

Comprehensive Analysis of Drug Residues from a Confiscated Pipe: GC-High Resolution Mass Spectrometry with Chemical Ionization to Facilitate Unknown Identification



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Key Words: Electron Impact Ionization, Chemical Ionization, High Resolution Time-of-Flight Mass Spectrometry

1. Introduction

The continuous influx of new synthetic drugs such as cannabis analogs into society is a major problem for law enforcement, forensic laboratories, and the medical community.^{1,2}

Relatively simple organic transformations produce novel and licit psychotics that can elude detection by standard analytical methods.^{3,4} Detection and characterization of synthetic drugs is complicated by 1) the wide range of active ingredients and variety of botanical matrices, 2) the rate at which new drugs and blends appear on the market, 3) the fact that these synthetic drugs and metabolites are often not targeted during routine forensic analyses,^{5,6} and 4) these newly emerging compounds are typically not present in commercially available mass spectral libraries. High performance time-of-flight mass spectrometry is a practical choice for the analysis of these moving targets.



This application note shows the utility of high resolution mass spectrometry with soft ionization to facilitate identification of unknown compounds which were present in extracted residues from a confiscated pipe. When a compound is detected that is not matched sufficiently to a commercially available library, the electronic impact ionization (EI) spectrum becomes difficult to interpret without confirmation of the molecular ion. Accurate mass chemical ionization (HR-CI) results in preservation of molecular ions which is very important for structural elucidation.

2. Results and Discussions

A confiscated pipe was obtained from a collaborating forensic laboratory. Residues from the pipe were dissolved in organic solvent and analyzed by GC-HRT. The resulting analytical ion chromatogram (AIC) is shown in Figure 1.

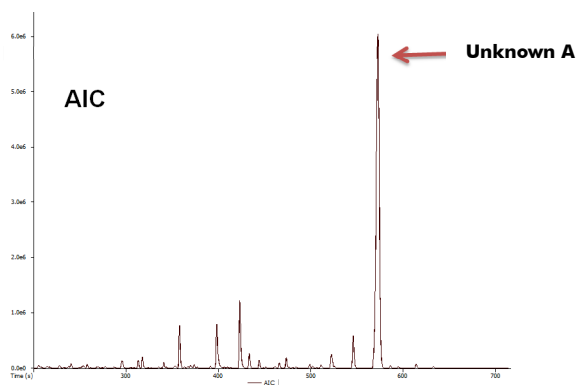


Figure 1. AIC obtained from EI analysis of pipe residue extract.

The EI mass spectrum of the most abundant analyte detected ("Unknown A") in the residue is shown in Figure 2. A library search of the mass spectrum of Unknown A resulted in Lepenine as the number one hit with a spectral similarity of 546 out of a possible 1000 points. The poor library match value and a quick inspection of the data suggests the unknown was not present in the commercially available libraries searched (NIST 2011 and Wiley 2009). The next step in the mass spectrometry work flow of unknown identification is to verify the molecular weight of the unknown compound. While the EI mass spectrum does contain a high mass ion at m/z 359.16861, there is no guarantee that this is the molecular ion peak without confirmation data from soft ionization mass spectrometry. Therefore, a second analysis of residue extract was conducted using HR-CI with methane as the reagent gas. The resulting methane HR-CI mass spectrum is shown in Figure 3. This spectrum contains an intense protonated molecular ion at m/z 360.17632 as well as a C_2H_5 adduct at 388.20798 confirming a molecular weight of 359 for the unknown and allows the analyst to proceed with structural elucidation of the obtained mass spectra. The excellent mass accuracies obtained using the Pegasus[®] GC-HRT allowed for confident formula assignments for molecular ions in both the EI and methane HR-CI spectra for the unknown. A formula search for the EI-MS ion at m/z 359.16861 resulted in $C_{24}H_{22}FNO$ (Mass delta = 0.00062, mass accuracy MA = 1.72 ppm). A similar search of the CI-MS ion at m/z 360.17632 resulted in the formula $C_{24}H_{23}FNO$ (MA = 1.38 ppm). A web-based search of the formula $C_{24}H_{22}FNO$ suggested the compound 1-(5-fluoropentyl)-3-(1-naphthoyl)indole, also known as AM-2201, as a likely candidate. A reference standard for this compound

was purchased and analyzed to confirm that this was in fact the unknown analyte identified in the residue extract. The protonated chemical structure is shown as an inset in Figure 3.

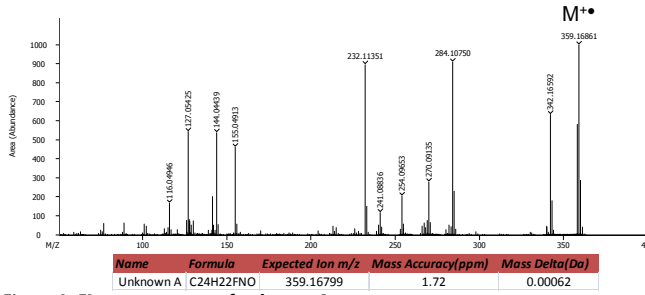


Figure 2. EI mass spectrum of unknown A.

