

JWH-018 and JWH-022 as Combustion Products of AM2201

Kathryn M. Donohue* and Robert R. Steiner

Virginia Department of Forensic Science

Controlled Substances Laboratory

700 North 5th Street

Richmond, VA 23219

[email: kathryn.donohue@dfs.virginia.gov]

ABSTRACT: The analysis of charred samples of synthetic cannabinoids led to the discovery of JWH-018 and JWH-022 as combustion products of AM-2201. The steps needed to separate these compounds for identification using GC/MS and AccuTOF-DART™ are discussed.

KEYWORDS: synthetic cannabinoids, AM2201, JWH-018, JWH-022, combustion, GC/MS, AccuTOF-DART™, forensic chemistry.

The emergence of synthetic cannabinoids continues to prove challenging to the forensic scientist. As the initially popular compounds, such as JWH-018 (1-pentyl-3-(1-naphthoyl)indole), have become controlled, several other synthetic cannabinoids have appeared to replace them for recreational use [1]. This laboratory has seen a surge in cases containing AM2201 (1-(5-fluoropentyl)-3-(1-naphthoyl)indole). As can be seen in Figure 1, AM2201 differs from JWH-018 by the replacement of a hydrogen atom on the end of the alkyl chain with a fluorine atom. In analyzing case specimens which contain AM2201, small amounts of JWH-018 and JWH-022 (1-(4-pentenyl)-3-(1-naphthoyl)indole) have been detected, interestingly, only in samples recovered from smoking devices or smoked cigar/cigarette butts. Due to the similarities in their structures (JWH-022 differs from JWH-018 by a double bond at the end of the alkyl chain), it was theorized that the JWH-018 and JWH-022 in the burnt residues may have occurred from the combustion of the plant material upon which the AM2201 was deposited.

Experimental

Standards and Reagents

A plant material sample was confirmed to contain AM2201 using GC/MS. A standard of JWH-018 was obtained from Cayman Chemical (Ann Arbor, MI) and ACS grade methanol (Fisher Scientific, Fair Lawn, NJ) was used as a solvent.

Methods and Instrumentation

In order to test the theory of JWH-018 and JWH-022 arising as combustion products of AM2201, a “pipe” was fashioned from a section of a glass (5 mL) pipette, with copper wool inserted in one end. Plant material that contained AM2201 was packed into the end, above the wool. A vacuum line was used to draw the combustion products through the pipe as a match was used to ignite the plant material. After cooling, the pipe was rinsed thoroughly with methanol. An additional sample of the un-burnt plant material was extracted with methanol for comparison.

An Ion Sense (Saugus, MA) Direct Analysis in Real Time (DART™) ionization source coupled with a JEOL, Inc. (Peabody, MA) Accurate Time of Flight Mass Spectrometer (AccuTOF™) was used to collect data in the 65-600 Da range. The AccuTOF™ orifice 1 voltage was set to 30V. The DART™ gas, Helium (He), was heated to 275°C with a flow rate of 2.5 L/min. The methanol extracts of both the burnt and un-burnt samples were introduced into the ionization source with a glass melting point tube. More detailed information about DART™ can be found in articles by Cody, *et al* [2,3] and Steiner [4].

An Agilent (Little Falls, DE) dual column 7890 GC using an Agilent HP-5MS column (0.25 mm ID x 15 m x 0.25 μm film) and coupled with a 5975 mass spectrometer was used to collect

