We will start momentarily at 2pm ET

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Upcoming ACS Webinars

Thursday, November 20, 2014
“Optimizing Potency for Nevirapine: The Drug that Saved Children from AIDS ”

Dr. Rebecca Anderson, Freelance Medical Writer and Author
Dr. Joseph Fortunak, Professor of Chemistry, Howard University

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Cannabis Chemistry 101: Review

- History of Cannabis
  - Legal status in the US

- Endocannabinoid System
  - Therapeutic benefits

- Chemical Complexity
  - Phytochemical constituents
  - Potential contaminants
  - Matrix complexity

- Biosynthetic Pathways
  - Formation of cannabinoids

- Cannabinoid Reactions
  - Degradation/Decarboxylation

- Opportunities for Analytical Chemistry
  - Application of modern technologies
  - Ensure consumer safety
  - Research opportunities

Role of Analytical Chemistry

- Ensuring Consumer Safety
  - Confirm products are free from contamination
  - Assist in determining proper dosage

- Optimization of Cultivation Practices
  - Monitoring nutrient uptake
  - Early identification of phenotypes

- Design and Development of Marijuana Infused Products (MIPs)
  - Optimization of extractions and processes
  - Quantitation required for product labeling
Audience Poll

What is typically the most abundant cannabinoid found in cannabis?

- THC (Tetrahydrocannabinol)
- CBD (Cannabidiol)
- THCA (Tetrahydrocannabinolic Acid)
- CBDA (Cannabidiolic Acid)

Analytes and Analytical Techniques

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Analytical Technique</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cannabinoids</td>
<td>TLC, GC, HPLC, UPLC, CC (SFC)</td>
</tr>
<tr>
<td>Terpenes</td>
<td>GC</td>
</tr>
<tr>
<td>Water (Residual Moisture)</td>
<td>Gravimetric, Water Activity</td>
</tr>
<tr>
<td>Heavy Metals</td>
<td>AA, ICP, ICP-MS, TXRF</td>
</tr>
<tr>
<td>Volatile Organic Compounds (VOCs)</td>
<td>Headspace GC, GC/MS</td>
</tr>
<tr>
<td>Mycotoxins</td>
<td>ImmunoAffinity (IA) Assays</td>
</tr>
<tr>
<td>Microbiological Contaminants</td>
<td>Cultures, qPCR</td>
</tr>
<tr>
<td>Pesticides/Plant Growth Regulators</td>
<td>LC/MS, GC/MS</td>
</tr>
</tbody>
</table>
Mycotoxins

- **Four Key Aflatoxins: B₁, B₂, G₁, G₂**
  - Produced by some Aspergillus molds
  - Results in liver damage

- **Ochratoxin A**
  - Produced by some Aspergillus and Penicillium molds
  - Results in kidney damage and immune suppression

- **Found in many commodities**

---

**ImmunoAffinity (IA) Assays**

- **Monoclonal Antibody Based Affinity Chromatography**
  - Extracted sample is loaded on to the column
  - Sample is flushed through the column
  - Mycotoxins are selectively bound to the antibodies
  - Additional constituents are passed through to waste
  - Mycotoxins are collected selectively for analysis
Mycotoxin Testing

Mycotoxin concentrations can be measured with a digital fluorometer. Provides total aflatoxin and total ochratoxin concentrations.

Analysis with LC or LC/MS/MS delivers additional sensitivity and specificity, providing separation and quantitation of the individual mycotoxins.

X-ray Fluorescence (XRF) Spectroscopy

- An X-ray quantum hits an inner shell electron in a (sample) atom. The electron is removed leaving the atom in an excited state (1).
- A electron from a higher orbital will drop down to fill the space. (2)
- The energy difference between the inner and outer shell is balanced by the emission of a photon quantum (fluorescence radiation, 3).
- These transitions are instantaneous. Fluorescence emissions are specific to individual elements, with intensities proportional the concentration of those elements.

Courtesy of Bruker-AXS
X-ray Fluorescence (XRF) Spectroscopy

- Each element shows a specific line pattern in a spectrum depending on the orbitals involved
  - L→K transition = Kα line
  - M→K transition = Kβ line
  - M→L transition = Lα line
  - N→L transition = Lβ line

- The higher the atomic number, the more "shells" (generally speaking)

Each element has its own set of "fingerprints"

Courtesy of Bruker-AXS

Quantitative Elemental Analysis

TXRF - Total reflection X-ray Fluorescence Spectroscopy

- Provides quantitative multi-element microanalysis
- Lower limits of detection in ppb range
- Meets USP requirements established for pharmaceutical products (USP 232/233)

Courtesy of Bruker-AXS
Quantitative Elemental Analysis

Cannabis Bud

Quantitative Elemental Analysis

- QC Testing for Soil, Fertilizers and Water During Cultivation
- Better Understand Nutrient Uptake by Plants
- Identify of Heavy Metal Contamination

