GC-MS 37

Drug Screening with Fast-GC/MS

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The productivity of a method is an important criteria, if it is an established method is in a laboraty. The requirement to analyze an increasing amount of samples together with the need to decrease the cost, makes it necessary to find a fast and cost effective method for the analysis.

Analysis cycles of 40 minutes are usual in drug screening analysis. The productivity can be increased by a higher through put on the same instrument. This can only be achived with fast chromatography.

The doors were opened for fast GC and GC/MS in the last few years with improvements in instrument technology as well as improvements in column technology.

Using high resolution columns with small internal diameters and short lenghts, analysis cycles can be decreased without any loss in separation efficiency.

The demands on a GC/MS system for fast chromatography are; high heating rates, qick cooling down times, as well as the requirement to work with high head pressures (up to 9.6 bar) and last, but not least, fast scan rates (6750 dalton/sec).

In addition a highly sensitive detector is required, as the injection volume is limited due to the low sample capacity of the column. Pressure programs for the carrier gas should be used, to guarantee an optimum flow through the column.

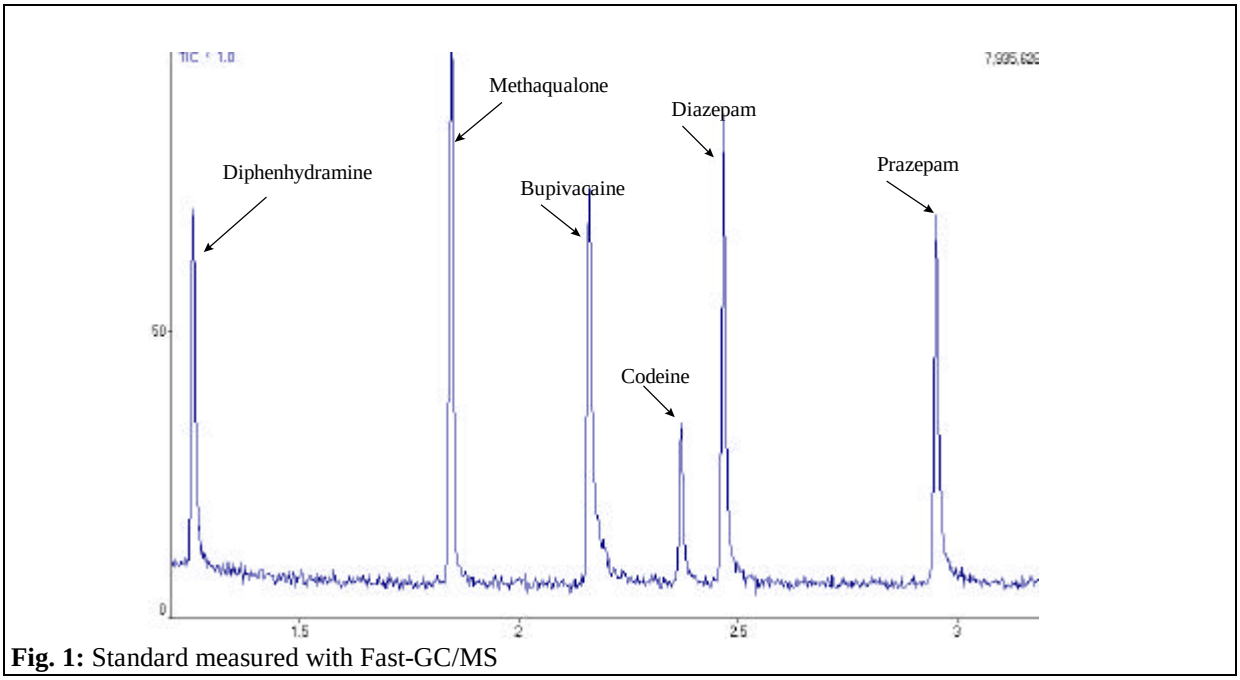

Fig. 1: Standard measured with Fast-GC/MS

Analysis of the real samples

Fig. 1 shows a standard chromatogram. This standard was measured with fast-GC/MS. Under regular conditions the analysis time is 14 minutes. Using the fast-GC/MS, the time can be reduced to 3 minutes.