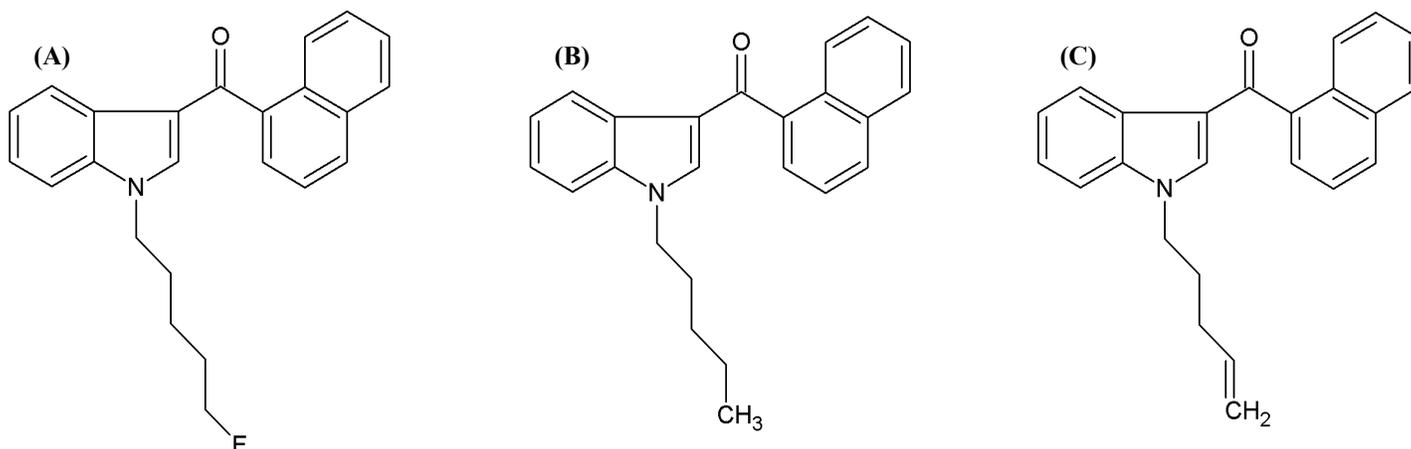


Figure 1 - Structures of (A) 1-(5-fluoropentyl)-3-(1-naphthoyl)indole (AM2201), Formula: C₂₄H₂₂FNO, Molecular weight: 359.4 Da; (B) 1-pentyl-3-(1-naphthoyl)indole (JWH-018), Formula: C₂₄H₂₃NO, Molecular weight: 341.5 Da; and (C) 1-(4-pentenyl)-3-(1-naphthoyl)indole (JWH-022), Formula: C₂₄H₂₁NO, Molecular weight: 339.4 Da.

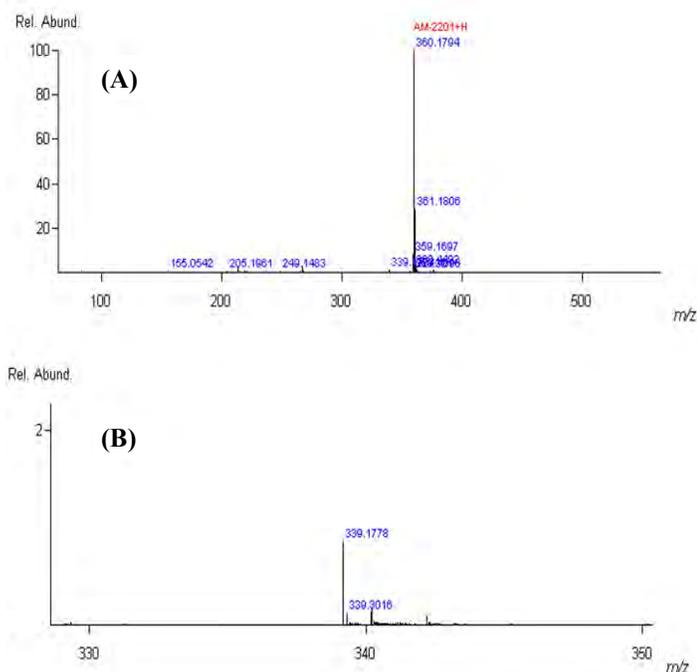


Figure 2 - Un-burnt plant material extract: (A) 30V AccuTOF-DART™ spectrum showing $[M+H]^+$ of AM2201; (B) enlarged section of spectrum showing no peaks for JWH-018 or JWH-022.

