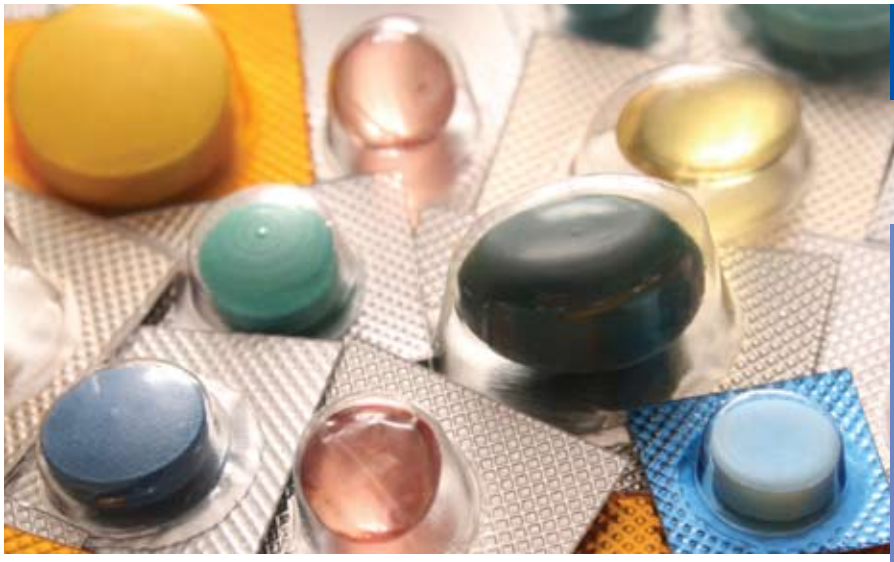

APPLICATION BRIEF

Thermogravimetric Analysis – Mass Spectrometry

Evolved Gas Analysis: a High Sensitivity Study of a Solvent of Recrystallization in a Pharmaceutical

Typical applications of TG-MS include:

- Detection of moisture/solvent loss from a sample (e.g. loss on drying or dehydration of a pharmaceutical)
- Thermal stability (degradation) processes
- Study reactions (e.g. polymerizations)
- Analysis of trace volatiles in a sample (e.g. volatile organic compound (VOC) testing)

Introduction

Thermogravimetric analysis (TGA) of materials is commonly used to measure weight loss as a sample is heated or held isothermally. In the pharmaceutical industry, materials often show weight losses associated with the loss of solvent/water, desolvation or decomposition of the sample. This information is then used to assess the purity and stability of the material and its suitability for use. The TGA gives a quantitative measure of mass lost from the sample, but it does not provide information on the nature of the products that are lost from the sample, and this information is often required for complete characterization.

Coupling a mass spectrometer (MS) to a TGA allows evolved gases to be analyzed and identified giving this additional valuable information.

Instrumental Setup

All of the TGA systems supplied by PerkinElmer (Pyris™ 1 TGA, STA 6000 and TGA 4000) can be easily interfaced to MS systems. PerkinElmer can supply systems with either the PerkinElmer Clarus® MS or with a Hiden Analytical MS. In this study, a Pyris 1 TGA interfaced to a Hiden Analytical HPR-20 MS was used.

Figure 1. Pyris 1 TGA is shown interfaced to a HPR-20 MS (left) and a Clarus 600 MS (right).

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The HPR-20 MS is optimized for the analysis of the evolved gases from the TGA and offers the following benefits:

- The ability to use either Faraday cup or secondary electron multiplier (SEM) detectors, depending on the sensitivity levels required. The SEM offers the ability to detect very low partial pressures of evolved gases below 10^{-8} bar, allowing identification of very low levels of contaminants. The system is able to operate in air, posing no issues for sample changing.
- Optional foreline and bypass vacuum pumping permits the most efficient pumping of helium which is normally used as a purge gas since it produces no interfering mass ions.
- A very flexible heated transfer line allows simple interfacing to the TGA systems. The lightweight heated line can be moved around in use without damage, making the system very robust. Gas transfer uses a wide-bore fused-silica capillary which gives 16 mL/min flow to the mass spectrometer for highest sensitivity.
- An anti-blockage filter has been added to catch high-molecular-weight material that might block the capillary. This single feature prevents hours of down time and cleaning with no loss of vacuum in the mass spectrometer.
- Soft ionization so the system can be optimized to reduce the splitting of ions leading to a simpler spectrum for analysis.

