrogen bonds for FUR—PRX [Å and deg.].

D-H···A	d(D-H)	d(H···A)	d(D···A)	<(DHA)
N(28)-H(28)···O(13)	0.86	2.25	3.091(2)	166.4
O(33)-H(33)···O(30)	0.82	1.82	2.538(3)	146.2
N(1)-H(1A)···O(42)$^{\#1}$	0.84(3)	2.17(3)	2.989(3)	162(3)
N(1)-H(1B)···O(3)$^{\#2}$	0.80(3)	2.21(3)	2.991(2)	166(3)
N(15)-H(15)···O(13)	0.86	2.10	2.704(2)	126.9
O(12)-H(12)···N(22)	0.82	1.85	2.662(2)	170.1

Symmetry transformations used to generate equivalent atoms:

#1 x-1,y,z #2 -x,-y+1,-z+1