TDTS 41

Analysis of the residual solvent dimethyl sulfoxide in a drug precursor

Summary

This Application Note describes the development of a method to analyse residual dimethyl sulfoxide in a sample of a drug precursor using direct thermal desorption.

Introduction

Many samples require intensive sample preparation before they can be analysed by GC or GC/MS methods. Conventionally, this is carried out by a single or multi-step solvent extraction, but this can be a complex and difficult procedure for some materials – including many pharmaceuticals. Critical aspects include selecting a solvent that is neither used in the drug manufacture nor likely to co-elute with the compounds of interest, but will completely dissolve the drug itself. Dissolution also limits the sensitivity of GC(MS) methods.

As described in Application Note TDTS 9, thermal desorption (TD) can provide a simple, high sensitivity and readily automated alternative to solvent extraction. If the sample is relatively homogeneous and in powder or granule form, like most drugs, small samples of the materials can be weighed directly into empty sample tubes or sample tube liners (Figure 1). These are then heated in a stream of carrier gas during the desorption process to extract the volatiles into the gas stream. The method works best for drugs whose crystal structure breaks down at a temperature below that at which the drug itself begins to decompose. Most drugs fall into this category.

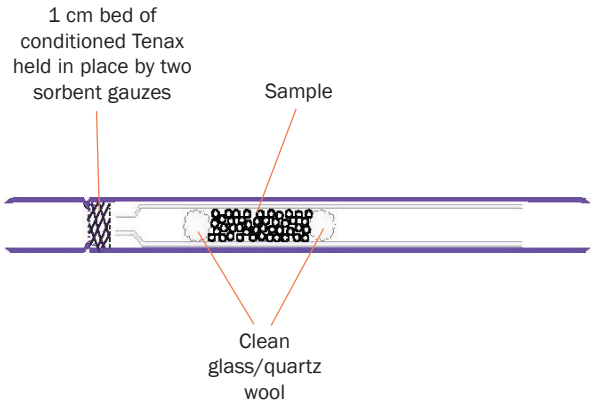

Figure 1: Diagram showing PTFE insert within a sorbent tube. The bed of Tenax® at the front of the tube is only necessary during method development.

Method development

The objective was to develop a TD–GC method for measuring residual DMSO in an insoluble drug precursor. A small amount (2–3 mg) of the powdered drug was introduced into a PTFE liner and held in place between two plugs of clean, silanised glass wool. During the early stages of method development, a 1 cm bed of Tenax was placed into the sorbent tube in front of the insert. This sorbent was held in place between two retaining gauzes. The purpose of the sorbent was purely to protect the analytical system from contamination should the drug decompose or sublime at a lower temperature than expected.

Keeping below the drug decomposition temperature, desorption conditions (temperatures, flows, times) were adjusted until >95% recovery of the residual DMSO was achieved in a single desorption. DMSO standard solution could then be introduced into a clean Tenax tube for external standard calibration. After method development, the PTFE liner containing the sample was inserted into an empty tube for routine analysis. Once analysis was complete, the liner was removed from the sorbent tubes and discarded.

Analytical conditions

TD (UNITY):

Primary desorption:	10 min, 225°C
Focusing trap:	Packed with Tenax
Focusing trap high:	280°C for 3 min
Focusing trap low:	30°C

GC:

Column:	30 m × 0.32 mm × 1 µm Carbowax 20M
Temp. program:	60°C (2 min), then 10°C/min to 115°C (7 min), then 30°C/min to 250°C (6 min)

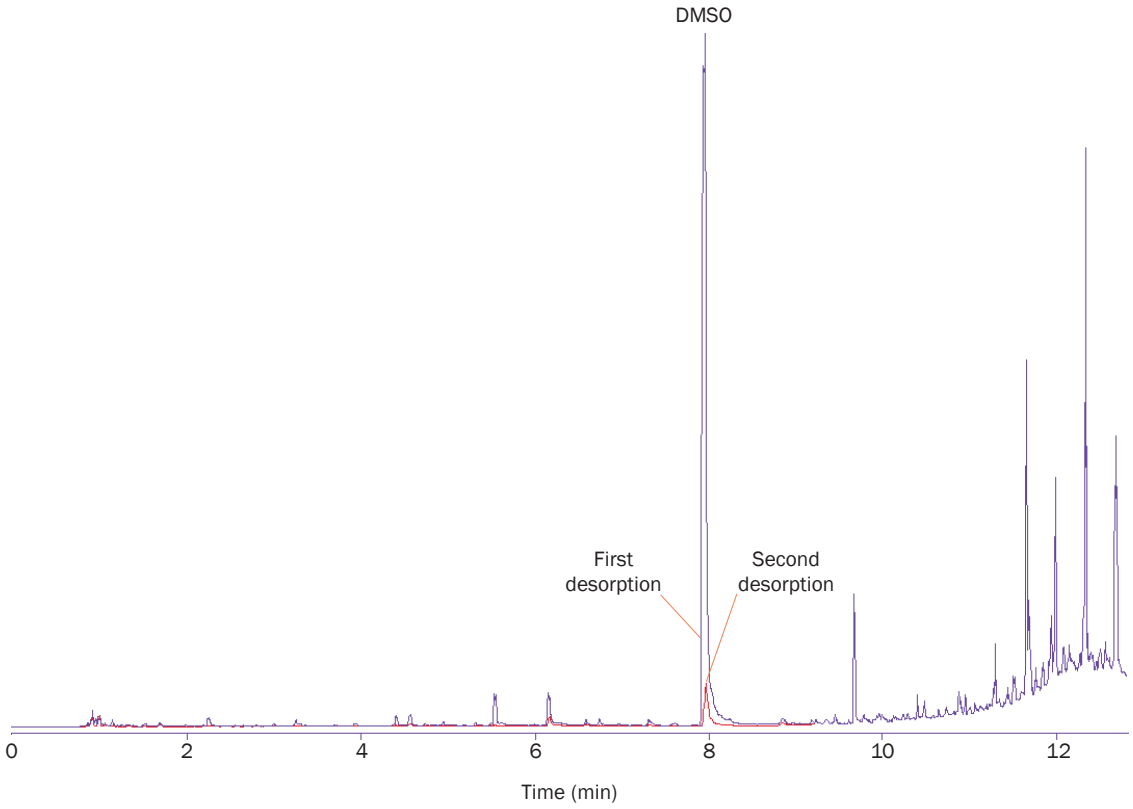

Figure 2: Analysis of a drug precursor, showing <3% carryover of DMSO.

Results

Figure 2 shows the first desorption of 3 mg of drug, and a second desorption of the same sample, illustrating <3% carryover.

Given such a high recovery, quantification of the mass/concentration of DMSO present in a weighed sample would be a one-step process after system calibration. As the use of automated TD allows desorption of a subsequent sample while GC analysis of the previous sample continues, sample throughput is typically limited solely by the GC cycle time.

Thermal desorption clearly offers significant advantages *versus* sorbent extraction for this pharmaceutical powder and many other drugs. Key enhancements include:

- Sensitivity (no dissolution)
- Automation (minimal sample preparation – just weighing)
- Productivity (automated throughput of 3–4 samples per hour).

Trademarks

Applications were performed under the stated analytical conditions. Operation under different conditions, or with incompatible sample matrices, may impact the performance shown.

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