Building the Chemical Foundation for Intelligent Breath Analysis

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Drug Sampling Options

Blood Sample

1.5 h – 4 h delay
Drug Sampling Options

Breath Sample

- H₂O
- N₂
- CO₂
- O₂
- Ar

Ethanol
0.4 mg / liter breath
at legal limit
Ethanol
Known correlation between conc. and impairment
Blood-breath ratio $\approx 2350$ (mean)
Simple elimination profile; not stored in fat tissue
Thermophysical properties – known

Cannabis
Unknown correlation between conc. and impairment
Blood-breath ratio $\approx ?$
Unknown elimination profile; stored in fat tissue
Thermophysical properties – unknown and difficult to measure
Cannabis is Challenging

\[
\text{Cannabis constituents:} \quad C_{21}H_{30}O_2 \quad \Delta-9\text{-tetrahydrocannabinol (THC)}
\]

\[
\text{Metabolites:} \quad \text{cannabigerol & cannabinol}
\]

\[
\text{Terpenes:} \quad \text{ethanol}
\]
Cannabis is Challenging

C₂H₅OH

Ethanol Blood Concentration
0 – 3,000,000 ng/mL

C₂₁H₃₀O₂

THC Blood Concentration
0 – 200+ ng/mL
Properties for Reliable Quantitation

Vapor Pressure

\[ P_{\text{SAT}} = \frac{m \cdot R \cdot T}{M \cdot V} \]

Partitioning

\[ K_{F/B} = \frac{[A]_{\text{FAT}}}{[A]_{\text{BLOOD}}} \]
\[ K_{B/A} = \frac{[A]_{\text{BLOOD}}}{[A]_{\text{AIR}}} \]
\[ K_{S/A} = \frac{[A]_{\text{PDMS}}}{[A]_{\text{AIR}}} \]
**P\textsubscript{SAT} – Standard Method**

**Concatenated Gas Saturation**

Mononitrotoluene taggants  

Low-volatility terpenes  

Internal eicosane control  

Influence of carrier gas  

Anti-oxidants for unstable chemicals  

**CARRIER GAS**

**SATURATOR**

**ADSORBER**

**SATURATOR**

**ADSORBER**

Time = 1 – 8 weeks

**30 °C – 90 °C**

ca. 20 °C
**P$_{\text{SAT}}$ – Rapid Method**

Porous Layer Open Tubular (PLOT) Cryoadsorption

![Diagram of PLOT cryoadsorption system]

- Carrier Gas
- Saturator: 30 °C – 300 °C
- Adsorber: -10 °C

**Time = 1 – 2 hours**

**Graph: ln[PSAT(Pa) • 10$^3$] vs. 1000 / T(K)**

- Eicosane ($\text{C}_{20}\text{H}_{42}$)
  - 282.5 g/mol
  - 30 °C

- Reference correlation (Lemmon and Goodwin 2000)
- Concatenated gas saturation method
- PLOT-cryo method

**Tetradecane validation**

**Cannabinoids**
**P_{SAT} – Rapid Method**

Porous Layer Open Tubular (PLOT) Cryoadsorption

Time = 1 – 2 hours

THC (C_{21}H_{30}O_{2})

314 g/mol

THC: 0.000115 Pa @ 40 °C
$P_{\text{SAT}}$ – Rapid Method

Porous Layer Open Tubular (PLOT) Cryoadsorption

CARRIER GAS

SATURATOR

30 °C – 300 °C

-10 °C

ADSORBER

THC ($C_{21}H_{30}O_{2}$)

314 g/mol

Ethanol: 18,000 Pa @ 40 °C

THC: 0.000115 Pa @ 40 °C

SOURCE: NIST REFPROP Database

Time = 1 – 2 hours
Can we capture and concentrate sufficient material at physiological temperatures?

How does ethanol impact blood/air partitioning?
**$K_{\text{Fat/Blood}}$ – Non-Invasive NMR Method**

Fat Surrogate = Octanol

Blood Surrogate = Water

Eugenol in D$_2$O

Octanol + D$_2$O

Eugenol in Octanol + D$_2$O

Octanol Signals

Eugenol Signals

$^1$H Chemical Shift

**FORENSICS @ NIST**

#NISTForensics
**$K_{PDMS/AIR} – Model Feasibility**

Is it feasible to predict sorbent-air partitioning with an empirical model?

$$K = \frac{[A]_{PDMS}}{[A]_{AIR}}$$

$n$ [moles] = $K \times V_s \times C_o$

**Partition Coefficient**

**PDMS Structure**

**Synthetic Designer Drugs**

**SPME Fiber**

**Capillary Microextraction of Volatiles (CMV)**
$K_{PDMS/AIR}$ – Chemicals for Model

**Functional Groups (18)**

<table>
<thead>
<tr>
<th>Non-Ring Groups</th>
<th>Ring Groups</th>
<th>Oxygen Groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>$&gt;\text{C}&lt;$</td>
<td>$&gt;\text{C}&lt;$</td>
<td>$-\text{OH}$ (alcohol)</td>
</tr>
<tr>
<td>$&gt;\text{CH}-$</td>
<td>$&gt;\text{CH}-$</td>
<td>$-\text{OH}$ (phenol)</td>
</tr>
<tr>
<td>$\text{-CH}_2-$</td>
<td>$\text{-CH}_2-$</td>
<td>$-\text{O}-$</td>
</tr>
<tr>
<td>$\text{-CH}_3$</td>
<td></td>
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<td>$=\text{C}&lt;$</td>
<td>$=\text{C}&lt;$</td>
<td>$&gt;\text{C}=\text{O}$</td>
</tr>
<tr>
<td>$=\text{CH}-$</td>
<td>$=\text{CH}-$</td>
<td>$-\text{CHO}$</td>
</tr>
<tr>
<td>$=\text{CH}_2$</td>
<td></td>
<td>$-\text{COO}-$</td>
</tr>
</tbody>
</table>

**Training Set Requirements**

1) Log K at three temperatures: 60 °C - 180 °C
2) Follows van’t Hoff Equation with $R^2 > 0.95$
Compare experimental values (x axis) with predicted values (y axis) for chemicals used to build model (N = 275).

\[ R^2 = 0.984 \]
**K\textsubscript{PDMS/AIR} – Model Predictions**

Predict values for chemicals not used to build model.

**Example: C\textsubscript{8} chemicals at 100 °C**

<table>
<thead>
<tr>
<th>Chemical</th>
<th>Experimental Data</th>
<th>Model Prediction</th>
<th>% Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>ethylidene-cyclohexane</td>
<td>2.128</td>
<td>2.112 + 0.002</td>
<td>0.8 %</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.989 + 0.001</td>
<td>0.4%</td>
</tr>
<tr>
<td>ethenyl-cyclohexane</td>
<td></td>
<td>1.996</td>
<td></td>
</tr>
</tbody>
</table>

Summary

Quantitative breath analysis of cannabinoids will be challenging due to their low volatility and their low concentration in blood.

Thermophysical property measurements for large, hydrophobic, low-volatility chemicals push the limits of existing experimental approaches.

Current Partnerships: Prof. Jerry King (University of Arkansas), Prof. Roger Giese (Northeastern University), Prof. April Hill (Metro State University), Prof. Lupita Montoya (University of Colorado)

Outreach: ASTM Committee D37 on Cannabis, Front Range Forensic Chemists Association, Colorado Bureau of Investigation, Cannabis Industry
Please contact any of us to discuss working together or to discuss postdoctoral opportunities.

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