Experiment

In the following study, a Pyris 1 TGA was interfaced to a HPR-20 MS. The sample was heated to 200 °C at 10 °C/min with helium purge gas at 30 mL/min. A sample weight of 6.1374 mg was used.

A sample of a pharmaceutical was found to exhibit an unusual recrystallization behavior over a period of time. This behavior is often associated with the loss of a solvent from the sample. A method was required to confirm the suspected identity of the solvent which had been used in the production of the sample.

6.1374 mg of the sample was run in the TGA; the HPR-20 MS was used in multiple ion detection (MID) mode using the high-sensitivity SEM detector. The mass ion chosen to identify the presence of the solvent was 49 amu (atomic mass units) for dichloromethane.

The thermogram in Figure 2 shows the TGA trace collected for the sample. An extremely small weight loss of just 1.2 µg (0.026%) was found, indicating the outstanding performance of the Pyris 1 TGA.

The gases evolved during this very small amount of weight loss were analyzed. The background partial pressure of mass 49 was observed at a 2 x 10^{-11} bar and a slight peak to 5 x 10^{-11} bar observed in the weight loss region as shown below (Figure 3). Despite the very small amount of volatile loss and the correspondingly small increase in partial pressure, the MS was clearly able to detect this small change. This trace clearly indicates the loss of dichloromethane from the sample, as suspected, and shows the power of this technique to identify very small amounts of residual contaminants in a sample.

The application of TG-MS to low-level contaminants that would be undetectable by TG-IR is an example of the power of this technique. For more information, please contact your sales representative.

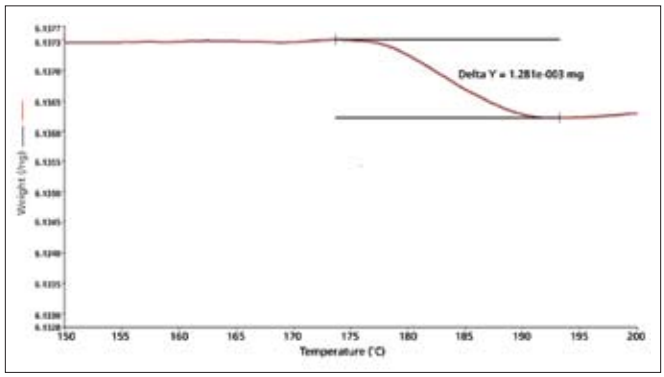

Figure 2. Weight loss due to the loss of solvent from the sample. Data has been expanded to show the weight loss clearly.

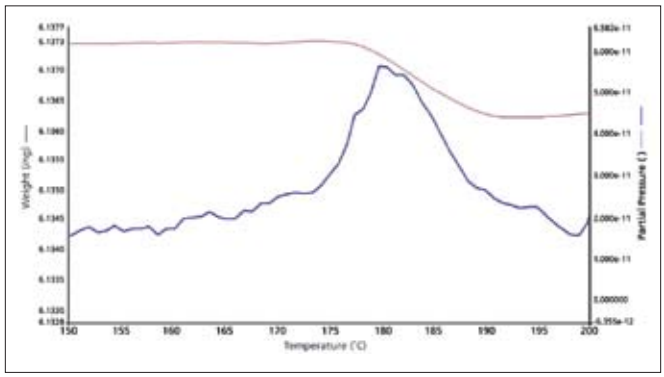

Figure 3. Weight loss curve and mass 49 (dichloromethane) in the 10^{-11} bar region.

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