Analysis of Designer Drugs Bath Salts by Quadrupole Ion Trap GC/MS

Application Note

Forensics

Authors

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Abstract

With more sophisticated production methods and ease of obtaining designer drugs of abuse, forensic laboratories face increasing challenges. The rapid influx of cases involving designer drugs sold as "Bath Salts" pose a unique opportunity to develop fast analytical methods which are analyte specific that can also reach the desired detection levels. A 29 analyte mixture of bath salts was analyzed using the benefits of Gas Chromatography coupled to Quadrupole Ion Trap Mass Spectrometry (GC/MS). GC/MS is proposed as one solution to the growing bath salts problem experienced by forensic laboratories.

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Introduction

Designer synthetic stimulants, sold as bath salts, often contain various amphetamine-like chemicals, such as methylenedioxypyrovalerone (MPDV), mephedrone, and pyrovalerone. MDPV is a psychoactive drug with stimulant properties which act as a norepinephrine-dopamine reupatake inhibitor. Mephedrone, also known as 4-methylmethcathinone (4-MMC), or 4-methylephedrone, is a synthetic stimulant drug of the amphetamine and cathinone classes which produce similar effects to MDMA, amphetamines, and cocaine. Pyrovalerone, a Schedule V controlled substance in the United States is used for the clinical treatment of chronic fatigue or as an appetite suppressant for weight loss purposes. Recently, bath salts containing MDPV, mephedrone, and pyrovalerone were being sold as a legal drug alternative. These drugs were originally developed as alternatives to those controlled by laws against illegal drugs and were marketed as designer drugs or bath salts. However, as of October 2011 the US Drug Enforcement Agency has temporarily classified MDPV and mephedrone as illegal since they are considered analogs of other illegal drugs and thus fall under the Federal Analog Act. These three analogs are just the starting point of designer drugs being sold in the public domain. As soon as one drug is regulated by authorities another analog is rapidly introduced as a substitute. GC/MS, full scan Electron Ionization (EI), along with Chemical Ionization (CI) confirmation (mode changes are software selected) provide the selectivity, specificity, and low levels of detection that place greater confidence in analytical results obtained in the laboratory when dealing with these types of forensic cases. This application note develops GC/MS conditions for 29 bath salts.

Experimental

GC/MS ion trap analysis

Bath salt analysis was performed on an Agilent 240 Quadrupole Ion Trap GC/MS system using the Agilent 7890A Gas Chromatograph (GC) with the Agilent 240 Mass Spectrometer (MS). The GC was equipped with a HP-5MS UI Column. The 240 MS was operated in both Electron Impact (EI) ionization mode and CI mode using a liquid reagent acetonitrile.

Agilent 7890A GC conditions

Column	Agilent HP-5MS UI 30 m × 250 μm, 0.250 μm (p/n19091S-433UI)
Injection mode	Split/splitless inlet, pulsed splitless injection Pulse pressure 40 psi until 0.8 minutes Purge flow 50 mL/min at 0.75 minutes
Inlet temperature	280 °C
Carrier gas	Helium, constant flow mode, 1.2 mL/min
Oven program	Initial 80 °C hold for 0 minutes 10 °C/min to 150 °C hold for 0 minutes 5 °C/min to 180 °C hold for 0 minutes 10 °C/min to 300 °C for 2 minutes
Total run time	27 minutes

Agilent 240 quadrupole ion trap MS conditions

Tune	Auto-tune
Acquisition	EI (electron ionization) target- 40,000 filament 10 μA Scan 35–500 da CI (chemical ionization) target- 15,000 filament 20 μA Scan 150–400 da
CI reagent gas	Acetonitrile - reagent low Mass 35 reagent high mass 60
Solvent delay	6.0 minutes
MS temperatures	Trap 230 °C, manifold 100 °C, transfer line 280 °C

Compounds were identified by full-scan spectra from reference standards, followed by CI to confirm compound identity for the analysis. Many compounds had a characteristic 58 ion, 44 ion, and 126 ion, making positive identification difficult except by retention time.

