A study of the influence of collision cell design on the fragmentation of cathinones by LCMSMS – Part 2

Dominic Aummunn[1], Olaf Drummer[2,3], Jochen Beyer[2,3], and Paul Wynne[4]

[1]Universität des Saarlandes, Saarbrücken, GERMANY, [2]Victorian Institute of Forensic Medicine, Melbourne, AUSTRALIA, [3]Monash University Department of Forensic Medicine, Melbourne, AUSTRALIA; [4]Shimadzu Australasia, Rowville, Victoria, AUSTRALIA

Introduction

The evolution of collision cells for tandem mass spectrometry is influenced by a variety of application needs and includes improved sensitivity, signal to noise and ion-transmission speeds. Ultrafast Mass Spectrometry (UFMS) on triple quadrupole instruments offers the opportunity to simultaneously acquire fragmentation data from a single compound at several different collision energies without compromising the integrity of the peak shape. In this application, we use UFMS to generate data for multiple analytes in a single run using complimentary pathways to improve the certainty of analyte identification.

Method

Standards of cathinones and related compounds were analysed on a Nexera LC-30-LCMS-8030 (Shimadzu, Kyoto, Japan) using a AT Zorbax Eclipse XDB, 150 x 4.2 mm column at 60 °C and a mobile phase of 50mM ammonium formate solution adjusted to pH 3.5 with formic acid (solvent A) and 0.1% formic acid in acetonitrile (solvent B). The following programme was used: 0-2 min (10% B at 0.6 min) then linearly to 17 min (100% B at 0.8 mL/min) and held for 3 min. MRM channels were optimised automatically for three major ions selected by the instrument. MRM parameters (protonated molecular ion, selected fragment ions, Q1 pre-rod bias voltage, optimised collision potential difference and Q3 pre-rod bias) are shown in Table 1. The drying line was 280 °C, N_2 nebulising gas 3L/min, heater block 450 °C, and the drying gas at 15L/min and the CID gas was argon at 230 kPa.

Discussion and Results

In this study, we examine the collision induced dissociation of a class of illicit drugs using the UFSweeper™ design of collision cell. In a previous part of this study, we compared the spectra with a conventional linear collision cell that uses collisional cooling with nitrogen and found that spectra were qualitatively and quantitatively similar. In this experiment, the passage of ions through the UFSweeper™ cell is cooled by the quadrupole field cooling and argon as the collision gas.

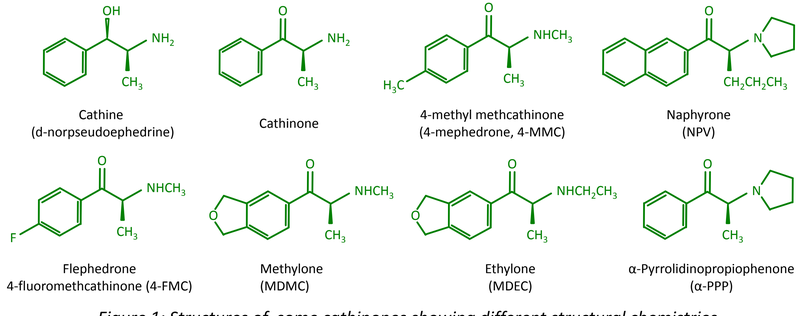

Figure 1: Structures of some cathinones showing different structural chemistries.

