

Quantitative Analysis of Crystallinity of Pharmaceutical Powders: Industrial Needs

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The majority of pharmaceutical compounds and excipients are manufactured or processed as powders. These pharmaceutical powders exhibit a wide range of crystallinity from almost perfect ordered crystalline lattices to completely disordered amorphous states. Variations in crystallinity can significantly alter physical and chemical properties such as the dissolution rate, reactivity and consequently stability, hygroscopicity and processability of the solid material.

Various analytical methods have been employed to assess the crystallinity of pharmaceutical powders, including X-ray powder diffraction, differential scanning calorimetry, isothermal microcalorimetry, solution calorimetry and moisture sorption analysis.

Applications of isothermal microcalorimetry and isothermal solution calorimetry will be discussed in more detail. Isothermal microcalorimetry is a highly sensitive technique used for the quantification of amorphous content of solids. In some cases, amorphous contents as low as 0.3% can be detected. This is, however, restricted to amorphous solids where recrystallization can be easily initiated, preferably using defined relative humidity conditions. The time taken for a single determination may require a full day, making it an expensive method if used on a routine basis for quality control of pharmaceutical solids.

Solution calorimetry is able to measure directly the heat change caused by the dissolution of a crystalline or partially crystalline powder. The observed heat of solution is a function of the variability in crystallinity displayed. The quantification of crystallinity, however, requires the availability of pure amorphous and pure crystalline standards. The substance must also have sufficient solubility in a suitable solvent.

References

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