Determination of Pyrolysis Products of Smoked Methamphetamine Mixed with Tobacco by Tandem Mass Spectrometry

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Abstract

This study examines the pyrolysis products of smoked methamphetamine mixed with tobacco that was trapped with a C₈ adsorbent cartridge and then detected by gas chromatography-tandem mass spectrometry. According to the results, the mainstream smoke contains 2-methylpropyl-benzene, 2-chloropropyl-benzene, 2,3-dihydro-3,5-dihydroxy-6-methyl-4H-pyran-4-one, 3-ethyl-phenol, methamphetamine, dimethylamphetamines, hydroquinone, 3-methyl-5-(1-methylethyl)-methylcarbamate phenol, N-methyl-N-(2-phenylethyl)-acetamide, 4-(3-hydroxy-1-butenyl)-3,5,5-trimethyl-2-cyclohexene-1-one, propanoic acid, N-acetylmethamphetamine, phenyl ester, and furfurylmethylamphetamine. In addition, the compounds in sidestream smoke are 2-propenyl benzene, phenylacetone, methamphetamine, dimethylamphetamines, benzyl methyl ketoxime, 3,4-dihydro-2-naphthalenone, N-folmylamphetamine, N-acetylamphetamines, bibenzyl, N-folmylmethamphetamine, N-acetylmetbamphetamine, N-propionymethamphetamine, and furfurylmethylamphetamine. Moreover, the presence of methamphetamine promotes the oxidation of the tobacco components.

Introduction

Abuse of narcotics and central nervous system stimulants have seriously threatened modern society. Clandestine laboratories manufacture large quantities of illegally synthesized amphetamines, particularly methamphetamine-HCl. Methamphetamine abuse among the youth population has accelerated in recent years, signaling a serious drug problem in Taiwan. Methamphetamine is abused primarily through subcutaneous or intravenous injection, but some abusers prefer to take it orally or through nasal inhalation. Abuse of methamphetamine by smoking a cigarette mixed with methamphetamine has also become an abuse pattern among the younger generation in recent years. Schmeltz et al. (1) reviewed several nitrogen-containing compounds in tobacco and tobacco smoke. In addition, previous investigations (2–4) have examined the pyrolysis products produced by smoking drugs with tobacco, including heroin, cocaine, and phencyclidine (PCP). In related work, Lue et al. (5) determined the polynuclear aromatics formed during the smoking of PCP-laden cigarettes. Sekine and Nakahara (6,7) performed spectral analysis of infrared spectra, mass spectra, and proton magnetic resonance spectra to examine the pyrolysis products of smoking methamphetamine in tobacco. They determined the major pyrolysis products of methamphetamine in tar to be methamphetamine, amphetamine, phenylacetone, dimethylamphetamine, N-formyl-, N-acetyl-, N-propionyl-, and N-cyanomethyl-methamphetamine.

Johnson and Yost (8) thoroughly described the difficulties associated with trace organic analysis and the application of tandem mass spectrometric (MS–MS) techniques to determine trace amounts of organic compounds in a complex matrix.

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Other workers demonstrated that MS–MS is a highly effective means of structurally elucidating trace amounts of organic compounds (9–11). In this study, we examine the pyrolysis products of smoked methamphetamine mixed with tobacco that was trapped on a C8 adsorbent cartridge and then detected by gas chromatography–tandem mass spectrometry (GC–MS–MS). The mainstream and sidestream smoke from cigarette mixed with methamphetamine was collected with a solvent trap and an adsorbent cartridge. GC–MS–MS was performed to determine the structure of pyrolysis products.

Materials and Methods

Reagents
All chemicals were of research grade and used without further purification. Standard methamphetamine was purchased from Sigma Chemical Co. (St. Louis, MO).

