



Evolved Gas Analysis

The Study of Materials using a Thermogravimetric Analyser (TGA) coupled to a Mass Spectrometer (MS)

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Introduction

Thermogravimetric Analysis (TGA) of materials is commonly used to provide information on the weight loss as a sample is heated or held isothermally. Pharmaceutical 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 characterisation.

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

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Typical applications of TGA-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. polymerisations

Analysis of trace volatiles in a sample e.g. Volatile Organic Content (VOC) testing



HPR20 interfaced to the STA6000

The HPR20 mass spectrometer is optimised 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 so allowing identification of very low levels of contaminants. The system is able to operate in air so 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 so making the system very

Instrumental Setup

All of the TGA systems supplied by PerkinElmer (Pyris 1 TGA, STA6000 and TGA4000) can be easily interfaced to MS systems. The example used in this note shows connection to the Hiden HPR20 quadrupole mass spectrometer.



HPR20 interfaced to the Pyris 1 TGA

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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.

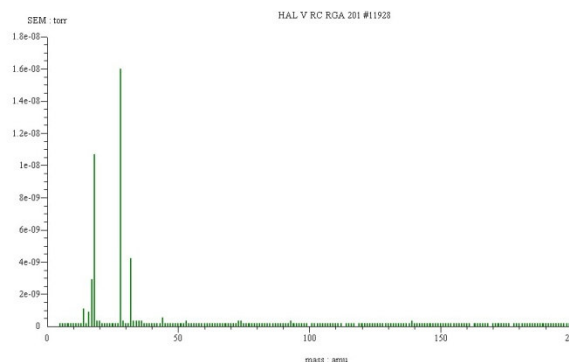
Soft Ionisation so the system can be optimised to reduce the splitting of ions leading to a simpler spectrum for analysis.

Experiment

In the example below a pharmaceutical sample was analysed using a PerkinElmer Pyris1 TGA connected to a Hiden HPR 20 mass spectrometer. The MS system had a mass range of 200 amu which is more than sufficient for most pharmaceutical analysis 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. Since 16 ml/min is taken to MS additional gas flow tends to dilute the evolved gases and reduce sensitivity.

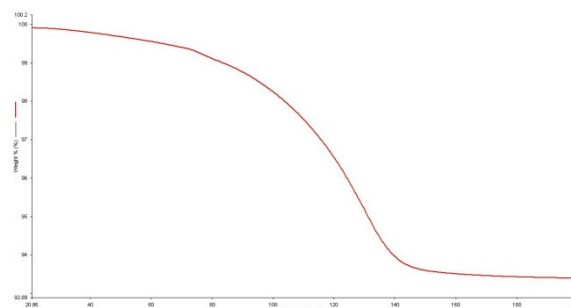
Often the ions of interest are unknown. In this case a typical approach to analysis is to run a sweep across the mass range to see what mass ions are being given off from a sample, and then to home in on the individual masses of interest in a second run known as an MID (multiple ion detection) trace. 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 analysing each mass ion.



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

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 crystallisation process. The example in figure 2 shows a broad weight loss of about 6% beginning around ambient and ending around 140 °C.

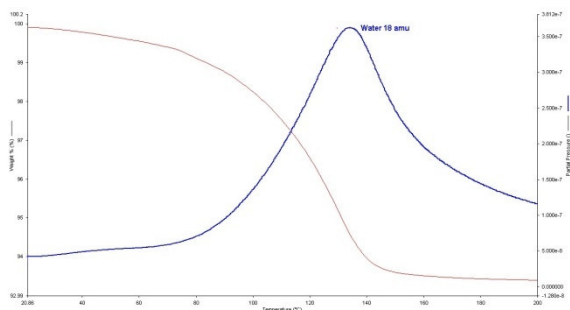


Moisture is found in many materials but it is unlikely that such a broad event is solely due to water loss. Accordingly the sample was analysed for ethanol and acetone which may have remained from the production process, together with water. Water has a mass ion of 18 amu (atomic mass units), and the 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.

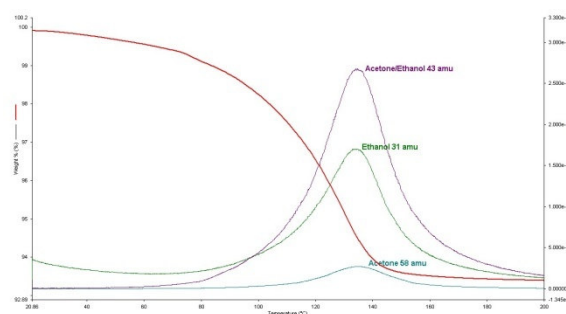
A sample was inserted into the TGA and the thermal program setup as normal. An additional trigger was programmed to start and stop the MS from the thermal software so that both systems were synchronised. During the run the data can be observed as it is collected in the respective software. At the conclusion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

Water was found to be present as expected from the mass 18 trace shown below with a partial pressure in the 10-7 range.



Weight loss and mass 18 (water) trace compared

Other mass ions were obtained at significantly lower concentration in the 10-8 range see below.



Weight loss compared with masses obtained in the 10-8 range

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. 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 was 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.

Acknowledgements

The authors would like to thank Peter Hatton, David Lundie and Luke Wells at Hiden Analytical for providing the HPR20 system and their assistance in developing this application.