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Building the Chemical Foundation for Intelligent Breath Analysis

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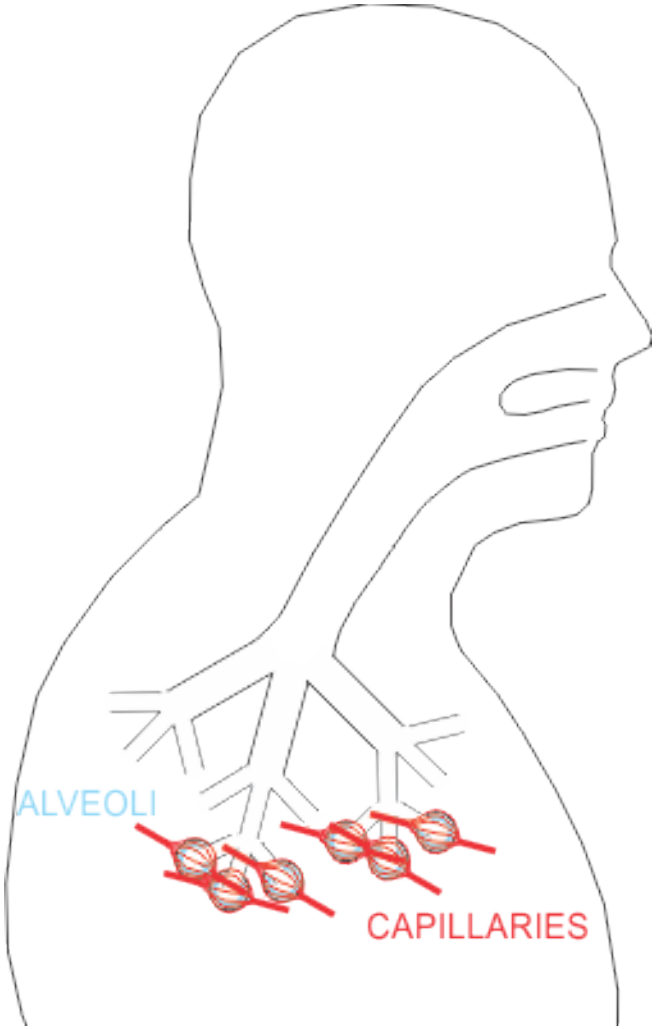
Funding: NIST Special Programs Office

