

Thermogravimetric Analysis –
Mass Spectrometry

Evolved Gas Analysis: Residual Solvent Contamination Measured by Thermogravimetric Analysis-Mass Spectrometry

Introduction

Thermogravimetric analysis (TGA) of materials is commonly used to measure weight loss from a sample as it is heated or held isothermally. In the pharmaceutical industry, many materials 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, delivering this additional valuable information.

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)

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 (Figure 1). The example used in this application brief shows connection to the Hiden Analytical HPR-20 quadrupole mass spectrometer. However, the PerkinElmer® Pyris 1 TGA can also be coupled to our own Clarus® MS as shown in Figure 2.

Experiment

In the example below, a pharmaceutical sample was analyzed using a PerkinElmer Pyris 1 TGA connected to a Hiden HPR-20 MS spectrometer. The MS system had a mass range of 200 amu (atomic mass units) which is more than sufficient for most pharmaceutical analyses where solvent mass ions are mostly less than 100 amu. TGA purge gas flow rates are normally kept between 20–30 mL per minute total flow.

Often the ions of interest are unknown. In this case, a typical approach to analysis is to run a sweep across the mass range to see what mass ions are being given off from a sample, and then to hone in on the individual masses of interest in a second run known as an MID (multiple ion detection) trace. The MID trace allows much better quality of data for the ions selected since they are the only ions being sampled rather than a wide mass range where much less time is spent analyzing each mass ion.

One frequently asked question revolves around the loss of volatiles and what residual solvents remain in the sample, and whether these are associated with solvents used in the crystallization process. The following example shows sample with a broad weight loss of about 6% beginning around ambient and ending around 140 °C.

Moisture is found in many materials but a question was raised as to whether this event was solely due to water loss. Accordingly, the sample was analyzed for ethanol and acetone which may have remained from the production process, together with water. Water has a mass ion of 18 amu, and the primary mass ions of ethanol and acetone were chosen from the software library as 31 and 43 respectively. The library also shows that ethanol has a secondary mass ion of 43 so the presence of this ion may not uniquely identify the acetone. For this reason, a secondary mass ion for acetone of 58 was also chosen.

A sample was inserted into the TGA and the thermal program set up as normal. An additional trigger was programmed to start and stop the MS from the thermal software so that both systems were synchronized. During the run, the data can be observed as it is collected in the respective softwares. At the conclusion of the run, MS data can be imported into Pyris software and the data overlaid in time or temperature.

Results

Water was found to be present as expected from the mass 18 trace shown below with a partial pressure in the 10^{-7} range (Figure 3). The associated TGA curve is shown in Figure 4.

Other mass ions were obtained at significantly lower concentration in the 10^{-8} range see below. The water peak from the MS is shown overlaid on the TGA thermogram in Figure 5.



Figure 1. HPR-20 MS interfaced to the STA 6000.



Figure 2. PerkinElmer Clarus 600 C MS interfaced to the Pyris 1 TGA.

The mass 31 trace clearly indicates the presence of ethanol. Acetone is also present as shown by the mass 43 trace and confirmed by the mass 58 trace (Figure 6). As it happens, the fact that the mass 43 trace is in much higher concentration than the mass 31 trace in itself indicates the presence of acetone. If mass 43 were solely due to the presence of ethanol, it would be found in much smaller quantities than the ethanol primary mass ion. In this example, the mass 43 ion probably had a small contribution from the ethanol secondary mass ion.

