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Short Communication

A comparison of single quadrupole mass detection and diode array ultraviolet detection interfaced to ultra-high performance supercritical chromatography for the quantitative analysis of synthetic cathinones

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ABSTRACT

A comparison of single quadruple mass spectrometry and diode array-ultraviolet (PDA-UV) detection interfaced to ultra-high performance supercritical fluid chromatography was performed for the quantitative analysis of synthetic cathinones. Synthetic cathinones, also known as “bath salts”, are derived from cathinone, a component of the khat plant. For 15 controlled solutes linearity, repeatability, and limits of detection were determined using both UV and MS detection. Quantitation studies were performed using the above detectors for 19 mixtures of up to 4 of the above compounds with an adulterant to simulate seized samples. MS detection provided approximately an order of magnitude greater linearity range and allowed for two to three orders of magnitude lower limits of detection than UV detection. Both detection techniques exhibited similar results of analysis and comparable repeatability. The latter detection mode which provided significantly high linearity correlation coefficients ($0.9994 \leq R2 \leq 1.0000$) would be preferred for quantitative analysis.

1. Introduction

Synthetic cathinones, or “bath salts”, are derived from the naturally occurring cathinone which comes from the khat plant, *Catha edulis* [1,2]. They have similar effects as amphetamines such as euphoria, increased libido, tachycardia, hypertension [1–3]. They have been marketed as “legal highs” and they are sold under different names, as well as labeled “not for human consumption” in order to bypass the laws [1]. These drugs come in powder or tablet form and are usually ingested or snorted but can also be inhaled or injected intravenously [1].

Ultra-high performance supercritical fluid chromatography (UHPSFC) employs significantly improved instrumentation with sub 3 µm particle columns or equivalent with sub or supercritical fluids employing carbon dioxide, an organic modifier, and possibly an additive, to produce highly efficient and rapid separations. UHPSFC is well suited for the rapid analysis of synthetic cathinones including excellent resolution of positional isomers [4,5]. It has the capability of being connected to a variety of analytical detectors including diode array ultraviolet (PDA-UV) and single quadrupole mass spectrometer (Single Quad MS). Single Quad MS is a low cost, small, and easy to use detector [6]. Both the UV and single quad MS detectors in series provide highly complementary structural information which aid in the identification of emerging drugs. This includes the ability to distinguish between positional isomers (UV detection) and the determination of molecular ion (electrospray ionization MS detection), which is lacking with gas chromatography electron ionization mass spectrometry (GC EI MS) [7]. The quantitation of seized drugs such as synthetic cathinones is important for both legal and intelligence purposes. GC EI MS [8] and liquid chromatography quadrapole time of flight MS (LC QTOF MS) [9] and GC vacuum UV (VUV) [10] have been shown to be viable techniques for the quantitation of synthetic cathinones.

In this study, a comparison is made between PDA-UV and Single Quad MS detection for the quantitative determination of synthetic cathinones in simulated seized exhibits using previously reported [5,6] UHPSFC conditions. For 15 controlled synthetic cathinones linearity, repeatability, limits of detection as well as quantitative accuracy is determined. Because both detectors are available for this instrument, a comparison of linearity, precision, and quantitation for both detectors was evaluated for mixtures of synthetic cathinones.

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2. Experimental

2.1. Materials and reagents

All synthetic cathinones were purchased from Cayman Chemicals, Inc. (Ann Arbor, MI, USA). These compounds had a certified ≥95.00% purity. The structure and protonated molecular mass of all of the investigated synthetic cathinones are shown in Table 1. LC/MS grade water and methanol, as well as certified A.C.S. ammonium hydroxide were obtained from Fischer (Fairlawn, NJ, USA). 99.9% liquid carbon dioxide was obtained from Roberts Oxygen (Rockville, MD, USA). Nitrogen for MS detection was delivered using a Peak Scientific Model NM32LA nitrogen generator (Inchinnan, UK).

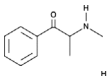
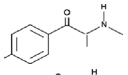
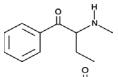
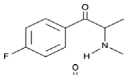
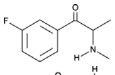
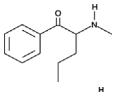
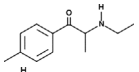
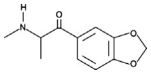
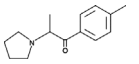
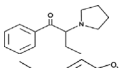
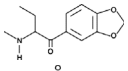
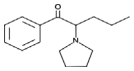
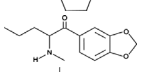
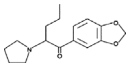
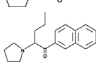
2.2. UHPSFC separation and data analysis

A Waters ACQUITY UPC^2 system consisting of a chiller, a binary solvent pump and an autosampler with a 10 µL loop for partial injection was interfaced to an ACQUITY PDA-UV detector and QDA single quadrapole MS detector (Milford, MA, USA). Makeup solvent was delivered by an isocratic solvent manager (Waters) and mixed with effluent (0.07% ammonium hydroxide in 95:5 methanol water) before MS detection. Empower Version 3 was used for instrument control, data acquisition, and data processing. The column of interest was a Torus DIOL (high density DIOL, 1.7 µm, 3.0 × 100 mm).