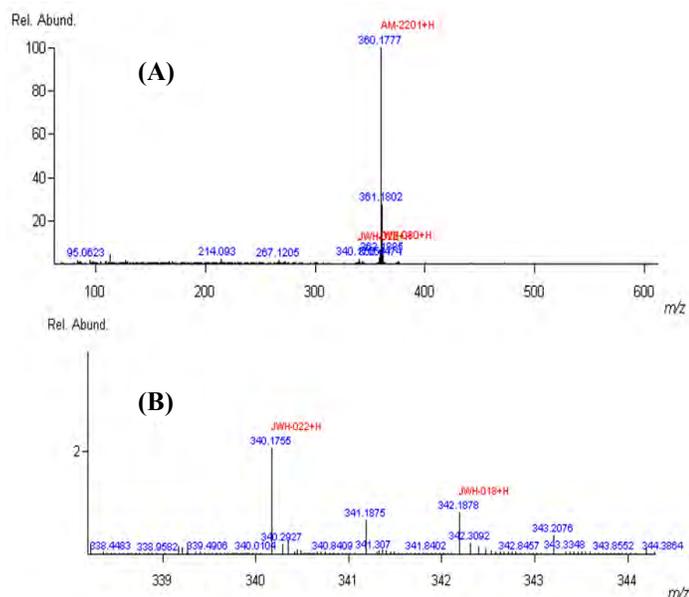


Figure 3 - Methanol extract of pipe after burning plant material: (A) 30V AccuTOF-DART™ spectrum; (B) enlarged section of spectrum showing presence of peaks for JWH-018 and JWH-022.

spectra in the 14-600 m/z range. An Agilent HP-1 column (0.25 mm ID x 15 m x 0.25 μm film) was attached to a flame ionization detector (FID). The columns are joined in one split/splitless injection port using a two-hole ferrule. This allows data to be simultaneously collected from the mass spectrometer and the FID signal. Using a split ratio of 60:1, the temperature program for the GC ran from 200-300°C at a ramp rate of 30°C/min, He flow was 1.8 mL/min, the injection port was set at 290°C, the mass spectrometer transfer line was set at 300°C

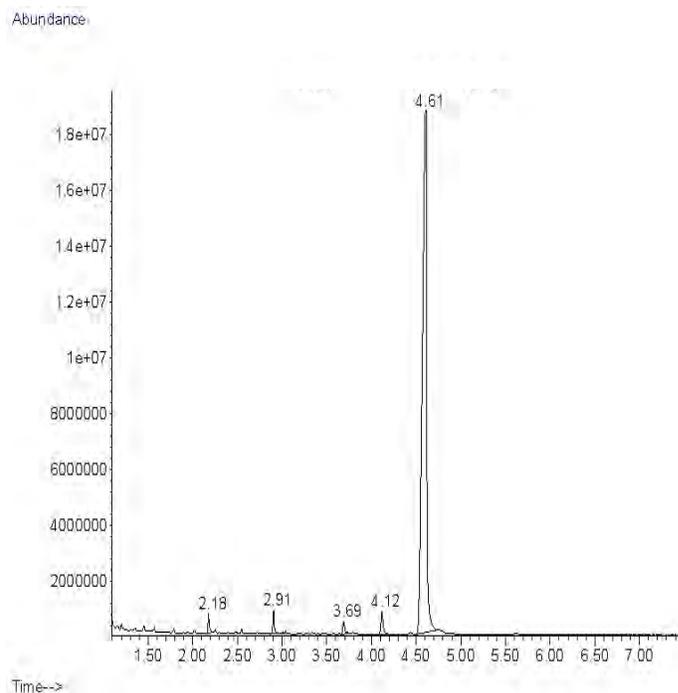


Figure 4 - Total ion chromatogram from HP-5MS column showing AM2201 at 4.61 min and co-eluted peak of interest at 4.12 min.

and the FID temperature was set at 290°C. For further separation and identification, a 30 meter HP-1MS column (0.25 mm ID x 0.25 μm film) was used under the same conditions in a different 7890/5975 GC/MS system. Using an Agilent HP-35 (0.25 mm ID x 15 m x 0.25 μm) column installed in an Agilent 6890 GC, a temperature program was run from 225-300°C at a ramp rate of 30°C/min, He flow was 1.8 mL/min, the injection port was set at 270°C and the detector was set at 280°C. An Agilent HP-1 column (0.25 mm ID x 15 m x 0.25 μm film) was also used with the Agilent 6890 GC under the same conditions.

Results and Discussion

The AccuTOF-DART™ data of the un-burnt plant material extract (Figure 2) shows a large peak for AM2201 ($[M+H]^+$ 360.1794 Da) and nothing at the expected masses for JWH-018 ($[M+H]^+$ calc. 342.1858 Da) and JWH-022 ($[M+H]^+$ calc. 340.1701 Da) within the 5 mDa acceptance criteria. Figure 3 displays the resultant spectrum obtained from the methanol extract of the smoking device. JWH-018 is seen well within the acceptance range (342.1878 Da). The JWH-022 peak is slightly out of range but, as these are relatively small peaks, in a mixture spectrum, there is likely noise or other interference in the mass assignment of this peak.

