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The Characterisation of Pharmaceutical Powders by Solution Calorimetry

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Solution calorimetry is a thermal technique that is able to measure the heat change produced by the dissolution of a crystalline or partially crystalline powder. This method can be used to measure solid-state properties such as crystallinity, amorphocity and polymorphism. It can also 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 50-500mg and energy changes as little as 10mJ/g can be determined.

Polymorphs or solvates can therefore be characterised by monitoring the heat of solution at a given temperature (typically between 25-50°C). It is of particular use where melting enthalpies cannot be determined by differential scanning calorimetry (DSC) owing to the interconversion of polymorphs upon heating or melting and simultaneous decomposition. The heat of solution however, incorporates several processes including wetting, which may be different for different polymorphs. In the presented example, the heat of solution measurements are correlated with differential scanning calorimetry (DSC) results.

Solution calorimetry was also used for the quantification of crystallinity and amorphous content which required the availability of a suitable solvent, in addition to pure amorphous and pure crystalline standards. The pure crystalline and pure amorphous forms, in this example, gave a heat of solution in ethanol of 18 kJ/mol and -5 kJ/mol respectively. Data were correlated with additional analytical techniques such as x-ray powder diffraction (XRPD) and differential scanning calorimetry (DSC).