Mass Spectrometry in Forensic Science

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Overview

- Introduction to forensic sciences
- Uses of mass spectrometry in forensic sciences
- Typical instrumentation in forensic sciences
- Applications of new instrumentation

Introduction to Forensic Sciences

Forensic Sciences is defined as: the application of a broad spectrum of sciences to answer questions of interest to the legal system.

Introduction to Forensic Sciences

Typical analytical sections within a forensic science laboratory:

Drug Chemistry – Analysis of pills, powders, liquids, plant materials, and other suspicious items for illegal drug content

Toxicology – Analysis of biological samples for alcohol, prescription medication, drugs of abuse, and other chemicals that are not naturally occurring in the body

DNA – Extraction and amplification of DNA from biological fluids for identification

Firearms – Bullet pattern recognition and analysis of gun powder

Fire Debris -- Identification of ignitable liquids used in arsons

Standards for Accepting the Scientific Validity of a Procedure, Technique, and Principle

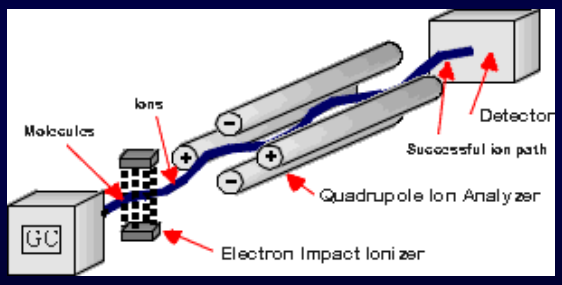
- Alabama
  - Frye standard: the court must decide if the questioned procedure, technique, and principles are “generally accepted” by a relevant community
  - Federal Rule 702: a witness qualified as an expert may testify in the form of an opinion
- Federal
  - Daubert:
    - Has it been tested?
    - Has it been published and peer reviewed?
    - Potential rate of error
    - Existence and maintenance of standards controlling the techniques operation
    - Accepted in the relevant scientific community

Mass Spectrometry in Forensic Science

A gas chromatograph with a mass spec detector is the final tool used in the analysis of drug chemistry and toxicology samples for identification and confirmation.

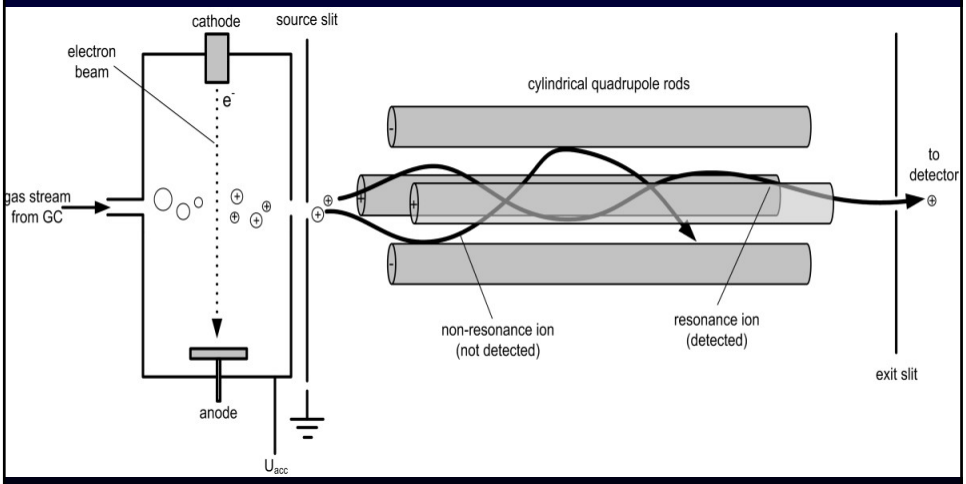
Typical forms of Mass Spectrometry in Every Forensic Science Lab

Gas Chromatography-Mass Spectrometry (GC-MS)