Using the fast-GC/MS a compromise between fast analysis cycles and sensitivity must be found. In the standard example, high concentrations were measured. In this case an injection volume of 0.1 µl is enough. For the analysis of street drugs a split ratio of 1:80 was used, using a lower split ratio, column overloading can occur.

Fig . 2 shows the chromatogram of a typical street drug. This example shows clearly, that the analysis time is increased, when analyzing compounds like Papaverine and Noscapine. Using the split injection, the peaks forms are sharp.

The abillity of the fast-GC/MS was checked afterwards with a couple of real samples, to see the sensitivity for small amounts of metabolites, like Oxazepam.

In general additional care has to be taken for sample preparation, when using the fast-GC/MS. Samples prepared with Liquid-Liquid-Extraction (LLE) were measured. Using LLE, in addition to the relevant drugs, also a lot of steroids were extracted. The elution time of the steroids is so long, that the cycle time in total is increased. The sample preparation has to be done carefully, so that interfering compounds are eliminated, to obtain short analysis cycles.

Good results were obtained when using the Solid-Phase-Extraction (SPE), with mixed bed cartridges.

In the first step, conditions were used, which gave good results for the analysis of street drugs. Using a split method, the necessary sensitivity could not be reached. Using a special Advanced-Flow-Control, a head pressure of up to 9.6 bar can be set on the GC-17A Ver. 3. The initial temperatures can be set higher for a splitless injection in fast GC/MS by using a high head pressure on the injector. Initial temperatures of 150 °C, 120 °C, 100 °C and 80 °C were selected for the determination of the optimum initial temperature.

