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Detecting New Designer Cannabinoids in Herbal Incense using LC-MS-MS with Fast Precursor Ion Scanning

TIAFT 2012 P-182

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Introduction

Forensics and anti-doping labs rely on LC-MS-MS for detection of controlled and banned substances. LC-MS-MS methods use MRM analysis for the highest sensitivity and selectivity, however these methods only detect analytes whose MRM transitions are known in advance. In order to circumvent drug laws, designer drugs are synthesized which are not detected by traditional MRM-based methods. Because designer drugs often share common product ions and neutral losses, precursor ion or neutral loss scanning could be used to detect them.

We developed LC-MS-MS methods that utilize extremely fast precursor ion scanning for detection of designer cannabinoids in herbal incense products. The urine of human subjects who reported synthetic cannabinoid exposure was also analyzed using a newly developed high sensitivity triple quadrupole mass spectrometer from Shimadzu, the LCMS-8040.

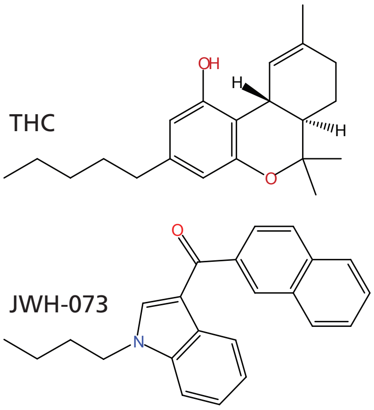
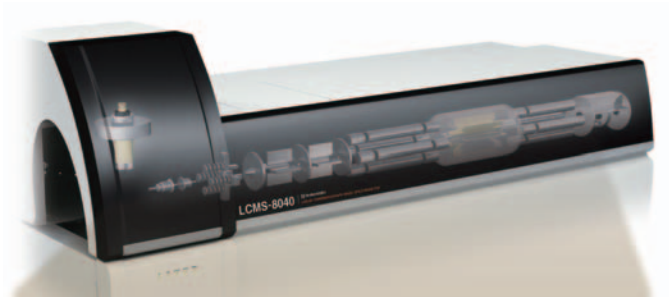


Fig. 1 Structures of THC, the active component in marijuana, and JWH-073, a designer cannabinoid

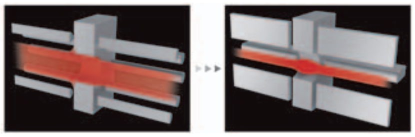
Fig. 2 Typical herbal incense product

Method

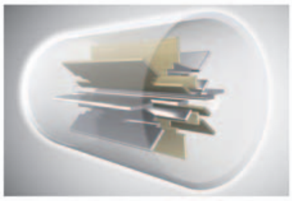
Electrospray ionization with continuous polarity switching was used on a new fast-scanning, high sensitivity triple quadrupole mass spectrometer, the LCMS-8040, and a Nexera ultra high performance liquid chromatograph. A precursor ion scan for each common product ion was carried out at a scan speed of 5,000 u/sec. Data dependent MS-MS were carried out at 15,000 u/sec. A Restek 3 µm Ulta Biphenyl column was used for improved LC separation of isomers and metabolites. The mobile phase was 0.1% formic acid in water (Pump A) and 0.1% formic acid in acetonitrile (Pump B), and the flow rate was 0.5 mL/min.



Improved ion optics of the LCMS-8040 for Ultra fast scan speed with enhanced sensitivity



UF Lens for better ion transmission



UF Sweeper-II® collision cell for better CID efficiency

Results and Discussion

The fragment ions at *m/z* 155 and 127 were observed as a common products among the napthoyl-indole cannabinoids. The fragments result from cleavage on either side of the carbonyl group. Precursor ion scans for these products were used to screen for designer cannabinoids of the napthoyl-indole class.