http://www.chem.arizona.edu/massspec/intro_html/intro.html

Typical forms of Mass Spectrometry in Every Forensic Science Lab

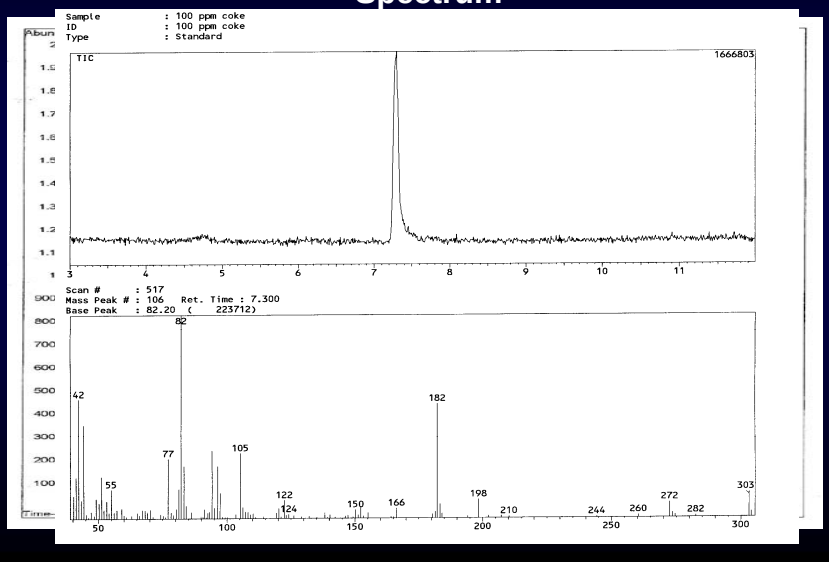


http://www.microbialcellfactories.com/content/figures/1475-2859-6-6-4-l.jpg

Typical forms of Mass Spectrometry in Every Forensic Science Lab

Gas Chromatography Mass Spectrometry (GC-MS)

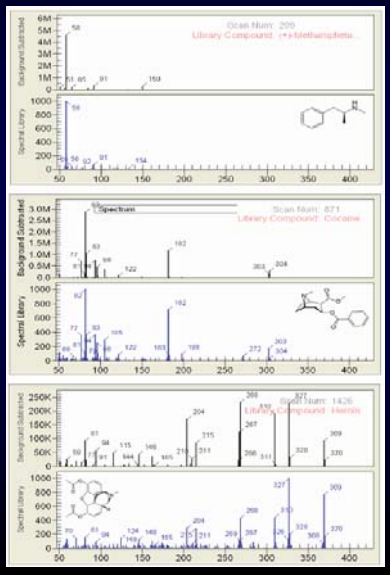
Spectrum



Typical forms of Mass Spectrometry in Every Forensic Science Lab

Gas Chromatography Mass Spectrometry (GC-MS)

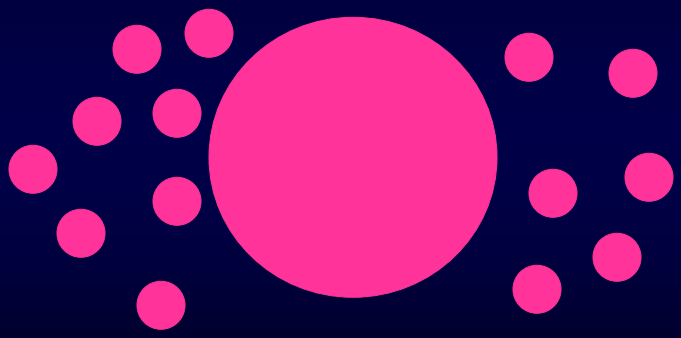
Spectrum



Spectra are searched against a library of known compounds in an effort to identify every peak in the TIC

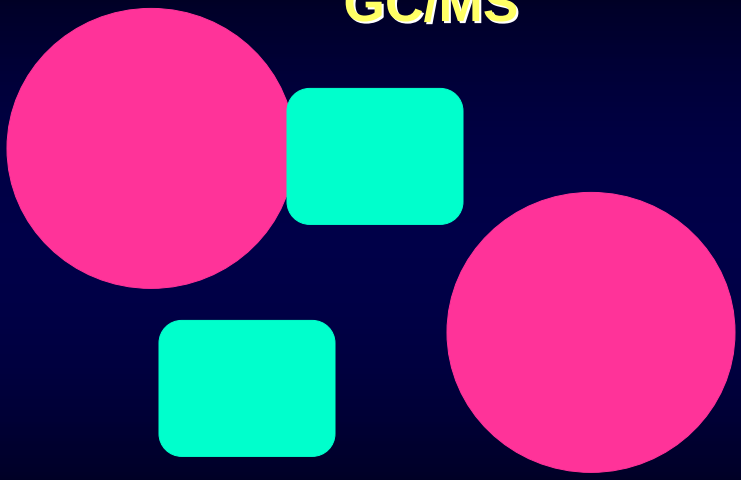
A standard is analyzed on the instrument to generate a known retention time and spectrum of the compound for that instrument

Problems Encountered with the GC/MS



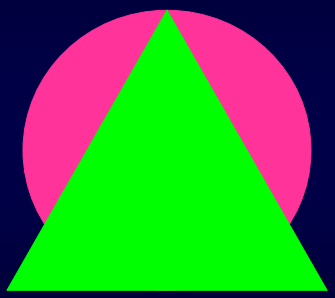
Lose the parent ion of the compound upon ionization in the instrument
Example: Methadone

