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USE OF DSC ROBOTIC SYSTEMS IN PHARMACEUTICAL ANALYSIS

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DSC is extremely valuable for analysis of pharmaceuticals. The introduction of robotic systems with data acquisition and processing makes it very competitive to other methods in the field of purity determination or solid state characterization of raw materials. Some applications are also possible to dosage forms. Applications of DSC robotics with statistical results are given.

I. Introduction

Differential scanning calorimetry may be widely used in all fields of pharmaceutical analysis [1–4] for raw materials and dosage forms: identifications, polymorphism and pseudo-polymorphism studies, purity and quantitative analysis.

The introduction of robotic systems with auto-sampling, data acquisition and data processing, makes it quite competitive to other routine analytical methods as melting point determination, spectroscopy or chromatography for routine control as well as for development work.

II. Instrument

Three companies offer robotic systems: Perkin–Elmer (DSC–4 and DSC–7), DuPont and Setaram.

The examples given here have been obtained with the Perkin–Elmer DSC–7 robotic system.

The system is composed of a removable 48 position sample carousel and a pneumatically controlled robotic sampling arm. This automatic loading and unloading system with the DSC sample holder forms an independant unit. Programming and activation are controlled by the Computer PE 7700. When in operation, the robotic arm automatically selects a desired sample from any of the 48

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carousel positions, places it in the DSC sample holder and closes the sample holder enclosure cover.

Several heating/cooling cycles are possible for each sample and are programmed with the computer. Data are aquired according to the given instructions and data processing is possible at any time after the measurement.

The repeatability of the system is demonstrated by the good standard deviations obtained for melting point and melting enthalpy of different samples of pure indium at 3 different heating rates, measured in one run as given in Table 1.

Table 1 Repeatability of the DSC–7 robotic system. Indium at different heating rates

Heating rate, deg·min^{-1}	Melting energy, J g^{-1}	*s*, rel.%	Onset, °C	*s*, rel.%	*n*
10	28.22	0.57	156.83	0.007	6
5	28.55	0.30	156.34	0.003	6
2.5	28.56	0.10	156.29	0.008	6

As expected the calorimetric accuracy is lower at high heating rate. The differences of the onset values are due to the thermal lag of the sample holder and are used for temperature corrections.

III. Rational applications

III.1 Calibration

Calibration of temperature and enthalpies are done very quickly, allowing frequent controls and therefore conforming to pharmaceutical SOPs. Table 2 is an example of a run overnight.

III.2 Raw material characterization

III.2.1 Glass transition

Table 3 demonstrates the reproducibility of glas transition determination of polyvinylpyrrolidone (anhydrous). The DSC scans are given in Fig. 1. The glas transitions of marketed polyvinylpyrrolidone types given in Table 4 can be used for identification.

III.2.2 Melting point determination

DSC allows more accurate melting point determination than classical methods. The onset temperature is defined as melting point.