

Mass Spectrometry

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Analysis of Cathinones in Bath Salts by Direct Sample Analysis TOF MS

Synthetic cathinones are gaining popularity as drugs of abuse and are often sold in bath salts. Currently, there is no standard method to quickly screen and confirm cathinones in bath salts. To address this issue, use of the AxION® Direct Sample Analysis™ (DSA™) integrated with the AxION 2 time-of-flight mass spectrometer (TOF) (PerkinElmer, Waltham, MA) was implemented. Cathinone standards and bath salt samples were rapidly screened and confirmed in seconds by accurate mass and isotopic distribution of parent and fragment ions using DSA/TOF and AxION Solo™ software.

Introduction

Cathinone is a beta-ketone amphetamine analogue that is found naturally in the *Catha edulis* plant. Derivatives of cathinone have been synthesized and are grouped together as cathinones.¹ Synthetic cathinones have gained popularity in the U.S. over the last few years as drugs of abuse, and are often sold as bath salts in head shops. The synthetic stimulants are used as legal substitutes for other illicit drugs, such as cocaine and methamphetamine. Bath salt components continually change as street chemists alter existing compounds to avoid detection. This in turn makes law enforcement surrounding bath salts and cathinones difficult. To date, the Drug Enforcement Agency (DEA) has only been successful in permanently banning two cathinones: mephedrone and methylenedioxyprovalerone (MDPV).²

There lacks a standard analytical methodology for the detection and confirmation of cathinones in bath salts. A variety of lengthy methods have been used to analyze cathinones, including an 18-min method utilizing GC/MS and LC/MS/MS to detect and confirm mephedrone, and a 20-min method implementing GC/MS to detect several cathinones.^{3,4} This article presents a fast and direct screening and confirmation method using the AxION DSA/TOF.

Due to the variety of bath salts available, it is advantageous to monitor the entire spectral range, which is easily performed using TOF MS. The ability to analyze samples rapidly is desirable, as drug seizures may result in thousands of samples. Fast screening of seized samples in seconds, without sample preparation, is easily performed using DSA/TOF MS. A proof of concept for the rapid analysis of 11 cathinones in bath salts is presented here.

AxION DSA/TOF MS analysis allowed for the screening of 11 cathinones, including butylone; methylone; naphyrone; mephedrone; 4-fluoromethcathinone (4-FMC); 4-methylethcathinone (4-MEC); ethcathinone; 3,4-methylenedioxy- α -pyrrolidinobutiophenone (MDPBP); α -pyrrolidinopentiophenone (α -PVP); 3-methyl- α -pyrrolidinopropiophenone (α -MPPP); and MDPV. Structures of the 11 cathinones studied are shown in Figure 1. The presence of the target analytes was confirmed using AxION Solo software by mass accuracy and isotopic abundances of parent and fragment ions produced by collision-induced dissociation (CID).

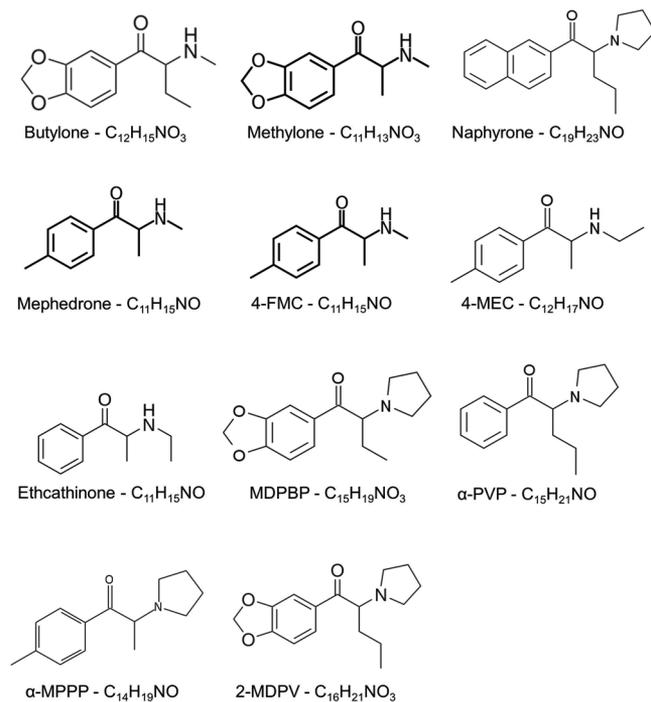


Figure 1. Structures of the 11 cathinones used in this study.

Experimental

Sample Preparation

Cathinone standards were prepared by placing a small amount of solid sample on the mesh target screen and applying 5 μ L of methanol. Due to their insolubility in methanol, confiscated bath salt samples were directly sampled by placing them in glass sampling tubes. Images of the mesh target screen and a glass sampling tube are shown in Figure 2.