Hemp Extract Based Product – Sourced out of China

<table>
<thead>
<tr>
<th>Element</th>
<th>USP Limits (ppm)*</th>
<th>Measured Conc.(ppm)</th>
<th>Limits of Detection (ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cr (Chromium)</td>
<td>2.5</td>
<td>ND</td>
<td>0.013</td>
</tr>
<tr>
<td>Mn</td>
<td>0.191</td>
<td>0.009</td>
<td></td>
</tr>
<tr>
<td>Fe (Iron)</td>
<td>0.169</td>
<td>ND</td>
<td>0.006</td>
</tr>
<tr>
<td>Ni (Nickel)</td>
<td>0.15</td>
<td>ND</td>
<td>0.006</td>
</tr>
<tr>
<td>Cu (Copper)</td>
<td>10</td>
<td>0.123</td>
<td>0.005</td>
</tr>
<tr>
<td>Zn</td>
<td>0.31</td>
<td>0.005</td>
<td></td>
</tr>
<tr>
<td>Ga</td>
<td>5</td>
<td>ND</td>
<td>0.004</td>
</tr>
<tr>
<td>As (Arsenic)</td>
<td>0.15</td>
<td>ND</td>
<td>0.003</td>
</tr>
<tr>
<td>Rb</td>
<td>0.907</td>
<td>0.004</td>
<td></td>
</tr>
<tr>
<td>Sr</td>
<td>0.41</td>
<td>0.004</td>
<td></td>
</tr>
</tbody>
</table>

Mercury concentration higher than acceptable limits

* Limits established for administration of pharmaceuticals by inhalation – United States Pharmacopeia USP 232/233
**Volatile Organic Compounds (VOCs)**

- Propane
- Ethanol
- iso-Butane
- 1-Propanol
- Methanol
- n-Butane
- Pentane
- Hexane
- Diethyl Ether
- iso-Propanol
- Diethyl Ether
- Propane
- n-Butane
- Iso-Butane
- 1-Propanol
- Methanol
- n-Butane
- Pentane
- Hexane
- Diethyl Ether
- iso-Propanol
- Propane
- n-Butane
- Iso-Butane
- 1-Propanol
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- iso-Propanol
- Propane
- n-Butane
- Iso-Butane
- 1-Propanol
- Methanol
- n-Butane
- Pentane
- Hexane
- Diethyl Ether
- iso-Propanol

**Headspace Gas Chromatography**

- **Measurement of Volatile Organic Compounds (VOCs)**
  - Measure residual solvents from cannabis extractions
  - Includes common extraction solvents: butane, propane, ethanol, etc..
  - Vial is heated to volatilize organic compounds
  - Sample is collected from the headspace above the bulk
  - Sample is injected for Gas Chromatographic (GC) analysis
Headspace Gas Chromatography: VOCs

Terpenes

Linalool

Limonene

Terpinolene

Myrcene

trans-Ocimene

α-Pinene

Camphene

Geraniol
Gas Chromatography: Terpenes

Gas Chromatography: Cannabinoids

THCA - Heat decarboxylation
THC - oxidation
CBN - oxidation

200-400°C
Liquid Chromatography

- **High Performance Liquid Chromatography (HPLC)**
  - Maintains the quantitative information of the acid and neutral cannabinoids

- **UltraPerformance Liquid Chromatography (UPLC)**
  - Ultra High Pressure Liquid Chromatography (UHPLC)
  - Faster and more efficient than HPLC

Both methodologies use organic solvents to achieve the separation and quantitation of analytes

Convergence Chromatography

- **UltraPerformance Convergence Chromatography System (UPC²)**

- Based on the theory of Supercritical Fluid Chromatography (SFC)
  - Uses liquid CO₂ as the primary mobile phase

- Reduces the hazardous waste generated relative to conventional liquid chromatography

- Captures quantitative information on both acid and neutral (decarboxylated) form of the cannabinoids

- Amenable to non-polar solvents, ideal for analysis of analytes in lipid-rich matrices
Analysis of Cannabis Flower

UltraPerformance Convergence Chromatography (UPC²)

Decarboxylation

Temperature: 260°F
Decarboxylation

Audience Poll

Which United States President was NOT a hemp farmer?

☐ George Washington
☐ Thomas Jefferson
☐ James Buchanan
☐ James Madison
Marijuana Infused Products

- Marijuana Infused Products (MIPs)
  - Becoming increasingly important to the industry
  - Provides delivery formats for patients that do not want to smoke cannabis
  - Some states allow, by regulation, only derivative products to be available

Cannabis Extractions

- Supercritical Fluid Extractions (SFE) using liquid CO$_2$
  - Safest Extraction Option: Non-toxic, non-flammable, environmentally neutral
  - Maintains terpene-rich extract profile
  - Extract can be used as the basis for many products
SFX Work Flow

Purification of Individual Cannabinoids

Hemp Extract

Purified CBD

Purified CBDA
Summary

- Analytical chemistry will play a key role in the expanding cannabis industry, with a primary focus on ensuring patient/consumer safety

- The complexity of cannabis, as a natural product, with the potential for a variety of contaminants provides a number of analytical challenges that requires multiple analytical techniques to understand more fully

- The current trends for increased acceptance of cannabis as a legitimate industry provides the opportunity for the application of current analytical technologies to address these challenges

References for Additional Information


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