Smoking experiments
Long Life (8-mm i.d., 85 mm, Taiwan Tobacco & Wine Monopoly Bureau), a cigarette filter, was used for the experiment. Figure 1 depicts the smoking apparatus used in this study. The collector consisted of a smoking chamber in which the smoke of a cigarette was mixed with the methamphetamine. The collector further consisted of two ice baths with methanol and ether trap tubes, a C8 adsorbent cartridge (Supelco, Bellefonte, PA), valve, transfer system, and water pump. The water pump was controlled at a flow rate of 1.5 mL/s. The cut-tobacco from a cigarette was drawn out and mixed with 25 mg of methamphetamine. The mixed tobacco was repacked into the cigarette. In the mainstream smoke experimental study, the cigarette filter (21 mm) was cut off to avert the detaining of pyrolysis products on the cigarette filter. The analytes were desorbed from the C8 adsorbent cartridge with 3 mL methanol. Next, the eluant, methanol extract and ether extract, was evaporated to dryness with a rotary vacuum evaporator (Tokyo Rikakikai, Tokyo, Japan). The residue was then redissolved in 1 mL methanol for analysis. Finally, a cigarette without any methamphetamine added was put through the same procedures to obtain the control data.

Instrumentation
A Hewlett-Packard (Palo Alto, CA) 5890 series II GC equipped with an HP 5898B MS engine detector (MS) or JEOL JMS SX/SX 102A (Tokyo, Japan) four-sector MS–MS. An HP-5 capillary column (30 m x 0.25-mm i.d., 0.5-µm film thickness, Hewlett-Packard) was used for chromatographic analysis. The GC was operated in the splitless mode, and the injector port temperature was set at 250°C. The GC–MS interface temperature was maintained at 280°C. Helium carrier gas was held at a rate of 1 mL/min by using electric...
pressure control. The initial GC temperature was maintained at 60°C for 30 s, increased to 120°C at 35°C/min, then increased to 190°C at 5°C/min, and finally increased to 225°C at 3°C/min.

The MS was operated in the electron impact (EI) ionization mode with an electron energy of 70 eV and a mass-to-charge ratio scan range of 40-500 amu. Methane was used as the reagent gas at 2 torr in the chemical ionization mode (CI). The electron energy for mass spectrum in CI mode was obtained at 100 eV.

The product ion experiments were performed with a JEOL JMS SX/SX 102A high-resolution double focusing four-sector tandem MS. The mass spectrometer was operated at a full accelerating voltage of 10 KeV. Spectra were obtained at a magnetic scan rate of 80 amu/s. The source pressure averaged at around 1.5 x 10⁻³ Pa (10⁻⁴ torr). Helium was used as the collision gas to attenuate the intensity of the ion beam from the source by 30%. Finally, MS–MS data were recorded by using a linked scan at a constant magnetic field/electrostatic field (B/E) ratio to record product ion mass spectra from reactions occurring in the first field-free region of the instrument. Notably, the resolution of the MS was approximately 3000.

Results and Discussion

The C₈ adsorbent cartridge was positioned behind the solvent traps in the experiments, in which the pyrolysis products of smoked methamphetamine mixed with tobacco were detected in the traps and the cartridge. No obvious signal was obtained from the solvent traps that were positioned after the cartridge in the smoking apparatus. This observation suggests that all the pyrolysis products were completely adsorbed by the adsorbent cartridge. Therefore, the experiments were performed with the cartridges set before the solvent traps.

**Sidestream cigarette smoke**

Comparing GC–MS analysis of C₈ cartridge eluate from a cigarette containing methamphetamine with that of a control cigarette reveals that many pyrolysis products are produced. Figure 2 presents the mass chromatograms. Pyrolysis products of methamphetamine were temporarily named P-1, -2, -3, -4...-12, and -13 according to the order of retention time, with the earliest being P-1. Figure 3 displays the EI mass spectrum of the pyrolysis product P-2 at retention time 3.5 min in Figure 2. From a library search of standard mass spectrum in data base, Figure 5. Chemical structures of pyrolysis products in sidestream smoke from smoked methamphetamine in a tobacco cigarette.

