

Moisture Sorption Studies in the Characterization of Drug Hydrates

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Moisture uptake is a significant concern in the development of pharmaceutical products and the ability of materials to absorb moisture is often a key factor in decisions related to processing, packaging, storage and shelf-life. Interactions of materials with moisture are manifold and may affect the physical and/or the chemical state of the material. One of the most important interactions is the formation of hydrates where water is situated in more or less defined lattice positions of crystalline compounds. About 30% of the drug substances and many excipients are known to form hydrates and due to the high complexity of such solids in terms of analytical aspects, manufacturing and storage, suitable analytical strategies are very important in order to shorten the time scale of the drug development.

Besides thermal analysis the most important methods in the characterization of hydrates are moisture sorption/desorption studies which provide information about the extend and the kinetics of the water uptake or loss. From the course of the moisture sorption-/desorption isotherms the state of water associated with the solid can be roughly estimated. Discontinuous changes in the isotherm indicate phase changes in the solid *i.e.* the formation of stoichiometric hydrates whereas discontinuous changes are mainly based on the absorption of water into structural voids. The latter is not connected with a phase change of the solid and concerns non-stoichiometric hydrates. However, in order to realize the kind and extend of changes of the crystal lattice it is important to combine moisture sorption studies with suitable methods like X-ray powder diffractometry.

As the evaluation of a complete water sorption/desorption isotherm with classic methods (saturated salt solution, integral isotherms) requires large amounts of sample and is time consuming because of hundreds of manual weighings, automated moisture sorption analyzer have been developed. These systems use highly sensitive Cahn balances and the weight changes small amounts of a sample can be continuously monitored in atmospheres of controlled composition (interval isotherms). Even though the instruments work fast because of a dynamic atmosphere the overall sample throughput is low since only one sample can be analyzed. Thus a new automatic analyzer (SPS11) has been developed which enables the investigation of 11 samples simultaneously. This instrument is designed for high throughput moisture sorption studies but requires larger amounts of samples (> 10 mg) than the analyzer based on Cahn balances. However, since sample weights up to 180 g and specimen diameters up to 5 cm can be analyzed, the device is usable for a wide variety of applications. In this contribution results from investigations of drug hydrates obtained with this analyzer as well as with classical moisture sorption methods are given and general concepts and strategies of hydrate studies are discussed.