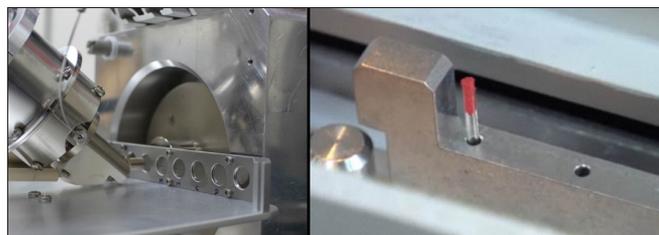


Figure 2. Images of the DSA TOF equipped with a mesh target screen (left) and a glass sampling tube (right).

AxION DSA/TOF MS Instrumentation

The AxION DSA conditions were as follows: corona current of 5 μ A, heater temperature of 350 $^{\circ}$ C, auxiliary gas (N_2) pressure of 80 psi, drying gas (N_2) flow of 4 L/min, and drying gas (N_2) temperature of 25 $^{\circ}$ C. The AxION 2 TOF MS was run in positive ionization mode with a flight tube voltage of 8000 V. The capillary exit voltage was set to 100 V for normal MS analysis and 160 V for CID analysis. Mass spectra were acquired with a mass range of 50–1000 m/z and an acquisition rate of 2 spectra/sec. To maintain mass accuracy, two lock mass ions were used (m/z 121.0509 and m/z 322.0481). All samples were analyzed for only 15 sec.

Results

Cathinone Standards

All eleven cathinone standards were analyzed by DSA/TOF, and the $[M+H]^+$ ion, as well as at least two fragment ions, were identified. The mass errors for the $[M+H]^+$ ion in each standard were determined to be less than 5 ppm and are listed in Table 1. The mass spectra collected from standards using CID, for the two cathinones that have been permanently banned (mephedrone and MDPV), are shown in Figure 3. In addition to the $[M+H]^+$ ion, all identified fragment ions, based on accurate mass and isotopic distribution, are also labeled in Figure 3. The same procedure was performed for the remaining cathinone standards. Many cathinones shared fragment ions, such as theoretical m/z 149.0233, 126.1277, and 91.0542, corresponding to fragment ions with formulas of $C_8H_5O_3$, $C_8H_{16}N$, and C_7H_7 , respectively.

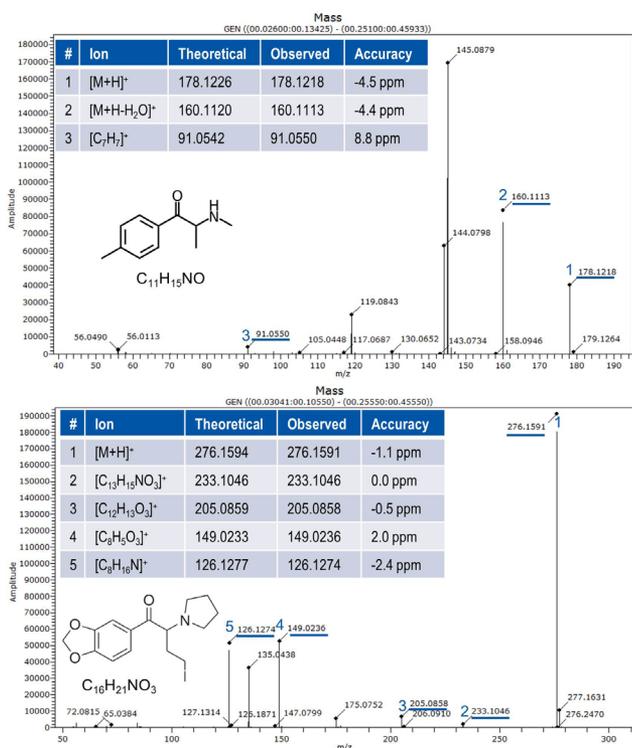


Figure 3. Mass spectra obtained in 15 sec each, directly on mesh, for mephedrone (top) and MDPV (bottom), demonstrating the mass accuracy of the AxION TOF/MS, and the ability to easily detect and identify cathinone standards.

Bath Salt Samples

Five different bath salt samples (labeled numbers 3, 5, 7, 8, and 9) were analyzed and found to contain a variety of the cathinones. These were easily confirmed from previously analyzed standards. The mass spectra of samples 3 and 8 were found to contain butylone and 4-MEC, and MDPBP, butylone, α -MPPP, and α -PVP, respectively (Figure 4). As shown in Figure 4, excellent mass accuracy was observed for real bath salt samples in only 15 sec, and no sample preparation, despite the large number of ions present. The remaining bath salt samples were found to contain: MDPV in sample 5; butylone in sample 7; and MDPBP, α -PVP, and 4-MEC in sample 9. All cathinones in the bath salt samples were confirmed by accurate mass and isotopic distribution of parent and fragment ions using AxION Solo software.