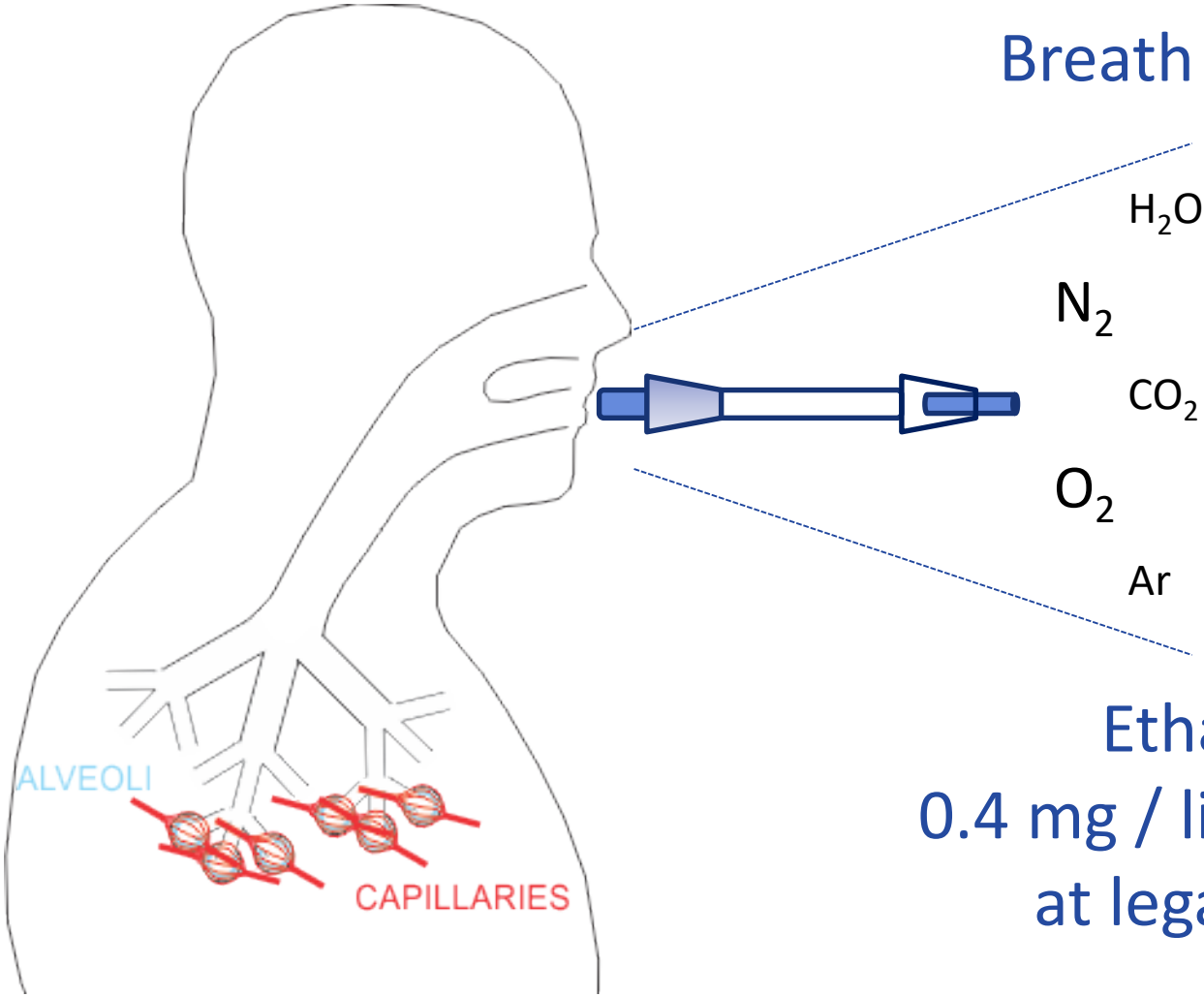
Drug Sampling Options



Blood Sample

1.5 h – 4 h delay

Drug Sampling Options



Breath Sample

H_2O

N_2

CO_2

O_2

Ar

Ethanol
0.4 mg / liter breath
at legal limit

Ethanol

Known correlation between conc. and impairment

Blood-breath ratio ≈ 2350 (mean)

Simple elimination profile; not stored in fat tissue

Thermophysical properties – known

Cannabis

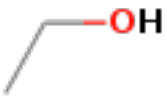
Unknown correlation between conc. and impairment

Blood-breath ratio ≈ ?

Unknown elimination profile; stored in fat tissue

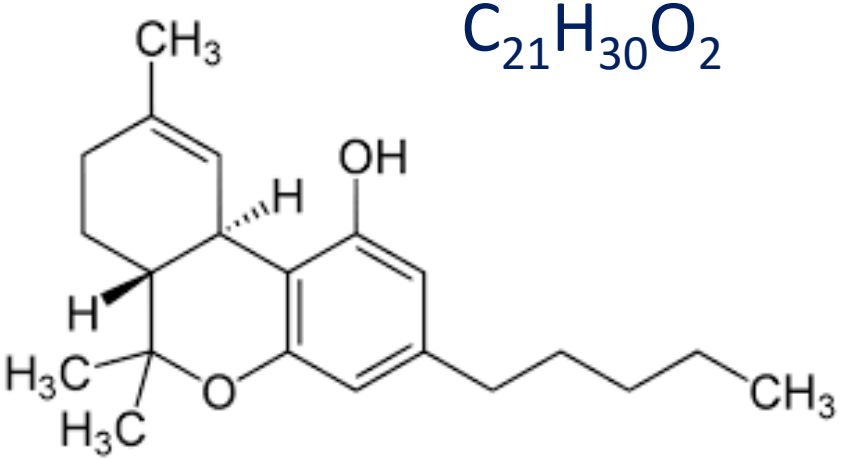
Thermophysical properties – unknown and difficult to measure

Cannabis is Challenging



C_2H_5OH

ethanol



$C_{21}H_{30}O_2$

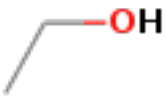
Δ-9-tetrahydrocannabinol (THC)

metabolites

cannabigerol & cannabinol

terpenes

Cannabis is Challenging

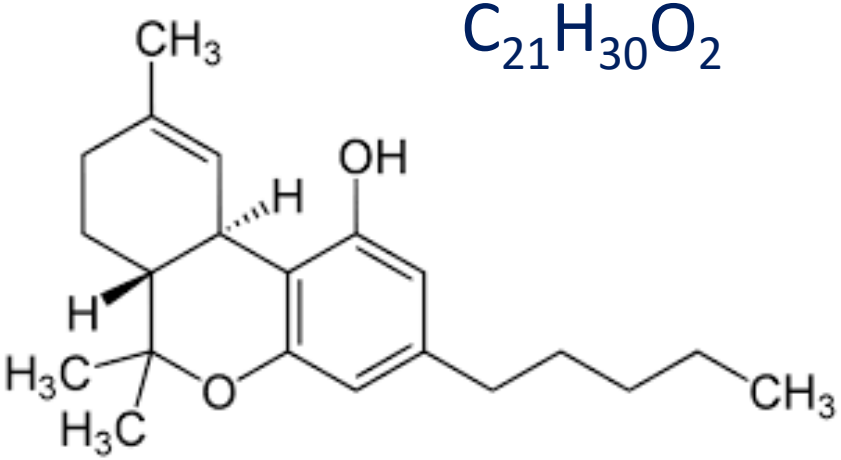


C_2H_5OH

Ethanol Blood Concentration

0 – 3,000,000 ng/mL

SOURCE: Jones et al. *J. Forensic Sci*. **41**, 1996.