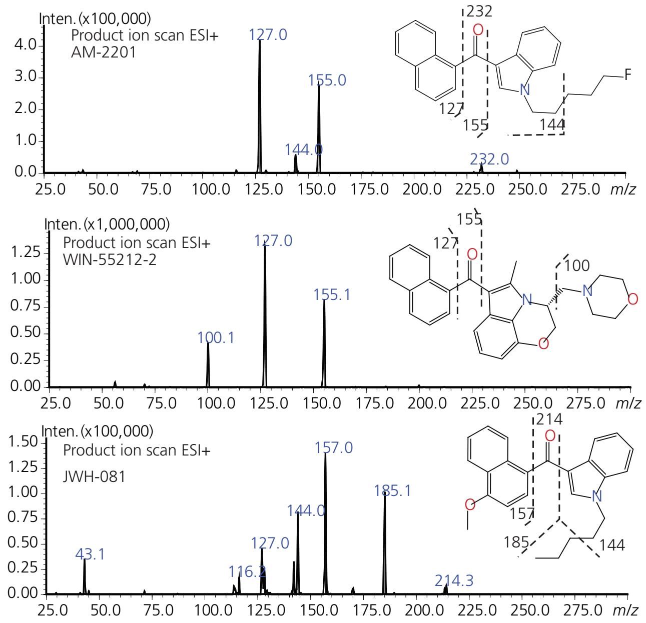


Fig. 3 Tandem mass spectra of three representative designer cannabinoids showing common product ions.

The precursor ion scan chromatograms of an extracted herbal incense product are shown in Fig. 5. The precursor ion spectra of the peak at 7.5 min indicate a precursor ion of *m/z* 342. Data dependent MS-MS of the *m/z* 342 peak is shown in Figure 8. As in this case, the product ion scans should detect any designer cannabinoids with modifications to the N-alkyl chain or indole group. Any designer cannabinoid with modifications to the napthalene group could be detected by the fragment of *m/z* 144 from the indole group. Therefore this method has the capability to detect a wide variety of modified napthoyl-indole designer cannabinoids.

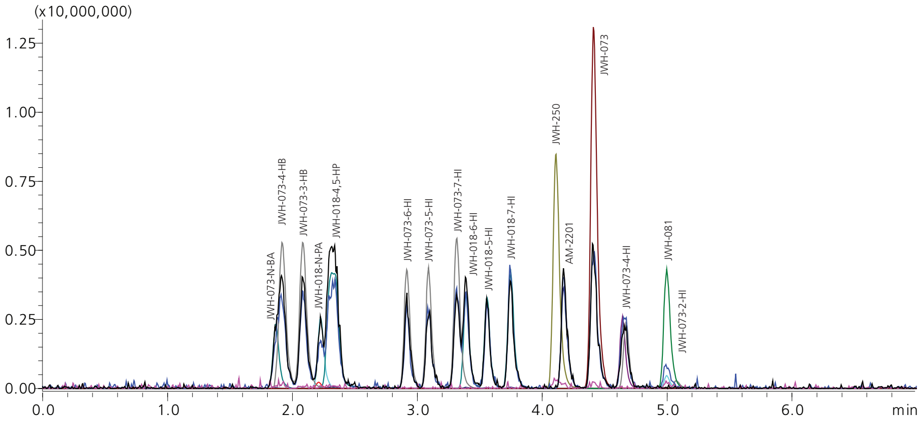


Fig. 4 Improved chromatography of cannabinoids and their metabolites using a Restek Ultra Biphenyl column (2.2 µm, 2.1 × 50 mm)

