

TOWARD A RATIONALIZATION OF THE HYDRATION-DEHYDRATION MECHANISM OF SODIUM DICLOFENAC

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Understanding the hydration behaviour of a pharmaceutical material is vitally important for its successful development and formulation. Sodium diclofenac is one of the marketed salts of 2-[2-(2,6-dichlorophenylamino)phenyl]acetic acid, and is a hygroscopic compound known to crystallize as a hydrated species, Figure 1 [1]. The crystal structures of two different hydrate species with two different stoichiometries, a tetrahydrate [2] and a pentahydrate [3], have been published. These crystal structures appear to be similar and were eventually rationalized by the publication of the 4.75 hydrate structure, [4], containing four moles of sodium diclofenac and 19 moles of water in the asymmetric unit of the crystal structure. Furthermore, a hemihydrate species [5] has also patented but no evidence of its existence has yet been found, despite intensive attempts on the characterization of this mysterious phase.

This work aims to completely rationalize the behaviour of the diclofenac sodium-water system by construction of the three component phase diagram and by the use of X-ray powder diffraction (both variable temperature and variable relative humidity) and also single crystal X-ray micro-diffraction studies.

Using high resolution, high quality data the dehydration/rehydration processes of this compound are revealed and a hitherto unknown 3.5 hydrate phase has been discovered and completely characterized. These data are used in conjunction with dynamic moisture sorption - desorption investigations and TGA-DSC to provide a full description of the system.

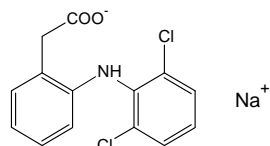


Figure 1: Sodium Diclofenac.

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