Problems Encountered with the GC/MS



Derivatize the compound for analysis with GC/MS which decreases detection of low level compounds
Example: THC

Problems Encountered with the GC/MS

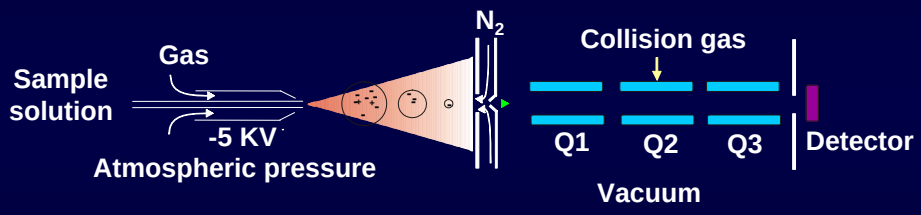


Heat labile compound will be identified as a related compound, but not the actual compound
Example: Clorazepate to Nordiazepam

New instrumentation is being introduced to combat the common problems encountered with GC/MS analysis

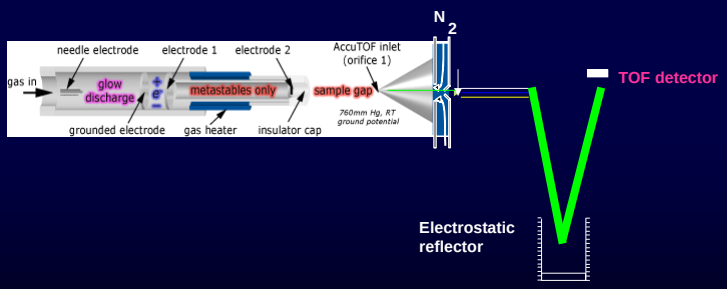
Different forms of Mass Spectrometry

Liquid Chromatography Electrospray Ionization Mass Spectrometry (LC-ESI-MS)

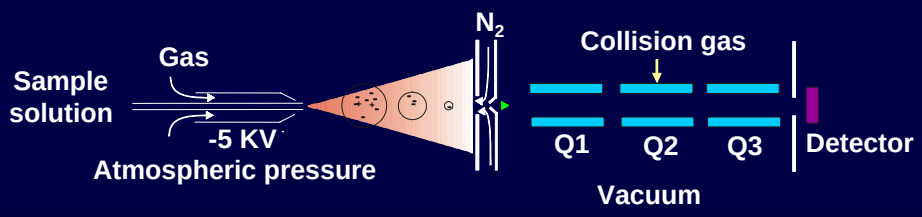


Different forms of Mass Spectrometry

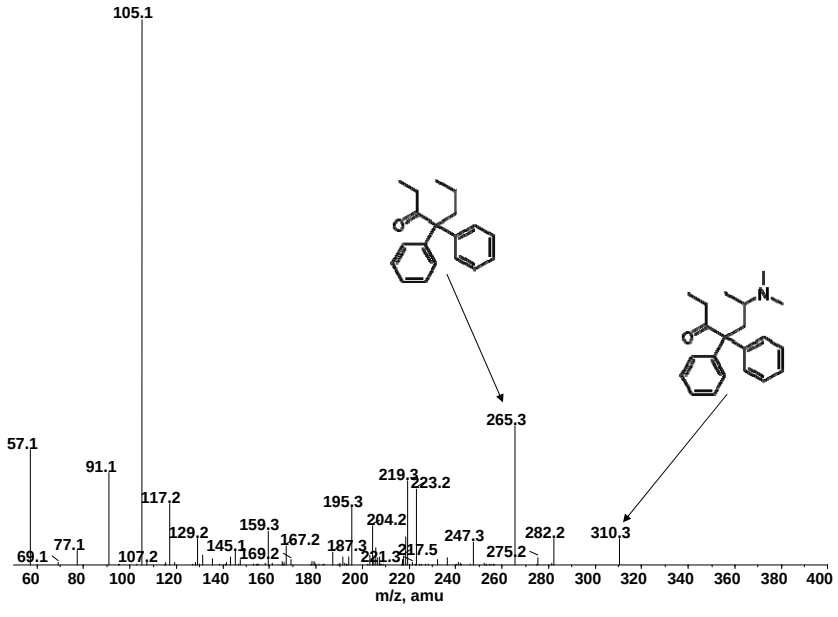
Direct Analysis in Real Time with Time of Flight Mass Spectrometry