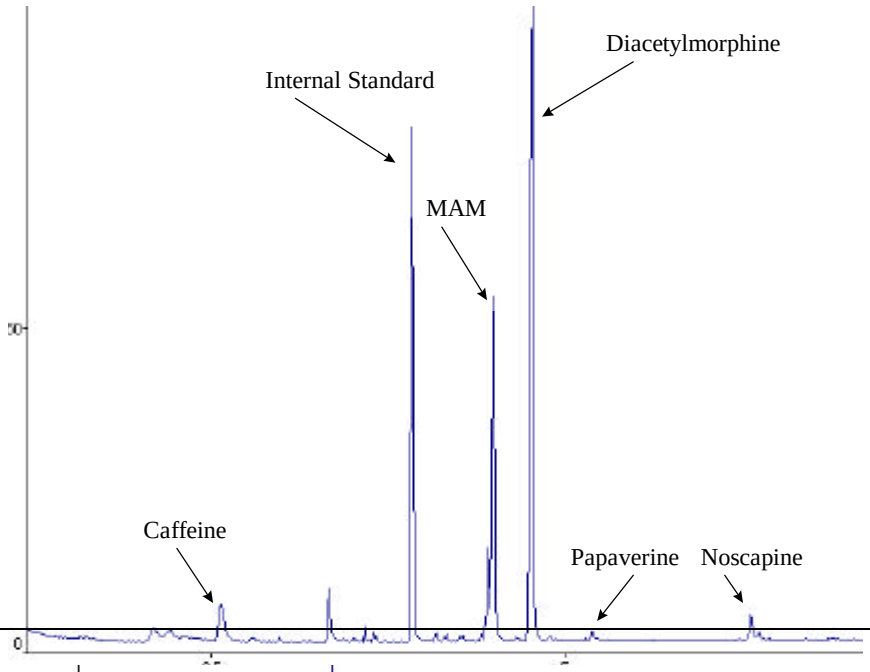

Fig. 2: Street dr

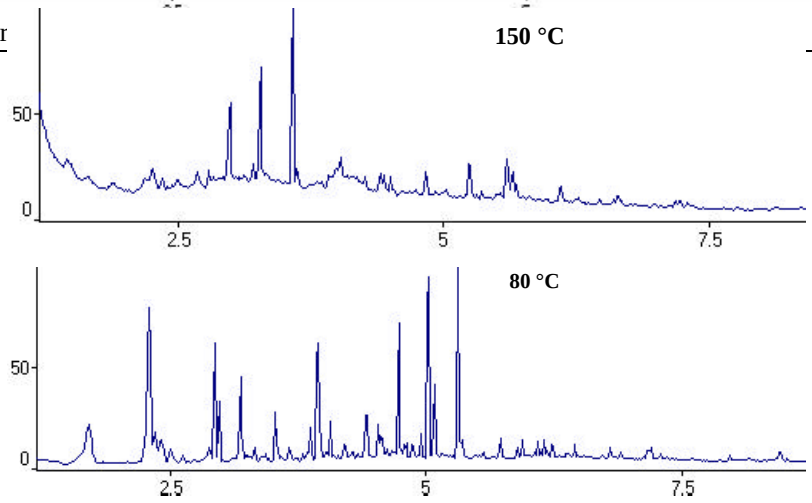

Fig. 3: Real sample measured with different initial temperatures

Fig. 3 shows chromatograms, detected at different initial temperatures. The later retention area is very well resolved due to good sample focussing on the column. The earlier retention area is the critical one in the fast-GC/MS, where compounds with low boiling points elute. Broad peaks result when the initial temperature for the splitless analysis is too high, lower boiling point compounds are not focussed on the column.

Up to a certain degree this can be corrected by a higher head pressure. In the case of a splitless analysis, it is usefull to work with an isothermal step at the beginning of the temperature program of at least 1 minute. Otherwise the peaks are too broad.

unknown samples a volume of 0.5 µl is necessary. Volumes higher than 0.5 µl again generate broad peaks and leading peak shape. If the volume is lower than 0.5 µl, small concentrations of Oxazepam and Diazepam might not be detected.

separate early eluting compounds like Amphetamine and Metamphetamine, as well as Morphine and it's metabolites. Alprazolam a late eluting compound also exhibits good GC.

