GC-TOFMS Study on Common Drugs of Abuse: Diphenylhydramine, Orphenadrine, Propoxyphene, Amitryptyline and Dothiepin

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Key Words: GC-TOFMS, Forensics

1. Introduction

Purpose of Analysis

The abuse of drugs, both pharmaceutical and recreational, is a worldwide phenomenon. Accurate identification of these components is required in clinical and forensic studies. This note describes methodology used for the analysis of some of these compounds, implicated in accidental deaths in South Africa.

Background

The prevalence and ready availability of drugs has increased dramatically in recent years. Many of these medicines have made major contributions to the alleviation of suffering and have resulted in a better quality of life for millions of people. A dark side of this drug explosion is the number of deaths caused by frequent overdose and abuse of these compounds. Consequently, better and faster methods for the detection of these substances are always needed.

This note describes the analysis of some common drugs of abuse by Gas Chromatography—Time-of-Flight Mass Spectrometry (GC-TOFMS). The samples submitted for analysis in this study were obtained from the Forensic Chemistry Laboratory, Department of Health in Johannesburg, South Africa. The compounds analyzed are frequently found in overdose situations. The drug standard for this work is used routinely to investigate possible causes of death and to evaluate overdose potential. In addition, two real-life samples of blood and urine extracts were analyzed to demonstrate the power of the technique in handling samples containing small amounts of drugs in demanding matrices.

2. Experimental Conditions

GC: Agilent 6890 GC

Standard

Column:	10 m x 0.18 mm x 0.18 µm DB-5
Oven Program:	100°C (1 minute), 20°/minute to 280°
Inlet Temperature:	250°C
Injection Volume:	1 µL
Split Ratio:	10:1
Carrier Gas:	He at a constant flow of 1 mL/minute
Transfer Line Temp:	250°C
Total Run Time:	10 minutes

Blood and Urine Samples

Oven Program:	100°C (1 minute), 20°/minute to 300° (1 minute)
Total Run Time:	12 minutes

MS:	LECO Pegasus® III GC-TOFMS
Ionization:	Electron ionization at 70 eV
Mass Range (u):	50 to 360
Acquisition Rate:	10 spectra/second
Source Temp:	220°C

3. Results

Standard Sample

The standard sample contained a mixture of the drugs diphenylhydramine, orphenadrine, propoxyphene, amitryptyline, and dothiepin. The major challenge here is that all five components have very similar mass spectra, making differentiation and accurate identification difficult when no standards are available.

The Total Ion Chromatogram (TIC) and the Peak Table for this sample are shown below as Figure 1 and Table 1. Only the portion of the chromatogram between 300 and 475 seconds is displayed.

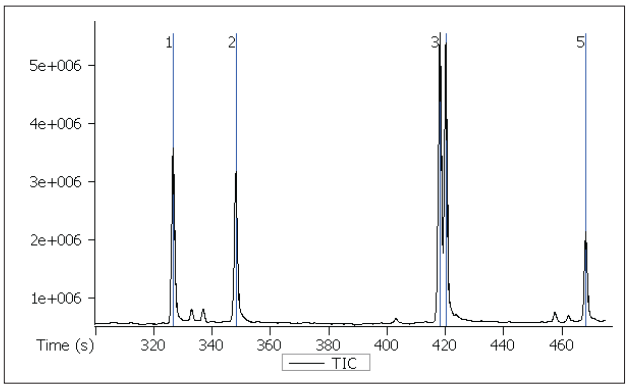

Figure 1. A portion of the TIC for the standard sample.

Only those peaks with a signal-to-noise ratio (S/N) greater than 1000:1 and a Peak Width greater than 4 seconds were added to the Peak Table (Table 1). Identifications are based on library search results, using the NIST library.

Table 1. Peak table for the standard sample.

Peak #	Name	R.T. (sec.)	Similarity	CAS
1	Diphenylhydramine	326.62	952	58-73-1
2	Orphenadrine	348.22	923	83-98-7
3	Propoxyphene	418.22	960	469-62-5
4	Amitryptyline	420.22	981	50-48-6
5	Dothiepin	468.22	902	113-53-1

Under the conditions used in this study, there is some overlap between the peaks corresponding to propoxyphene and amitryptyline, as shown in Figure 2.