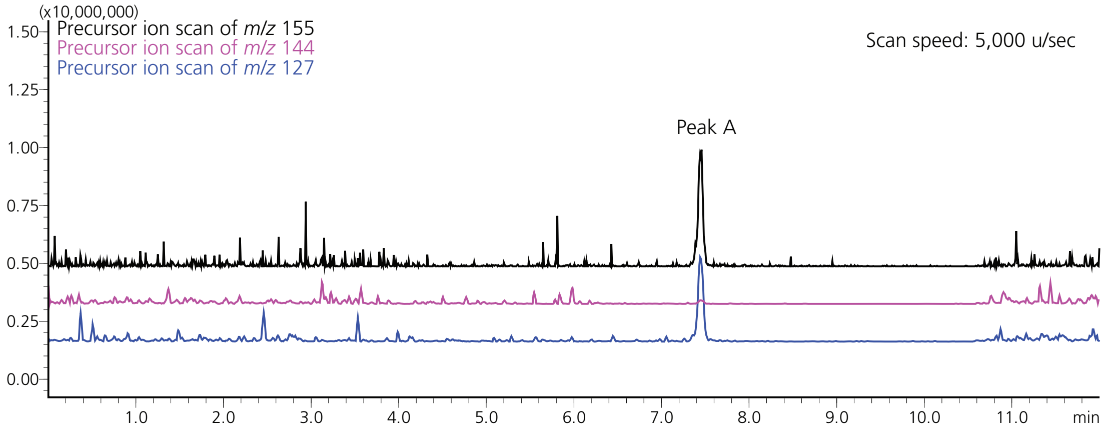


Fig. 5 Chromatograms of three precursor ion scans for the K2 Spice cannabinoid product. Peak A, eluting at 7.5 min, was investigated as a designer cannabinoid.

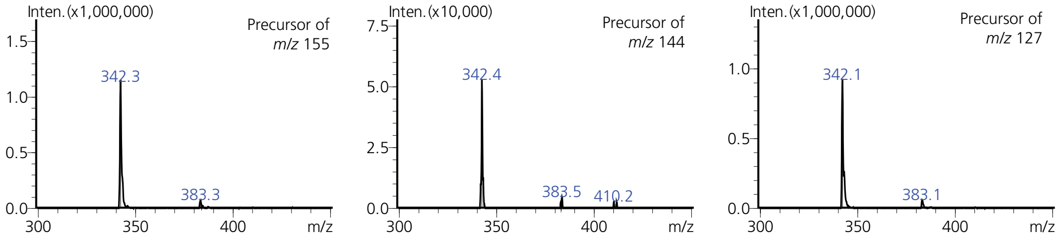
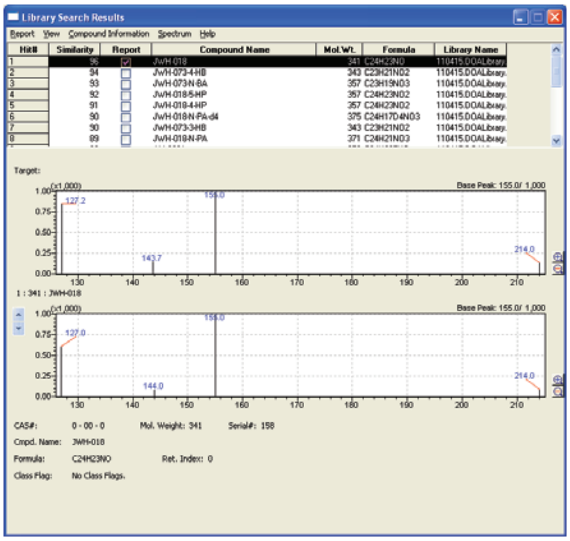


Fig. 6 Precursor ion spectra for Peak A

Because the possibility remains that some designer drugs might still not be detected by these precursor ion scans, full scan MS at a fast scan speed combined with fast data-dependent product ion scanning was used. A similar approach, using tailored fast precursor ion and neutral loss scanning with data dependent tandem MS, could be used to screen for designer barbiturates, amphetamines, and other classes of drugs as well.



Hit#	Similarity	Report	Compound Name	Mol.Wt.	Formula	Library Name
1	96	☑	JWH-018	341	C24H23NO	110415.DOALibrary.
2	94	☐	JWH-073-4-HB	343	C23H21NO2	110415.DOALibrary.
3	93	☐	JWH-073-N-BA	357	C23H19NO3	110415.DOALibrary.
4	92	☐	JWH-018-5-HP	357	C24H23NO2	110415.DOALibrary.
5	91	☐	JWH-018-4-HP	357	C24H23NO2	110415.DOALibrary.
6	90	☐	JWH-018-N-PA-d4	375	C24H17D4NO3	110415.DOALibrary.
7	90	☐	JWH-073-3-HB	343	C23H21NO2	110415.DOALibrary.
8	89	☐	JWH-018-N-PA	371	C24H21NO3	110415.DOALibrary.

CAS#: 0 - 00 - 0 Mol. Weight: 341 Serial#: 158
Cmpd. Name: JWH-018
Formula: C24H23NO Ret. Index: 0
Class Flag: No Class Flags.

