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The role of ultra high performance liquid chromatography with time of flight detection for the identification of synthetic cannabinoids in seized drugs

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ABSTRACT

Separation and mass spectrometric techniques are integral parts of forensic drug analysis for both screening and confirmation. The Scientific Working Group for the Analysis of Seized Drugs (SWGDRUG), which is responsible for setting standards for drug analysis, requires for drug identification a Category A test such as mass spectrometry with an additional test from either Category B or C. If a Category A method is not used at least two uncorrelated tests from Category B must be included, for which separation techniques such as gas chromatography and liquid chromatography would qualify. The utility and validity of using ultra high performance liquid chromatography (UHPLC) and time-of-flight (TOF) mass spectrometry (MS) for the analysis of synthetic cannabinoids is presented. The separation of 32 solutes, including 23 controlled substances and nine non-controlled positional isomers of JWH-018, are compared using UHPLC with TOF detection and capillary GC with electron ionization (EI). For these solutes, the reversed phase UHPLC separation on three different 2.1 mm × 150 mm × 2.7 μm superficially porous (SPP) columns (C18, Phenyl-Hexyl and Dimethylpentafluorophenylpropyl (PFP)) compared favorably with the capillary gas chromatography (GC) separation using an Elite-5MS column 0.25 mm × 30 m × 0.25 μm. Principal component analysis revealed that all three UHPLC separations for the separation of the controlled substances are orthogonal to the capillary GC separation. It was also revealed by principal component analysis that the separation of JWH-018 and the nine non-controlled positional isomers for the various techniques were significantly more correlated than the separation of the controlled substances. Although most of the controlled synthetic cannabinoids gave unique TOF in-source collision-induced dissociation MS spectra and EI spectra, it was not possible to discriminate among the geometric isomers (CP47, 497, Epi CP47, 497; Cp47, 497 C8 homologue, Epi CP47, 497 C8 homologue). JWH-018 could be distinguished from the non-controlled isomers based on its EI spectra. In contrast, several of the non-controlled JWH-018 isomers give identical TOF in-source collision-induced dissociation MS spectra to JWH-018.

1. Introduction

The use of new designer drugs created to circumvent the controlled substances laws has greatly increased over the last few years. New structurally similar compounds are created by slightly modifying the chemical structure of a controlled substance. Emerging drugs such as synthetic cannabinoids are easily available over the Internet and at local "head shops". Synthetic cannabinoids are typically sprayed on plant material. Presently there are over 20 synthetic cannabinoids under permanent or temporary federal control in the United States [1]. For the analysis of these solutes, the desired analytical methodology would have the ability to distinguish between similar solutes (analogs including stereo-isomers and positional isomers), whether for screening or confirmation purposes. In practice multiple techniques have been used for their analysis including thin layer chromatography (TLC) [2], gas chromatography (GC)–single quadrapole mass spectrometry (SQ MS) [2], high performance liquid chromatography photo diode array ultra violet detection (HPLC)-PDA UV [2], nano-HPLC-PDA UV [3], nano-HPLC Ion Trap MS [3], HPLC-chemiluminescence nitrogen detection [4], ultra high performance liquid chromatography (UHPLC)-PDA UV-SQ MS [5,6], HPLC-Orbitrap MS [7], UHPLC-time-of-flight (TOF) MS [2,8], UHPLC Q-TOF MS [9–11], flow injection MS/MS [12], direct

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analysis in real time (DART)-TOF MS [13–15], matrix assisted laser desorption/ionization (MALDI)-TOF MS [12,16], capillary electrophoresis (CE)-PDA UV [17], CE-triple quad (TQ) MS [18], nuclear magnetic resonance (NMR) [10,11,19], and Fourier transform infrared (FT-IR) [10,20].

UHPLC offers higher speed and/or peak capacity than HPLC (but not as high as GC) and is well suited for the analysis of synthetic cannabinoids. TOF MS detection, which provides exact mass capabilities for molecular ions, isotope ions and fragment ions, provides selective detection of the above solutes. In comparison to unit mass resolution quadrupole and ion trap techniques, TOF can provide accurate mass (potential empirical formula) information.

