Qualitative and Quantitative Applications of Non-ambient X-ray Diffractometry

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Variable temperature powder X-ray diffractometry (XRD) is a technique wherein XRD patterns are obtained while a sample is subjected to a controlled temperature program. It is an excellent complement to other thermoanalytical techniques such as differential scanning calorimetry and thermogravimetric analysis. This technique has been used to detect a metastable anhydrous phase formed during dehydration of theophylline monohydrate.

Aminophylline monohydrate transformed to theophylline, either directly or through aminophylline anhydrate as an intermediate. Since XRD permitted simultaneous quantification of the reactant, intermediate and product phases, it was possible to study the effects of temperature, water vapor pressure and processing on the kinetics of this complex reaction.

Finally, low temperature XRD enabled the physical characterization of solutes in frozen aqueous solutions. By attaching a vacuum pump to the low temperature stage of the diffractometer, it was possible to carry out the entire freeze-drying process *in situ*, in the sample chamber of the XRD. This enabled real time monitoring of phase transitions during all the stages of the freeze-drying process. Several pharmaceutical excipients including mannitol, trehalose, glycine, sodium chloride and also excipient mixtures were investigated by this technique.

Keywords: XRD, low temperature, reaction kinetics