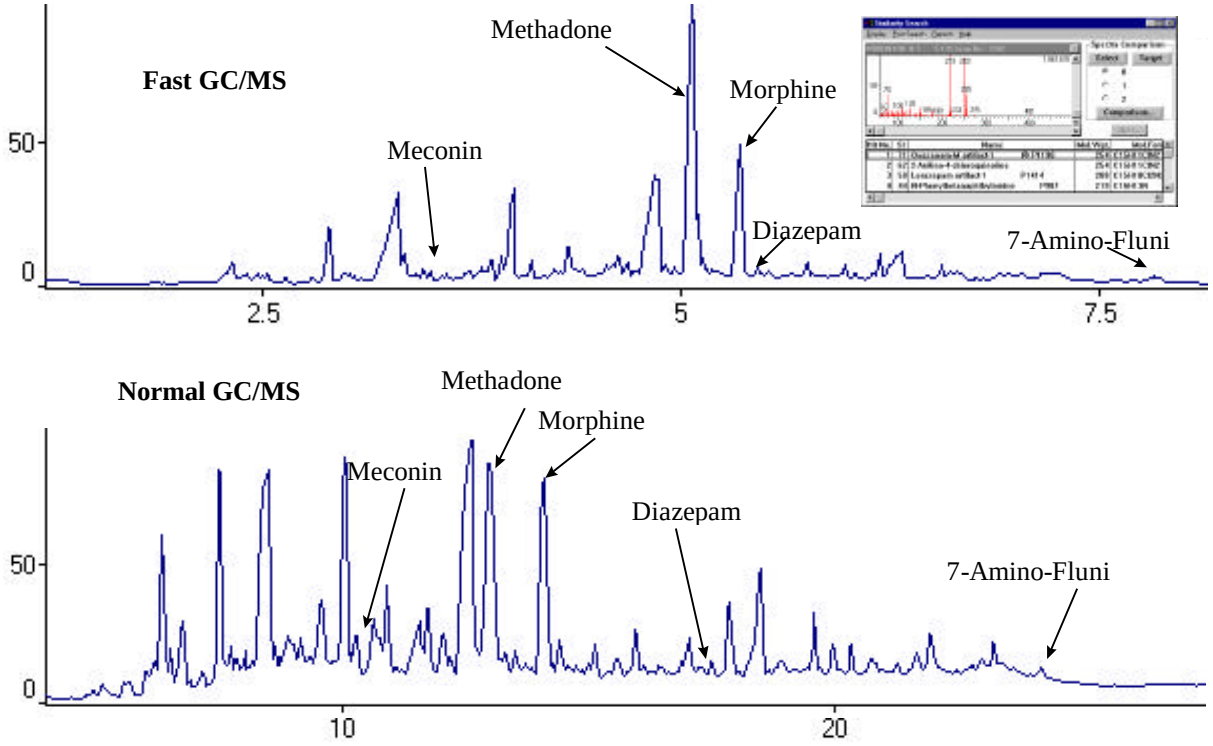

Fig. 4: Urine, measured with normal GC/MS and fast-GC/MS

Fig. 4 shows the difference between the fast GC/MS and the normal GC/MS. For this example the same urine was measured with both methods. In general, the analysis cycle can be decreased from 40 minutes to 14 minutes with fast GC/MS. The only exclusions are urine samples with Dihydrocodeine and its related metabolites.

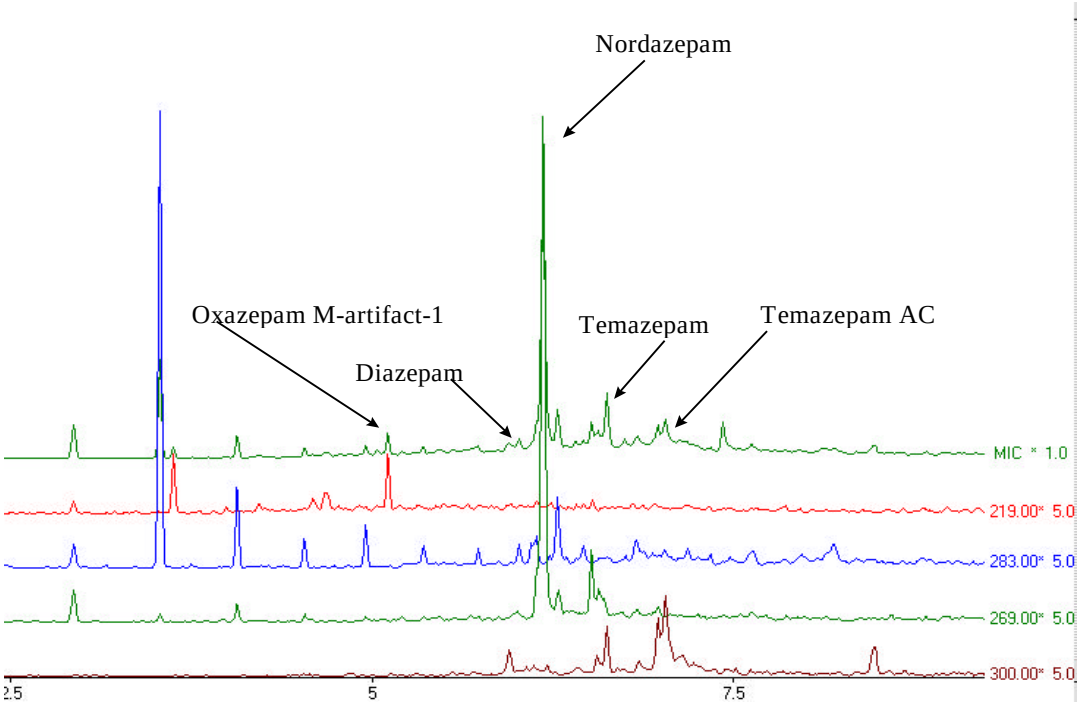

Fig. 5: Real sample measured with Fast-GC/MS

Fig. 5 shows a drug urine with the identification of some of the relevant substances. It makes sense to work with Multi-Ion-Chromatograms, to ease the identification of the Benzodiazepines. All relevant substances could be identified with fast-GC/MS, which were previously detected with normal GC/MS.

Fig. 6 shows a Lyphocheck control from Biorad. This control was prepared with Solid-Phase-Extraction. The marked compounds were included in the control with a concentration of 400 ng/ml. The compounds could be detected on both systems with a good sensitivity.