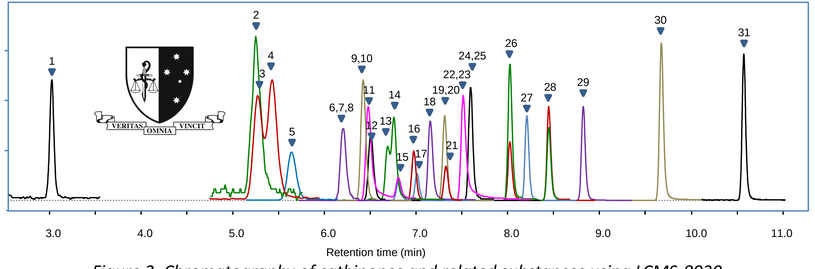

Figure 2: Chromatography of cathinones and related substances using LCMS-8030

Parent ion	Fragment	Dwell	Q1	CE (V)	Q3
(1) phenylephrine					
168.0	150.1	50	-8	-16	-50
	109.1	50	-8	-22	-20
	91.1	50	-8	-24	-34
(2) norephedrine					
152.0	134.1	50	-16	-16	-8
	115.1	50	-16	-20	-46
	91.1	50	-16	-36	-34
(3) d3-norephedrine					
155.1	137.1	50	-6	-16	-14
	119.1	50	-6	-22	-22
	120.0	50	-6	-14	-40
(4) norpseudoephedrine					
152.0	134.1	50	-16	-16	-8
	115.1	50	-16	-20	-46
	91.1	50	-16	-36	-34
(5) S-cathinone					
150.0	132.1	50	-8	-18	-34
	117.2	50	-4	-22	-10
	105.0	50	-16	-24	-10
(6) pseudoephedrine					
166.1	148.2	15	-12	-16	-6
	115.0	15	-14	-28	-40
	91.1	15	-12	-34	-34
(7) d3-pseudoephedrine					
169.1	151.0	15	-12	-16	-46
	115.0	15	-8	-28	-44
	91.1	15	-8	-40	-32
(8) methcathinone (MC)					
164.2	146.1	10	-16	-16	-14
	131.0	10	-16	-22	-26
	130.1	10	-14	-34	-26
(9) methylone (MDMC)					
208.0	159.9	10	-8	-18	-16
	190.2	10	-8	-14	-20
	132.1	10	-8	-30	-48
(10) d3-methylone					
211.2	163.0	10	-20	-20	-10
	192.8	10	-20	-14	-20
	135.0	10	-8	-30	-44

Parent ion	Fragment	Dwell	Q1	CE (V)	Q3
(11) N,N-dimethylcathinone (DMC)					
178.1	105.1	10	-8	-22	-10
	77.1	10	-8	-44	-28
	72.1	10	-8	-26	-12
(12) methylephedrine					
180.1	162.0	10	-8	-18	-10
	117.0	10	-8	-22	-40
	91.1	10	-8	-34	-32
(13, 14) 3 or 4-fluoromethcathinone (3-FMC, 4-FMC)					
182.2	164.0	10	-16	-16	-16
	149.0	10	-16	-24	-48
	148.0	10	-18	-32	-50
(15) ethcathinone (EC)					
178.1	160.0	10	-8	-16	-10
	132.1	10	-8	-20	-28
	130.0	10	-8	-34	-24
(16) ethylone (MDEC)					
222.1	174.0	10	-10	-20	-18
	204.3	10	-10	-14	-22
	146.1	10	-10	-30	-48
(17) 4-methoxymethcathinone (PMMC)					
194.1	175.9	10	-8	-14	-18
	160.9	10	-8	-22	-16
	146.0	10	-8	-32	-48
(18) pyrrolidinopropiophenone (PPP)					
204.1	105.1	10	-6	-26	-10
	132.9	10	-6	-20	-26
	98.2	10	-6	-26	-36
(19) methylenedioxypyrrolidinopropiophenone					
248.1	98.1	10	-12	-26	-18
	147.0	10	-6	-26	-48
	91.0	10	-12	-46	-30
(20) Butylone					
222.2	174.0	10	-16	-18	-18
	204.3	10	-10	-14	-14
	146.0	10	-6	-28	-30
(21) d3-butylone					
225.1	177.1	10	-10	-18	-18
	207.1	10	-10	-14	-22
	134.1	10	-10	-40	-48