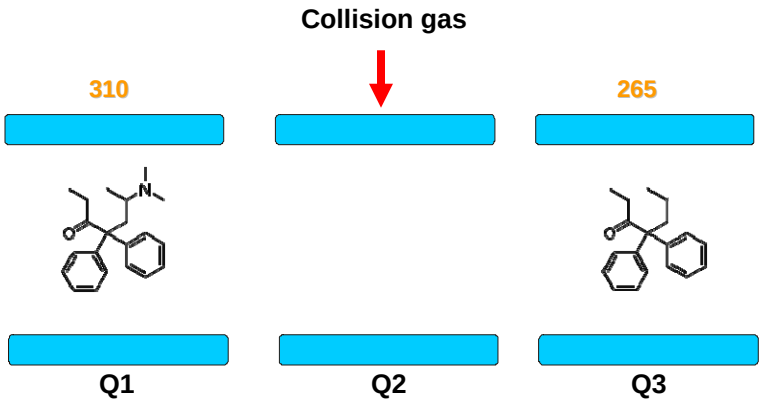
LC-MRM-MS assay for Drug Detection and Quantitation



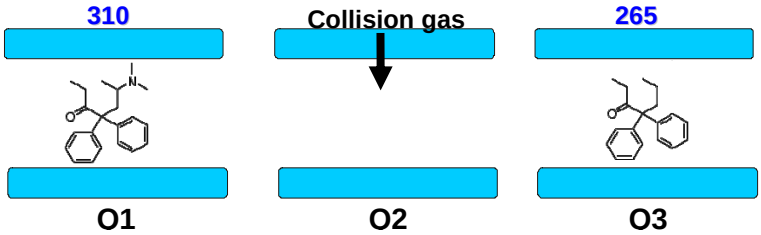
LC-ESI-MS/MS Spectrum of Methadone



LC-MRM-MS analysis for Drug Quantitation

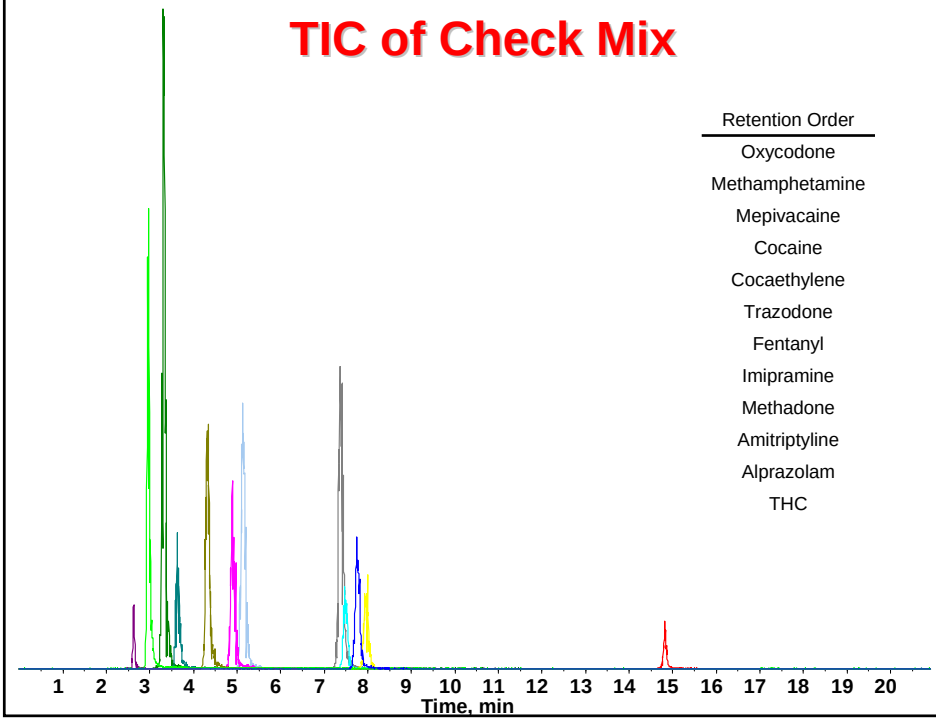


LC-ESI-MRM-MS

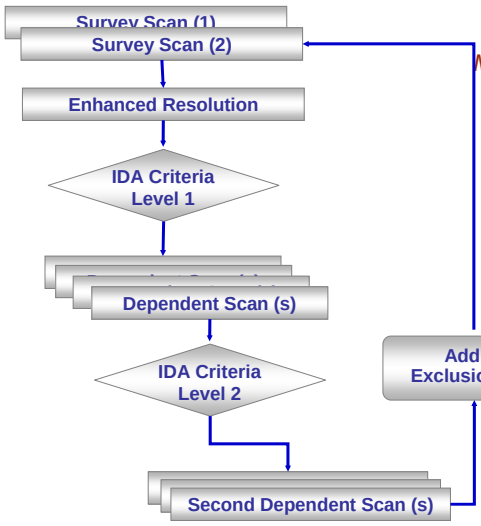


Compound	Molecular Weight	Parent ion	Product ion	Dwell Time (msec)	Declustering Potential (DP)	Collision Energy (CE)	Retention Time	pKa
Alprazolam	308.0829	309.1	205	25	60	50	8.03	2.4
Amitriptyline	277.183	278.2	91	25	45	42	7.8	9.4
Cocaethylene	317.37	318.2	196	25	40	39	4.32	--
Cocaine	303.1471	304.1	82	25	30	40	3.6	8.6
Fentanyl	336.2202	337.2	188	25	55	43	5.18	8.4
Imipramine	280.1939	281.2	86	25	35	32	7.41	9.5
Mepivacaine	246.1732	247.2	98	25	42	28	3.32	7.6
Methadone	309.2093	310.1	265	25	30	35	7.56	8.6
Methamphetamine	149.1204	150.1	91	25	34	27	2.96	8.6
Oxycodone	315.1471	316.1	241	25	50	40	2.6	8.5
THC	314.2246	315.1	193	25	37	34	14.91	10.6
Trazodone	371.1513	372.2	176	25	60	42	4.87	6.1

TIC of Check Mix



*I*nformation *D*ependent *A*cquisition *(IDA)*



Survey scan be EMS, EMC, Neutral Loss, Precursor Scan, MRM or EPI (combinations of 2 surveys)

Improve Resolution/Accuracy

Two levels of criteria

Multiple dependant scans (EPI, Product Ion and MS3)

Inclusion/Exclusion List

Second Level Dependant Scan (MS^3)

