Fast Analysis Workflow with No Sample Preparation for Forensic Applications using Open Probe Fast GC/MS: Unit and High Resolution MS

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Introduction

Positive identification of drugs and other chemicals in bulk samples is critical during screening in crime laboratories. Drug analysis often requires sample preparation that includes dissolution, dilution and several reagent-based assays to classify the type of drugs followed by GC/MS analysis for confirmation. A simple and fast analysis workflow that does not require sample preparation is demonstrated with Open Probe Fast GC/MS. Correct compound identification of drugs in liquid and solids is achieved through NIST library search when using a single quadrupole (SQ) mass spectrometer (unit resolution) or additionally by mass accuracy when using a quadrupole time-of-flight (Q-TOF) high resolution mass spectrometer.

Experimental

A variety of drug samples were obtained, including drug mixtures (40-75 ng/µL) in solvent, an oxycodone tablet (whole) and a Vicodin tablet (pulverized). Individual samples (liquid, solid, powder) were touched with the closed end of a clean melting point vial and introduced into an Open Probe Fast GC/MS (Aviv Analytical LTD, Israel) system with Agilent's SQ or Q-TOF (Figure 1) for 3-6 seconds prior to data acquisition. An Extractor electron ionization (EI) source was used with the SQ whereas a prototype EI source modified to be tuned and operated at different ionization energies was used with the Q-TOF. The system was equipped with 1.5mx0.25mm (0.1µm 100% dimethylpolysiloxane film) and 1mx0.18mm (0.18µm 100% dimethylpolysiloxane film) restrictor columns using a ~400 °C/min temperature ramp and allowed for chromatographic separation in under 1 minute. The data was analyzed using MassHunter Qualitative Analysis, NIST library searches and accurate mass analysis for compound identification.

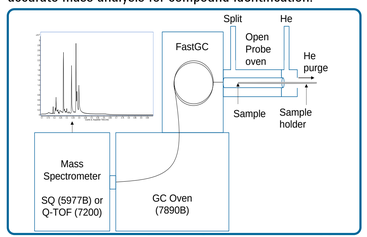

Figure 1. Schematic for the Open Probe Fast GC/MS instrument configuration.

Experimental

Sample preparation: No sample preparation required. Touch the sample with a sample holder and start analysis.

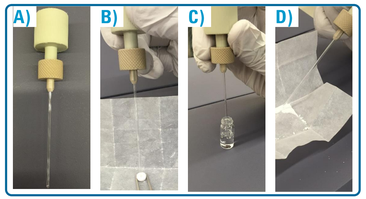

Figure 2. Sample preparation consists of touching the sample with the sample holder (A) as shown for B) solid (pill), C) liquid or D) powder (pulverized pill).

Fast Sample Analysis (~1 min)

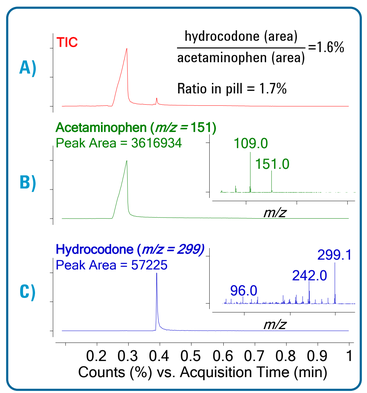

Figure 3. Pulverized Vicodin pill (5:300 mg of hydrocodone:acetaminophen) analysis in ~1 min using the Open Probe Fast GC/MS configuration with a SQ. A) Total ion chromatogram (TIC). Extracted ion chromatograms (EIC) for acetaminophen *m/z* 151 (B) and hydrocodone *m/z* 299 (C). The hydrocodone:acetaminophen peak area ratio is in excellent agreement with the components ratio in the pill.

Results Summary

The fast chromatographic separation, direct sample introduction and short acquisition (~1 minute) allowed for rapid and high throughput analysis of different types of bulk samples - liquid, solid, powder - containing drugs. For the pulverized Vicodin tablet (powder), acetaminophen and hydrocodone were confidently identified, regardless of hydrocodone accounting for 1-2% of the tablet mass (Figure 3). The hydrocodone:acetaminophen peak area ratio is in excellent agreement at 1.6% to the pill's manufacturer mass ratio of 1.7%. Drug compounds in a solution containing caffeine, methadone, cocaine, codeine, 6-monoacetylmorphine (6-MAM) and diacetylmorphine (i.e., heroin) were all identified with match scores greater than 800 when using a SQ mass spectrometer equipped with an Extractor source tuned at 70 eV and additionally with mass accuracy better than 2 ppm when using a Q-TOF equipped with a prototype EI source tuned at 12 eV (Figures 4 and 5, Table 1). The combination of fast analysis, compound identification and no sample preparation allows for a fast workflow that involves screening and confirmation in under 5 minutes (Figure 4). This workflow can expedite analysis of bulk drug samples in forensic laboratories while saving solvent, sample preparation and reagent disposal costs.