$C_{21}H_{30}O_2$

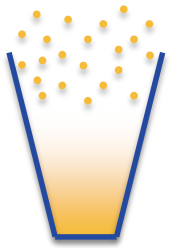
THC Blood Concentration

0 – 200+ ng/mL

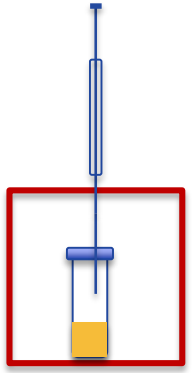
SOURCE: Huestis *Chem. Biodivers*. **4**, 2007.

Properties for Reliable Quantitation

Vapor Pressure



$$P_{SAT} = \frac{m \bullet R \bullet T}{M \bullet V}$$



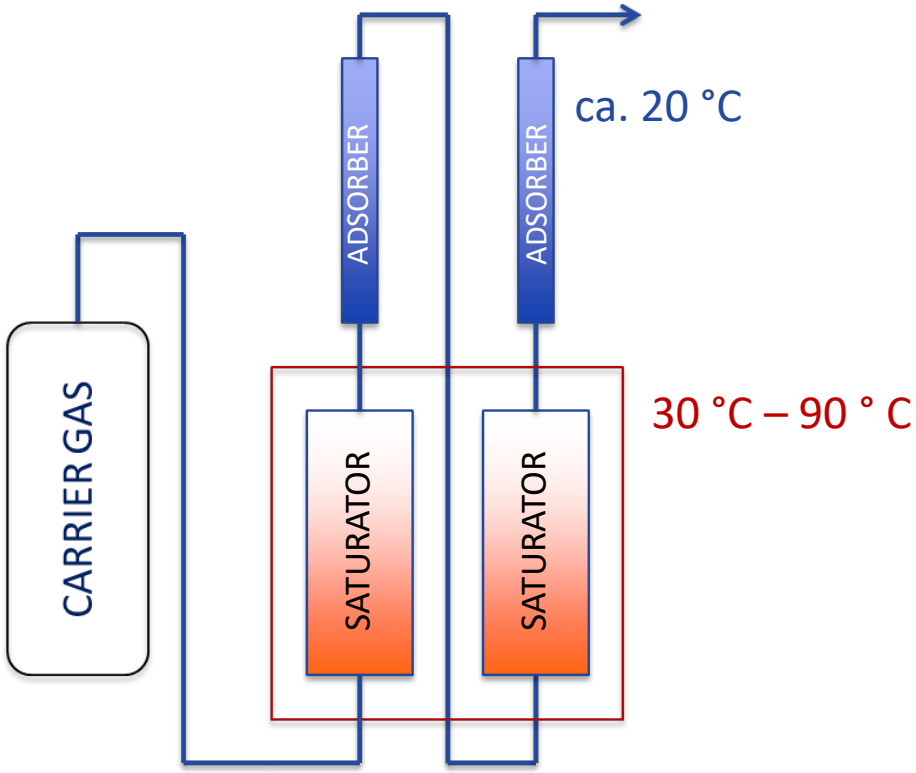
Partitioning

FAT ⟷ BLOOD ⟷ BREATH ⟷ SORBENT

$$K_{F/B} = \frac{[A]_{FAT}}{[A]_{BLOOD}} \qquad K_{B/A} = \frac{[A]_{BLOOD}}{[A]_{AIR}} \qquad K_{S/A} = \frac{[A]_{PDMS}}{[A]_{AIR}}$$

P_{SAT} – Standard Method

Concatenated Gas Saturation



Time = 1 – 8 weeks

Mononitrotoluene taggants
Widegren et al. *J. Chem. Eng. Data* **55**, 2010.

Low-volatility terpenes
Widegren et al. *Environ. Sci. Technol.* **44**, 2010.

