Vaporization as a Smokeless Cannabis Delivery System:

A Pilot Study

Donald I. Abrams, M.D[1,2,4]., Hector P. Vizoso, R.N[1,4]., Starley B. Shade, M.P.H., Ph.D.c.[1,4], Cheryl Jay, M.D.[3,5], Mary Ellen Kelly, M.P.H.[1,2,4], and Neal L. Benowitz, M.D[4,6].

From the Community Consortium, Positive Health Program[1], Hematology-Oncology[2] and Neurology[3] Divisions at San Francisco General Hospital, Department of Medicine[4] and Neurology[5] and the Division of Clinical Pharmacology and Experimental Therapeutics[6] at the University of California, San Francisco.

Correspondence: Donald I. Abrams, M.D.

San Francisco General Hospital

Ward 84, 995 Potrero Avenue

San Francisco, CA 94110

Phone: 415-476-4082 Fax: 415-502-2991

Email: dabrams@php.ucsf.edu

Word Count: Abstract: 248 Body of Text: 3210

Acknowledgements: Supported by the University of California Center for Medicinal Cannabis Research and NIH Grant 5-MO1-RR00083.

ABSTRACT

Context: Although cannabis may have potential therapeutic value, inhalation of a combustion product is not a desirable delivery system.

Objective: To investigate vaporization using the Volcano® device as an alternative means of delivery of inhaled *Cannabis sativa,* to characterize preliminary pharmacokinetic and pharmacodynamic effects and to determine whether vaporization may be an appropriate system for use in clinical effectiveness studies.

Design, Setting and Participants: Eighteen healthy subjects were admitted to the inpatient General Clinical Research Center at San Francisco General Hospital to compare the delivery of cannabinoids by vaporization of marijuana to marijuana smoked in a standard cigarette. One dose (1.7, 3.4 or 6.8% tetrahydrocannabinol) and delivery system (smoked cannabis cigarette or vaporization system) was randomly assigned for each of the six study days.

Main Outcome Measures: Plasma concentrations of delta-9-tetrahydrocannabinol (THC), resulting from inhalation of cannabis by vaporization versus smoking. Expired carbon monoxide was measured to evaluate exposure to gaseous toxins. Physiologic and neuropsychologic effects were evaluated.

Results: 18 participants (15 men and 3 women) completed the 6-day inpatient study. The peak plasma concentrations of THC after inhalation of vaporized cannabis were similar to those of smoked cannabis. Carbon monoxide levels were substantially reduced with vaporization. Neuropsychologic effects were equivalent and participants expressed a clear preference for vaporization as a delivery method. No adverse events were observed.

Conclusion: Vaporization of cannabis is a safe and effective mode of delivery of THC. Further trials of the clinical effectiveness of cannabis could utilize vaporization as a smokeless delivery system.

INTRODUCTION

The Institute of Medicine report on Marijuana as Medicine published in 1999 concluded that "scientific data indicate the potential therapeutic value of cannabinoid drugs, primarily THC, for pain relief, control of nausea and vomiting, appetite stimulation; smoked marijuana, however is a crude THC delivery system that also delivers harmful substances" (1). The report recommended that clinical trials of cannabinoid drugs for symptom management should be conducted with the goal of developing rapid onset, reliable, and safe delivery systems. While acknowledging therapeutic potential, the IOM report stressed that cannabis is not a completely benign substance, but a powerful drug with a variety of effects, but "except for the harms associated with smoking, the adverse effects are within the range of those tolerated for other medications." The report comments that "because of the health risks associated with smoking, smoked cannabis should generally not be recommended for long-term medical use. Nonetheless, for certain patients, such as the terminally ill or those with debilitating symptoms, the long-term risks are not of great concern." The Institute of Medicine sends a clear message suggesting that smoking is not a desirable delivery system for the potential therapeutic effects of cannabis.