The Scientific Working Group for the Analysis of Seized Drugs (SWGDRUG) [21], which is responsible for setting minimum standards for the analysis of seized drugs, allows for the identification of a drug using a combination of various instrumental, microscopic and wet chemical techniques which are included under three categories in descending order of specificity (A, B, C). Two possible combinations include a mass spectrometric technique (Category A) and a separation technique (Category B); or – when a Category A technique is not available – two uncorrelated separation techniques such as GC and liquid chromatography (HPLC, UHPLC) and a less specific Category C technique. To ensure quality, SWGDRUG also suggest that two separate samplings be employed. Also, as indicated by Logan et al. [2], positive results should only be reported if confirmed by two independent analytical techniques, with hybrid techniques such as GC–MS counting as one technique. In this vein it is of interest to show how an emerging technology such as positive electrospray ionization (ESI^+) TOF MS compares to the gold standard of electron impact quadrupole mass spectrometry in terms of specificity. In addition it is of interest to compare the orthogonality of UHPLC with the well-established capillary GC separation technique.

For this purpose the UHPLC–TOF MS of 32 synthetic cannabinoids including 23 controlled and nine non-controlled isomers of JWH-018 (see Figs. 1 and 2) is compared with capillary GC–MS.

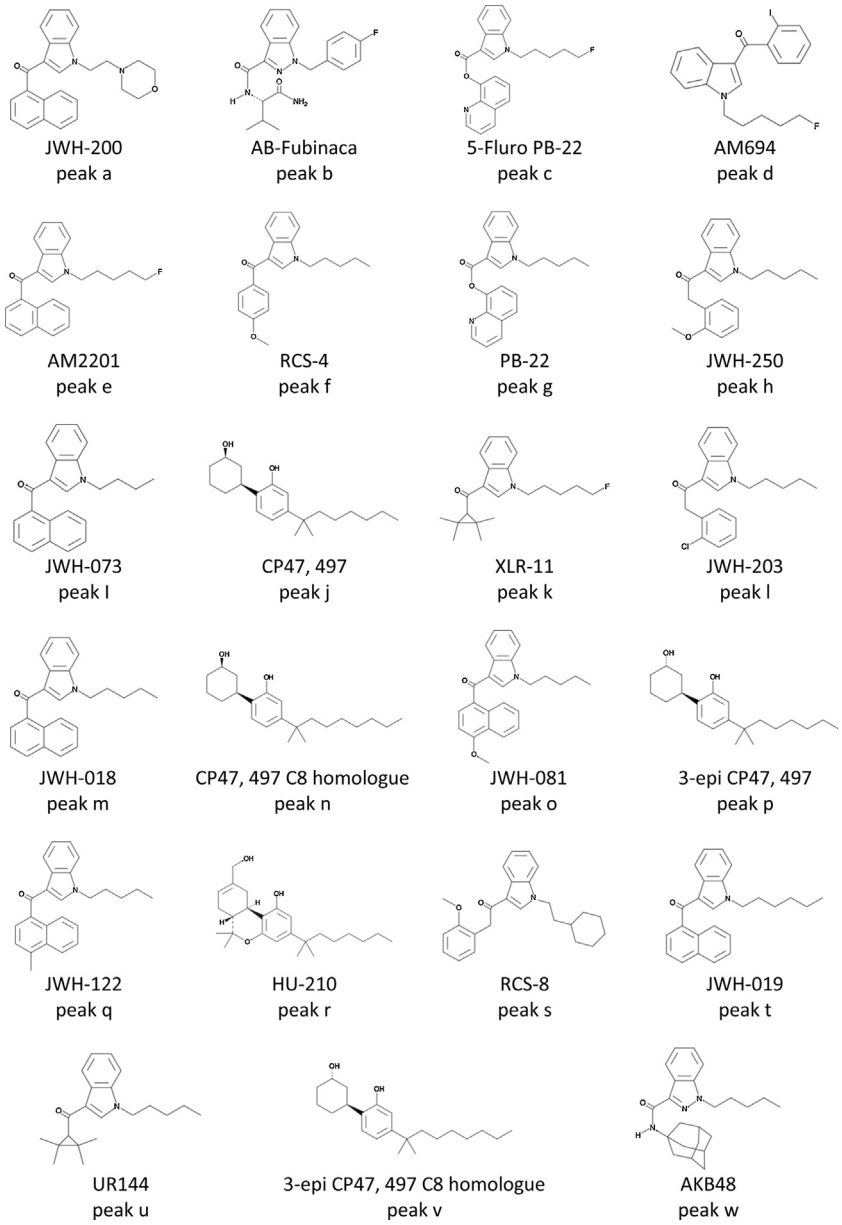

Fig. 1. Structure of controlled synthetic cannabinoids.