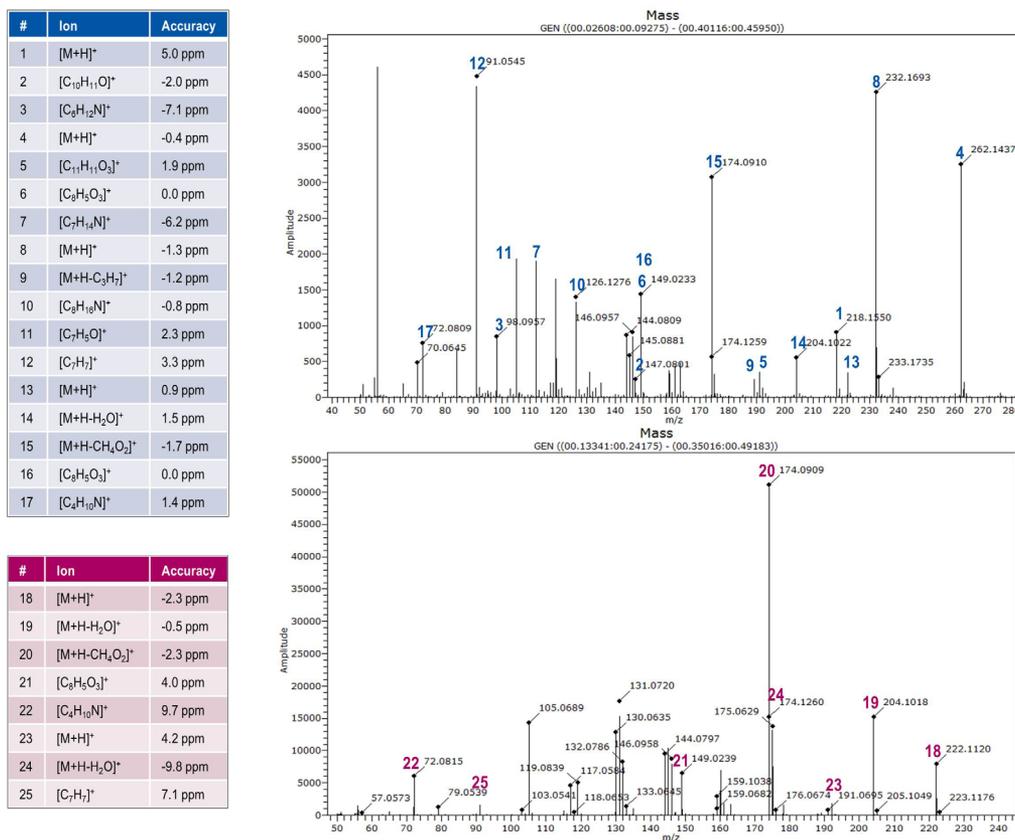


Figure 4. Mass spectra of two different bath salt samples, one sample containing four cathinones (sample 8, top) and the other sample (sample 3, bottom) containing two cathinones, demonstrating the ability to perform rapid confirmation of multiple analytes, in 15 sec or less, with AxION DSA/TOF/MS. Peak numbers 1–17 were found in sample 8 and correspond to α -MPPP (#1–3), MDPBP (#4–7), α -PVP (#8–12), and butylone (#13–17). Peak numbers 18–25 were found in sample 3 and correspond to butylone (#18–22) and 4-MEC (#23–25).

Conclusion

This article offers the first solution for screening and/or confirmation of bath salts in seconds without sample preparation using DSA/TOF and AxION Solo software. Eleven cathinone standards were screened, without sample preparation, in 15 sec per sample. Accurate masses of parent and fragment ions were determined and used to confirm the presence of cathinones in various bath salts. The accurate mass of the [M+H]⁺ ion of each of the cathinones, in standard and bath salt samples, was determined and observed to be <5 ppm mass error. Some bath salts contained up to four different cathinones. In conclusion, the AxION DSA/TOF can screen and confirm multiple cathinones in bath salts by accurate masses of both parent and fragment ions, as well as isotopic distributions. DSA/TOF applied in labs responsible for screening and confirming the presence of illegal substances could replace traditional, lengthy techniques, such as GC/MS and LC/MS/MS. The AxION DSA/TOF work flow will decrease training and analysis time, lower costs, and improve laboratory productivity.

Table 1. Comparison of the accurate mass and the observed mass for each cathinone standard; all mass errors were less than 5 ppm.

Cathinone	Ion Observed	Theoretical Mass	Measured Mass	Error (ppm)
Butylone	[M+H] ⁺	222.1125	222.1127	0.9
Methylone	[M+H] ⁺	208.0968	208.0973	2.4
Naphyrone	[M+H] ⁺	282.1852	282.1851	-0.4
Mephedrone	[M+H] ⁺	178.1226	178.1218	-4.5
4-FMC	[M+H] ⁺	182.0976	182.0978	1.1
4-MEC	[M+H] ⁺	192.1383	192.1382	-0.5
Ethcathinone	[M+H] ⁺	178.1226	178.1218	-4.5
MDPBP	[M+H] ⁺	262.1438	262.1438	0.0
α-PVP	[M+H] ⁺	232.1696	232.1685	-4.7
α-MPPP	[M+H] ⁺	218.1539	218.1532	-3.2
2-MDPV	[M+H] ⁺	276.1594	276.1591	-1.1

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