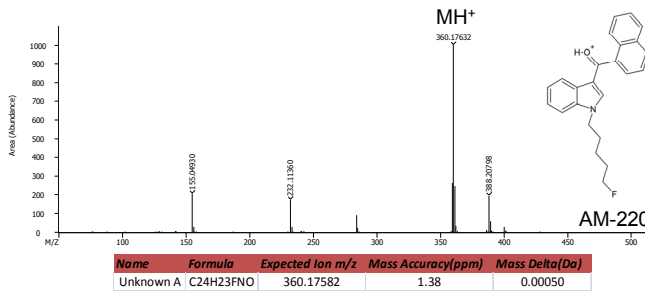


Figure 3. HR-Cl mass spectrum of unknown A.

The sample also contained Δ^9 -tetrahydrocannabinol (Δ^9 -THC) and other synthetic cannabinoids including JWH-018, JWH-122, JWH-081, and an additional suspected synthetic drug, Unknown B (labeled with an asterisk in Figure 4). MA values for these compounds ranged from -1.39 to -0.12 ppm. The mass spectrum for Unknown B was also absent in the commercial libraries. The workflow described for Unknown A was employed for Unknown B and led to JWH-022 as a proposed candidate for this compound. Figures 5 and 6 display its EI and methane HR-Cl spectra, respectively.

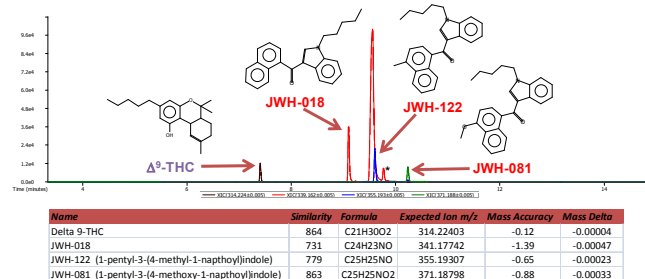


Figure 4. Extracted ion chromatogram (XIC) showing THC and synthetic cannabinoids in pipe sample.

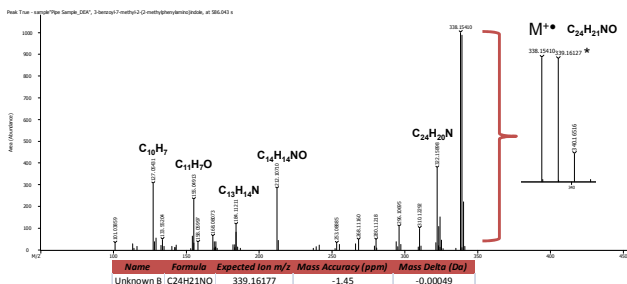


Figure 5. EI mass spectrum of unknown B.

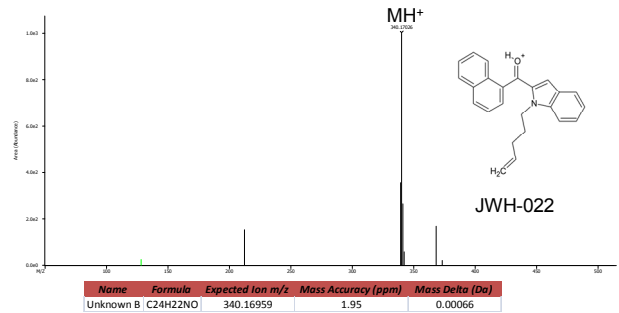


Figure 6. HR-Cl mass spectrum of unknown B.

Forensic samples can be a complex mixture of illicit and licit substances as evident from the wide variety of compounds found in this pipe. This is most likely the result of multiple uses of the pipe with different drug substances; however, the complexity may also be due to poor or non-existent quality control in the production of these materials. A partial list of compounds in the sample, including sterols, indole derivatives, nitriles, and phenols appears in Table 1.

Table 1. Miscellaneous compounds in pipe sample.