**Table 1. The Characteristic Mass Spectral Data of Pyrolysis Products for Sidestream Cigarette Smoke**

<table>
<thead>
<tr>
<th>Product</th>
<th>CI-MS [M+H]^+ (%)</th>
<th>Base peak (100%)</th>
<th>Precursor ion (100%)</th>
<th>Major fragment ion (100%)</th>
<th>MS-MS M⁺ (%)</th>
<th>Base peak (100%)</th>
<th>MW (amu)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-Propenyl benzene</td>
<td>19(33%)</td>
<td>91</td>
<td>91</td>
<td>91 (M-28)</td>
<td>118(78%)</td>
<td>117 (M-1)</td>
<td>118</td>
</tr>
<tr>
<td>Phenyacetone</td>
<td>135(100%)</td>
<td>135</td>
<td>135</td>
<td>93 (M-92)</td>
<td>134(11%)</td>
<td>91 (M-43)</td>
<td>134</td>
</tr>
<tr>
<td>Methamphetamine</td>
<td>150(100%)</td>
<td>150</td>
<td>150</td>
<td>91 (M-59)</td>
<td>149(2%)</td>
<td>58 (M-91)</td>
<td>149</td>
</tr>
<tr>
<td>Dimethylamphetamine</td>
<td>164(100%)</td>
<td>164</td>
<td>164</td>
<td>91 (M-73)</td>
<td>163(1%)</td>
<td>72 (M-91)</td>
<td>163</td>
</tr>
<tr>
<td>Benzyl methyl ketoxime</td>
<td>178(100%)</td>
<td>178</td>
<td>178</td>
<td>91 (M-59)</td>
<td>177(8%)</td>
<td>86 (M-91)</td>
<td>177</td>
</tr>
<tr>
<td>3,4-Dihydro-2-naphthalene</td>
<td>182(100%)</td>
<td>182</td>
<td>182</td>
<td>77 (M-70)</td>
<td>182(30%)</td>
<td>91 (M-91)</td>
<td>182</td>
</tr>
<tr>
<td>N-Furfurylmethylmethamphetamine</td>
<td>192(100%)</td>
<td>192</td>
<td>192</td>
<td>91 (M-101)</td>
<td>191(1%)</td>
<td>58 (M-133)</td>
<td>191</td>
</tr>
<tr>
<td>N-Acetylmethamphetamine</td>
<td>206(100%)</td>
<td>206</td>
<td>206</td>
<td>91 (M-87)</td>
<td>205(1%)</td>
<td>58 (M-147)</td>
<td>205</td>
</tr>
<tr>
<td>Furfurylmethamphetamine</td>
<td>230(100%)</td>
<td>230</td>
<td>230</td>
<td>91 (M-148)</td>
<td>229(1%)</td>
<td>81 (M-148)</td>
<td>229</td>
</tr>
</tbody>
</table>

* Relative intensity to 100%
1 The ion was selected as the precursor ion
the pyrolysis product P-2 is identified as phenylacetone (Figure 3). This figure indicates that a characteristic ion at m/z 134 corresponds to the molecular ion. The base peak ion at m/z 91 can be formed from the cleavage of the CH₃CO group of the molecular ion. The ion at m/z 77 is derived from the most abundant ion m/z 91 with a loss of CH₂ or with β-cleavage of the molecular ion by a loss of a CH₃COCH₂ radical. Herein, positive chemical ionization technique was applied to confirm the molecular ion of the P-2 compound. The base peak ion is at m/z 135, which comes from the protonated molecular ion (M+H)⁺ (Figure 4A). The adduct ion at m/z 163 is also a characteristic ion that comes from (M + C₂H₅)⁺ in CI mass spectra with methane as a reagent gas. Therefore, according to these results, we can conclude that the molecular weight of the pyrolysis compound P-2 is 134 amu. Moreover, a series of GC-MS–MS experiments was performed to further confirm the structure of the P-2 compound. Figure 4B presents the product ion spectrum of the protonated molecular ion (M + H)⁺ at m/z 135. The fragmentation ion in the product ion spectrum resembles that in the normal EI spectrum of standard phenylacetone. Under collisionally activated dissociation (CAD) conditions, fragmentation of the ion at m/z 135 yielded several abundant product ions. The major product ions were m/z 117, 91, 77, and 43. From the product ion spectra, we can infer that the structure of this pyrolysis product P-2 is phenylacetone.