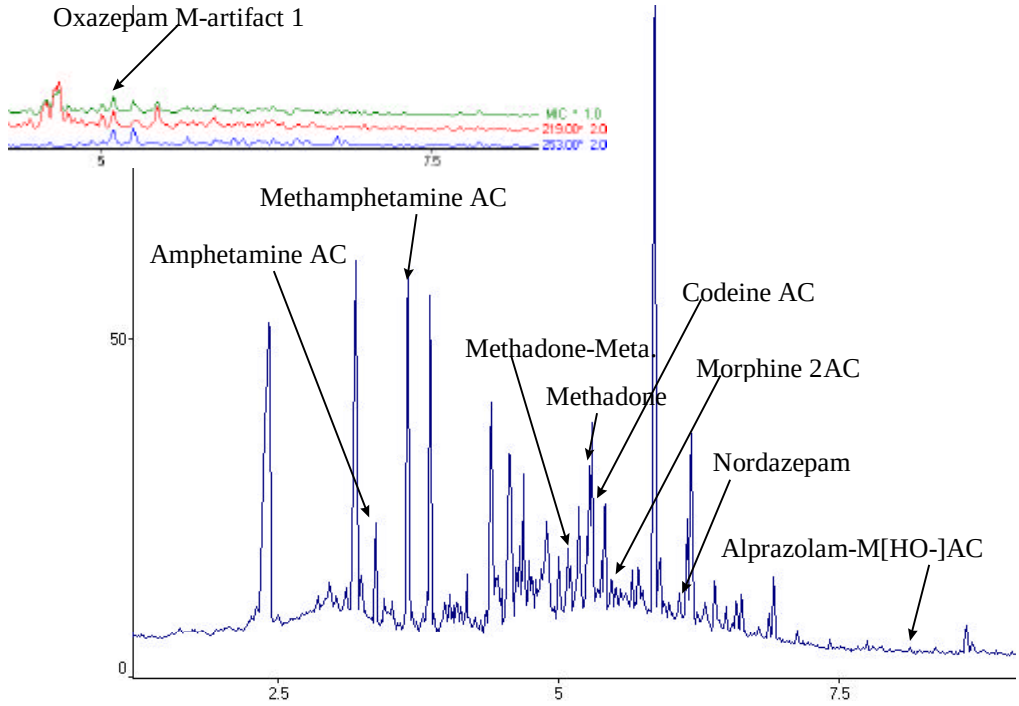

Fig. 6: Lyphocheck control

Instrumentation

GC/MS System:	QP-5050A
Gaschromatograph:	GC-17A Ver. 3
GC/MS Software:	CLASS 5000, NIST 75.000, PMW-TOX 2
Carrier gas:	Helium
Columns:	Fast GC ; Chrompack CP-SIL5, 10m, 0.1 mm I.D.; 0.12 µm film Normal GC; J&W DB5-MS; 30m, 0.25 mm I.D., 0.25 µm film
Temperature Program:	Fast GC: 80°C/1 min with 40°C/min to 320°C; 0.5 min splitless, 0.5 µl injection volume Normal GC: 70 °C/ 2 min with 20 °C/min to 200 °C with 7 °C/min to 300/ 3min with 25 °C/min to 320/2.5min
Split ratio:	1 min splitless
Injection volume:	1 µl
Injector temperature:	280 °C
Detector temperature:	320 °C
Scan rate:	Fast-GC/MS, 6000 dalton/sec, normal GC/MS 1000 dalton/sec
Mass range:	55-499 dalton
Gain:	1.6 kV

Conclusion

Fast-GC/MS will be used more frequently in future, as the same results, or better, can be obtained when compared to a normal GC/MS. The productivity of a method can easily be doubled by using fast-GC/MS. The necessary sensitivity can be reached when using a „Continuous Dynode Detector“as in QP-5050A. Separation problems can be solved by choosing the right columns, with a reduction of the cycle time at the same time. A good application for fast-GC/MS is the analysis of tricyclic antidepressants. Hopefully the GC column suppliers will follow this trend and produce the necessary stationary phases required for fast-GC/MS.