Sildenafil–Resorcinol Cocrystal: XRPD Structure and DFT Calculations

Rafael Barbas[1], Vineet Kumar,[2] Oriol Vallcorba[3], Rafel Prohens[1, 2,*] and Antonio Frontera[4,*]

[1] Unitat de Polimorfisme i Calorimetria, Centres Científics i Tecnològics, Universitat de Barcelona, Baldiri Reixac 10, 08028 Barcelona, Spain

[2] Center for Intelligent Research in Crystal Engineering S.L., Parc Científic de Barcelona, Baldiri Reixac, 4-8, 08028, Barcelona, Spain.

[3] ALBA Synchrotron Light Source, Cerdanyola del Vallès, Barcelona, Spain

[4] Departament de Química, Universitat de les Illes Balears, Crta. de Valldemossa, km 7.5, 07122 Palma (Baleares), Spain; e-mail: toni.frontera@uib.es

[*] Correspondence: rafel@ccit.ub.edu (R.P.); toni.frontera@uib.es (A.F.)

Electronic Supplementary Information

1. Experimental Methods

XRPD pattern of the Sildenafil-resorcinol cocrystal was obtained on a PANalytical *X'*Pert PRO MPD diffractometer in transmission configuration using Cu Kα1+2 radiation (λ = 1.5406 Å) with a focusing elliptic mirror and a PIXcel detector working at a maximum detector's active length of 3.347° θ. Configuration of convergent beam with a focalizing mirror and a transmission geometry with flat sample sandwiched between low absorbing films measuring from 2 to 70° θ in 2θ, with a step size of 0.013° θ and a total measuring time of 5 hours.

1.1. DFT Geometry Optimization

The initial Rietveld plot of the crystal structure obtained by the direct space strategy implemented in TALP is shown in figure S1. As a consequence of the adjustment, the obtained crystallographic information file (CIF) shows the deformation of one of the phenol rings. Thus, the atomic positions of this resorcinol molecule were optimized with dispersion-correction DFT methods as provided by the module DMOL3 in Materials Studio software using the LDA/PWC functional and the double numerical with polarization (DNP) basis set. Comparative of both molecules of resorcinol is shown in figure S2.

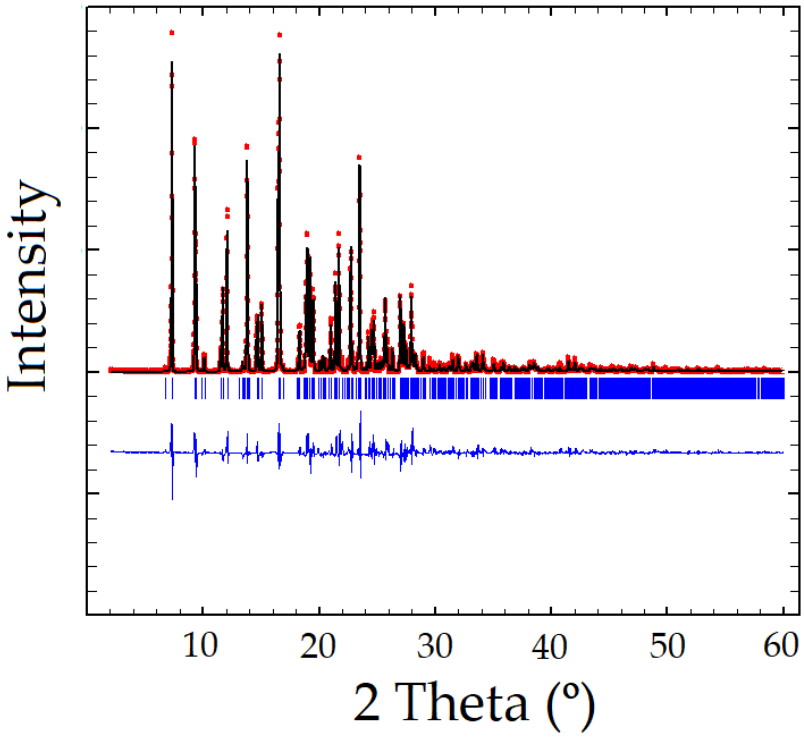

Figure 1. prf plot for the crystal structure refinement of sildenafil–resorcinol cocrystal determined by TALP. The plot shows the experimental powder XRD profile (red marks), the calculated powder XRD profile (black solid line), and the difference profile (blue, lower line). Tick marks indicate peak positions.