Since most bath salts are typically sold in pure form with little or no cutting agents, pure standards were analyzed. For method development and optimization purposes, a 100 ng/mL standard solution of all bath salt analytes was prepared in ethyl acetate. For quantitation purposes, the 100 ng/mL standard mixture of 29 bath salts was used.

No analyte derivatization was required for the analysis of the 29 bath salts studied in this application note.

Results and Discussion

For the IUPAC names, full scan spectra, and structures of each bath salt analyte used in this application note, refer to Agilent Technologies Designer Drugs Analysis by GC/MS Application Compendium.

Figure 1 shows an overlay of the total ion chromatogram for the 29 bath salts mixture EI and CI modes. Based on the observed area responses for each analyte, most bath salts can be easily detected at levels of 10 ng/mL.
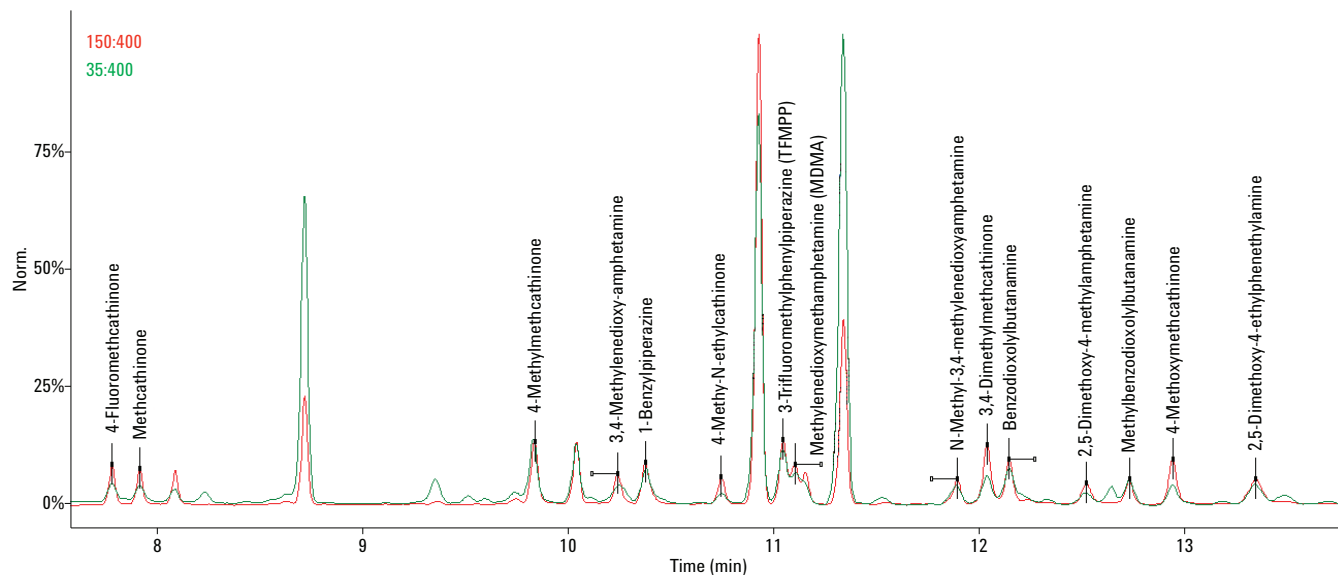

Figure 1.   EI and CI total ion chromatogram of the standard mixture of 29 Bath Salts (1 of 3).

After method optimization, the EI and CI quantitation ions for the 29 bath salts are listed in Table 1. It is good analytical practice to use the strongest signal (ion) for quantitation. which is listed for each analyte in Table 1. This provides a unique retention time, EI quantifying, and CI quantifying ions for each analyte of interest, which yields greater confidence in the analytical results obtained and reduces false positives or negatives.