Cannabis vaporization is a technology for delivering inhaled THC and other cannabinoids while reducing toxic byproducts of smoked cannabis primarily caused by combustion (2, 3). By heating cannabis to a temperature between 180° to 200° C, it is possible to vaporize the cannabinoids that reside on the trichomes on the surface of cannabis flowers and leaves, while avoiding combustion (which occurs at 230° C and above) and attendant smoke toxins. Vaporization is a relatively new technology. Various vaporizer designs are currently under development. The feasibility of vaporization of THC has been demonstrated in a series of laboratory studies involving different vaporizer designs (2). An electric vaporizer was shown to

release substantial amounts of the THC while producing no measurable amounts of the benzene, toluene, and naphthalene, which are generated when marijuana is smoked. Reductions in carbon monoxide and tar generation were also observed under vaporization compared to smoking. While no measurements were made of other smoke toxins, it is quite possible that the vaporizer eliminated or substantially reduced the polycyclic aromatic hydrocarbons and other combustion-generated toxins commonly found in cannabis smoke, since they form at the higher temperatures of pyrolysis.

A recent evaluation of the Volcano® vaporizer device used herbal cannabis or pure cannabinoid ethanolic solution preparations to test the efficacy and reproducibility of THC delivery into the balloon receptacle (4). Cannabinoids recovered from vapor phase inside the balloon by condensation onto glass fiber filter were analyzed by high-pressure liquid chromatography or nuclear magnetic resonance. The results validated the Volcano® vaporizer as an efficient and reproducible mode of delivery of Δ-9-THC. On average, 54% of the applied dose of THC was recovered in the balloon receptacle.

The present study investigated vaporization using the Volcano® device compared to smoked cannabis. This is first pharmacokinetic and pharmacodynamic evaluation conducted in humans to determine whether the Volcano® may be an appropriate system for use in clinical effectiveness studies.

METHODS

Study Patients

Participants were healthy adults between the ages of 21-45 who were current cannabis users and had smoked cannabis within the past 30 days but in an amount totaling less than 10

cannabis cigarettes or the equivalent. Subjects with active substance abuse (e.g., recurrent or continuous drug and/or alcohol use) or diagnosed with marijuana dependence as defined in DSM-IV code #304.30. were excluded. Subjects were required to abstain from smoking cannabis for 48 hours prior to their admission into the General Clinical Research Center (GCRC) at San Francisco General Hospital (SFGH). The study was approved by the Institutional Review Board at the University of California San Francisco, the Research Advisory Panel of California, the Drug Enforcement Administration, the Food and Drug Administration, and the National Institute on Drug Abuse. Written informed consent was obtained from all patients. The trial was monitored by an independent Data Safety Monitoring Board (DSMB) established by the University of California Center for Medicinal Cannabis Research.

Study Medication

The National Institute on Drug Abuse provided pre-rolled cannabis cigarettes, weighing on average 0.9 gm and containing 1.7%, 3.4% and 6.8% delta-9- tetrahydrocannabinol, respectively. The cigarettes were kept in a locked and alarmed freezer until they were dispensed to a locked freezer in the San Francisco General Hospital General Clinical Research Center where the inpatient study was conducted. The cigarettes were bisected; one half to be smoked and the contents of the other half to be vaporized. The half cigarettes were re-hydrated in a humidifier overnight prior to their use. Patients were housed in a room with a fan ventilating to the outside. Research staff monitored patients during smoking sessions, weighed the cannabis cigarettes immediately before and after they were administered to patients, and returned all leftover material to the pharmacy. To maximize standardization of inhaled doses, patients followed the Foltin uniform puff procedure where inhalation for five seconds is followed by a 10

second breath hold, then exhalation; the entire process being repeated after 45 seconds (5). Study participants smoked or vaporized cannabis once a day.

The Vaporizer Device

The Volcano® vaporizer was obtained from Storz & Bickel GmbH & Company (Tuttlingen, Germany) and was employed according to the manual provided. The device works as a vaporizer that evaporates the active substances or aromas from plant material by using a hot air flow (Figure 1). Cannabis placed in the filling chamber is heated by the device to 190° C. The vaporized compounds are collected in the inflatable, detachable bag fitted with a mouthpiece and a one-way valve that allows the vapor to remain in the balloon until inhalation. It required two to three balloon inflations to vaporize each half cigarette. Subjects also followed the Foltin puff procedure when inhaling the vaporization product.

Study Design and Procedures

The study was a 6-day "proof of concept" pilot study to investigate the delivery of cannabinoids by way of vaporization of cannabis compared to cannabis smoked in a standard cigarette. The inpatient setting permitted us to measure plasma THC levels over time and to rigorously assess the primary and secondary outcome variables in a controlled clinical environment.

