application

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Gas Chromatography/Mass Spectrometry | Fast Drug Analysis

Fast GC/MS Methods for Routine Drug Analysis

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Introduction

Drug testing laboratories are under increasing pressure to reduce costs and increase productivity without sacrificing analytical quality. Recent advancements in instrumentation, the separation sciences, and software have provided the tools that can dramatically increase productivity. Current column technology and the increased sensitivity of the Agilent Technologies 6890 GC/5973 MSD now allow rapid confirmation of drugs of abuse.

Historically, typical run times for drugs of abuse were from 5–15 min using 12–15-m, 0.25-mm o.d. columns in gas chromatographs with a constant column head pressure (manual pressure control). The introduction of electronic pressure control allowed programmable head pressures which shortened run times and improved the chromatography. The introduction of "fast" GC ovens provided more rapid oven ramps, further decreasing run time and cycle time. Increases in mass spectrometer sensitivity, such as that provided by the 5972A MSD, allowed split injections, thus reducing the amount of sample on column. Split injections combined with fast GC oven temperature ramping made it possible to program a "column burnout" between samples. And raising the column temperature between samples removes residual components from the column, which lengthens the time the column can be used without maintenance.

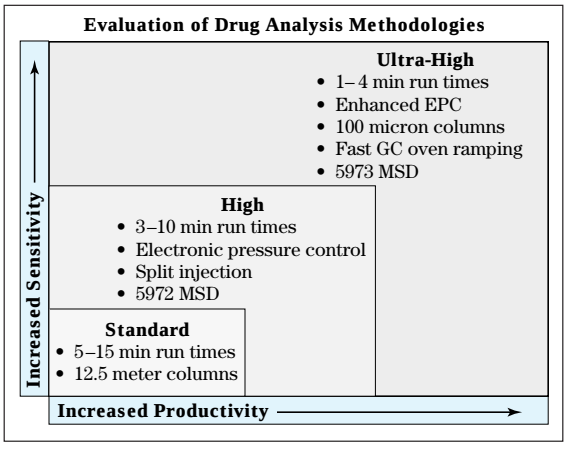

Figure 1. Advances in the separation sciences, faster GC ramping, and more sensitive instruments account for today's increases in productivity.

Ultrahigh Productivity

Today, an ultrahigh level of productivity can be reached with the highly sensitive 6890 GC/5973 MSD system. The sensitivity of the 5973 MSD now allows either split or very small volume injections (1-µl or less) or both to be used for all assays. The greater sensitivity of the MSD and the smaller sample injection volumes that are required allow use of very short (5-m) 100-µm diameter columns. These columns have very high resolving power and reduce chromatographic run times without loss of chromatographic integrity. Injection volumes as small as 0.1-µl extend the time between maintenance procedures by minimizing the amount of sample being introduced (Figure 1).

As sample analysis productivity continues to improve, more intelligent software is required to evaluate analyte chromatography and to decide if re-injection is required. Productivity tools for software will be discussed in a separate application brief.

The following are examples of some of the more important drugs analyzed in a toxicology laboratory. For each example, a chromatogram representing the typical approach and the new ultra-high-productivity method is provided.

Instrumentation

The GC/MSD system consists of a 6890 GC with 7673 or 7683 autosampler coupled to the highly sensitive 5973 Mass Spectrometer. The G1701BA Productivity ChemStation software and Windows NT® operating system provide data acquisition and an application-specific drug analysis mode of operation for data processing. The entire system was designed for high speed, high sensitivity, and increased productivity

THC / THCA

Tetrahydrocannabinol (THC) has traditionally been analyzed using a 12.5-m column in splitless mode injection. The resulting retention time is 5.4 min. The ultra-fast chromatography method, utilizing a 100-µm column and 0.2-µl splitless mode injection, provides a good signal-to-noise ratio, rapid run-time and eliminates interfering compounds (Figure 3).

Amphetamines

In some cases, high chromatographic resolution is desired. In this example, resolution of the deuterated internal standards from the analytes was desired by the laboratory. The chromatogram shown in Figure 4 illustrates that both high resolution and high speed are possible with 100-µm columns.

Figure 2. The 6890 GC / 5973 MSD system.