Fast Analysis Workflow: Screening to Confirmation in Under 5 minutes

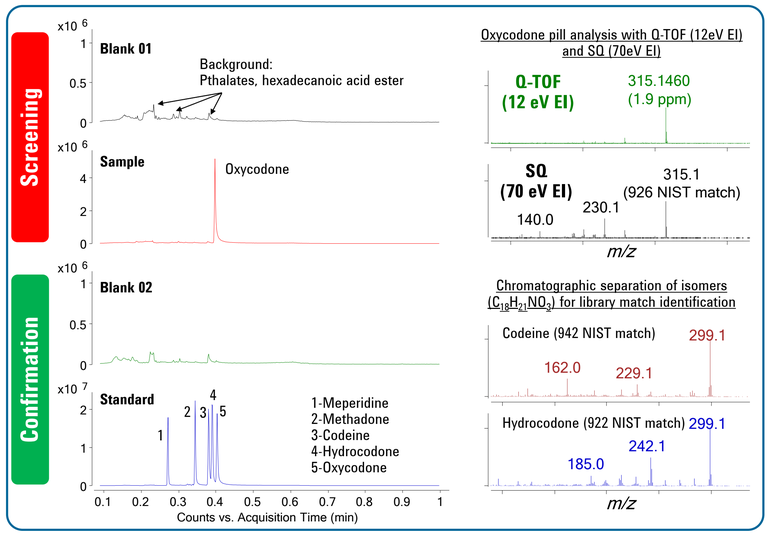

Figure 4. Fast workflow analysis for screening and confirmation of an oxycodone pill (whole) in under 5 minutes with the following steps: 1) Blank, 2) Sample, 3) Blank and 4) Standard. No sample preparation is required. Spectra shows the capabilities of using 12eV (with Q-TOF) vs 70 eV (SQ) electron ionization for compound identification. Additionally, chromatographic separation of isomers allows for library match identification. Note: Depicted chromatograms were acquired with a SQ, but similar results were also obtained with the Q-TOF.

Drug Mix Compound Identification with Q-TOF (12 eV EI) or SQ (70 eV EI)

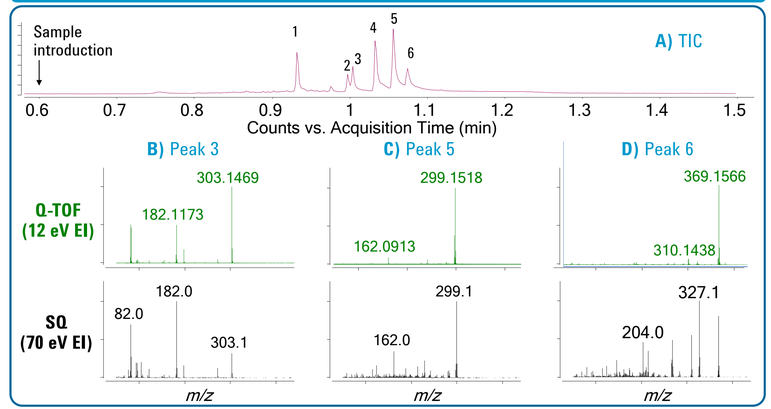

Figure 5. A) Total ion chromatogram for a multicomponent drug standard (listed in Table 1) showing excellent chromatographic separation in ~1 min for MS identification. Panels B-D show the spectra obtained for the chromatographic peaks 3, 5 and 6 when analyzed using the Open Probe Fast GC with a Q-TOF equipped with a prototype EI source tuned at 12 eV ionization energy (**green**) or with a SQ equipped with an Extractor EI source tuned at 70 eV (**black**). See Table 1 for the results summary for all 6 peaks. Note: Depicted chromatogram was acquired with a Q-TOF but similar results were also obtained with the SQ.

Table 1. List of compounds from Figure 5A showing mass accuracy (Q-TOF) and NIST library matches (SQ)

Peak	Compound	Formula	*m/z* (Theory)	*m/z* (Exp.)	Mass error (ppm)	NIST lib. match
1	Caffeine	$C_8H_{10}N_4O_2$	194.0798	194.0797	0.65	924
2	Methadone	$C_4H_{10}N^+$	72.0808	72.0807	1.05	907
3	Cocaine	$C_{17}H_{21}NO_4$	303.1465	303.1467	-0.63	877
4	Codeine	$C_{18}H_{21}NO_3$	299.1516	299.1518	-0.69	934
5	6-MAM	$C_{19}H_{21}NO_4$	327.1465	327.1465	0.03	913
6	Diacetylmorphine	$C_{21}H_{23}NO_5$	369.1571	369.1566	1.28	882

*fragment

Conclusions and Acknowledgements

Conclusions: Fast sample analysis for identification of drugs in bulk samples (powder, solid, liquid) was demonstrated using unit resolution and accurate mass spectrometers. In addition to drug identification, the fast analysis allows for the determination of relative content within a sample such as in a Vicodin pill (powder sample). The fast analysis did not require sample preparation and allowed for a simple workflow to expedite screening in a forensics application and included the following steps: 1) run blank, 2) run sample, (3) run blank and (4) run standard for confirmation. This analysis workflow resulted in overall screening and confirmation (when running a standard) of < 5 minutes for target analysis of drugs. Using a high resolution accurate mass Q-TOF, it can be expanded to non-targets and emerging targets as well. It can also be expanded to other fields that require fast screening and identification such as homeland security and organic synthesis.

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