Figure 4 shows the GC/MS data for the burnt plant material, with the peak at 4.61 min being AM2201 and the peak at 4.12 min showing the co-elution of JWH-018 and JWH-022 (Figure 5). Some distinction can be seen on the FID HP-1 column between these two compounds in the peak at 4.32 min (Figure 6).

It is of interest to note that very small amounts of JWH-018 and JWH-022 also appear to form as combustion products of AM2201 in the injection port of the GC. Recalling that the AccuTOF-DART™ analysis of the unburned plant material

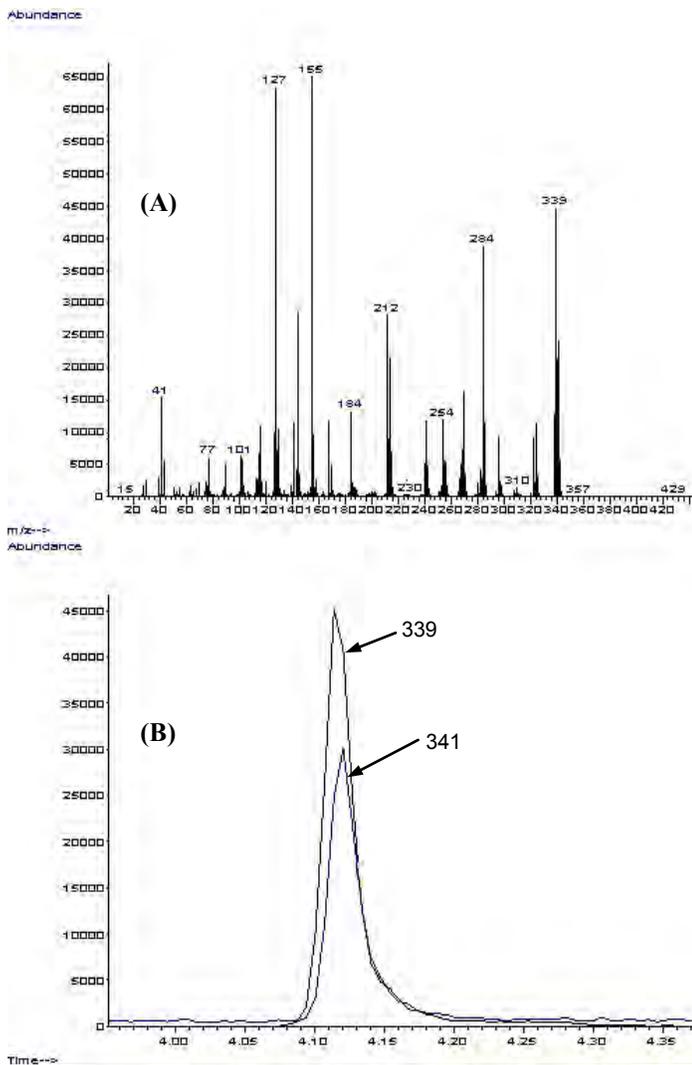


Figure 5 - (A) Co-eluted mass spectrum of JWH-018 and JWH-022; (B) reconstructed ion chromatogram showing coelution on the HP-5MS column.