Screening Visit

Once a subject for the protocol had been identified, details of the study were carefully discussed and the subject was asked to read and sign a consent form. Subjects were asked questions about their medical history including psychiatric illness and substance abuse. Subjects were asked to abstain from smoking or ingesting cannabis 48 hours prior to their hospitalization based on our prior studies which indicated that after 24 hours of abstinence, plasma THC levels

are sufficiently low so that the concentration-time curve could be determined after the experimental exposure (6).

GCRC Inpatient Hospitalization (Days 1-6)

Subjects inhaled three THC doses of cannabis (1.7, 3.4 and 6.8 percent) as smoked cigarettes and three as vaporized product using the Volcano® device. Half of one cigarette was inhaled via one of the two delivery systems on each of the six in-patient GCRC days. Blood was drawn at 2 minutes, 30 minutes, one hour, three hours, and six hours after smoking on each of the six inhalation days to measure the concentrations of THC. Expired carbon monoxide was measured using the Ecolyzer® prior to inhalation, then 2, 30, 60, 180, and 360 minutes after inhalation.

Subjects rated the subjective "high" they experienced using a 100 mm visual analog scale anchored by "none" and "highest ever". On Day 5 prior to discharge subjects were asked to choose which inpatient day they preferred. Subjects were asked to rate their preferences from 1-5 with 1 indicating very satisfied and 5 indicating very dissatisfied.

All adverse events were spontaneously reported by the subject or observed by the study personnel and/or GCRC nursing staff, documented along with any medical intervention, and evaluated according to standardized criteria in terms of severity, frequency, duration and relationship to study drug. Adverse events were graded using the NIH Division of AIDS table for scoring severity of adult adverse experiences (7).

Randomization

We used a Latin-square randomization scheme to ensure balance in the order assignments. Randomization was computer-generated, and dosing was managed by a research pharmacist. Subjects and study personnel were blinded to the dose.

Statistical Analysis

The 18 patient target sample size was based on a standardized effect size to calculate sample size and power for the study. With a sample of 18 subjects, we had an 80% power to detect a true standardized effect size (E/S) of 0.70, using an alpha of 0.05, where E is the effect size and S is the standard deviation of the mean of the paired differences (8, 9). This calculation assumes use of a paired t-test using data at a single concentration.

The primary outcome was the within-person difference in the six-hour area under the curve (AUC) for tetrahydrocannabinol, comparing the vaporizer with smoking cannabis cigarettes. AUC was computed using the linear trapezoidal method, assuming zero THC at baseline. We were able to make this assumption based on our prior research which observed undetectable levels of THC eight hours after smoking in all patients (6). For each mode of administration and THC concentration, we plotted the mean and 95% confidence intervals (CI) of the observed values at each time point and estimated the mean AUC and maximum concentration (with 95% confidence intervals and coefficient of variation). We compared the within-person difference in six-hour AUC for THC using vaporization compared to smoking using paired t-tests for each concentration of THC. To assess whether the order of randomization impacted these observed differences, we also created mixed effect models to assess paired differences in AUC for THC by concentration of THC controlling for randomization (vaporizer vs. smoking) and study day.

To explore possible dose-dependent changes in bioavailability we also compared the numbers of puffs taken during each session, plasma THC AUC normalized by THC dose, as well as AUC per puff during vaporization and smoking for each concentration of THC. As above, for each mode of administration and THC concentration we computed the group mean, 95%

confidence interval and coefficient of variation. The paired difference in values observed during vaporization and smoking of cannabis cigarettes were compared at each concentration of THC using paired t-tests. Dose-dependent changes in bioavailability were assessed by including concentration of THC (in addition to randomization and study day) in mixed effect models for number of puffs, plasma THC AUC normalized by THC dose, and AUC per puff.

We also explored the potential bioequivalence of vaporization and smoking of cannabis cigarettes. We compared the within-person ratio of six-hour AUC for THC using vaporization compared to smoking. The median ratio (with 90% confidence intervals) was calculated for each THC concentration. Non-parametric assessment was necessary due to skewed distributions in these values. A ratio of 1.0 is considered completely bioequivalent. The FDA determines two drugs or modes of administration to be bioequivalent if the estimate of the ratio of the AUC lies between 0.80 and 1.25. To establish bioequivalence, the 90% confidence intervals for the ratios of the AUCs must be fully contained within this interval (10).