Courtesy of Ricky Ciner

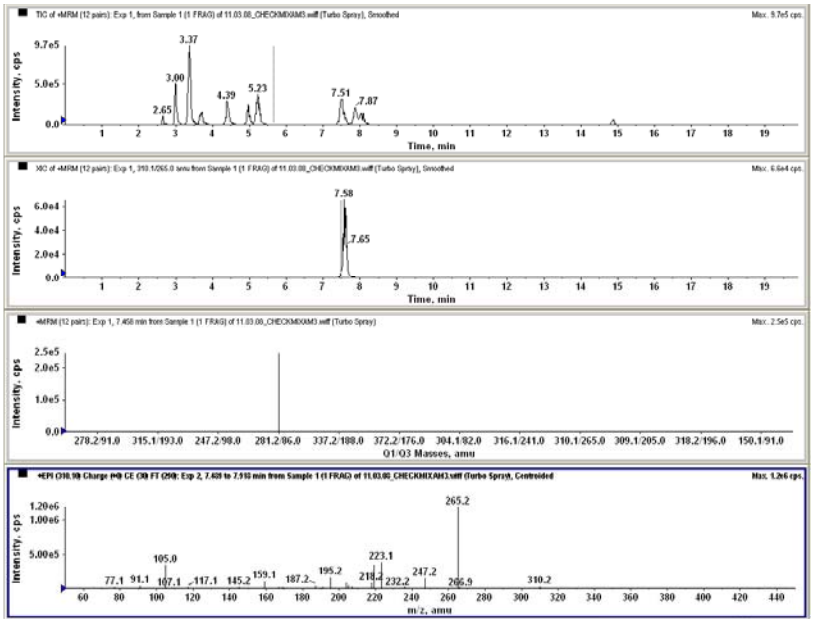
IDA Analysis of Check Mix

TIC

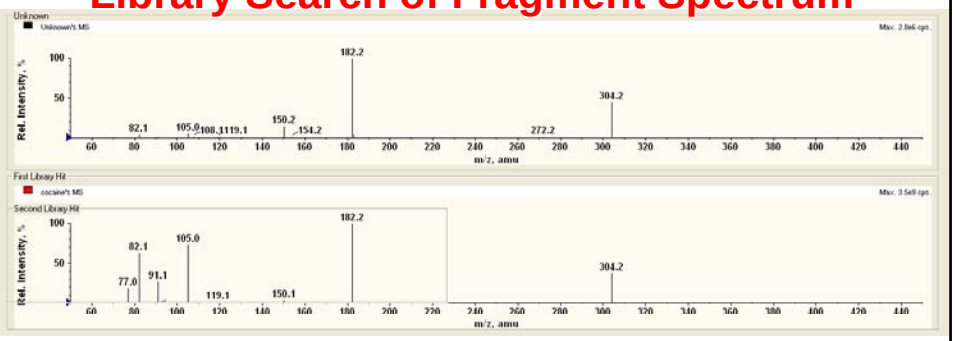
XIC

MRM

EPI



Library Search of Fragment Spectrum



	Name	Formula	Molecular weight (amu)	Fit	RevFit	Purity	CE
1	cocaine	C17H21NO4	303.1470	76.392	75.193	74.384	20.000
2	norpropoxyphene (3200)	C21H27NO2	325.2041	58.738	0.392	0.222	20.000
3	phenytoin (3200)	C15H12N2O2	252.0898	45.442	45.056	22.367	25.000
4	atomoxetine	C17H21NO	255.1623	44.991	43.158	21.116	20.000
5	methadone	C21H27NO	309.2092	33.970	2.092	1.360	20.000
6	diltiazem	C22H26N2O4S	414.1613	32.815	6.350	3.150	20.000
7	gabapentin (3200)	C9H17NO2	171.1259	32.126	1.196	0.730	20.000
8	scopolamine	C17H21NO4	303.1470	28.540	36.795	10.921	20.000
9	cocaethylene	C18H23NO4	317.1627	27.416	6.327	3.437	20.000
10	MDMA	C11H15NO2	193.1102	26.564	0.828	0.615	20.000
11	phenmetrazine	C11H15NO	177.1154	20.907	0.410	0.323	20.000

Summary

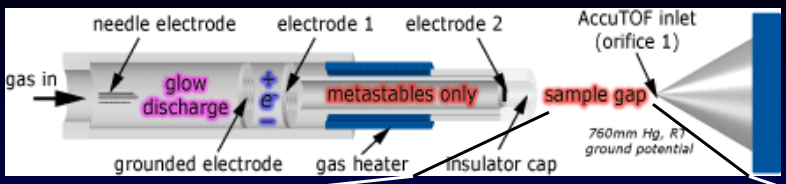