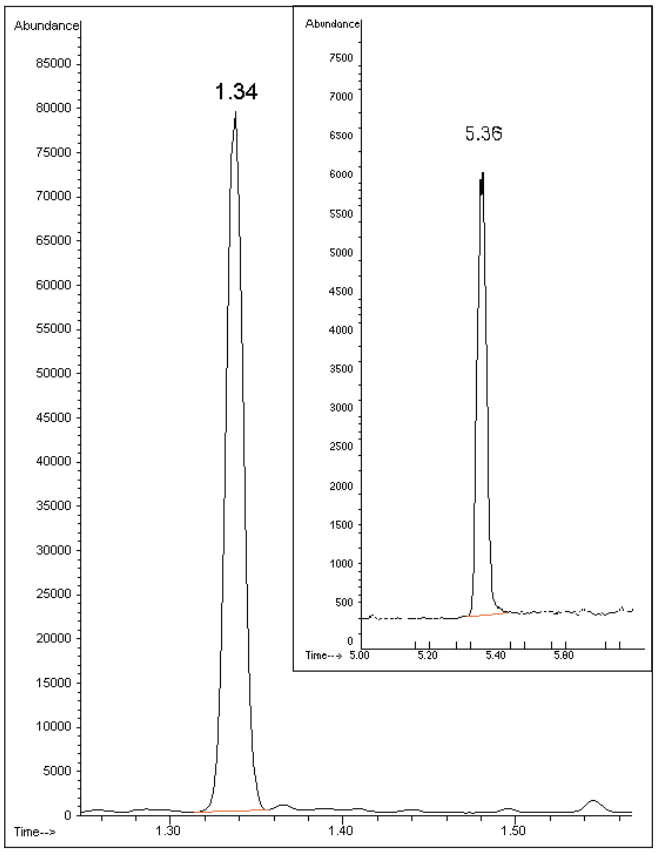

Figure 3. Ultra-fast chromatography of 15 ng/ml of TCHA cutoff. Injection volume 0.2-µl; analysis run time less than 1.5 min. Standard THC analysis with retention time of 5.4 min shown in insert.

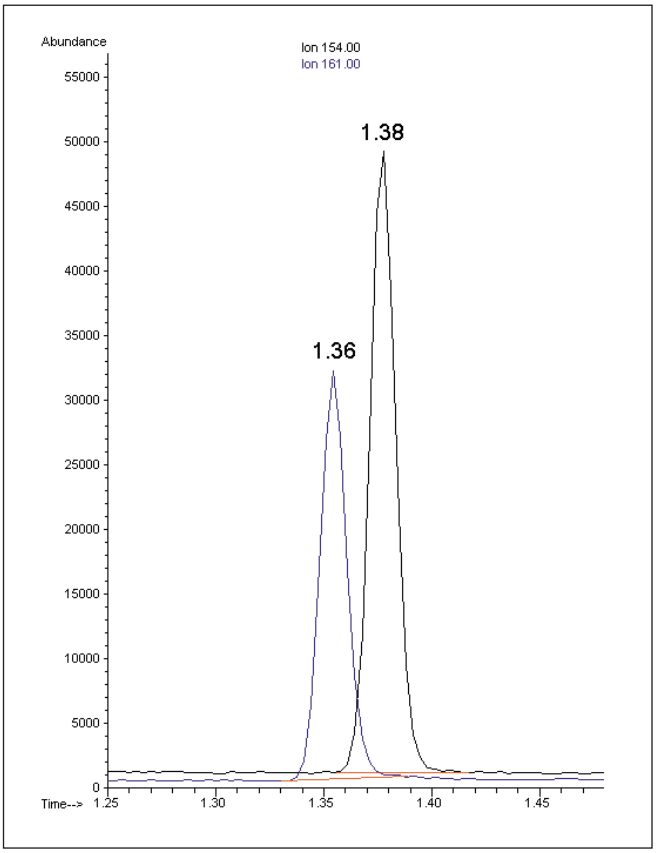

Figure 4. Example of a 200-ng/ml, 0.1-µl injection of TFA derivatives of amphetamine and deuterated internal standard with 50:1 split; analysis run time slightly more than 1 min.

d,l-Methamphetamine

The chromatography of d,l-methamphetamine can be difficult; however, with 100-µm column technology, baseline separation is easily achieved in less than 3 min (Figure 5).

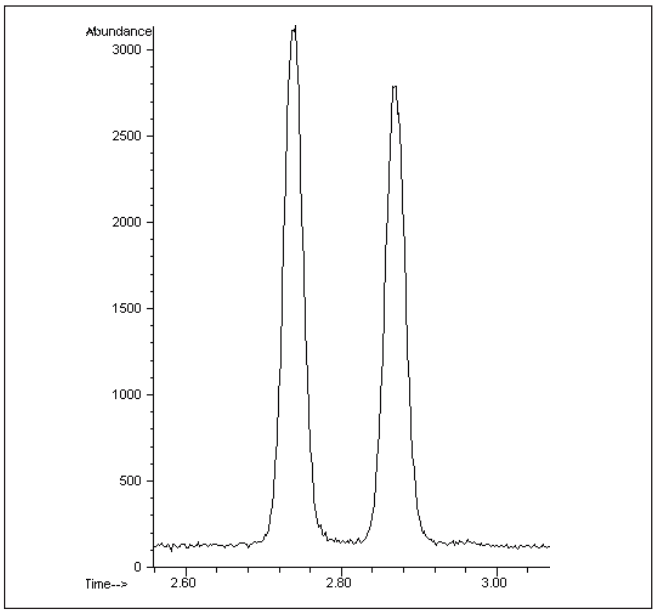

Figure 5. Example of a 200-ng/ml, 0.1-µl injection of d,l-methamphetamine at a 10:1 split; analysis run time less than 3 min.