Table 1. Analyte EI and CI Quant. Ions and Retention Times with Respective Molecular Ions

Chemical name	R.T	M. ion	EI Quant. ion	CI Quant. ion
4-Fluoromethcathinone	7.74	181.206	58.3	182.1
Methcathinone	7.909	163.22	58.3	164.1
4-Methylmethcathinone	9.839	177.242	58.3	178.2
3,4-Methylenedioxy-amphetamine	10.242	179.22	44.3	163
1-Benzylpiperazine	10.383	176.258	91.1	177
4-Methyl-N-ethylcathinone	10.753	191.27	72.3	192.2
3-Trifluoromethylphenylpiperazine (TFMPP)	11.046	230.23	188.2	231.1
Methylenedioxymethamphetamine (MDMA)	11.113	193.24	58.3	194.1
N-Methyl-3,4-methylenedioxyamphetamine	11.903	207.27	72.3	208.2
3,4-Dimethylmethcathinone	12.047	191.27	58.3	192.1
Benzodioxolylbutanamine	12.158	193.242	58.2	177
2,5-Dimethoxy-4-methylamphetamine	12.534	209.29	166.2	193.2
Methylbenzodioxolylbutanamine	12.739	207.27	58	208.2
4-Methoxymethcathinone	12.949	193.242	72	194
2,5-Dimethoxy-4-ethylphenethylamine	13.371	209.29	180.2	193.2
3,4-methylenedioxymethcathinone	14.493	207.23	58.3	208.2
2,5-Dimethoxy-4-chloroamphetamine	14.736	229.7	44.3	213.3
Ethylone	15.3	221.2524	72.2	222.1
Butylone	15.476	221.2524	72.3	222.1
4-Bromo-2,5-dimethoxyphenethylamine	15.951	260.13	232	244.2
2,5-Dimethoxy-4-bromoamphetamine	16.008	274.15	44.3	258
Pryovalerone	16.774	245.36	126.3	246.2
2,5-Dimethoxy-4-iodophenethylamine	17.343	307.13	278	291.1
2,5-Dimethoxy-4-ethylthiophenethylamine	17.546	241.35	212.1	242.3
2,5-Dimethoxy-4-propylthiophenethylamine	18.464	255.38	226.1	256.3
5-Methoxy-dimethyltryptamine	18.642	219.298	58.3	219.2
Methylenedioxypyrovalerone (MDPV)	19.857	275.343	126.4	276.2
N,N-diallyl-5-methoxytryptamine	21.516	270.375	110.3	271.3
Naphyrone	21.697	281.391	126.4	282.3

The upper chromatograms show an overlay of EI and CI total ion chromatograms. The peaks to the right show the EI peak is a combination of peaks and interference.

Spectra 2A and 2B, lower right, show the interference spectra and the naphyrone spectra.

Spectra 1a shows the clean CI spectra of Naphyrone and no interference as the interference did not CI.

