Crystal structure of fluconazole polymorph V, $C_{13}H_{12}F_2N_6O$

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Fluconazole (CAS Registry number 86386-73-4) is used to treat a number of fungal infections, particularly candidiasis, and has many polymorphs. There are five low-precision experimental patterns of fluconazole in the Powder Diffraction File (00-057-1444, 00-058-1926, 00-059-1308, 00-062-1568, and 00-062-1569); one of them, 00-059-1308, corresponds to polymorph V, but does not contain all of the peaks observed here. In this study a commercial sample of fluconazole crystallized in the orthorhombic space group *Pbca* (#61) with $a = 12.97949(12)$, $b = 6.13624(7)$, $c = 35.1757(5)$ Å, $V = 2801.57(8)$ Å^3, and $Z = 8$ at 295 K. A reduced cell search in the Cambridge Structural Database (Groom *et al.*, 2016) yielded a previously reported crystal structure of polymorph V (Karanam *et al.*, 2012; Refcode IVUQOF02) collected at 100 K. In this work, the sample was ordered from Sigma-Aldrich (Product # F8929-100 mg) and analyzed as received. Other commercial samples evaluated as part of this study were found to have consisted of mixtures of polymorphs. The room-temperature crystal structure was refined using synchrotron ($\lambda = 0.412708$ Å) powder diffraction data, density functional theory, and Rietveld refinement techniques. The diffraction data were collected on beamline 11-BM at the Advanced Photon Source, Argonne National Laboratory (see crystallographic details in the supplementary material). Figure 1 shows the powder X-ray diffraction pattern of the compound. The thermal expansion between 100 and 295 K is anisotropic; the expansion is 0.40, 1.86, and 0.98% along *a*, *b*, and *c*, respectively. The cell volume is 3.27% larger at room temperature. The hydroxyl group forms a strong hydrogen bond to a ring nitrogen atom along the *a*-axis, but the crystal packing is dominated by ring–ring interactions. The pattern and room-temperature crystal structure have been submitted to ICDD for inclusion in the Powder Diffraction File.

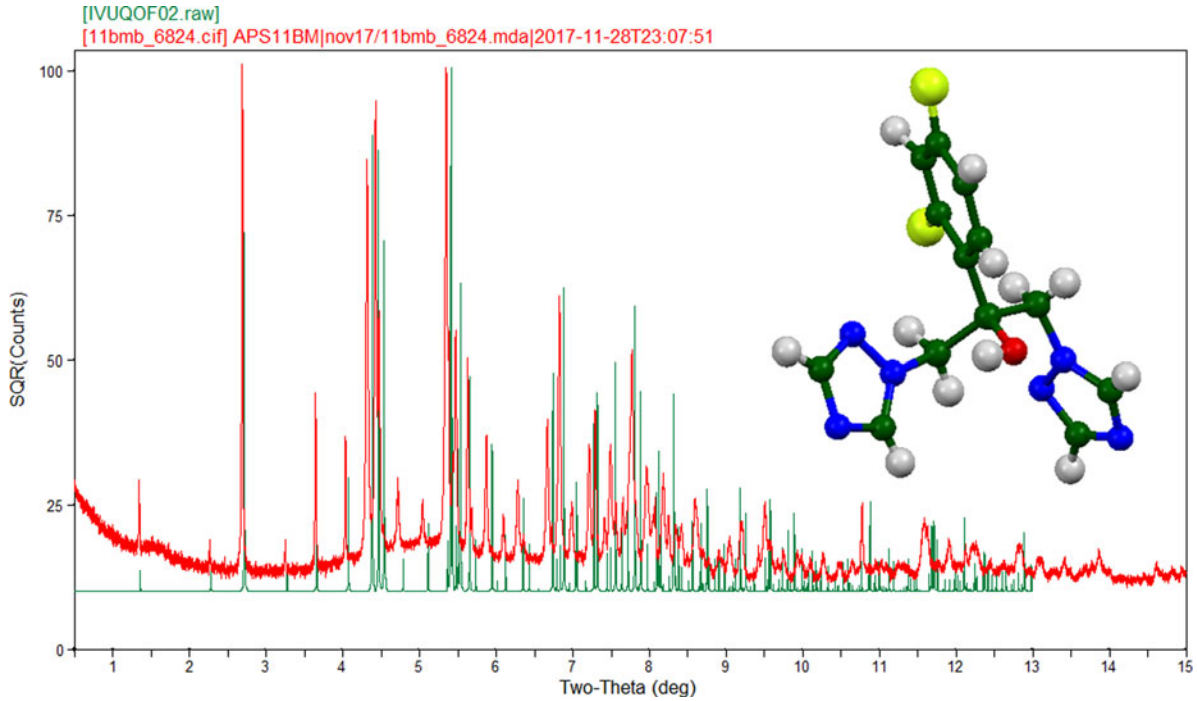

Figure 1. (Color online) Observed (295 K, red) and calculated (100 K, green) powder X-ray diffraction patterns of fluconazole polymorph V. Note the shift to higher 2θ (smaller d-spacing) for the 100 K diffraction pattern when compared to the 295 K diffraction pattern.

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SUPPLEMENTARY MATERIAL

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