We compared the observed values for expired carbon monoxide (CO) and self-reported high using similar methods. We plotted the mean and 95% confidence intervals at each time point for each mode of administration and THC concentration. We also computed the mean, 95% CI and coefficient of variation (CV) for the six-hour AUC for CO, the AUC per puff and the six-hour AUC for self-reported high for each mode of administration and THC concentration. We compared the paired differences in these values using paired t-tests and mixed models controlling for randomization and study day.

RESULTS

Baseline characteristics of study subjects

A total of 68 patients were screened for eligibility between August 2004 and May 2005 (see Figure 2). Of these, 47 were not enrolled (33 were unavailable to commit to a 6-day hospitalization, 10 were excluded as a result of their medical history or concurrent illness, and 4 because of active substance abuse). Twenty-one patients were randomly assigned; however, three patients did not complete the intervention of the study phase (1 for non adherence to GCRC rules of comportment, 1 for acute Influenza and 1 withdrew consent) leaving 18 total patients for analysis.

Participants were predominately male (83%), Caucasian (72%), with some college education (94%). All the participants were active marijuana users (median 5-6, range 3-10 marijuana cigarettes in the past 30 days). None had used the Volcano® device, although one participant had previously experienced vaporized marijuana using a similar device.

Primary Outcome Measure

The mean and 95% confidence intervals for the observed plasma concentrations of THC for each concentration of THC using both vaporization and smoking are presented in Figure 3. The vaporizer resulted in higher plasma THC levels compared to smoked marijuana at 30 minutes ($p=0.023$, $p=0.018$, and $p=0.026$ for THC concentrations of 1.7%, 3.4% and 6.8% respectively using paired t-tests) and one hour ($p=0.008$, $p=0.049$, and $p=0.067$ for THC concentrations of 1.7%, 3.4% and 6.8% respectively using paired t-tests) at each concentration. The two modalities were not significantly different at different product concentrations (1.7%, 3.4% or 6.8% THC) in the overall six-hour area under the plasma THC concentration-time curve, or for the peak THC concentrations measured at two minutes (Table 1).

There was evidence of decreasing in bioavailability with increasing concentrations of THC. The plasma THC AUC derived from the vaporizer normalized for the dose of THC was highest at 1.7% THC and was progressively lower at higher THC concentrations ($p<0.001$), suggesting higher bioavailability at lower THC concentrations..

There was also some evidence of titration of intake of THC with increasing concentrations of THC. The number of puffs taken using both vaporized and smoked marijuana tended to decrease with increasing concentrations of THC ($p=0.25$). The decrease in puffs was significantly greater in the smoked arm compared to the vaporized arm ($p=0.029$). As expected, the amount of THC (AUC) inhaled per puff increased with increasing concentrations of THC ($p<0.001$ for increase in THC% using mixed model).

When we computed the within-person ratio of the AUC for THC using 1.7% THC cannabis cigarettes, we found that the use of a vaporizer resulted in AUCs for THC that were almost twice as high as those when smoking cannabis (median ratio 1.99, 90% CI=1.04, 3.27). This difference was not observed for other THC concentrations (median ratio = 0.90; 90% CI=0.58, 1.70 for 3.4% THC and median ratio = 1.20; 90% CI=0.89, 2.07 for 6.8% THC). We did not observe any statistically significant differences ($p<0.05$) in the within-person ratio of plasma THC with vaporizer versus smoked marijuana at any THC concentration.

Secondary Outcome Measures

The levels of exhaled carbon monoxide increased very little after vaporization (see Figure 4; mean = -1.9; 95% CI = -4.4, 0.6 for 1.7% THC; mean = -1.8; 95% CI = -3.7, 0.7 for 3.4% THC; and mean = -0.5; 95% CI = -1.9, 0.9 for 6.8% THC), while there was a substantial increase after smoking marijuana (mean = 15.5; 95% CI = 11.0, 20.1 for 1.7% THC; mean = 11.9; 95% CI = 6.8, 17.1 for 3.4% THC; mean = 7.0; 95% CI=4.0, 10.0 for 6.8% THC). This difference

was statistically significant ($p<0.001$) at each concentration of THC). The increase in carbon monoxide decreased during smoking ($p=0.003$ for trend), but not vaporization ($p=0.25$) with increasing THC concentration. The expired CO AUC per puff is an indicator of how much smoke is inhaled per puff for the smoked marijuana. The CO AUC per puff decreased progressively (1.7% THC: mean = 2.8; 95% CI = 2.2, 3.3; 3.4% THC: mean = 2.1; 95% CI = 1.1, 3.0; 6.8% THC: mean = 1.2; 95% CI = 0.6, 1.9; $p=0.003$ for trend), consistent with taking smaller puffs with increasing THC concentrations in the marijuana.