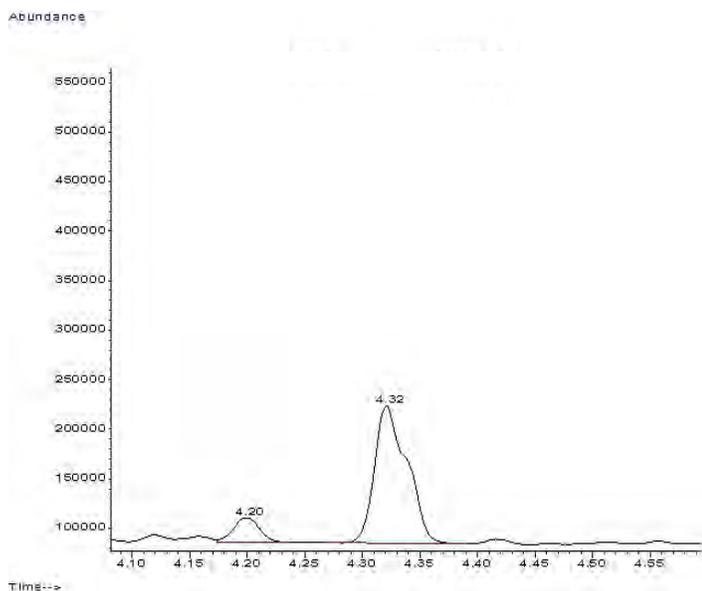


Figure 6 - Enlarged portion of chromatogram from HP-1 (FID) column showing slight separation of peaks of interest (GC/MS conditions).

(Figure 2) did not show evidence of either of these products, the GC/MS data of the un-burnt material (Figures 7 and 8) shows their presence, with JWH-022 forming at a greater rate than JWH-018. The temperature to which the AM2201 is exposed in the AccuTOF-DART™ (275°C) is not as high as the temperature in the injection port of the GC (290°C), which in turn is less than the burning temperature in an actual flame. Given the relative ratio of AM2201 to the combustion products formed and, as the conversion in the injection port is not very aggressive, it is likely that the peak at 4.12 min, in unburned samples of AM2201, would not be seen under normal dilution. However, since the amount of JWH-018 in the burnt sample is roughly ten times greater, it is very probable that the JWH-018 would be in sufficient quantity for identification.

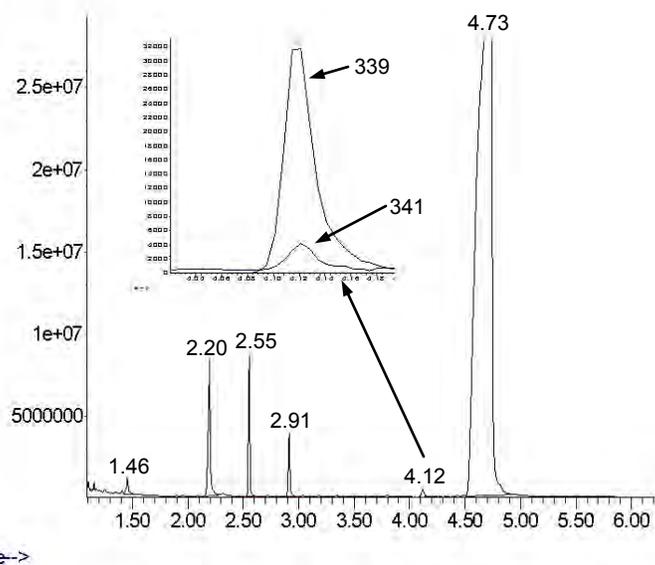


Figure 7 - Total ion chromatogram and (inset) reconstructed ion chromatogram of methanol extract of un-burnt plant material showing formation of JWH-018 and JWH-022 from heat of injection port. Note relative abundance of peak at 4.12 min to AM2201 peak at 4.73 min.

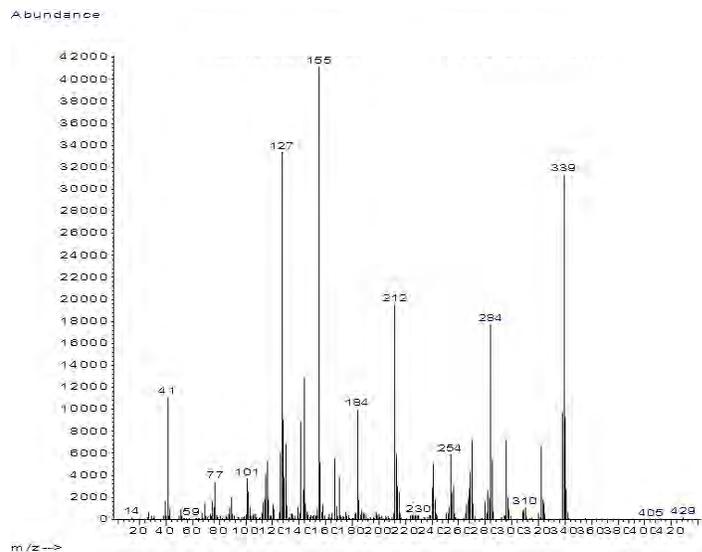


Figure 8 - Spectrum of peak at 4.12 min in Figure 7.

