Applications of Solution Calorimetry in Characterisation of Pharmaceutical Powders

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Solution Calorimetry is a thermal technique able to measure directly the heat change caused by the dissolution of a crystalline or partially crystalline powders. This technique can be used to measure solid-state properties such as crystallinity, amorphocity and polymorphism. It can distinguish between solid-state changes caused by processes such as milling and micronisation. Furthermore, it is sensitive enough to detect temperature changes to 1µK corresponding to an energy of 1-4 mJ. Typical sample weights are 100mg-500mg and energy changes as little as 10mJ/g can be determined.

Solution calorimetry is used to characterise different polymorphs or solvates by monitoring the heat of solution recorded at constant temperature (typically between 25° - 50°C). In particular, this technique is useful in cases were melting enthalpies can not be measured by DSC as polymorphs interconvert upon heating or melting and decomposition occurs at the same temperature. However, heat of solution includes several processes such as wetting, which may de different for different polymorphs. In the shown example heat of solution measurements are correlated with DSC results.

Furthermore, solution calorimetry was used for quantification of crystallinity or amorphous content. 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. For the shown example the pure crystalline and pure amorphous forms gave a heat of solution in ethanol of 18 kJ mol^{-1} and -5 kJ mol^{-1} respectively. Data were correlated with other analytical techniques such as x-ray powder diffraction (XRPD) and differential scanning calorimetry (DSC).