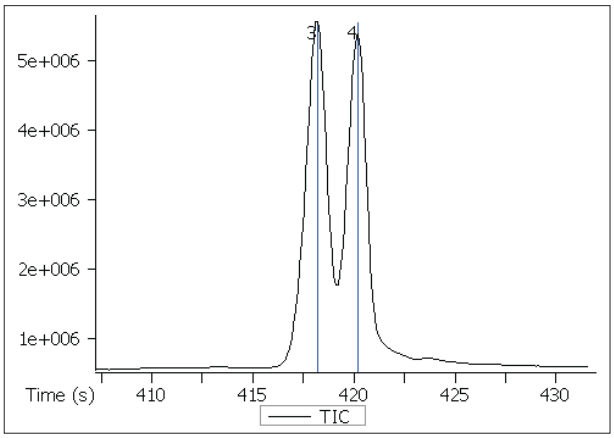

Figure 2. Overlap of propoxyphene and amitryptyline peaks.

Despite this overlap, the mass spectra corresponding to these two components match the spectra contained in the NIST library to an excellent degree (960 and 981 similarities, out of 999 possible, respectively) showing the efficacy of the Deconvolution algorithm (Figures 3 and 4).

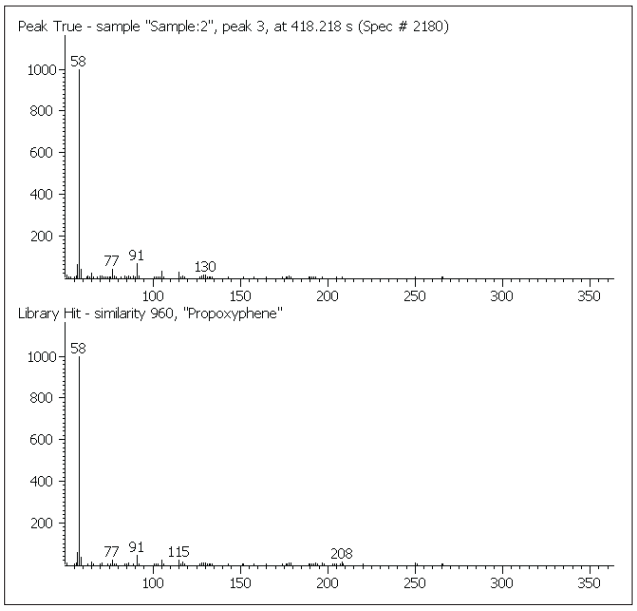

Figure 3. Deconvoluted (top) and NIST library (bottom) spectra for propoxyphene.

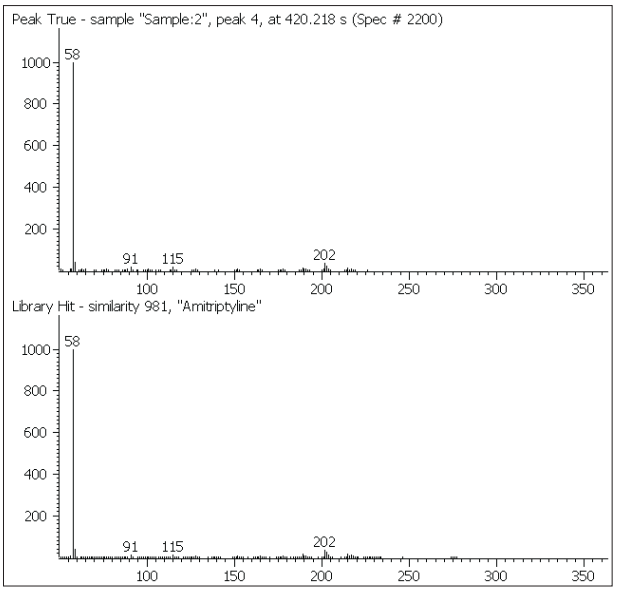

Figure 4. Deconvoluted (top) and NIST library (bottom) spectra for amitryptyline.

Blood Sample

A blood sample, which contained the drugs propoxyphene and amitryptyline at overdose levels, was extracted and provided for analysis by the Forensic Chemistry Laboratory. This sample provided a test of instrument and methodology in a complex matrix, where matrix components would dominate the drug components. The TIC for the blood extract is shown in Figure 5.