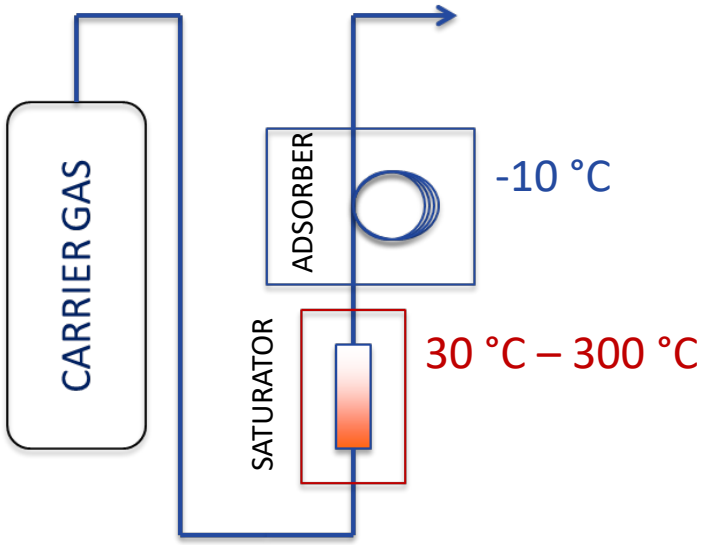
Internal eicosane control
Widegren et al. *Fuel* **90**, 2011

Influence of carrier gas
Widegren et al. *J. Chem. Eng. Data* **60**, 2015.

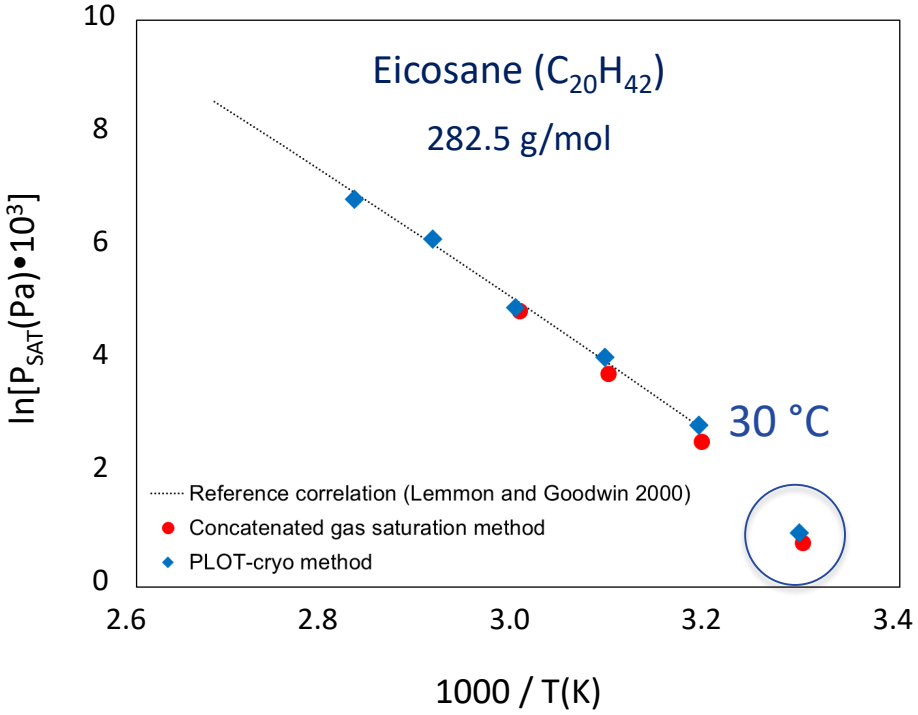
Anti-oxidants for unstable chemicals
Widegren et al. *J. Chem. Eng. Data* **62**, 2017.

P_{SAT} – Rapid Method

Porous Layer Open Tubular (PLOT) Cryoadsorption



Time = 1 – 2 hours



Tetradecane validation

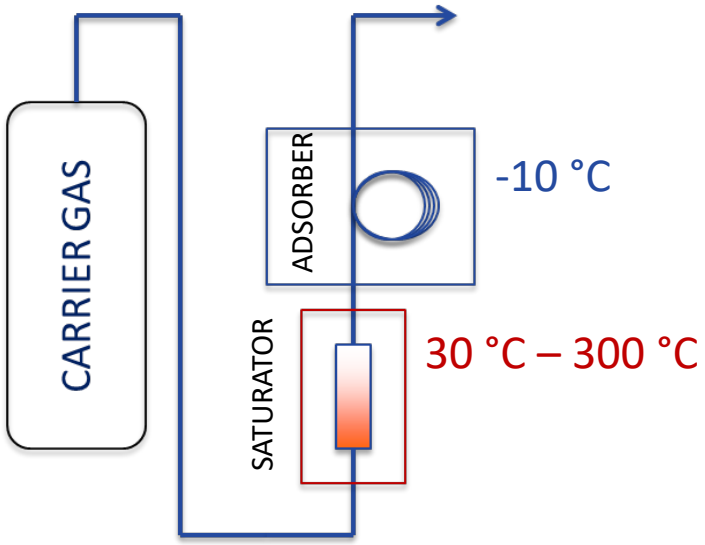
Lovestead et al. *Anal. Chem.* **82**, 2010.