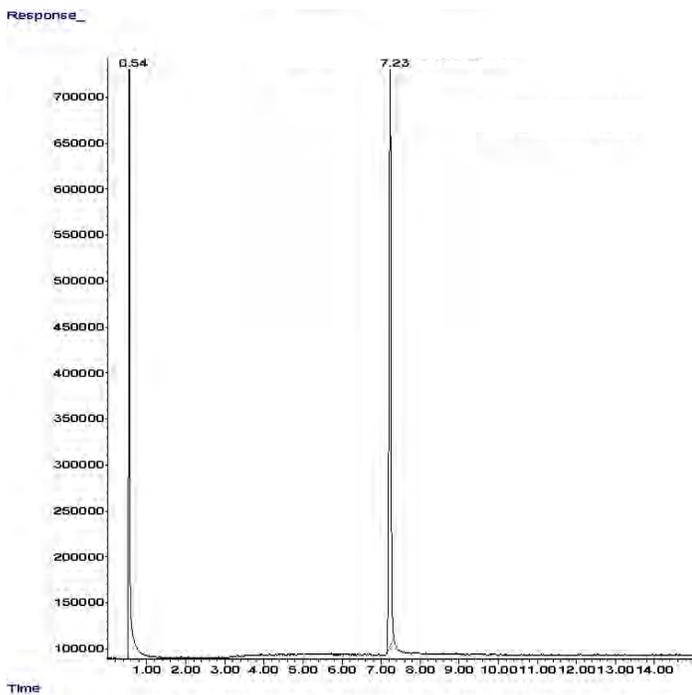


Figure 9 - JWH-018 standard run under GC-only conditions (FID) on HP-35 column.

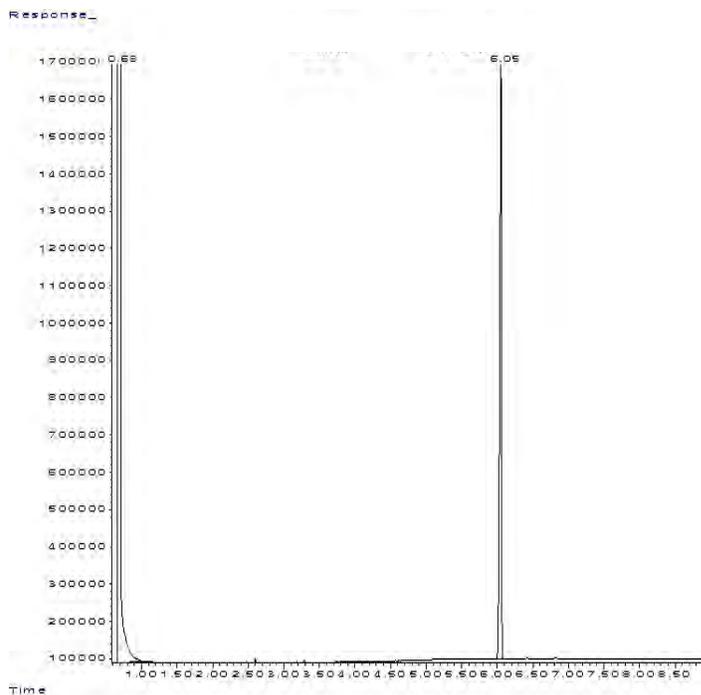


Figure 11 - JWH-018 standard run under GC-only conditions (FID) on HP-1 column.

