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Solid State Characterization of Fluconazole

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Abstract: Two polymorphs and three solvates of fluconazole were isolated and characterized by X-ray powder diffractometry (XRPD), IR spectroscopy, differential scanning calorimetry (DSC), thermogravimetry (TGA) and their dissolution rates. The different forms were prepared by crystallization of the original powder in different solvents at different cooling rates. The X-ray diffraction patterns of the five solid modifications exhibited substantial differences in both the intensity and position of the peaks. FTIR spectrums of the five different solid-state modifications also exhibited differences in the peaks' positions and intensities. DSC thermogram of anhydrate form I showed a single melting point at 139.2°C. Anhydrate form II showed two endothermic peaks at 136.5°C and at 139.2°C and one exothermic peak in between. The DSC thermogram of acetone 1/4 solvate exhibited two endothermic peaks at 75.5°C and at 139.2°C. Benzene 1/7 solvate exhibited two endothermic peaks at 131.5°C and 138.8°C. Hydrate E exhibited two endothermic peaks at 102.7°C and 139.2°C. The DSC thermogram of anhydrate form II showed that this form is sensitive to the application of a mechanical force. The solubility study showed that anhydrate form II and acetone 1/4 solvate have higher solubilities than anhydrate form I, while benzene 1/7 solvate and monohydrate have lower solubilities than anhydrate form I. The intrinsic dissolution study confirmed these results.