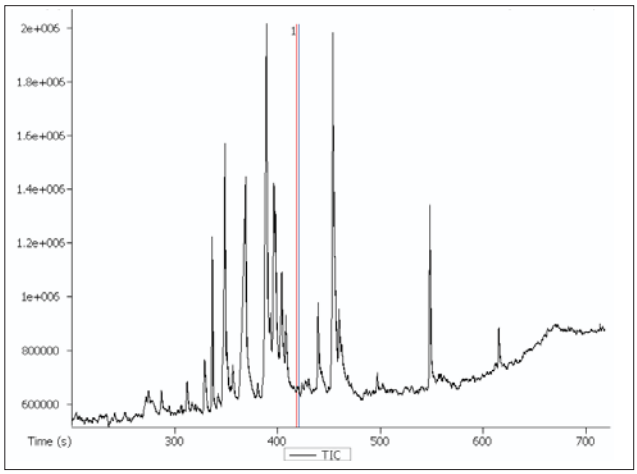

Figure 5. TIC of the extracted blood sample.

The Peak Table for the analysis is shown below. It has been restricted to the two components of interest.

Table 2. Restricted Peak Table for the extracted blood sample.

Peak #	Name	R.T. (sec.)	Similarity	Unique Mass	Weight	Formula
1	Propoxyphene	418.427	805	58	339	C22H29NO2
2	Amitriptyline	420.527	838	58	277	C20H23N

Despite the complex nature of the matrix, spectral quality was good with similarities greater than 800 (out of 999). Recorded mass spectra, after deconvolution, and library matches are shown in Figure 6 below.

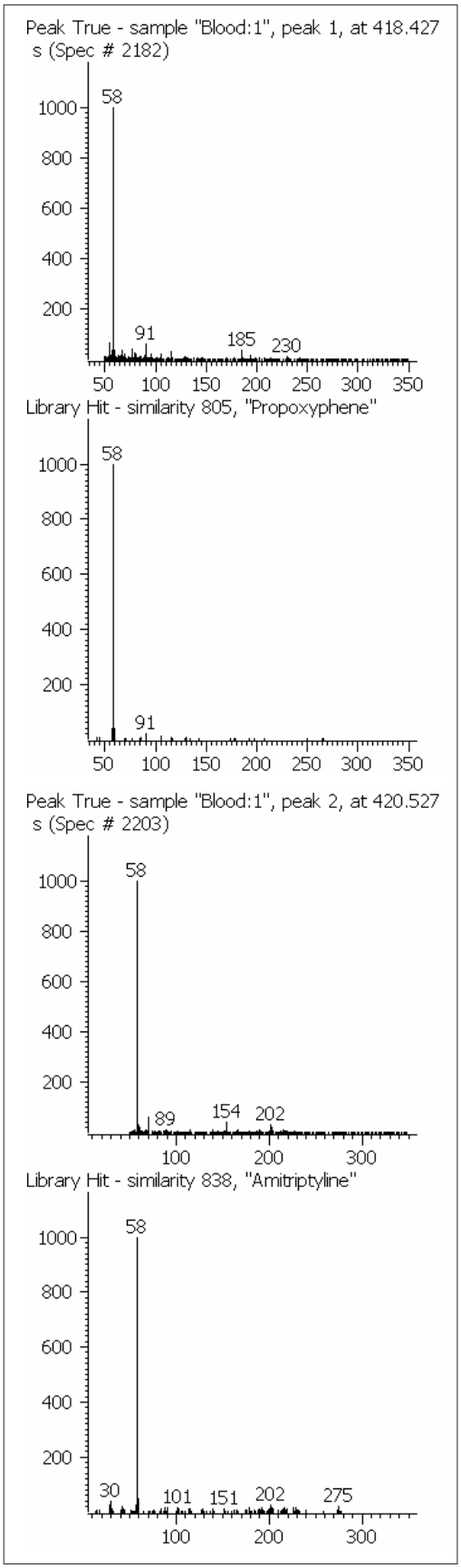

Figure 6. Mass spectra of propoxyphene and amitryptyline obtained from the extracted blood sample.

Even in a complex blood matrix, the automated Peak Find capability of the ChromaTOF® software is able to locate the drugs of interest, and the quality of the deconvoluted mass spectra allows unambiguous identification with excellent library matching.