- LC-ESI-MS can be used in the qualitative and quantitative analysis of drugs in toxicological specimens
  - The instrumentation is advantageous in that chemicals do not have to be derivatized
  - The soft ionization aids detection of the parent ion of the compound

AccuTOF-DART MS

- The DART is the first open air, ambient ion source for a mass spectrometer
- Coupled to a time of flight instrument exact mass measurements can be used in the putative identification of compounds

http://www.jeolusa.com/Portals/2/prodshots/AI/accutof-dart-tm.jpg

AccuTOF-DART MS Ionization



- Penning ionization: energy is transferred from metastable ions (M*)
- Positive ions: He* ionized water which transfers a proton to the sample
- Negative ions: Penning electrons are rapidly thermalized and capture by oxygen which ionizes the sample

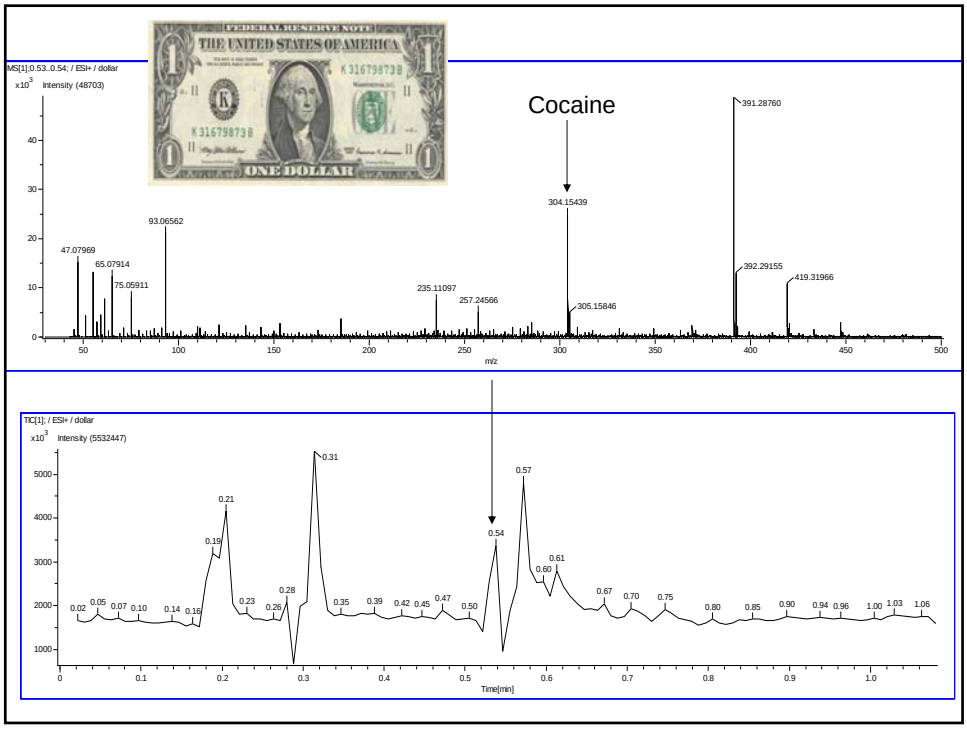
http://www.jeolusa.com/PRODUCTS/AnalyticalInstruments/MassSpectrometers/AccuTOFDART/AccuTOFDARTIonizationMechanisms/tabid/450/Default.aspx

