Electronic Supplementary Information

For

Article

Crystal structure of Febuxostat marketed polymorph determined by electron diffraction and reinforced by X-ray crystallography

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Table S1. Crystallization experiments targetting form A.

Solvent used	Concentration of FEB [mg/mL]	Crystallization method	Form by X-ray powder diffraction
2-Ethoxyethanol	30	Determination of MSZW	Form A + Q
	60		
	120		Form A
	240		
	360		
Ethanol	30		Form F3
	60		
	120		
	180		
Acetonitrile/Water	5	Anti-solvent vapor diffusion	Form A
2-Ethoxyethanol	-	Solvent-drop grinding	Form Q
THF	-		Form A + Q
2-Ethoxyethanol	125	Recrystallization of solvent-drop grinding materials	Form A
2-Ethoxyethanol	100	Cooling evaporative crystallization	Form A
THF	75		Form A + Q
Ethanol	35		Form F3

Table S2. Calculation settings of the force fields used in the molecular mechanics calculations.

Variable	Setting
Forcite	
Optimization algorithm	Smart
Convergence energy	2.0×10^{-5} kcal/mol
Convergence force	0.001 kcal/(mol Å)
Convergence stress	0.001 GPa
Conv. displacement	1.0×10^{-5} Å
Max. iterations	1000
External pressure	0
Optimize cell	yes
E^- static sum method	Ewald
Ewald accuracy	1.0×10^{-5} kcal/mol
Buffer width	0.5 Å
vdW sum method	Ewald
Ewald accuracy	1.0×10^{-5} kcal/mol
Buffer width	0.5 Å
Repulsive cutoff	6.0 Å
H-bond sum method	atom based
Cutoff distance	6.0 Å
Spline width	0.5 Å
Buffer width	0.5 Å

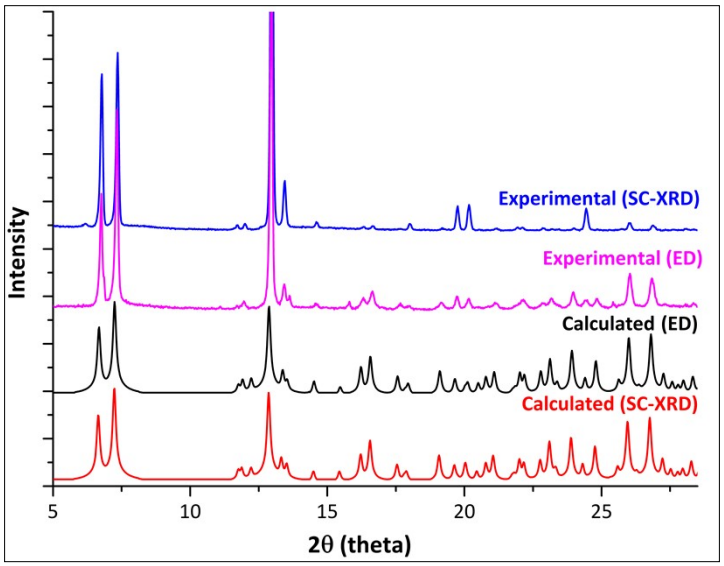

Figure S1. Experimental and calculated X-ray powder patterns of form A based on the SC-XRD and ED data.

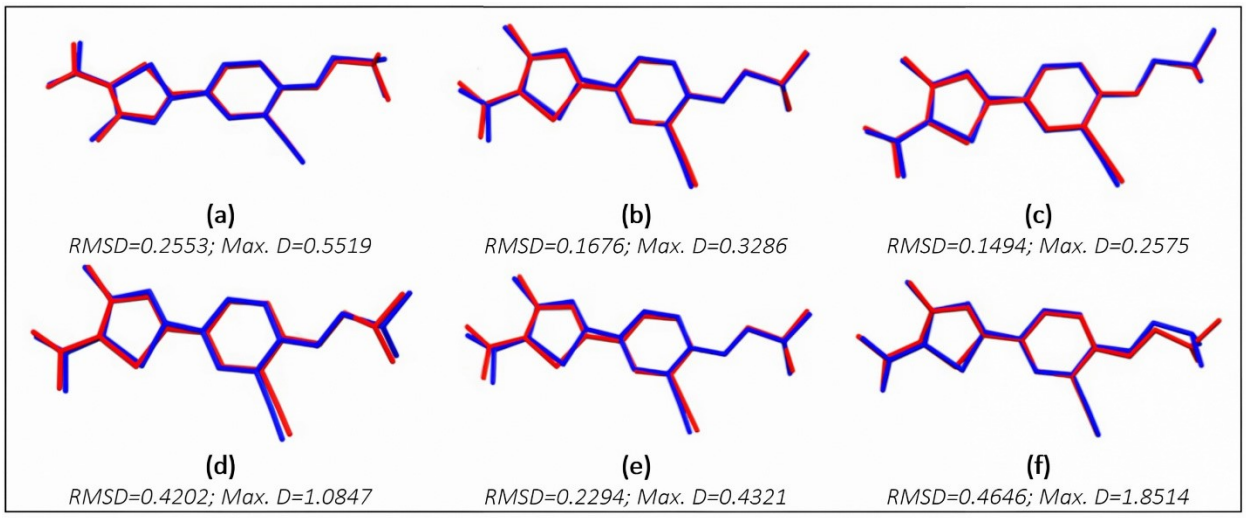

Figure S2. Overlays of the FEB molecules from the CSD structures with the unique conformers identified by the Boltzmann method: **(a)** HIQQAB02→molecule 1 (red) *versus* conformer F1 (blue); **(b)** HIQQAB02→molecule 2 (red) *versus* conformer F2 (blue); **(c)** UREQOY (red) *versus* conformer F2 (blue); **(d)** HIQQIJ (red) *versus* conformer F2 (blue); **(e)** HIQQUV (red) *versus* conformer F2 (blue) and **(f)** HIQQEF (red) *versus* conformer F5 (blue). All values are in Å.