Subjective and Safety Observations

Self-reported high did not differ during vaporization compared to smoking overall (six-hour AUC) or at any observation after consumption of cannabis (Figure 5). Self-reported high did increase significantly during both vaporization and smoking with increasing concentrations of THC ($p<0.001$).

While blinded with regard to dose, 8 participants selected the day they received 3.4% THC (7 vaporized, 1 smoked) as their most preferred treatment day; 4 selected the day they received 6.8% THC via vaporization and 6 had no treatment day preference. Overall vaporization was the preferred method of administration by 14 participants, smoking was preferred by 2, and 2 reported no preference. During the course of the study no adverse events were reported.

DISCUSSION

Our study provides novel data on the absorption of THC from marijuana dosed via the Volcano® vaporizer system compared to smoking marijuana cigarettes. We found that THC levels were generally similar for the two types of dosing, although there was a marginally higher

within-subject exposure to THC for the vaporizer compared to smoking at the lowest dose level. The vaporizer also was associated with higher plasma THC concentrations at 30 minutes and 1 hour compared to smoking at each concentration, suggesting that absorption was faster with the vaporizer.

Bioequivalence criteria developed for drugs require that the confidence intervals for the ratios of AUC for the test and reference products be between 80 to 125% to be judged bioequivalent (10). Using these criteria, we were not able to establish the bioequivalence of vaporization and smoking of marijuana. A much larger study would be needed to establish bioequivalence in this setting.

Of interest was that the systemic dose of THC, as estimated by the plasma AUC, varied with dose; the dose of THC normalized for concentration of THC in the marijuana, was greater at lower compared to higher levels of THC. This observation is consistent with the concept of titration of THC intake. That is, smokers adapted their smoking behavior to obtain desired levels of THC from the particular delivery system – inhaling more effectively at lower concentrations compared to higher concentration THC dose levels.

While smoking marijuana increased carbon monoxide levels as expected for inhalation of a combustion product, there was little if any increase in carbon monoxide after inhalation of THC from the vaporizer. This indicates little or no exposure to gaseous combustion toxins. Combustion products are harmful to health and reflect a major concern about the use of marijuana cigarettes for medical therapy as expressed by the Institute of Medicine. Although we did not measure other combustion products such as polycyclic aromatic hydrocarbons and oxidant gases, the observation of little or no carbon monoxide exposure suggests little or no exposure to these other compounds. The vaporizer was well tolerated, with no reported adverse

effects. Most subjects preferred the vaporizer compared to marijuana smoking, supporting its potential for medical therapy. Thus the Volcano® seems to be a safer and acceptable way to dose with THC than smoking marijuana cigarettes.

In summary, we provide data indicating that the bioavailability of THC delivered by the Volcano® vaporizer is comparable from that of marijuana cigarettes. Vaporization of marijuana does not result in exposure to combustion gases, and therefore is expected to be much safer than smoking marijuana cigarettes. The vaporizer was well tolerated and preferred by most subjects compared to marijuana cigarettes. The Volcano® device is an effective and apparently safe vehicle for THC delivery, and warrants further investigation in clinical trials of THC for medicinal purposes.

ACKNOWLEDGEMENTS

We are grateful to our study participants; the General Clinical Research Center nursing staff for their meticulous adherence to protocol; to Sheila Huang, Pharm.D.; Peter Bacchetti, Ph.D. at the UCSF Department of Biostatistics and Epidemiology for his assistance in creating the randomization scheme; and to Heather Bentley at the University of California Center for Medicinal Cannabis Research for her invaluable assistance with regulatory affairs, data quality management and interaction with the Data Safety Monitoring Board.