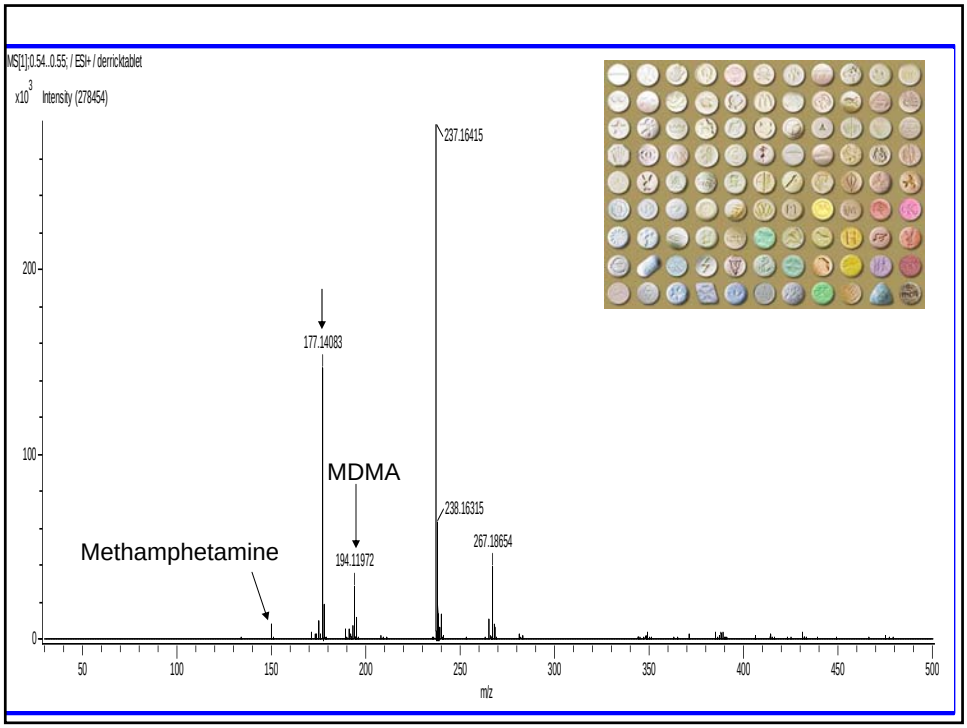
Types of Samples Analyzed with the AccuTOF-DART MS

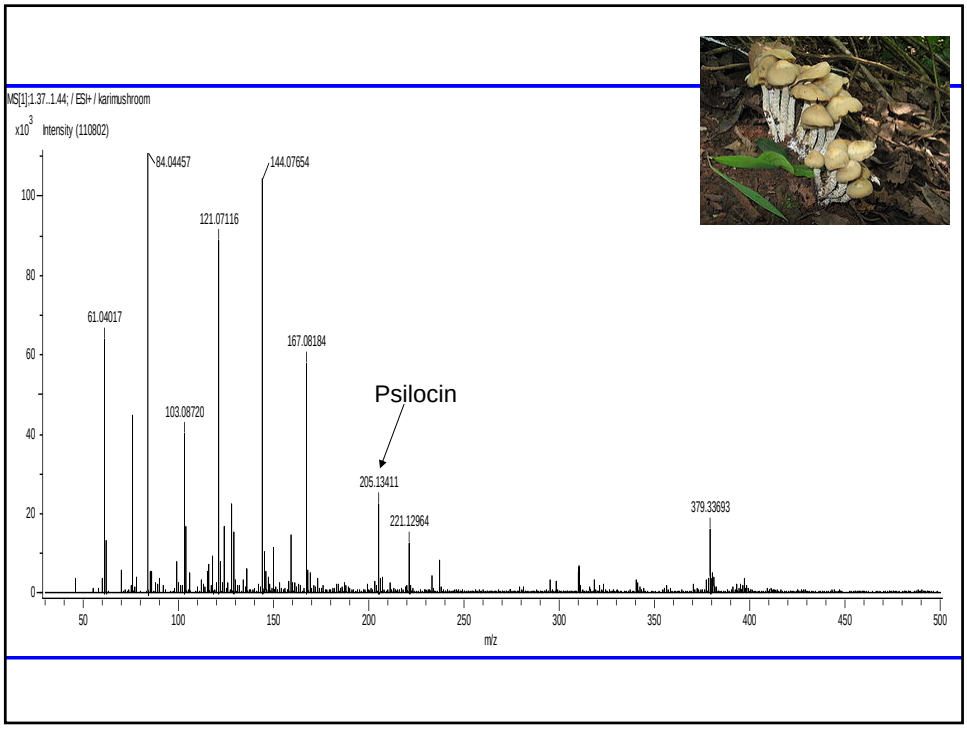
http://www.ecstasy2.com/img/ecstasy_pill_collage1.jpg

