APPLICATION NOTE

Thermal Analysis

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TG-IR Analysis of Decomposition Products of a Drug

Introduction

Ramoplanin is an oral antibiotic produced by the fermentation of Actinoplanes spp. It is active against both Gram-positive aerobic and anaerobic bacteria.

The complexity of the molecule, its amorphous form and lack of conventional crystallization means that the drug cannot easily be identified via DSC thermal analysis. After loss of humidity and residual solvents, it decomposes while releasing gaseous products.

The analysis performed by PerkinElmer set out to identify the gaseous products resulting from the decomposition of Ramoplanin.

Sample preparation

The sample was supplied in a sealed vial. TG-IR analysis does not require any kind of sample preparation; the amount of sample just needs to be weighed before the analysis. In this study, the analysis was performed in an air environment over a weighed sample of 1.262 mg, with a heating ramp of 25 °C/min in a temperature range of 20 °C - 900 °C.

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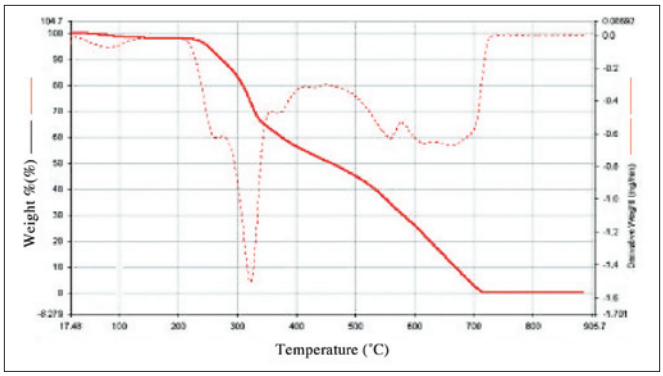

Figure 1. The TGA weight loss curve (solid) shows the loss of material as a function of temperature. The dotted line is the derivative curve which shows the rate of change and highlights various components coming off.

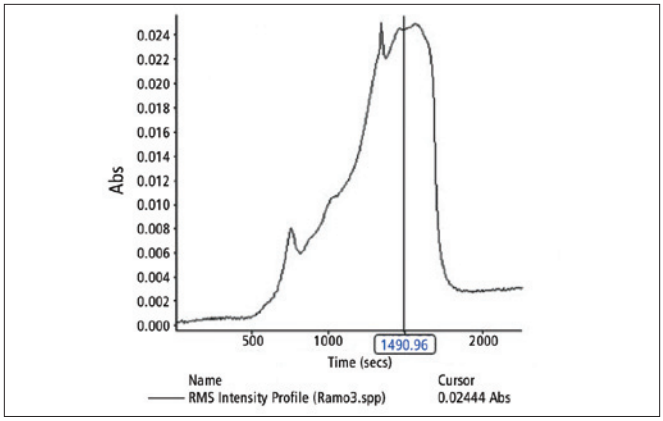

Figure 2. The gas emission intensity profile shows the overall intensity of the IR signal. Note the number of peaks matches the number of peaks in the derivative curve in Figure 1.

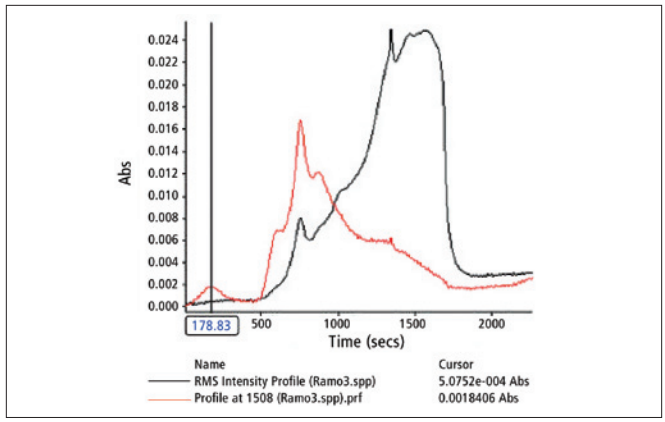

Figure 3. The intensity profile from Figure 2 is overlaid with the emission spectrum of water.

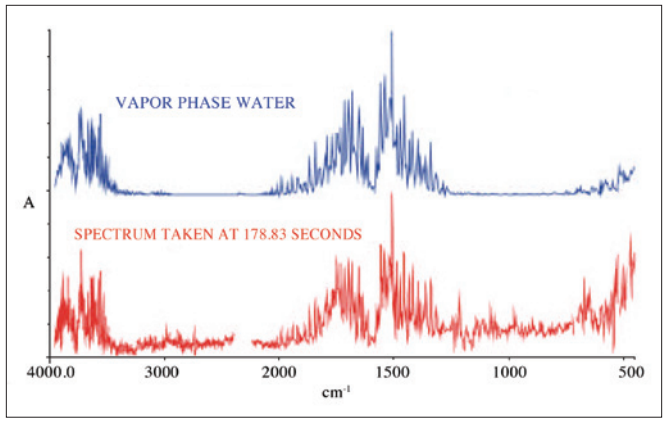

Figure 4. Water in vapor phase compared with the sample's spectrum acquired at 178.83 seconds.

