Disposition of Cannabinoids in Oral Fluid and Whole Blood after Vaporized and Smoked Cannabis

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Outline

- Background on “vaping”
- Study goals
- Pharmacokinetics (Ed Cone)
- Pharmacodynamics (Ryan Vandrey)
Background: “Vaping” Cannabis is Gaining Momentum and Widely Used

- Combustion of cannabis produces a similar profile of carcinogens as tobacco
- Vaporization eliminates these toxins and is perceived to be a “safe” alternative
- The technology of vaporization has led to sale of hundreds, if not thousands, of devices for vaping
- Devices can be portable or table-top
- Used with “raw” cannabis or extracts/oils
- Portable devices can be used to “conceal” cannabis use
Examples of “Vaping” Devices
Study Goals

Much of the science of cannabis is based on studies of combusted cannabis

- Profile the distribution of cannabinoids after vaporization in comparison to smoked cannabis
- Infrequent user population (no use in past 30 days; mean time since last use >1 year)
Participant Demographics

- Healthy adults; drug-free non-smokers
- 8F/9M
- 11 Caucasian/3 AA/3 “Other” (hispanic)
- Mean Age: 27 (+/- 6; range 22-44)
- Mean BMI: 26 (+/- 3; range 21-34)
Study Design

- Six 8-hr sessions
  - Vaporize raw cannabis containing 0, 10, 25 mg THC
  - Smoke raw cannabis containing 0, 10, 25 mg THC
  - Route clustered in 3 consecutive sessions, not blinded, random dose order within each route
- Blood, oral fluid, urine, PD measures
Cannabis Plant Material

- NIDA supplied cannabis
- 13% total THC
- 0.1% Cannabidiol (CBD)
- 0.8% Cannabinol (CBN)
Biospecimens

- Whole blood, oral fluid, and urine obtained post-dosing
- Blood and oral fluid analyzed by LC/MS/MS
- LOQ concentrations (ng/mL)
  - Blood: THC, 11-OH-THC, THCCOOH = 0.5
  - Oral fluid: THC = 1; THCCOOH = 0.02
Deposition of THC in Blood After Vaporization and Smoked Cannabis
Deposition of THC and Metabolites in Blood After Vaporization and Smoked Cannabis (25 mg)

**Vaped**

**Blood Cannabinoids**
- L/L BL THC Vaped 25
- L/L BL 11-OH-THC Vaped 25
- L/L BL THCCOOH Vaped 25
- L/L BL THCCOOH-GLUC Vaped 25

**Smoked**

**Blood Cannabinoids**
- L/L BL THC Smoked 25
- L/L BL 11-OH-THC Smoked 25
- L/L BL THCCOOH Smoked 25
- L/L BL THCCOOH-GLUC Smoked 25
Deposition of THC in Oral Fluid After Vaporization and Smoked Cannabis
Deposition of THCCOOH in Oral Fluid After Vaporization and Smoked Cannabis

Oral Fluid THCCOOH

- OF THCCOOH Vaped 25
- OF THCCOOH Smoked 25
- OF THCCOOH Vaped 10
- OF THCCOOH Smoked 10

Cutoff = 0.050 ng/mL
Deposition of CBN in Oral Fluid After Vaporization and Smoked Cannabis
Deposition of CBD in Oral Fluid After Vaporization and Smoked Cannabis

Oral Fluid CBD

- OF CBD Vaped 25
- OF CBD Smoked 25
- OF CBD Vaped 10
- OF CBD Smoked 10

ng/mL

Hours
Pharmacokinetic Conclusions

- Vaporization of cannabis plant provides higher blood levels of THC than by the smoked route
- Oral fluid concentrations after vaporization appeared to be equivalent to smoking
- THCCOOH in oral fluid was erratic and often negative
Pharmacodynamic Measures
Pharmacodynamic Measures

Do you feel a drug effect?

not at all  
Extremely

2
VAS: “Drug Effect”

**10 mg THC**
- Smoke*
- Vaporized*

**25 mg THC**
- Smoke*
- Vaporized*

**Plot Details:**
- VAS (mm) on the y-axis.
- Time (Hours) on the x-axis.
- Graphs show the effect of THC at 10 mg and 25 mg levels over time, comparing smoke and vaporized methods.
Heart Rate

10 mg THC

25 mg THC

Beats Per Minute Δ from Baseline

Time (Hours)

Smoke *
Vaporized *

BL 0.16 0.5 1 1.5 2 3 4 5 6 8

BL 0.16 0.5 1 1.5 2 3 4 5 6 8
Paced Serial Addition Task

10 mg THC

Number Correct Δ from Baseline

Time (Hours)

25 mg THC

Number Correct Δ from Baseline

Time (Hours)
Digit Symbol Substitution Task

10 mg THC

25 mg THC

Number Correct Δ from Baseline

Time (Hours)

Smoke
Vaporized

BL 0.5 1 1.5 2 3 4 5 6 8

BL 0.5 1 1.5 2 3 4 5 6 8

*
Divided Attention Task

10 mg THC

25 mg THC

Distance from Target Δ from Baseline

Time (Hours)

Smoke

Vaporized *

Smoke

Vaporized *
Blood THC vs VAS Drug Effect at 25mg THC dose
Blood THC vs VAS Drug Effect at 25mg THC dose

Blood THC

Drug Effect

[Graph showing Blood THC levels and VAS effects over time for different dosing methods: Smoke, Vape, Oral.]
# PK/PD Correlations at 25mg THC dose

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<th></th>
<th>Blood THC</th>
<th>Blood 11-OH-THC</th>
<th>Blood THCCOOH</th>
<th>OF THC</th>
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<tr>
<td><strong>Smoked</strong></td>
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<tr>
<td>Drug Effect</td>
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<td>−0.03</td>
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<tr>
<td><strong>Vaporized</strong></td>
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<tr>
<td>Drug Effect</td>
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<td>0.14</td>
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</table>
Additional Observations

- Higher ratings of paranoia, dry mouth, red/irritated eyes following vaporization
- 2 instances of vomiting, one in each route of admin at 25mg dose
- 1 instance of “hallucinatory” effects at 25mg dose when vaporized
Limitations

- Only infrequent cannabis users enrolled
- Limited range of doses
- Only one type of cannabis (high THC, low CBD) studied
- Other routes of administration and product types still need to be evaluated (transdermal, suppository, oils/concentrates, etc.)
Summary

- Vaporization appears to be a more efficient method of delivery (greater blood THC and subjective drug effects)
- Different time course across assessments
  - Blood THC and HR shorter than subjective DE and cognitive effects
- Correlations btw PK and PD modest at best
- THC in blood and oral fluid returned to zero within 4 hours of exposure