Solvent Exchange Mechanisms among Pharmaceutical Crystals: From Topotactic to Destructive-Reconstructive Processes

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The development of systematic procedures for the research of polymorphic forms and solvates of pharmaceutical compounds has induced a drastic increase of the number of crystalline forms identified as solvates or even mixed solvates [1]. Simultaneously, recent studies have highlighted that phases identified as non solvates could actually consist of solvates undergoing a spontaneous and non-destructive desolvation during drying [2].

Since it is now well established that both storage and experimental conditions of manufactoring processes (grinding, compaction, tabletting, wet granulation, freeze-drying, etc.) can induce physical transformations of solid state samples [3,4], the understanding of solid-solid transformations which can occur between crystalline forms of pharmaceutical compounds is of major importance.

The present communication investigates the mechanisms involved in two extreme situations of solvent exchanges occurring between crystalline pharmaceutical solvates. In the case of Roxithromycin, it was observed that the acetonitrile solvate can be transformed into the monohydrate through a smooth and cooperative exchange of solvent molecules. By contrast, the DMSO and EtOH solvates of Dexamethasone Acetate evolved towards a sesquihydrate when single crystals of the former solvates were immersed in water, and this transformation was shown to be associated to the formation of whisker-like crystals [5].

The characterization of each form by means of XRPD and thermal techniques, the use of optical and electronic microscopies, and the analysis of crystal structures allowed to perform a comparative analysis of these solvent exchanges, and to elaborate hypothetical mechanisms allowing to account for these transformations. Our interpretations and classifications show that the associated mechanisms can be, at least to a certain extent, compared to that developed in the case of dehydration processes [6].

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