Screening and Quantitation of Drugs from Blood and Urine by Paper Spray MS
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Overview

- Paper spray is a method for performing rapid drug analysis by mass spectrometry without sample preparation.
- Analyte extraction and ionization is performed by applying a spray solvent by initiating an electrospray plume from a porous substrate (i.e. paper) after application of solvent and high voltage.
- The sample (blood, urine, saliva, etc) is dried and stored on the paper.
- Here, results for three experiments related to drug analysis by paper spray are shown:
  1. Screening of drugs and drug metabolites in urine.
  2. Quantitative analysis of drugs in dried blood spots.
  3. Separation of three opiate isomers using FAIMS ion mobility filtering coupled to a triple quad mass spectrometer.

Introduction

- A cone-jet of charged solvent droplets can be generated from wet paper by applying high voltage (Figure 1).
- The spray solvent that is applied to the paper also acts as the extraction solvent to extract drugs and other compounds from the dried sample (Figure 2).
- Typical solvents:
  - Methanol or acetonitrile with a small amount of water (<10% usually)
  - Sodium or ammonium acetate can be substituted for the acid if adduct formation is desired rather than protonation.

Experiment 1: Drug Screening in Urine using Paper Spray on an Exactive

- Figure 3. Picture of an automated paper spray MS attachment and Experiment 1: Drug Screening in Urine using Paper Spray on an Exactive

Experiment 2: Quantitative Analysis Directly from Dried Blood Spots

- Figure 6. The eight compounds shown to the left were quantitated from dried blood spots by paper spray MS/MS. Isotope labeled internal standards were mixed into the blood sample prior to spotting it onto the paper. The first 7 were quantitated simultaneously. THC was analyzed separately because it required a different solvent.
- Instrument: Thermo TSQ Access Max
- Solvent: 95:5 methanol-water with 0.2% hydroxyamine

Experiment 3: Opiate Separation by FAIMS Filtering Prior to MS/MS

- Figure 8. paper spray MS/MS spectra of three opiate isomers. They cannot be distinguished adequately by MS/MS

Table: Drug Analysis by Paper Spray MS

<table>
<thead>
<tr>
<th>Drug</th>
<th>Paper Spray LOD directly from DBS (ng/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amphetamine</td>
<td>1</td>
</tr>
<tr>
<td>Methamphetamine</td>
<td>0.3</td>
</tr>
<tr>
<td>MDMA</td>
<td>2</td>
</tr>
<tr>
<td>NMDA</td>
<td>0.04</td>
</tr>
<tr>
<td>Morphine</td>
<td>0.5</td>
</tr>
<tr>
<td>Cocaine</td>
<td>0.01</td>
</tr>
<tr>
<td>THC</td>
<td>4</td>
</tr>
</tbody>
</table>

Figure 9. FAIMS Separation of norcodeine and hydromorphone using the H-ESI ion source. A: both electrodes at 100°C. B: inner electrode decreased to 70°C. C: Three opiate mixture analyzed by H-ESI using the same conditions as B. D: Paper spray FAIMS separation of the three opiate mixture with 0.2% hydroxyamine