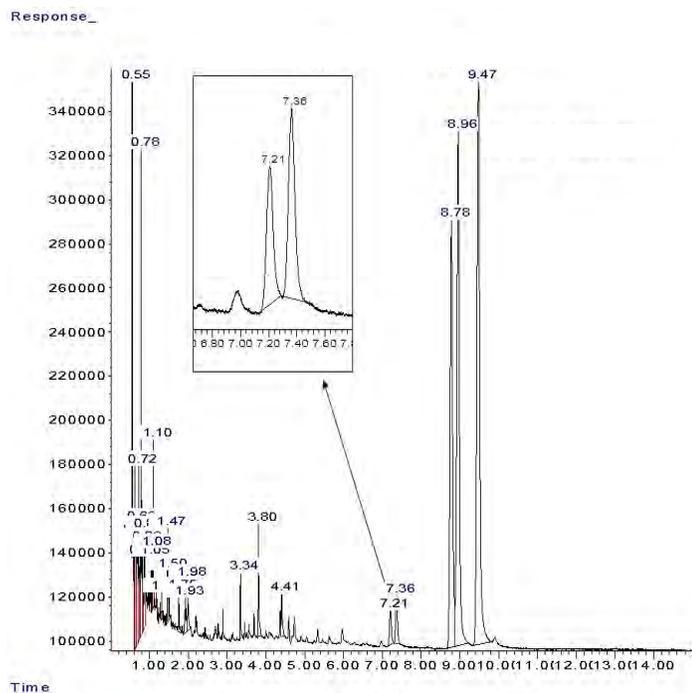


Figure 10 - Burnt plant material extract with GC-only conditions (FID) on HP-35 column.

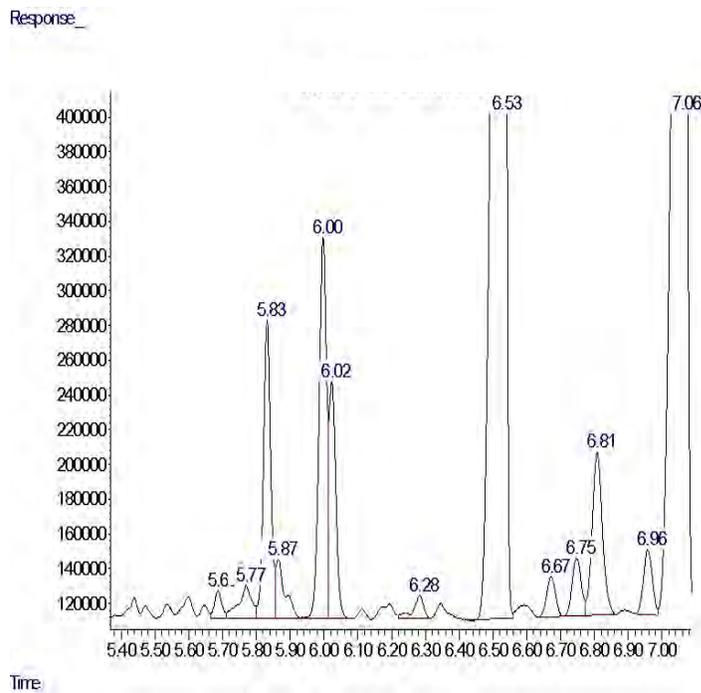


Figure 12 - Burnt plant material extract with GC-only conditions (FID) on HP-1 column.

As co-elution between the two compounds does occur under the normal operating conditions of this laboratory; the identification of JWH-018 in burned samples requires additional measures. Thin Layer Chromatography does not provide significant chromatographic separation for synthetic cannabinoids [5], however, gas chromatography using an Agilent HP-35 column provided nearly baseline separation between JWH-018 and JWH-022 (Figures 9-10). While the separation is not as prominent on the GC using the HP-1

column, it did give enough separation to provide comparison to the JWH-018 standard (Figures 11 and 12). It should be noted that Figures 10 and 12 represent actual casework data of a cigarette butt containing charred AM2201. The additional peaks present are not identified in the scope of this paper.

In order to obtain a 'clean' mass spectrum of JWH-018 for structural confirmation, a 30 meter HP-1MS column afforded enough separation, with ion reconstruction, to provide a good spectrum (Figure 13).

