STUDYING STRUCTURAL ASPECTS OF SALT HYDRATION BY VT-PXRD

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Pharmaceutical molecules containing ionisable groups can be formulated as salts to optimise key physicochemical properties including solubility, melting point, hygroscopicity and crystal habit.[1] Contact with water during processing and storage can result in the incorporation of water molecules into the crystal lattice to produce a hydrate with different physicochemical properties to the anhydrous material.[2] Hydrate formation is a key parameter in the selection of a suitable pharmaceutical salt form and the comparison of anhydrous and hydrated salt structures is investigated here to inform on the relationship between molecular packing and hydrate formation in organic salts. We have selected a range of hydrated salts from a bespoke library synthesized from organic bases and a range of pharmaceutically acceptable organic acid counterions. Variable-temperature X-ray powder diffraction (VT-XRPD) and structure determination from powder diffraction data (SDPD) using DASH[3] is employed to characterise the corresponding dehydrated salt structures. The structures of anhydrous tartaric acid salts have been determined and key structural features including hydrogen bond motifs and crystal packing arrangements are compared with the corresponding hydrates, to examine the structural consequences of the removal of water from the lattice. Structural comparisons are carried out using a range of software packages including Mercury [4] and xPac.[5]

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