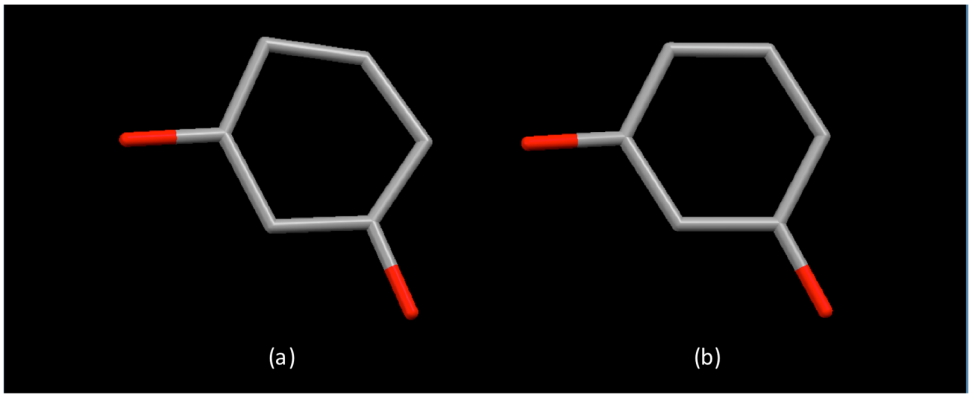

Figure 2. Comparative of the deformed resorcinol molecule: (**a**) after TALP crystal structure determination; (**b**) after DFT calculations.

Finally, the root-mean-square distance (RMSD) value between the asymmetric unit of the crystal structure before and after the DFT calculation computed using Mercury (4.3.0) is 0.0003 Å. (figure S3). Only a light adjustment of the resorcinol molecule was necessary, which had only a small effect in the final refinement by the Rietveld method.

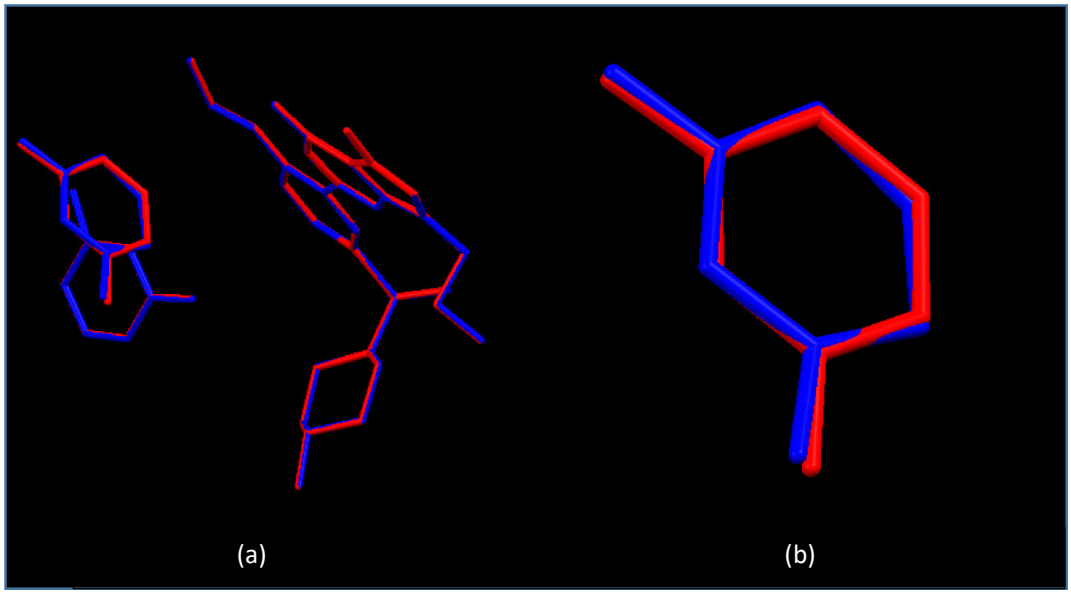

Figure 3. (**a**) Overlapping of sildenafil-resorcinol cocrystal structure initially determined by TALP (blue) and final structure refined by the Rietveld method (red). The computed root-mean-square distance (RMSD) is 0.0003 Å. (**b**) Detail of the overlapped resorcinol molecules.