Benzoylegconine (BE); Cocaine Metabolite

In many toxicology laboratories, the highest volume assays are for THC and cocaine metabolites. Figure 6 shows a typical chromatogram of a benzoylegconine analysis with BE eluting in 4.1 min on a 12.5-m column. However, benzoylegconine can be analyzed in less than 1 min with a very short sample-to-sample cycle time. The total sample-to-sample cycle time is less than 3 min, including a pressure-pulse, high-temperature "burn out" to eliminate interferences and a short oven cool down time (Figure 6).

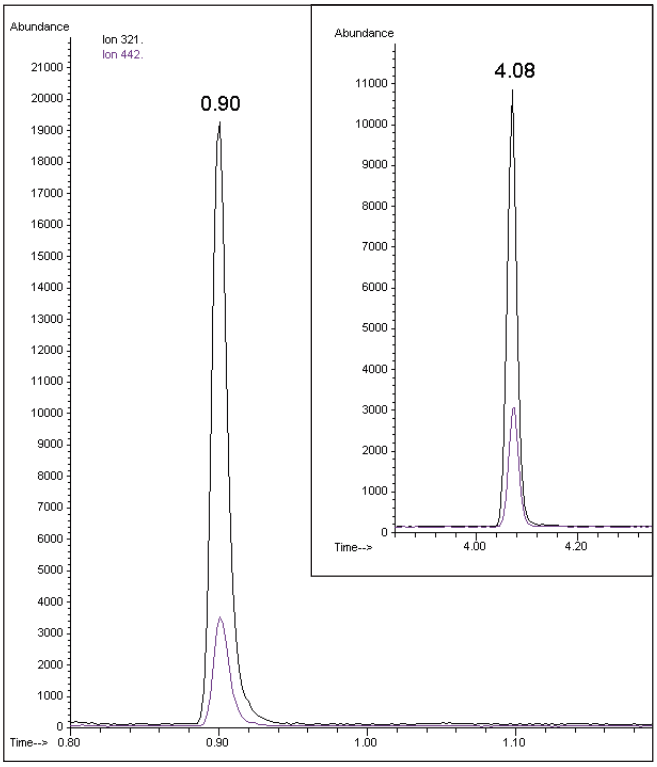

Figure 6. Example of ultra-fast BE (PFPA/HFIP derivative); 0.1-µl injection at a 10:1 split; analysis run time is less than 1 min. An example of typical BE (PFPA/HFIP derivative) analysis is shown in the insert.

Opiates

In the traditional methods for opiate-TFA derivatives, a 12.5-m capillary column is used and the derivatives elute in 5 min. Hydrocodone and hydromorphone are separated from codeine and morphine (Figure 7).

Ultra-high-speed methods for opiates eliminate commonly interfering compounds when analyzing for hydromorphone and hydrocodone (Figure 8).