Cannabinoids

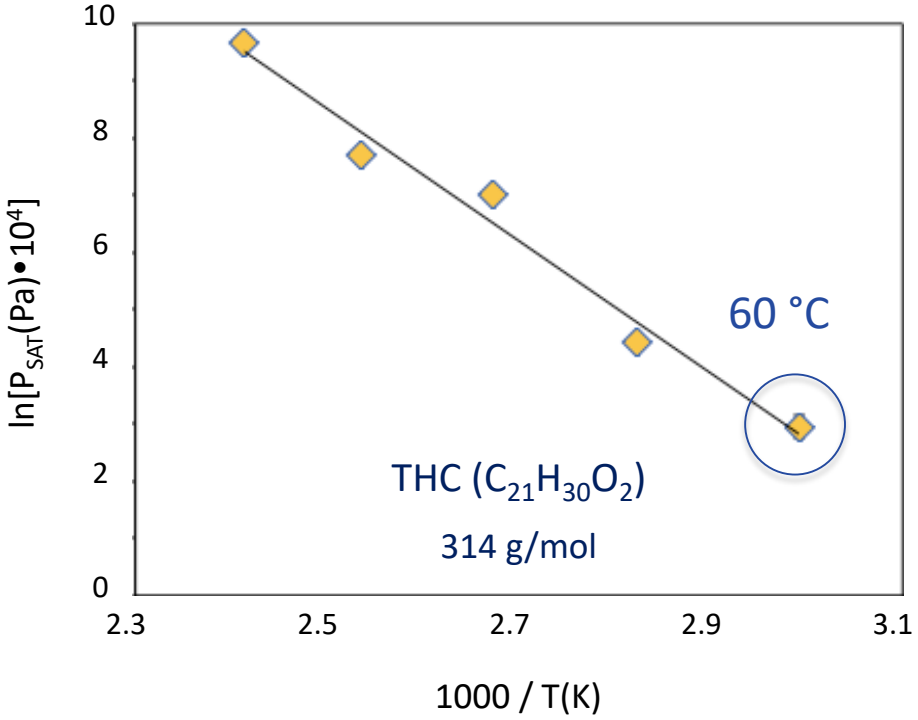
Lovestead et al. *Forensic Chem.* **5**, 2017.