Parent ion	Fragment	Dwell	Q1	CE (V)	Q3
(22) amfepramone					
206.1	105.0	10	-6	-24	-10
	100.1	10	-10	-24	-18
	77.1	10	-10	-50	-30
(23) d10-amfepramone					
216.1	105.1	10	-10	-24	-10
	110.1	10	-10	-26	-40
	77.0	10	-22	-52	-26
(24) mephedrone (4-MMC)					
178.2	160.2	10	-8	-12	-10
	145.0	10	-8	-22	-50
	143.9	10	-16	-36	-48
(25) d3-mephedrone (4-MMC-d3)					
181.05	163.1	10	-32	-16	-10
	147.9	10	-12	-24	-30
	147.0	10	-12	-24	-48
(26) 4-methyl ethcathinone (4-MEC)					
192.1	174.3	15	-8	-16	-18
	144.1	15	-18	-32	-48
	91.1	15	-8	-34	-22
(27) pentylone (PENT)					
236.1	188.0	15	-6	-18	-12
	218.0	15	-6	-14	-14
	175.0	15	-10	-22	-32
(28) 3,4-methyl methcathinone (3,4-DMMC)					
192.1	174.0	15	-36	-16	-18
	159.0	15	-14	-24	-50
	158.0	15	-14	-34	-48
(29) methylenedioxypyrovalerone (MDPV)					
276.1	126.1	15	-8	-32	-40
	175.0	15	-8	-24	-18
	135.0	15	-8	-30	-46
(30) pyrovalerone (PV)					
246.1	105.1	15	-26	-24	-10
	174.9	15	-6	-18	-18
	91.1	15	-12	-48	-32
(31) naphyrone (NPV)					
282.1	141.1	15	14	-26	-14
	211.0	15	-8	-20	-22
	127.1	15	-8	-56	-46

Table 1: Optimised MRM transitions for cathinones and related substances using LCMS-8030 Q1 and Q3 are prerod bias voltages, dwell is dwell time in milliseconds,

Standards of 20 cathinones including S-cathinone, mephydrone, methylone, ethylone, and pyrrolidinopropiophenone in methanol were analysed by automatically selecting and optimising three fragment ions. The fragmentation pathways for MRM transitions were studied mechanistically for their importance in structural identification.

The fragmentation of cathinones is dependent on the pattern of nitrogen substitution. Fragmentation of disubstituted or pyrrolidine containing analytes (*e.g.* naphyrone) is typified by neutral loss of the amine at low energy and formation of the aryl (naphthyl fragment at m/z 127) at high energy. The pyrrolidinyl cathinone analogues show atypical spectra because of the amine substituent (Figure 3). Mono substituted cathinones (*e.g.* methcathinone and ethcathinones) show a low energy loss of 18 Da (H_2O) and a higher energy loss of the amine substituent (33 or 34 Da for methcathinones and 48 Da for ethcathinones). The loss of water is driven from the enol tautomer while loss of the alkyl substituent may be either by dealcoholysis or by concerted rearrangement and loss of hydrogen to a number of possible structures including an indole (Figure 3).

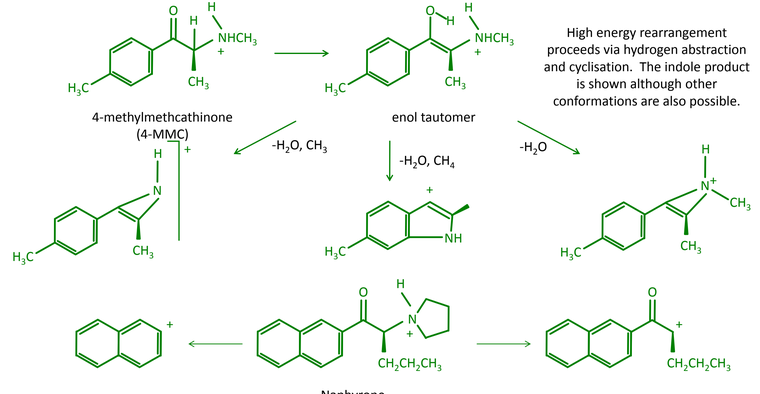

Figure 3: Fragmentation of the cathinones proceeds via high and low energy pathways. UFMS analysis with multiple collision energies allows complimentary identification of analytes.

Novel aspects

The use of both low and high collision energies in MRM experiments provides for the more robust identification of analytes as there is opportunity for fragments to be derived from mechanistically different pathways. This outcome is enabled in multiple analyte methods by high speed instruments and is particularly suited to the UFMS approach to triple quadrupole mass spectrometry.