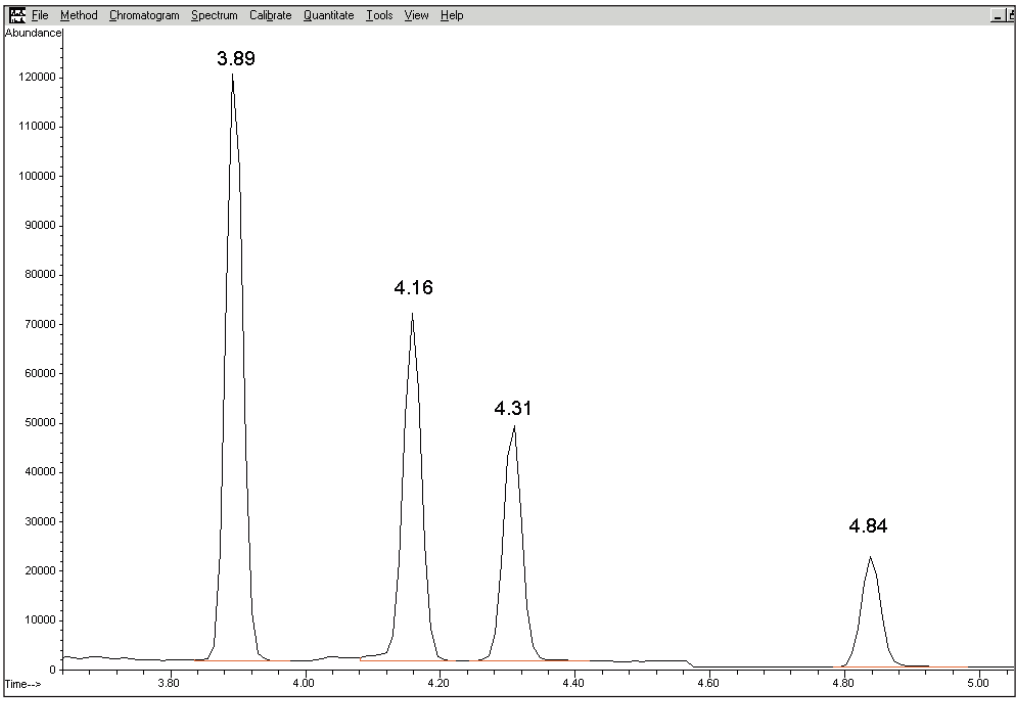

Figure 7. Example of typical opiate analysis: hydrocodone, hydomorphone, codeine and morphine.

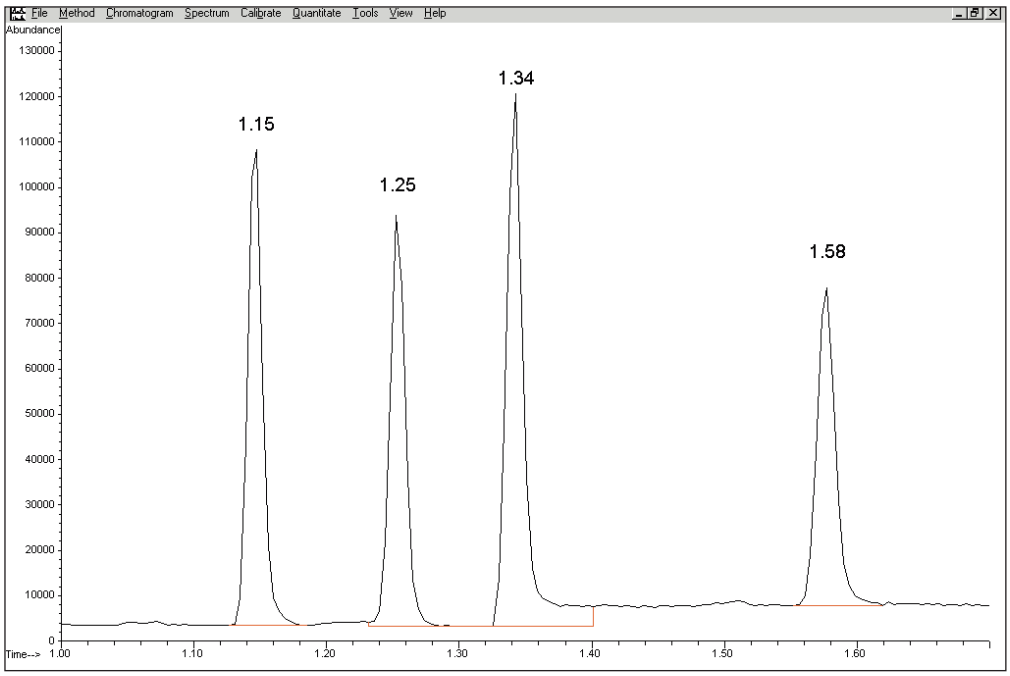

Figure 8. Example of ultra-high-speed 0.1-µl injection of opiates with 10:1 split; analysis run time less than 5 min. The baseline shift at 1.3 min on the total ion chromatogram reflects a programmed SIM group change between codeine and hydromorphone.

Summary

The preceding examples demonstrate that ultra-high-speed analysis is possible and that it has been developed and implemented by several of our customers for many of the common drugs of abuse. Significant increases in productivity are achieved by short run-times and cycle times with lowered maintenance requirements (Table 1). Even more rapid analysis times for selected analytes are possible and have been achieved based on the analytical methodologies (i.e., sample preparation and derivatization schemes) and analytical criteria.

Table 1. Summary of elution times for common drug analyses by means of ultra-fast methods on the 6890 / HP 5973 GC/MSD. All injections are in split mode unless otherwise noted.

Analysis	Elution Time (min)
THCA	1.34, splitless
Opiates	1.5
Barbituates	2.7
Amphetamines	1.3
Benzoylegconine	0.9
Benzodiazepines	4.0
d,l-methamphetamine	3.0
6-monoacetylmorphine	2.4, splitless
Phencyclidine (PCP)	1.0

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