Non-Stoichiometric Hydrates: Classification & Composition Determination using VH-PXRD with Moisture Sorption Profiles

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For small molecule crystalline pharmaceuticals, hydrates are a common occurrence. Hydrates are often classified as stoichiometric or non-stoichiometric. Typically, stoichiometric hydrates have well defined water content and often have a different crystal structure to their anhydrous equivalent. Conversely, non-stoichiometric hydrates have a variable composition of water depending on the water activity or RH of the environment. The crystal structure of non-stoichiometric hydrates typically expand or contract anisotropically to account for the variability of lattice water.

It is important to determine the type of hydrate and the composition of pharmaceutical hydrates as stability, handling, labeling and biopharmaceutical properties may be impacted. For non-stoichiometric hydrates characterization can be complicated. Single crystal XRD (SCXRD) is often the gold standard to determine structure, stereochemistry, conformation and composition of materials. However, the lattice water in non-stoichiometric hydrate structures may appear to be disordered and therefore hard to be resolved by SCXRD. Also for SCXRD it is necessary to obtain single crystals of reasonable size and that retain their diffraction quality through ingress/egress of water, which may not always be the case.

The poster will highlight the refinement of the SCXRD unit cell against the bulk PXRD at a given RH to show the expansion of the unit cell as function of humidity. Given that the moisture sorption profile gives water weight gain as a function of humidity, the unit cell dimension change is compared to the gravimetric moisture sorption data as a function of RH and is in good agreement. Compositional information of a particular unit cell can therefore be inferred from the extent of water uptake observed in the moisture sorption data at a particular humidity. In order to obtain in-situ VRH-XRD data, the poster will highlight a low tech method for collecting data without the need for an expensive stage but by using environmentally controlled, sealed capillaries.

Different types of hydrate/anhydrate systems categorized based on their moisture sorption isotherms and SCXRD structures were evaluated: (a) a non-stoichiometric hydrate with linear increase in water uptake as a function RH; (b) a non-stoichiometric hydrate with a non-linear water uptake as a function of RH; (c) an anhydrous/ hydrate system that is isostructurally related but exhibits a step change in the moisture sorption profile.