P_{SAT} – Rapid Method

Porous Layer Open Tubular (PLOT) Cryoadsorption



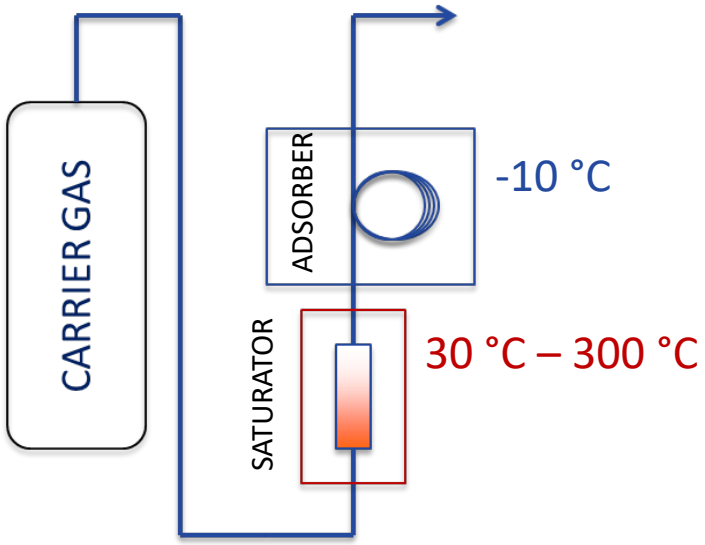
Time = 1 – 2 hours



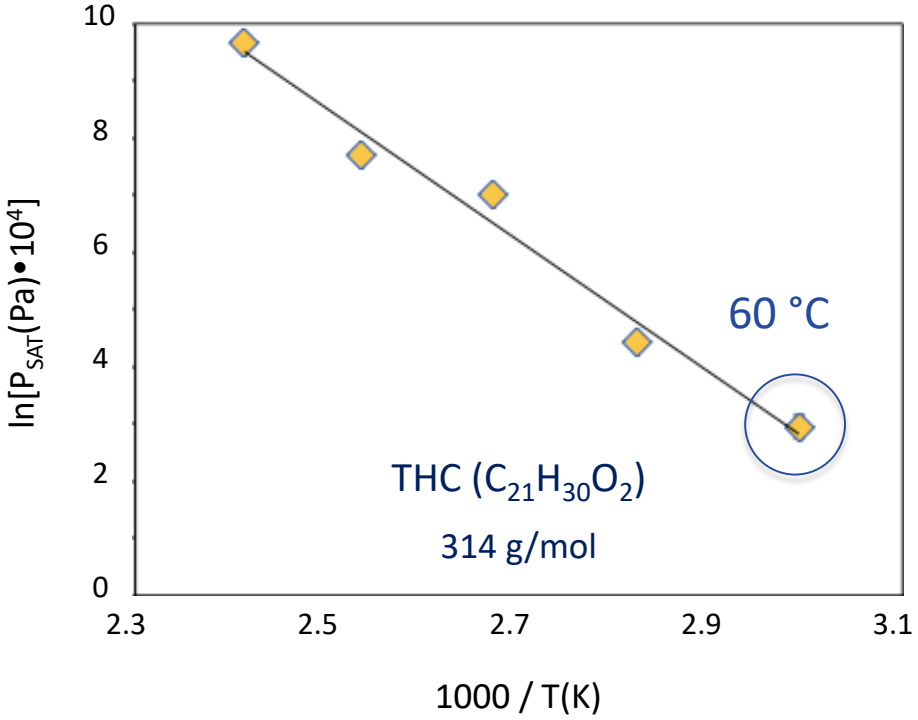
THC: 0.000115 Pa @ 40 °C

P_{SAT} – Rapid Method

Porous Layer Open Tubular (PLOT) Cryoadsorption



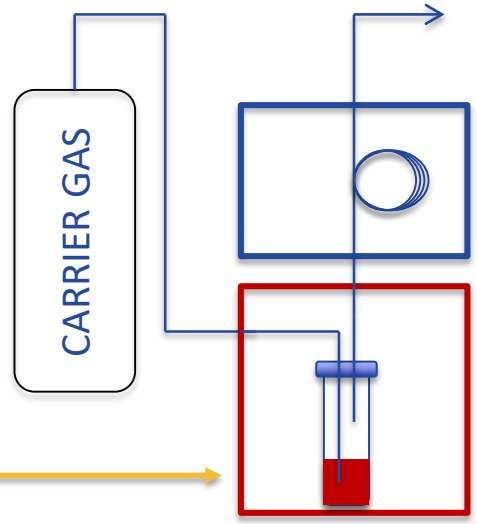
Time = 1 – 2 hours



THC: 0.000115 Pa @ 40 °C