Clean spectra without interference shown in EI trace
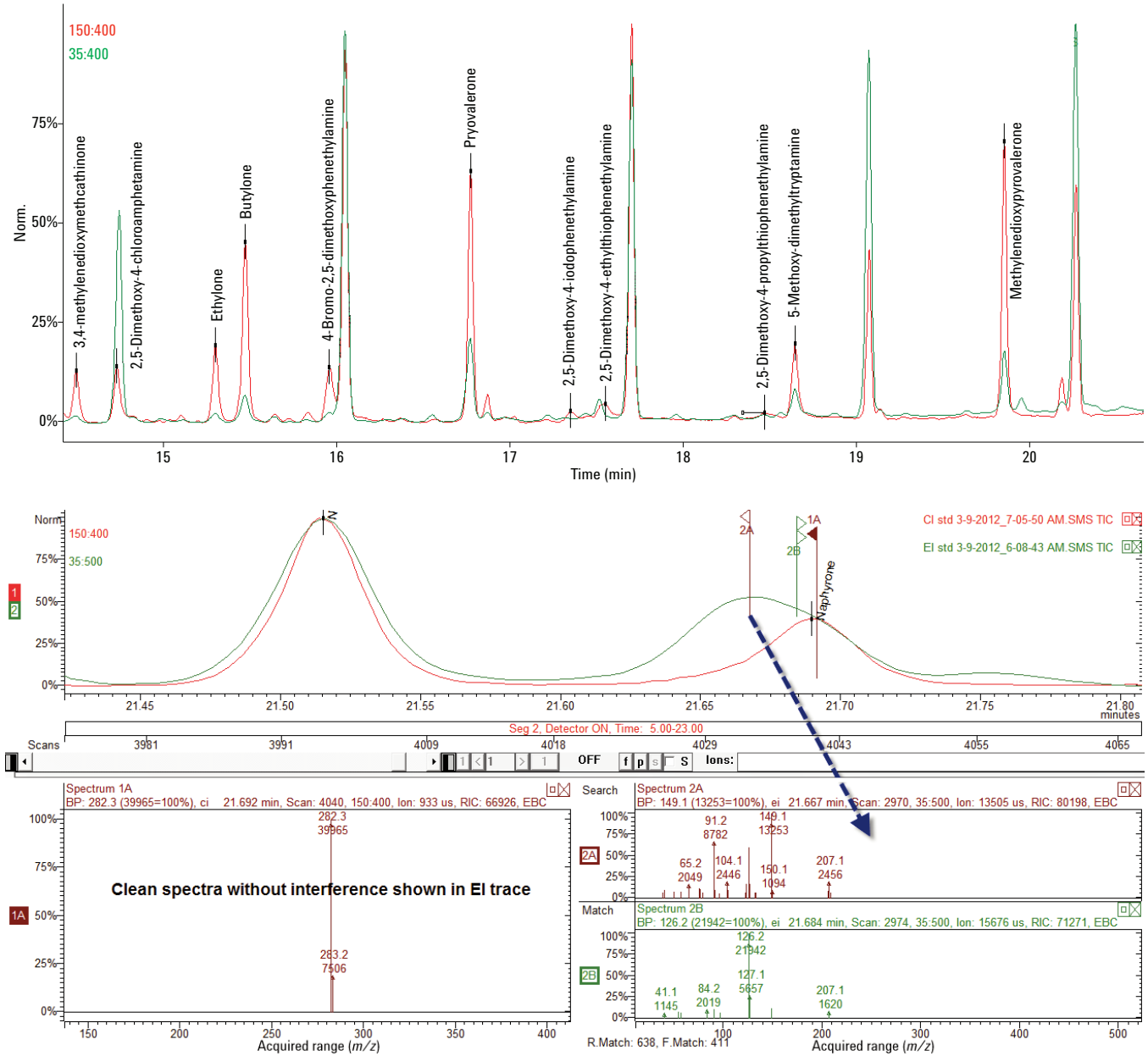
Conclusion

For the analysis of designer drugs such as bath salts, the benefits of GC Quadrupole Ion Trap MS cannot be underestimated. In terms of reducing sample matrix interference, improving signal-to-noise, and coupling its high selectivity and sensitivity, the GC/MS Ion Trap provides a more confidence driven solution for bath salt analysis. GC/MS Quadrupole Ion Trap analysis has the potential to reduce false positives and negatives as well as provide an additional degree of confidence in the results obtained. Using the optimized method listed above, a fast, targeted GC/MS method can be used to solve the current bath salt analysis problem facing forensic laboratories. The use of CI for matrix reduction verification and identification gives the analyst a higher level of confidence than EI alone.

References

1. "Chemicals Used in "Bath Salts" Now Under Federal Control and Regulation". News Release. Public Affairs, U.S. Drug Enforcement Administration. October, 21, **2011** http://www.justice.gov/dea/pubs/pressrel/pr102111.html

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3. "Confirmation and Quantification of Synthetic Cannabinids in Herbal Incense Blends by Triple Quadrupole GC/MS". Agilent Technologies, Inc. Application Note p/n 5990-8987EN. January **2012**.

4. SOFT-TIAFT International Conference on Forensic and Analytical Toxicology Sept 25-30, Poster- Ion Trap GC-MS/MS analysis of designer drugs in biological matrix, Joe Crifasi, Ron Honnold.

Acknowledgement

For More Information

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