

Preparation and Crystal Characterization of a Polymorph, a Monohydrate and an Ethyl Acetate Solvate of the Antifungal Fluconazole

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**Abstract:** The preparation and solid-state characterization of three crystalline modifications of the antifungal agent fluconazole [2-(2,4-difluorophenyl)-1,3-bis(1H-124-triazol-1-yl)-propan-2-ol] are reported. Recrystallization of fluconazole from propan-2-ol yielded a polymorph (Form III) whereas the solvents water and ethyl acetate yielded the solvated products fluconazole monohydrate and fluconazole·(ethyl acetate)<sub>0.25</sub> respectively. These species were analysed by thermogravimetry (TGA), differential scanning calorimetry (DSC), FTIR spectroscopy, powder X-ray diffractometry (PXRD) and single crystal X-ray diffraction. Availability of the hitherto unknown crystal structures facilitated interpretation of the thermal data and clarified previous findings relating to the polymorphism of this compound. Fluconazole was found to exist as a centrosymmetric hydrogen bonded dimer in Form III. For the solvated phases, the solvent locations within the drug host matrices were established as isolated sites for water molecules and constricted channels for ethyl acetate molecules. Desolvation of the monohydrate and ethyl acetate solvate yielded polymorphic Form I. Reference PXRD patterns computed from the refined single crystal X-ray data for the title compounds are presented.