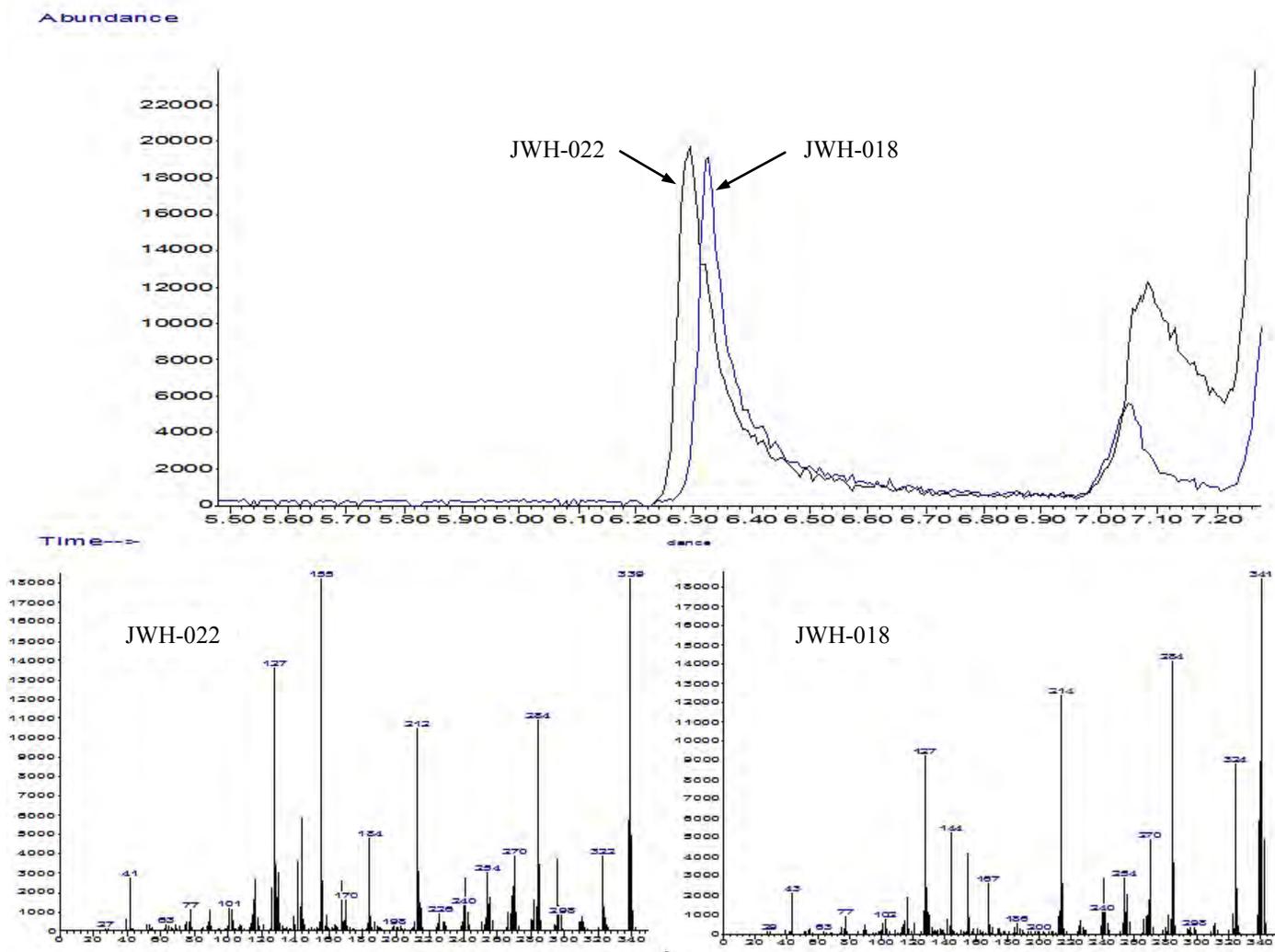


Figure 13 - Reconstructed ion chromatogram and subtracted spectra of JWH-022 and JWH-018 run on GC/MS with 30m HP-1MS column.

References

1. Wiley JL, Marusich JA, Huffman JW, Balster RL, Thomas BF. (2011). Hijacking of basic research: The case of synthetic cannabinoids. RTI Press publication No. OP-0007-1111. Research Triangle Park, NC: RTI Press. <http://www.rti.org/rtipress>. Retrieved March 13, 2012.
2. Cody RB, Laramée JA, Nilles JM, Durst HD. Direct Analysis in Real Time (DART™) mass spectrometry. JEOL News 2005;40(1):8-12.
3. Cody RB, Laramée JA, Durst HD. Versatile new ion source for the analysis of materials in open air under ambient conditions. Anal. Chem. 2005;77(8):2297-2302.
4. Steiner RR, Larson RL. Validation of the Direct Analysis in Real Time source for use in forensic drug screening. J Forensic Sci. 2009; 54(3):617-622.
5. <http://www.atk.gov.tr/pdf/huestissyntheticcannabinoids.pdf>. Retrieved March 12, 2012.