Crystal Polymorphism of Norfloxacin

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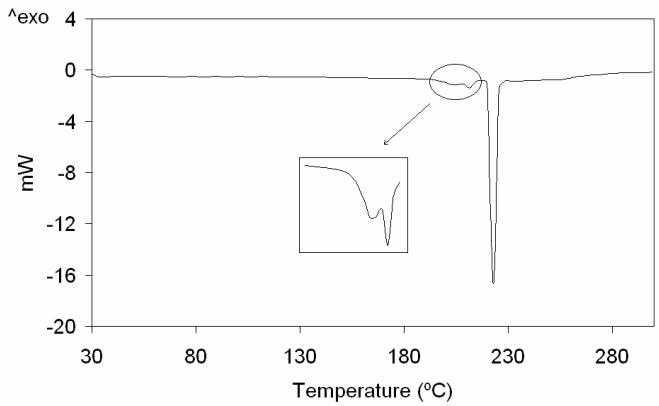
Polymorphism and crystallization have become an increasingly important and relevant topic in the pharmaceutical/generic drug market. Delivering an active pharmaceutical ingredient with the desired crystal form, size, purity and acceptable yield is always a challenge. Many drugs exhibit polymorphism and their physical forms are vital for obtaining the desired therapeutically effective product. The ability of a particular polymorph to crystallize is usually determined by both thermodynamic and kinetic factors. These factors must be well understood in order to explore and control the polymorphic behaviour of a substance.

Norfloxacin is a synthetic broad antibacterial fluoroquinolone compound used in the treatment of gonorrhea, prostate and urinary tract infections. Norfloxacin was known to exist in two polymorphic forms.[1] A new interpretation of this polymorphic system is described. We prove that the previous knowledge of this active pharmaceutical ingredient was erroneous due to a wrong identification of the system as a monotropic type. Our results of solvent mediated transformation experiments are in concordance with the fact that the observed solid-solid transition by DSC is endothermic.[2] These evidences are enough to demonstrate the enantiotropic relationship between both solid forms, being Form B the most stable one at room temperature. This can be important because many commercial samples of Norfloxacin are provided as the metastable form at room temperature and then, undesirable transformations could occur. Full characterization of both forms by X-ray crystallography, DSC, IR, Raman and solid-state NMR spectroscopy is provided. Moreover the crystal structure of Form A has been solved.



(1) Sustar, B.; Bukovec, N.; Bukovec, P. *Journal of Thermal Analysis* **1993**, *40*, 475-481.

(2) Barbas R.; Martí, F.; Prohens, R.; Puigjaner, C. Submitted for publication.