Table I summarizes the characteristic mass spectral data of pyrolysis products. According to a library search and with product ion spectra, a series of the sidestream smoke pyrolysis products P-1, P-2...P-12, and P-13 is proposed as 2-propenyl benzene, phenylacetone, methamphetamine, dimethylamphetamine, benzyl methyl ketoxime, 3,4-dihydro-2-naphthalenone, N-folmylamphetamine, N-acetylamphetamine, bibenzyl, N-folmylmethamphetamine, N-acetylmethamphetamine, and furfurylmethylamphetamine, respectively.

**Mainstream smoke experiments**

In the mainstream smoke experiments, the cigarette filter was cut off to prevent the pyrolysis products from adsorbing on the filter while the smoke passed through the filter. The procedures adopted herein were the same as those in the sidestream smoke studies. The mass chromatogram of the mainstream smoke from a cigarette containing methamphetamine was compared with that of a control cigarette. According to those results, the major compound in the pyrolysis
whether was methamphetamine added. In addition, most components of the higher boiling point are clearly produced only by smoking tobacco. Chemical ionization with methane as reagent gas was used to obtain the molecular weight data for pyrolysis products. In the tandem mass spectrometer, product ion scanning of the selected protonated molecular ion obtained in the structure of the monitored pyrolysis product. Therefore, by using mass spectrometric data and library search of standard mass spectral data, a series of pyrolysis products of mainstream smoke from a cigarette containing methamphetamine are proposed as 2-methylpropyl-benzene, 2-chloropropyl-benzene, 2,3-dihydro-3,5-dihydroxy-6-methyl-4H-pyran-4-one, 3-ethylphenol, methamphetamine, dimethylamphetamine, hydroquinone, 3-methyl-5-(1-methylthyl)-methylcarbamate phenol, propanoic acid, phenyl ester, N-methyl-N-(2-phenylethyl)-acetamide, N-acetyltrimethylamine, 4-(3-hydroxy-1-butyl)-3,5,5-trimethyl-2-cyclohexene-1-one, phenyl ester, and furfurylmethylamphetamine. Table II summarizes the characteristic mass spectral data of pyrolysis products in mainstream of smoking experiments.

Smoking of methamphetamine mixed with tobacco leads to various pyrolysis products by oxidation, acetylation, propionylation, formylation, furfurylation, demethylation, etc. (Figures 5 and 6). The undecomposed methamphetamine was also detected in both mainstream and sidestream smoke. In mainstream smoke studies, the collected smoke was drawn through the cigarette; in the sidestream smoke experiment, the collected smoke was generated by the burning end of the cigarette. The different collection points contributed different pyrolysis products. In sum, these results demonstrate that the presence of methamphetamine promotes the oxidation of the tobacco components.

Conclusions

This study reveals that a C8 adsorbent cartridge can completely trap the pyrolysis products from smoking methamphetamine mixed with tobacco. The pyrolysis products can be determined by using EI, CI, and tandem mass spectrometric data. According to those results, only a slight amount of methamphetamine itself still exits in mainstream and sidestream smoke. The pyrolysis products identified in sidestream were 2-propanyl benzene, phenylacetone, methamphetamine, dimethylamphetamine, benzyl methyl ketoxime, 3,4-dihydro-2-naphthalenone, N-folymethylamphetamine, N-acetyltrimethylamine, bibenzyln, N-folmylmethylamphetamine, N-acetyltrimethylamine, N-propionylmethamphetamine, and furfurylmethylamphetamine. In mainstream smoke, the pyrolysis products determined were 2-methylpropyl-benzene, 2-chloropropyl-benzene, 2,3-dihydro-3,5-dihydroxy-6-methyl-4H-pyran-4-one, 3-ethylphenol, methamphetamine, dimethylamphetamine, hydroquinone, 3-methyl-5-(1-methylthyl)-methylcarbamate phenol, propanoic acid, N-methyl-N(2-phenylethyl)-acetamide, N-acetyltrimethylamine, 4-(3-hydroxy-1-butyl)-3,5,5-trimethyl-2-cyclohexene-1-one, phenyl ester, and furfurylmethylamphetamine.

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References


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