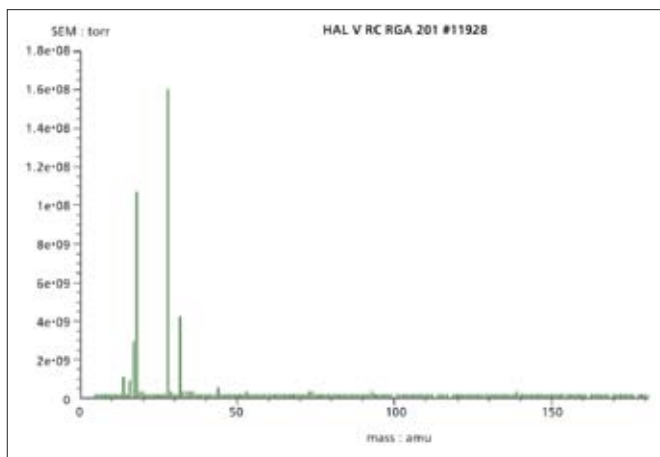


Figure 3. Bar graph initial sweep to assess what mass ions should be investigated.

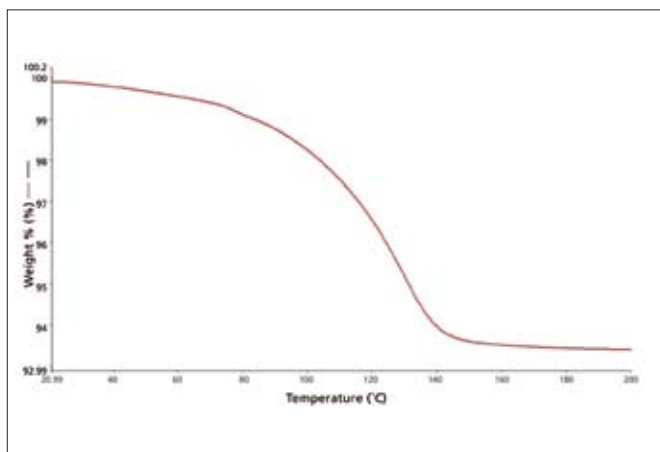


Figure 4. Sample showing a broad weight loss between ambient and 140 °C.

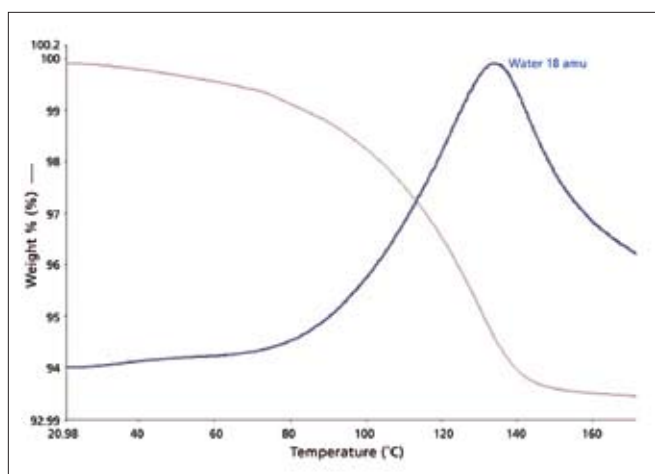


Figure 5. Weight loss and mass 18 (water) trace compared.

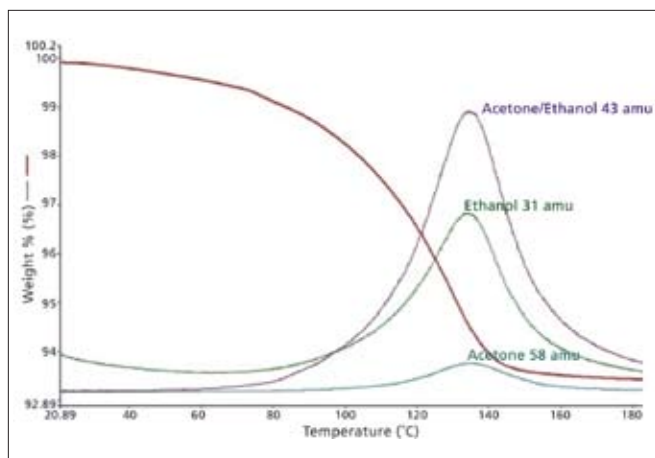


Figure 6. Weight loss compared with masses obtained in the 10⁻⁸ range.