Experimental conditions

TG-IR analysis was performed using a PYRIS® TGA thermobalance interfaced via a data transmission link to a FT-IR Spectrum™ 2000 infrared spectrophotometer.

The analysis was carried out in a nitrogen and air environment, with an almost identical sample decomposition seen in both settings. However, in the nitrogen environment, the product did not fully decompose – even at 900 °C – resulting in a consistent carbon residue. In air, the drug fully decomposed at a temperature of approximately 700 °C, releasing a large quantity of carbon oxides.

Discussion on results

TGA and DTGA curves are shown in Figure 1. Note the two main decompositions at temperatures of approximately 300 °C and 600 °C. This analysis demonstrates the highly complex decomposition process of the sample, with a variety of gases being released from different parts of the molecule – this will be discussed in more detail later.

TG-IR Analysis

Figure 2 shows the gas emission intensity profile. The TGA curve can be clearly seen and the number of peaks in the chromatogram equals the number of DTGA peaks. At around 100 °C on the TGA curve, a mass loss of the sample can be noted. Analysis of the gas released in this phase led us to conclude that the substance was water. Figure 3 illustrates the water emission intensity profile (shown in red) and Figure 4 shows the humidity spectrum against a standard spectrum of gaseous water.

The sample first started to decompose at temperatures ranging between 200 °C - 450 °C, losing approximately 22% of its mass. The IR analysis of the gas released in this phase shows that between 200 °C - 275 °C the sample releases water and a small quantity of hydrochloric acid (Figure 5).

As the temperature rose to between 280 °C - 450 °C, the sample released ammonia, water, CO_2, CO, plus an unidentified gas presenting a single rotation-vibration IR band at 2268 cm^{-1}, a typical absorption band of the -C=N group. Figure 6 shows the spectra acquired at 325 °C = 765 seconds, which shows the bands of these gases as a whole.

Starting from 460 °C up to 700 °C, the sample burned completely, releasing CO_2. Figure 7 shows the spectrum acquired at 650 °C compared with the carbon dioxide standard spectrum.

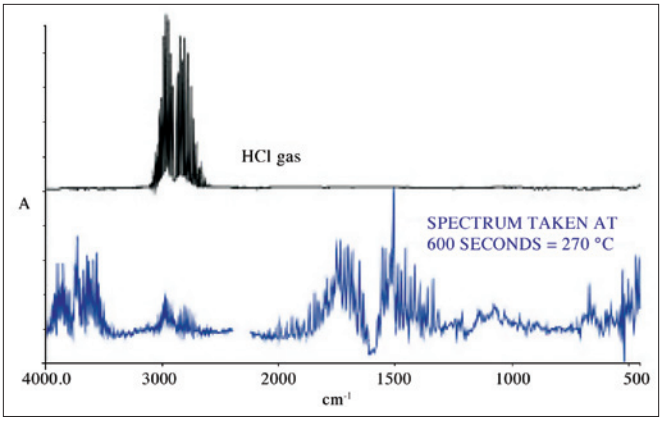

Figure 5. Spectrum at 600 seconds = 270 °C compared to spectrum at 600 seconds.

Conclusion

In conclusion, the Ramoplanin sample starts decomposing at about 210 °C, releasing water, hydrochloric acid, ammonia, CO_2, CO, plus an unknown gas (possibly cyanide acid).

PerkinElmer offers both Thermal Analysis and IR for better and more complete sample characterization from a single supplier.

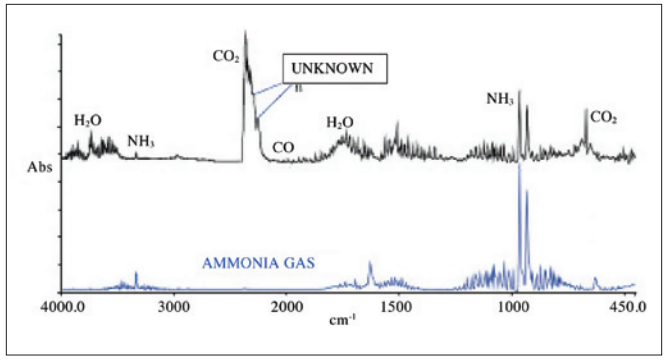

Figure 6. Ammonia compared to the sample spectrum.

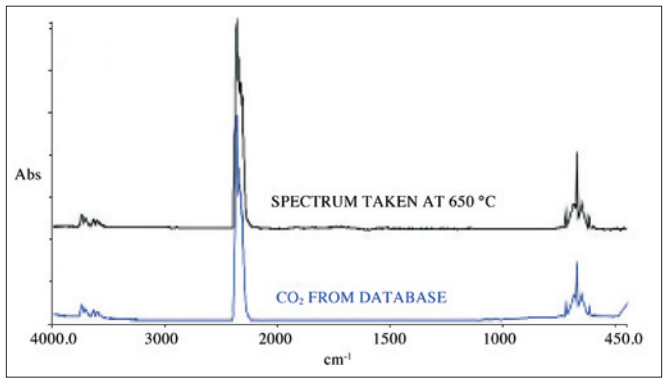

Figure 7. Spectrum acquired at 650 °C compared to CO_2 – standard spectrum.

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