394c Polymorphic Behaviour and Morphology of an Anti-Viral/HIV Drug: Stavudine

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Different characterization methods (optical and thermo-microscopy, DSC, TGA, XRD and solid state FTIR) were used to identify the two polymorphs and one hydrate of stavudine. The two forms are monotropically related and Form 1 is the stable polymorph. The effects of solvent, impurities, supersaturation (S) and mixing on the polymorphic occurrence of stavudine are investigated in detail. Hydrogen bonding analysis is employed to qualitatively predict the role of the solvent and structurally related impurities (thymine and thymidine) on polymorphism and morphology of stavudine crystals. The impurities showed significant changes in the morphology and crystal bulk density of solid stavudine but no influence on the polymorphic structure. Depending on the degree of supersaturation at T = 25 „aC, a specific polymorph or a mixture of Forms 1 and 2 was obtained. In isopropanol, below S *f*° 2.05, only pure Form 1 was obtained and above S *f*° 2.12, pure Form 2 was the product. Between S *f*° 2.05 and S *f*° 2.12 a mixture of the two polymorphs was produced concomitantly. These experiments showed that supersaturation is a critical factor in isolating the two polymorphs of stavudine. On the other hand, the impurities did not have a significant effect on the polymorphic outcome of stavudine. The morphology and the density of stavudine crystals, however, were strongly influenced by the presence of impurities.