The following chromatographic conditions were employed: 0.5 µL injection, 40 °C column temperature, 2200 PSI back pressure flow, 1.25 mL/min flow rate, 3% methanol with 10 mM ammonium formate and 97% carbon dioxide. For qualitative assessment, the UV detector was set at 230 nm. For quantitation, each individual compound was processed at the wavelength of 224 nm, 240 nm, or 250 nm, based on its lambda max(s). For quantitation using MS, each compound was evaluated using extracted ion chromatogram from its $[M + H]^+$.

Paired *t*-test was performed using Excel 2016.

Table 1
UV and MS data synthetic cathinones.

Solute	Structure	$[M + H]^+$	UV_{MAX} (nm)
Methcathinone (l)		164	239
Mephedrone (n)		178	250
Buphedrone (g)		178	239
4-Fluoromethcathinone (j)		182	242
3-Fluoromethcathinone (h)		182	242
Pentedrone (f)		192	239
4-Methylethcathinone (i)		192	250
Methylone (o)		208	224, 271, 304
4-MePPP (e)		218	249
α-PBP (b)		218	238
Butylone (m)		222	224, 270, 304
α-PVP (a)		232	238
Pentylone (k)		236	225, 270, 304
MDPV (c)		276	224, 269, 302
Naphyrone (d)		282	239, 280

2.3. Preparation of standard and simulated sample solutions

For linearity mixtures of individual synthetic cathinone standards at 80 µg/mL in methanol were serially diluted to the appropriate concentrations with methanol.

For quantitation, a total of 19 simulated sample solutions (prepared in duplicate) featuring either 2 or 4 synthetic cathinones along with an adulterant were created. From 1 mg/mL solutions of standard cathinones, secondary solutions were created by diluting synthetic cathinone standard(s) in methanol so that the final concentration of each solute was 12.5 µg/mL–75 µg/mL. Each secondary solution contained an adulterant (either lidocaine, benzocaine, caffeine, or pancake mix), where either a known amount of solute was weighed and added to the secondary solutions or a known concentration of adulterant was pipetted in order to create the secondary solution. Standards were prepared to be within a factor of four of sample concentration of synthetic cathinones. To stay in linear range for the mass spectrometer, a 1:100 dilution was prepared for the standard and samples. All standards and samples were vortexed, filtered using a 0.22 µm PTFE syringe filter into LC vials, prior to duplicate injections on the UHPSFC instrument.

3. Results and discussion

3.1. Single quadrupole mass detection versus PDA UV detection

A mixture of 15 synthetic cathinones was analyzed using positive electrospray single quadrupole mass detection in series with PDA-UV detection. The MS detection was able to provide better selectivity over UV detection for non-isomeric compounds. Comparison between the selectivity of the two detectors can be seen in Fig. 1. Where co-eluted peaks occurred, MS detection could easily resolve them using an extracted ion chromatogram from the compound's $[M + H]^+$. Since no positional isomers coeluted, all peaks were able to be resolved. In order to compare the utility of single quadrupole mass detection and diode array UV detection interfaced to UHPSFC for the quantitative analysis of synthetic cathinones, figures of merit were established, including linearity, limits of detection and repeatability. In addition, 19 simulated samples were analyzed.

3.2. Figures of merits

Linearity and limits of detection were performed and detected using UV and MS detection (Table 2). For the most part MS detection affords at least two order of magnitude linearity range, in contrast to UV detection which offers at least one order of magnitude linearity range. MS detection offers lower correlation coefficients than UV detection. For MS detection $0.9900 \leq R^2 \leq 0.9992$ while for UV detection $0.9994 \leq R^2 \leq 1.0000$. MS detection afforded two to three orders of magnitude lower limits of detection than UV detection. Run-to-run repeatability was examined for retention time (UV detection) and peak area (UV and MS detection) for each of the selected synthetic cathinones, at three concentrations representing low, moderate and high linearity concentration ranges (Table 3). For the most part good precision (0.01 ≤ % RSD ≤ 0.55, 0.31 ≤ % RSD ≤ 3.0, 0.31 ≤ %