Non-ambient Applications of X-ray Diffractometry for the Characterization of Pharmaceutical Systems

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X-ray diffraction patterns obtained while subjecting the sample to an elevated temperature program enabled the characterization of a variety of physical transformations including polymorphic conversion, dehydration and crystallization. In amorphous drugs as well as in amorphous solid dispersions (homogenous drug-polymer mixtures), the drug crystallization kinetics was evaluated by performing X-ray diffractometry under isothermal conditions at several elevated temperatures. This served as a measure of the physical stability of these systems.

Low temperature XRD was used to characterize the solid-state of the solutes in multi-component systems during all the stages of the freeze-drying process. Phase transitions during drying were monitored by simulating the entire freeze-drying process, in situ, in the sample chamber of the diffractometer (both laboratory source and synchrotron radiation). Trehalose, a widely used lyoprotectant, crystallized as a dihydrate when the frozen solution was annealed. Annealing also facilitated mannitol crystallization and low annealing temperature facilitated the formation of mannitol hemihydrate. The concentration of the active ingredient (typically a protein) as well as the processing conditions (annealing temperature and time, drying temperatures) influenced the physical form of excipients in the final lyophile. The formulation components have the potential to influence the physical form of one another during the different stages of the freeze-drying cycle.