Applications of X-ray powder diffractometry in preformulation and formulation studies

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Conventionally, X-ray powder diffractometry (XRD) has been used extensively for the identification of crystalline solid phases. Recent advances in instrumentation and software have extended the utility of the technique to the characterization of complex, multicomponent systems. Thus the active pharmaceutical ingredient in a complex dosage form, and more importantly, phase transitions induced during processing and storage were evaluated and quantified. For example, the water released by dehydration of the active pharmaceutical ingredient mediated cocrystal formation in intact tablets. The use of an X-ray microdiffactometer with an area detector permitted us to monitor phase transformations in intact tablets. The spatial information, gained by monitoring the tablet from the surface to the core (depth profiling), enabled the quantification of the transformation in different regions of tablets. Low temperature XRD enabled the physical characterization of solutes in frozen aqueous solutions. By appropriate modification of the instrument, the entire freeze-drying cycle (cooling, annealing, primary and secondary drying) was carried out in the sample chamber of the XRD. This allowed real time monitoring of phase transitions during all the stages of the freeze-drying process. The phase transitions of multiple analytes were simultaneously monitored and quantified. The use of synchrotron radiation, by substantially enhancing sensitivity, extended the applications of XRD. The crystallization onset and kinetics were monitored, both in neat drug and from amorphous solid dispersions.

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