Application of microcalorimetry in pharmaceutical industry

Michael Mutz
Novartis Pharma AG, Chemical and Analytical Development Basel

Microcalorimetry in the pharmaceutical area is applied in different fields of application as solid state properties of drugs and excipients, chemical stability studies or biological calorimetry. Among those the application of microcalorimetry for determination of amorphous contents or crystallinity of pharmaceutical drugs and excipients will be discussed in the presentation.

Processing powders by milling or micronization often generates amorphous regions at the particle's surface. The amorphous regions can alter the physical properties of the material, which may have an impact on further pharmaceutical processes or the quality of the material.

Microcalorimetry is a very sensitive way to measure amorphous contents well below 1%. The heat of recrystallization of the amorphous parts can be measured and by a suitable calibration the amorphous content can be determined. Solution calorimetry is able to measure directly the heat change caused by the dissolution of a crystalline or partially crystalline powders. The observed heat of solution is a function of the variability in crystallinity displayed. The quantification of amorphous contents, however, requires the availability of pure amorphous and pure crystalline standards.

The health authorities require that for bringing a drug product to man appropriate quality control measures and cGMP concepts should be applied. This requires qualification of the analytical instruments and validation of the test procedure to demonstrates that a test procedure is adequate for its intended purpose. Some concepts for microcalorimetry will be discussed.

References

K. Fiebich and M. Mutz, Evaluation of calorimetric and gravimetric methods to quantify the amorphous content of Desferal, J. Thermal Analysis and Calorimetry, 57 (1999) 75-85.

D. Gao and J. H. Rytting, Use of solution calorimetry to determine the extent of crystallinity of drugs and excipients, Int. J. Pharm. 51 (1997) 183-192.

G. Buckton et al. The use of isothermal microcalorimetry in the study of small degrees of amorphous content of powders, Int. J. Pharm. 117 (1995) 253-256.