Fig. 7 Library search results for the tandem mass spectrum of Peak A. The top hit is the designer cannabinoid JWH-018. The other hits found are metabolites of synthetic cannabinoids which have different precursor masses and therefore can be distinguished from JWH-018.

A spectrum search in a private library matched several cannabinoids, including JWH-018. The retention time anrd mass spectra of the unknown matched an authentic standard of JWH-018. Urine of a human subject testing positive for synthetic cannabinoid exposure also revealed the presence of synthetic cannabinoid metabolites of JWH-018 as shown in Fig. 9.

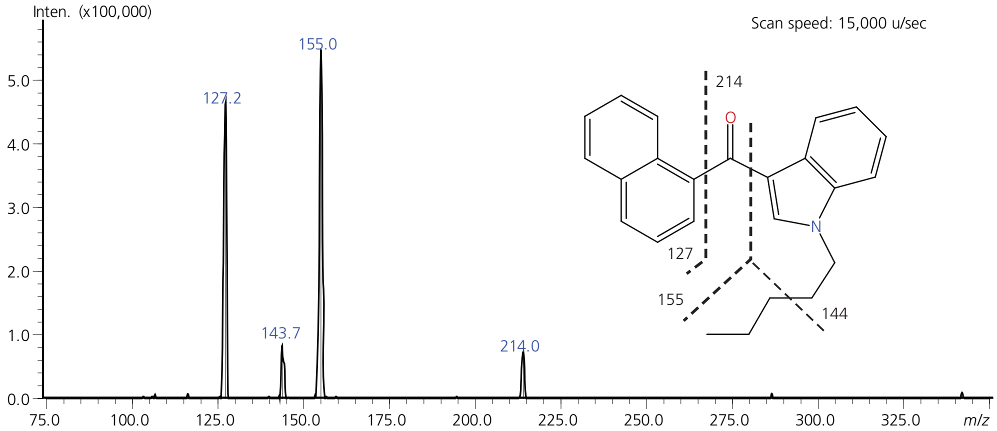


Fig. 8 Tandem mass spectrum of Peak A, identified as JWH-018, and fragment assignment

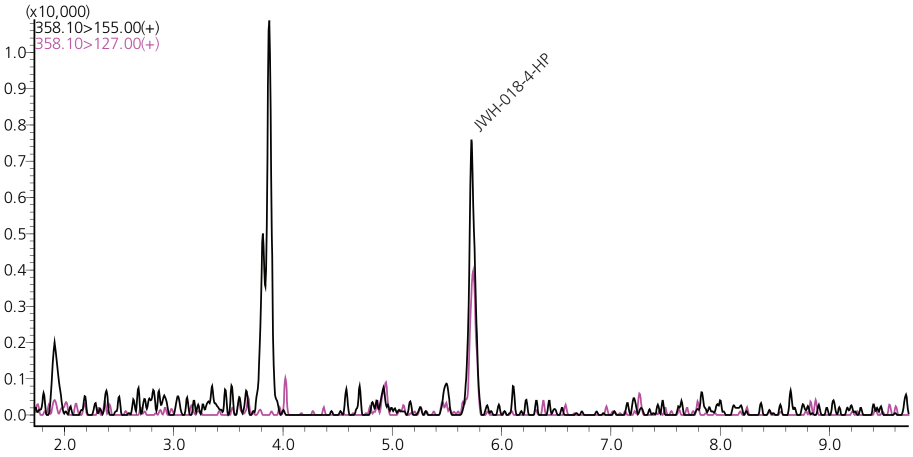


Fig. 9 Chromatograms for the metabolite JWH-018-4-HP from urine of a human subject with reported synthetic cannabinoid exposure.

Conclusion

Fast precursor ion scanning with data dependent MS-MS was used to detect designer drugs in herbal incense products. Metabolites of the drugs could also be detected using the higher sensitivity of the LCMS-8040 in the urine of human subjects with reported synthetic cannabinoid exposure. This fast precursor ion scanning method will enable screening for the latest designer drugs even before they are discovered by law enforcement.

First Edition: June, 2012

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