Ethanol: 18,000 Pa @ 40 °C
SOURCE: NIST REFPROP Database

$K_{Blood/Air}$ – PLOT Cryoadsorption Method



Capture = Multiple Components
water may compete for
adsorption sites

TEMP: 30 °C – 40 °C

Sample = Mixture
human blood with cannabinoids
or terpenes

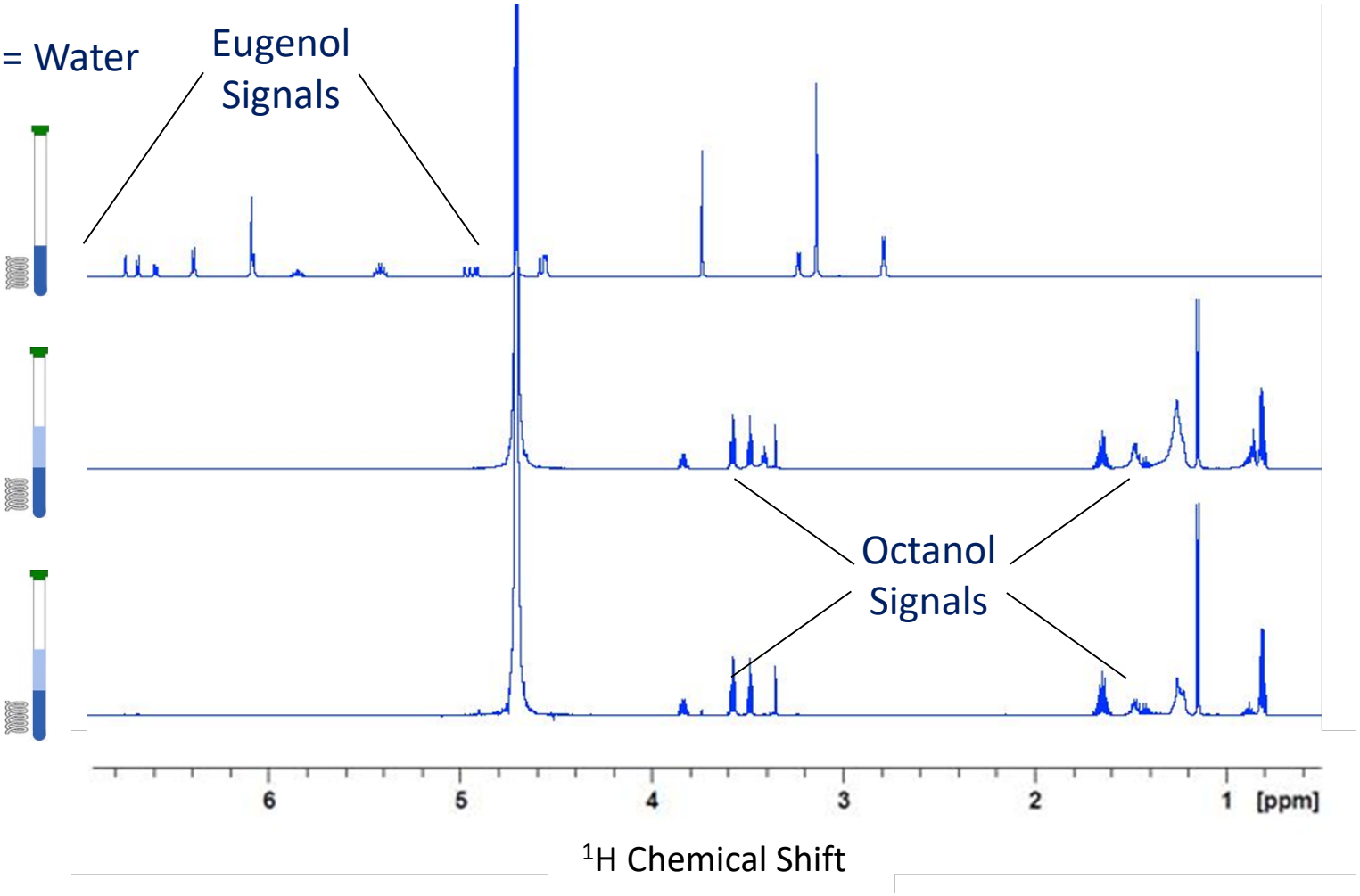
Can we capture and concentrate sufficient material at physiological temperatures?

