A Better Understanding of Cannabis Chemistry to Aid in Vapor Phase Detection of Intoxication

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Collaborators

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Cannabis/Marijuana Decriminalization

• Medical marijuana – 22 states and Washington D.C.
• Recreational marijuana
  – Legal in Colorado, Washington, Alaska and Oregon
  – Voting today! CA, AZ, NV, MA and ME
• Feb 2014 - Congress enabled financial institutions to do business with legal sellers

➢ Made imperative the need to detect cannabis-induced intoxication for both law enforcement and workplace safety.
The Endocannabinoid System

• Cannabinoid receptor types (CB):
  • CB$_1$ – nerve cells in brain, spinal cord, eyes
  • CB$_2$ – immune system, spleen, peripheral nerves

• Endocannabinoid neurotransmitters
• Regulate fear, stress, memory, pain, inflammation, appetite, immune function, depression

• Phytocannabinoids
• Synthetic cannabinoids
Synthetic Cannabinoids

• Sprayed onto plant material, paper
• Sold as “potpourri” or “herbal incense”
• Innervate with the cannabinoid receptors
  – More potent than endo- or phyto-cannabinoids
  – Tremors and seizures, hallucinations, delusions, and violent behavior
• Active ingredients in constant flux

Spice
  K2
  Bliss
  Fake Weed
  Yucatan Fire
  Skunk
  Moon Rocks
  Genie
  Scooby Snacks

Poisons yield unpredictable results by Ben Wallace, theadvocate.com/csp/mediapool/sites/Advocate/assets/templates…
Cannabis Chemistry

- Made up of over 400 compounds
- 100+ **phyto**cannabinoids
  - cannabidiol (CBD)
  - $\Delta^9$-tetrahydrocannabinol ($\Delta^9$-THC)
    - Main psychoactive cannabinoid
    - Responsible for “high” feeling
  - Effects pain sensation, mood (euphoria/paranoia), memory, appetite, coordination
  - Innervate with CB$_1$ and CB$_2$
- Terpenes - aroma
- Challenge - Schedule I drug
Physiological Complexities

• \(\Delta^9\)-THC levels spike within minutes, drop rapidly
• Body mass index
• Detect 1-2 ng/ml THC in the blood
  – Chronic user – 2 days
  – Occasional user – 8 hours
• \(\Delta^9\)-THC detected depends on how consumed
  – Smoking, eating, tinctures, teas, vaporization, patch
Detecting $\Delta^9$-THC

- Readily detect in blood, urine, hair, sweat, oral fluid (saliva), breath
- $\Delta^9$-THC in blood
  - *Per se* limits: CO limit, 5 ng/mL
  - “zero tolerance” laws
- Does not correspond to intoxication

- Other chemical markers indicative of intoxication?
  - Synthetic cannabinoids
Breath Tests for $\Delta^9$-THC

- Advantages
  - Non-invasive
  - Portable
  - Indicate recent use (0.5 – 2 hours)

- Challenges
  - Impairment may last longer than 2 hours
  - Passive exposure?
  - Does it determine degree of intoxication?

Our Approach

Fundamental Data
- Vapor pressures
- Molecular interactions
- Partition coefficients

“Breathalomics”
- Artificial breath
- Determine the chemical signature of intoxication
- Develop data analytics

Materials Development
- Material selection for adsorption
- Develop desorption techniques
- Begin with pure compounds and breath surrogates
Fundamental Data: Vapor Pressure

• Volatile substance - evaporates or sublimes readily at normal temperatures and pressures
  – Evaporation: liquid phase to gas phase
  – Sublimation: solid phase to gas phase
Characterization of $\Delta^9$-THC & CBD

- Large molecules with low vapor pressures
- Reactive with oxygen, heat, light
- Unstable for long measurement times

Accurate measurements are especially challenging for mixtures!
Porous Layer Open Tubular (PLOT)-Cryoadsorption

A dynamic HS sampling technique

Robust, reusable, cheap, large temperature operability (less volatile solutes), and sorbent phases can be tailored for application.
**PLOT – Cryoadsorption (PLOT-Cryo)**

Sweep Gas

- **COLD!**
  - $T_{\text{cryostat}} = -20 \, ^\circ\text{C}$

- $T_{\text{oven}} = 60, 80, 100, 120 \& 140 \, ^\circ\text{C}$

Gas Chromatography – Mass Spectrometry
Quantitative, Sensitive Recovery of Δ⁹-THC

\[ \ln\left( \frac{g}{L \times 10^7} \right) = 1000/T, \text{K}^{-1} \]

\[ \Delta H = 91.0 \text{ kJ/mol} \]

A linear relationship provides enthalpy of interaction

\[ T_{\text{oven}} = 140, 120, 100, 80, 60 ^\circ \text{C} \]
Vapor Pressure (Pa x 10^5) for Δ⁹-THC

\[ PV = nRT \]
Vapor Pressure ($Pa \times 10^5$) for both $\Delta^9$-THC and CBD
Breath Collection: PLOT – Cryo

A single PLOT capillary embedded in an epoxy wafer.

Tom Bruno demonstrating the hand piece and portable PLOT-Cryo.

Fundamental thermophysical properties data and adaptable technology for in-the-field sampling and pre-concentration.

Breath Collection: Capillary Microextraction of Volatiles (CMV)

**CMV Device**
- High sensitivity
- Low sampling time
- Ability for on-site sampling of VOC compounds

**CMV Device Specifications**
- 2 cm long open ended glass capillary tube
- Seven 2-mm wide by 2-cm long sorbent (PDMS) coated glass fiber strips
- Surface area 5000 times greater than SPME fiber
- Sampling time as low as 30 s
- Vacuum pump suction is 1L/min

Use CMV device for breath collection of cannabis-related metabolites.

Thermal Desorption: CMV

TD-CMV-GC/MS

Thermal Separation Probe (TSP)
“Breathalomics” - Artificial Breath Generator Breakthrough

Permeation Tube Vapor Generator

CMV Breakthrough Experiment

2,5-dimethylfuran
caryophyllene
tetradecane

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![Permeation Tube Vapor Generator Diagram](image)

![CMV Breakthrough Experiment Chart](chart)

*Calculations based on SIM AUC (n=3)
Summary

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Funding – Special Programs Office

Thank you!