Sample Introduction with the AccuTOF-DART MS

www.jeoluk.com/images/DART01.jpg

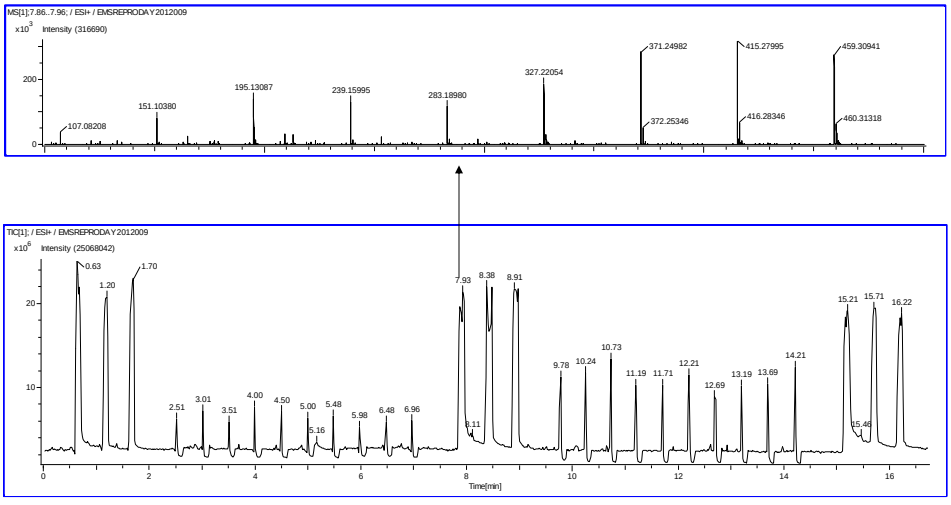



MS[1]:0.54..0.55; / ESI+ / derricktablet
x10^3 Intensity (278454)
237.16415
177.14083
MDMA
238.16315
267.18654
194.11972
Methamphetamine
m/z

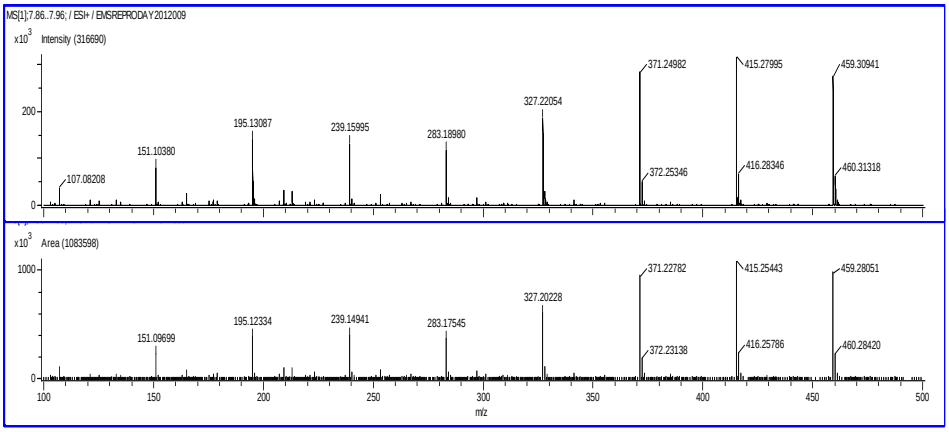

MS[1]:1.37..1.44; / ESI+ / karimushroom
x10^3 Intensity (110802)
84.04457
144.07654
121.07116
61.04017
167.08184
103.08720
Psilocin
205.13411
221.12964
379.33693
m/z

Sample Introduction with the AccuTOF-DART MS

Autosampler Sample Introduction into the DART



Within Run Calibration with PEG



Sample mass measurements must be with 5 mmu for putative drug ID

Summary

- The AccuTOF-DART will be used as a screening tool for compound analysis
  - The instrumentation is advantageous in that chemicals do not have to be derivatized
  - The open air ionization allows a wide variety of samples to be analyzed without extraction

Overall Summary

- Mass spectrometry is a powerful tool in a forensic science lab
- New instrumentation is expanding the sample analysis possibilities beyond current limitations
- No one technique is robust enough for everything, therefore a combination of techniques is ideal for screening and confirmation of drug and toxicology samples

Acknowledgements

UAB	ADFS
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