How does ethanol impact blood/air partitioning?

$K_{Fat/Blood}$ – Non-Invasive NMR Method

Fat Surrogate = Octanol

Blood Surrogate = Water



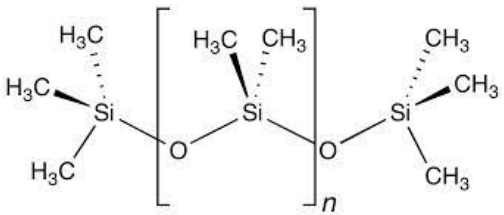
$K_{PDMS/AIR}$ – Model Feasibility

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

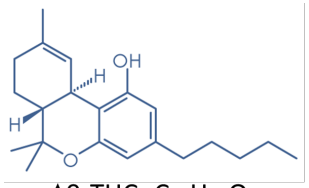
$$K = \frac{[A]_{PDMS}}{[A]_{AIR}}$$

$$n\ [moles] = K * V_S * C_O$$

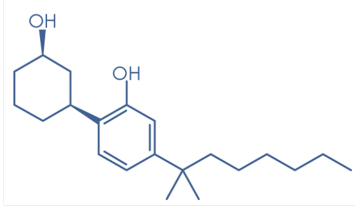
Partition Coefficient



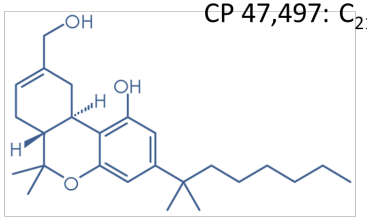
PDMS Structure



Δ9-THC: $C_{21}H_{30}O_2$



CP 47,497: $C_{21}H_{34}O_2$



HU-210: $C_{25}H_{38}O_3$

Synthetic Designer Drugs

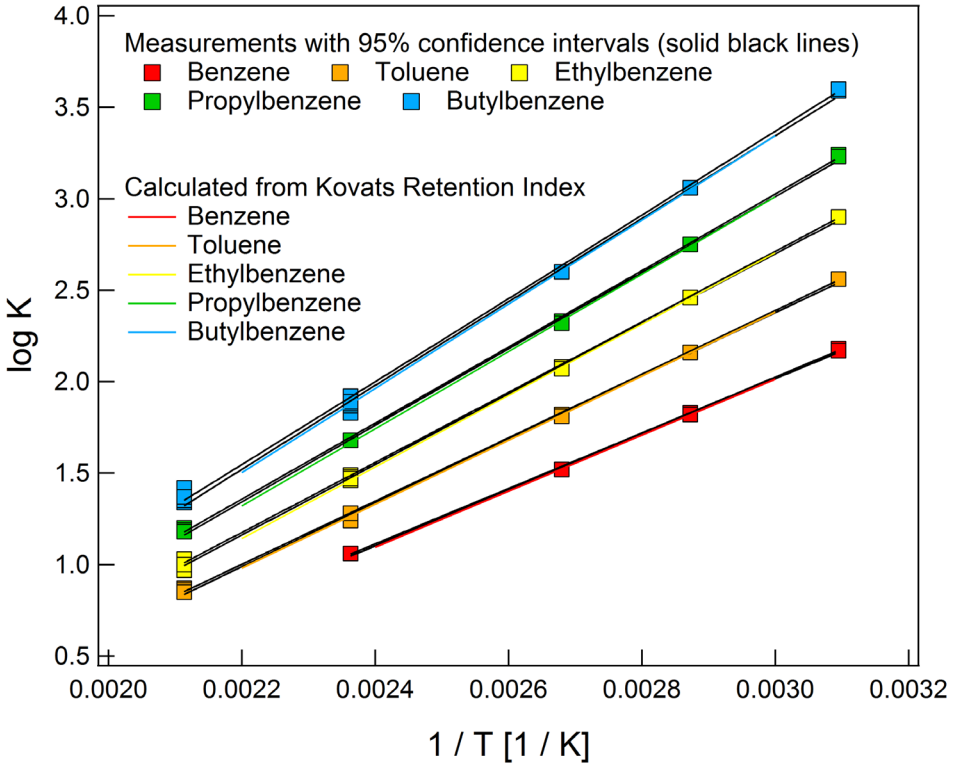
SPME Fiber

Capillary Microextraction of Volatiles (CMV)

$K_{PDMS/AIR}$ – Chemicals for Model

Functional Groups (18)

Non-Ring Groups	Ring Groups	Oxygen Groups
>C<	>C<	-OH (alcohol)
>CH-	>CH-	-OH (phenol)
$-CH_2-$	$-CH_2-$	-O-
$-CH_3$		
=C<	=C<	>C=O
=CH-	=CH-	-CHO
$=CH_2$		-COO-



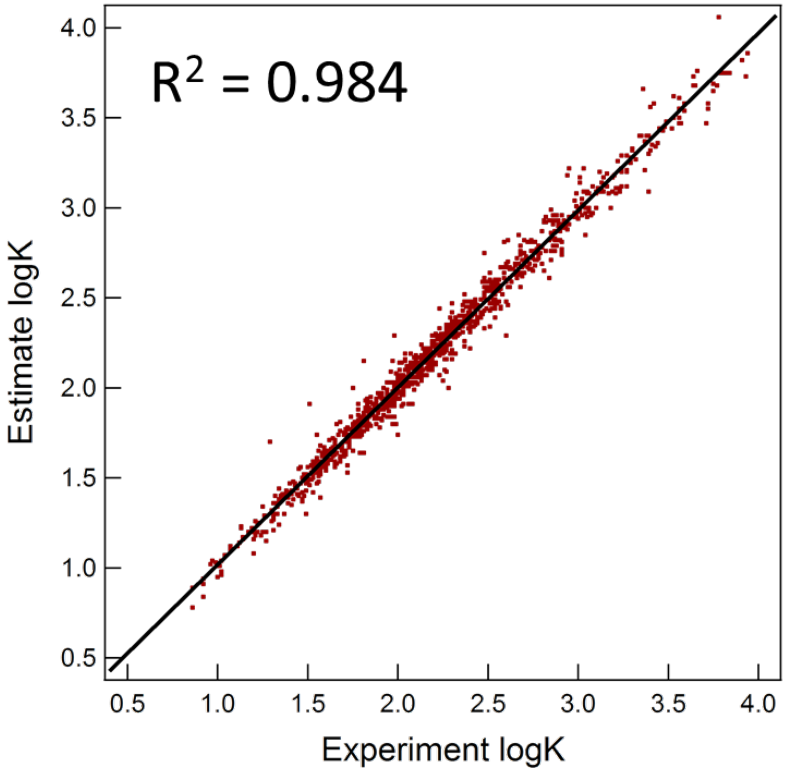
Training Set Requirements

1) Log K at three temperatures: 60 °C - 180 ° C

2) Follows van't Hoff Equation with $R^2 > 0.95$

$K_{PDMS/AIR}$ – Model Evaluation

Compare experimental values (x axis) with predicted values (y axis) for chemicals used to build model (N = 275).

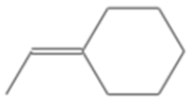


K. Jeerage et al. *20th Symposium on Thermophysical Properties*, June 2018.

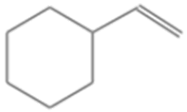
$K_{PDMS/AIR}$ – Model Predictions

Predict values for chemicals not used to build model.

Example: C_8 chemicals at 100 °C



ethylidene-cyclohexane



ethenyl-cyclohexane

2.112 + 0.002	Experimental Data	1.989 + 0.001
2.128	Model Prediction	1.996
0.8 %	% Difference	0.4%

K. Jeerage et al. *J. Breath Res*. (in preparation)

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

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Chris L. Suiter Jason A. Widegren

Boulder Cannabis Research Team

Please contact any of us to discuss working together or to discuss postdoctoral opportunities.

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