Name	Formula	R.T. (s)	Area	Expected Ion m/z	Mass Accuracy (ppm)
Phenol, 3-methyl- (CAS)	C7H8O	205.149	282908	108.05697	-0.87
1H-Imidazole, 2-methyl- (CAS)	C4H6N2	206.376	263641	82.05255	0.44
Phenol, 2-methoxy- (CAS)	C7H8O2	208.767	45543	124.05188	0.26
4[1H]-Pyridinone (CAS)	C5H5NO	213.548	397571	95.03657	-0.33
Phenol, 3-ethyl- (CAS)	C8H10O	228.263	162252	122.07262	0.13
Naphthalene	C10H8	234.075	51896	128.06205	0.29
Methylphenylguaiacol	C7H8O3	236.362	83989	140.04680	0.41
Catechol	C6H6O2	237.614	183354	110.03623	-0.64
4-vinylphenol	C8H8O	240.441	512207	120.05697	0.24
Benzenepropionitrile	C9H9N	243.873	42046	131.07295	-0.50
Cinnamionitrile	C9H7N	247.059	44083	129.05730	0.21
1,4-Benzenediol	C6H6O2	253.334	516706	110.03623	-0.47
1H-Indole	C8H7N	257.923	508162	117.05730	-0.18
4-vinyl-guaiacol	C9H10O2	261.488	80190	150.06753	-0.09
5-ethyl-pyrogallol	C8H10O3	268.299	181932	154.06245	0.35
1H-Indole, 3-methyl-	C9H9N	277.262	251291	131.07295	-0.46
ATRANOL	C8H8O3	278.703	38855	152.04680	-0.34
4-methyl-6(2-methylpropenyl)-2H-pyran-2-one	C10H12O2	288.459	50850	164.08318	-0.94
1-cyano-naphthalene	C11H7N	298.871	58725	153.05730	-0.21
2,3,5-Trimethoxytoluene	C10H14O3	301.771	39244	182.09375	1.90
(3a,5a-trans)-dodecahydropyrrrolo[1,2-a]quinoxaline	C11H20N2	308.857	58336	180.07810	-0.51
octylphenol	C14H22O	317.535	1871006	206.16652	-0.85
(+)-3-(2'-METHYLBUTYL)INDOLE	C13H17N	318.341	67100	187.13555	-0.94
9H-Carbazole	C12H9N	357.229	65287	167.07295	-0.47
octylphenol-ethoxylate	C16H26O2	357.776	5107445	250.19273	-0.38
9H-Pyrido[3,4-b]indole, 1-methyl-	C12H10N2	376.271	51137	182.09385	0.26
9H-Pyrido[3,4-b]indole	C11H8N2	377.278	132740	168.06820	-0.52
Pentalene, 1,2,3,3a,4,6a-hexahydro-	C8H12	395.052	17052	108.09335	-0.87
Ethanol, 2-[2-(4-(1,1,3,3-tetramethylbutyl)phenoxy)ethoxy]ethoxy-	C18H30O3	398.148	2909944	294.21895	-0.18
9-OCTADECENAMIDE	C18H35NO	423.04	4358976	281.12732	0.87
Oleanitrile	C18H33N	423.416	150791	263.26075	0.35
octylphenol-triethoxylate	C20H34O4	433.317	1111259	338.24516	-0.33
Ethanol, 2-[2-[2-[2-[1,1,3,3-tetramethylbutyl)phenoxy]ethoxy]ethoxy]ethoxy]-	C22H38O5	465.887	322409	382.27138	-0.23
9H-Carbazole, 9-phenyl-	C18H13N	473.060	51386	243.10425	-1.13
1H-Quinoln-2-one, 3,4-diphenyl-	C21H15NO	498.817	179143	297.11482	-1.28
Tocopherol	C28H48O2	510.43	82866	416.36488	-1.13
Vitamin E	C28H50O2	523.46	312844	430.38053	0.21
Stigmasteran-3,5-diene	C29H48	525.666	49994	396.37505	-0.47
Sitosterol	C29H50O	568.389	64162	414.38562	0.02
2-isopropyl-3,4-diphenyl-1-isoquinolone	C24H21NO	572.918	3961353	339.16177	0.17
3-benzoyl-7-methyl-2-(2-methylphenylamino)indole	C23H20N2O	586.043	161486	339.16177	-1.45

3. Conclusion

High performance time-of-flight mass spectrometry provides the necessary resolution, mass accuracy, and spectral quality to analyze complex forensic samples. Comprehensive data acquisition allows for complete analysis of samples and a combination of high resolution EI and HR-Cl data facilitates confident characterization of novel synthetic drugs. The Pegasus GC-HRT was shown as an ideal analytical tool for the fight against illegal drugs.

4. References

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5. Sample Preparation

A small quantity of residue (93 mg) was scraped from the inside of the drug pipe and transferred to a small vial. This material was dissolved in 3 mL of 2:1 methanol/dichloromethane. A 1 mL aliquot of the solution was transferred to an autosampler vial for analysis.

6. Experimental Conditions

Mass Spectrometry

MS: LECO Pegasus HRT
Source Temp.: 250°C (CI = 180°C)
EI: 70 eV (CI = 140 eV)
Acq. Delay: 200 s
Acq. Rate: 10 spectra/s
M/Z Range: 50-550
Mode: High Resolution (R = 25,000)
CI Reagent Gas: Methane

Gas Chromatography

GC: Agilent 7890
Injection: 1 µL, splitless @ 280°C
Carrier Gas: Helium, 1.0 mL/min.
Column: Restek Rxi-5HT
(30 m, 0.25 mm ID, 0.10 µm df)
Oven Program: 60°C (1 min), 40°C/min to 310°C,
hold 8 min
Transferline: 300°C