Urine Sample

Similarly, a urine extract containing diphenylhydramine at overdose levels was analyzed. The TIC (Figure 7) and a restricted Peak Table (Table 3) are shown below.

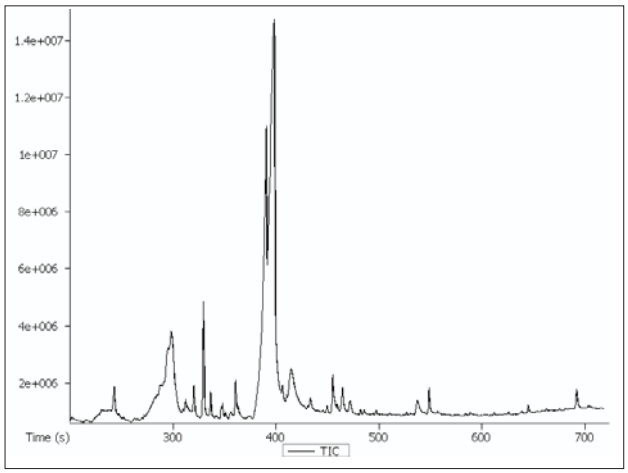

Figure 7. TIC of the extracted urine sample.

Table 3. Restricted Peak Table of the extracted urine sample.

Peak #	Name	R.T. (sec.)	Similarity	Unique Mass	Weight	Formula
39	Diphenylhydramine	341.317	787	58	255	C17H21NO

The TOF mass spectrum of the diphenylhydramine, as well as that of the corresponding library match, are shown in Figure 8.

Spectral quality is good, as is the library match, affirming the validity of the method for the analyses of these drugs in complex matrices.

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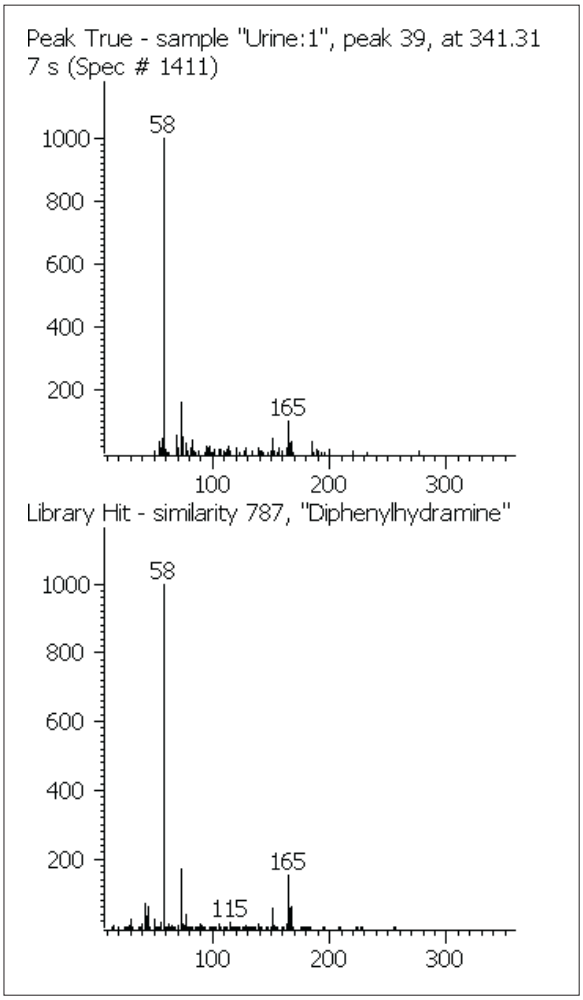

Figure 8. Mass spectra of propoxyphene and amitryptyline obtained from the extracted urine sample.

4. Conclusions

The described work demonstrates the use of GC-TOFMS to locate and identify common drugs of abuse. The use of a Time-of-Flight Mass Spectrometer in this work demonstrates a number of advantages over other types of mass spectrometers.

The strength of the Pegasus GC-TOFMS for the analysis of these sample types lies in its automated data handling capabilities. Peak finding, spectral determination (deconvolution), and library searching are all automatic. This is possible due to the high degree of spectral continuity generated, as well as the large data density allowed by the Pegasus GC-TOFMS system—up to 500 full mass spectra per second. Peaks are located and full range mass spectra obtained for all components, even when peaks coelute, allowing confident structural determination.

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