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## Detection of Low Crystalline Amounts of a Drug Substance in Solid Dispersions by DSC

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The poor oral bioavailability of drug substances with a low aqueous solubility can be improved by the application of solid dispersions as a formulation principle. In these systems the drug is finely dispersed in an amorphous form within a water soluble inert carrier. For the development of an optimal solid dispersion formulation and manufacturing process and prediction of the physical stability sensitive analytical tools are necessary to enable detection of low levels of the crystalline content of the drug in these systems since such amounts can act as seeds for further crystal growth resulting in deterioration in the product performance.

In this study the use of the conventional Differential Scanning Calorimetry (DSC) to charcterise the physical stability of the model system was not possible because of interfering thermograms of the individual consistuents of the formulation and a complex polymorphism of the drug substance. A simple washing technique was therefore developed to isolate the drug from the matrix for further characterisation making use of a sufficient difference in the aqueous solubilities between the drug and matrix which is usually the case in solid dispersion systems and a prerequisite for a successful application.

The results were confirmed by XRPD, mass- and enthalpy balances.

The procedure could be used qualitatively to characterise systems which consisted of drug concentrations at 1% w/w. A quantification seems to be possible in systems where the drug concentration exceeded about 3%. Below this, semiquantitative conclusions can be drawn.

The concept described within this work was not only applicable to cases where the individual components of a drug-matrix system gave interfering DSC thermograms but also to enrich the drug substance with the aim to improve the detection limit of small crystalline phases. The technique was found to be simple to use and applicable to a range of drug-matrix systems. The technique has been successfully applied to various drug - solid dispersion systems with different polymers and surfactants.

The limits of the technique are also discussed.

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