REFERENCES

1. Joy JE, Watson SJ, Benson JA (eds). Institute of Medicine. Marijuana and Medicine: Assessing the Science Base. National Academy Press, Washington, 1999.
2. Gieringer D. Cannabis vaporization: a promising strategy for smoke harm reduction. Journal of Cannabis Therapeutics, 1:3-4, 2001.
3. Russo E. An interview with Markus Storz: June 19, 2002. Journal of Cannabis Therapeutics, 3:67-78, 2003.4.
4. Hazekamp A, Ruhaak R, Zuurman L, van Gerven J, Verpoorte R. Evaluation of a vaporizing device (Volcano®) for the pulmonary administration of tetrahydrocannabinol. J. Pharm Sci, 95:1308-1317, 2006.
5. Foltin R, Fischman M, Byrne M. Effects of smoked marijuana on food intake and body weight of humans living in a residential laboratory. Appetite 1988; 25:577-582.
6. Abrams DI, Hilton JF, Leiser RJ, Shade SB, Elbeik TA, Aweeka FT, Benowitz NL, et al. Short-term effects of cannabinoids in patients with HIV-1 infection. Ann Int Med 2003; 139:258-266.
7. NIH Division of AIDS Table for Grading Severity of Adult Adverse Experiences, August 1992. Available at http://rcc.tech-res-intl.com/tox_tables.htm. Accessed August 28, 2006.
8. Dupont, WD, Plummer, WD. Power and Sample Size Calculations: A Review and Computer Program Controlled Clinical Trials, 1990; 11:116-28.
9. Hulley, SB, Cummings, SR. Designing Clinical Research. Baltimore: Williams and Wilkins; 1988.

10. Center for Drug Evaluation and research. Guidance for industry: Bioavailability and bioequivalence studies for orally administered drug products- general considerations. Revision 1, March 2003. Available at http://www.fda.gov/cder/guidance/index.htm . Accessed August 29, 2006.

Table 1. THC pharmacokinetics: summary statistics for THC AUCs, C_{max} and puffs taken[a]

THC concentration	PK parameter	Mode of administration	No.	Mean	95% CI	CV (%)	t-test p≤
1.7%	**AUC**	**Vaporizer**	18	46.0	34.9, 57.1	48.6	0.23
		Smoked	18	37.3	27.1, 47.5	55.0	
	C_{max}	**Vaporizer**	18	73.4	53.2, 93.7	55.5	0.28
		Smoked	18	60.3	45.1, 75.4	50.5	
	Puffs	**Vaporizer**	18	10.1	8.8, 11.3	24.9	0.001
		Smoked	18	6.1	4.8, 7.3	41.0	
	AUC/THC %	**Vaporizer**	18	27.1	20.5, 33.6	48.6	0.23
		Smoked	18	22.0	16.0, 28.0	55.0	
	AUC/Puff	**Vaporizer**	18	5.0	3.5, 6.5	61.6	0.16
		Smoked	18	7.0	4.4, 9.6	73.5	
3.4%	**AUC**	**Vaporizer**	18	69.8	52.9, 86.6	48.6	0.69
		Smoked	18	75.6	49.9, 101.3	68.4	
	C_{max}	**Vaporizer**	18	112.5	84.5, 140.4	49.9	0.51
		Smoked	18	126.4	92.2, 160.5	54.3	
	Puffs	**Vaporizer**	18	9.2	8.2, 10.1	20.6	0.001
		Smoked	18	5.9	4.9, 6.8	32.4	
	AUC/THC %	**Vaporizer**	18	20.5	15.6, 25.5	48.6	0.69
		Smoked	18	22.2	14.7, 29.8	68.4	
	AUC/Puff	**Vaporizer**	18	7.6	6.0, 9.2	43.2	0.006
		Smoked	18	13.3	9.6, 17.0	56.1	
6.8%	**AUC**	**Vaporizer**	18	81.3	60.0, 102.6	52.5	0.65
		Smoked	18	75.1	56.3, 93.9	50.2	
	C_{max}	**Vaporizer**	18	142.3	100.7, 183.8	58.7	0.81
		Smoked	18	135.7	98.8, 172.6	54.6	
	Puffs	**Vaporizer**	18	8.6	7.7, 9.4	19.7	0.003
		Smoked	18	6.4	5.3, 7.6	35.4	
	AUC/THC %	**Vaporizer**	18	12.0	8.8, 15.1	52.5	0.65
		Smoked	18	11.0	8.3, 13.8	50.2	
	AUC/Puff	**Vaporizer**	18	10.1	7.3, 12.9	56.6	0.27
		Smoked	18	19.1	2.4, 35.9	175.9	

[a] AUCs in ng* h/ml; C_{max} values in ng/ml

Figure 1: Volcano Apparatus

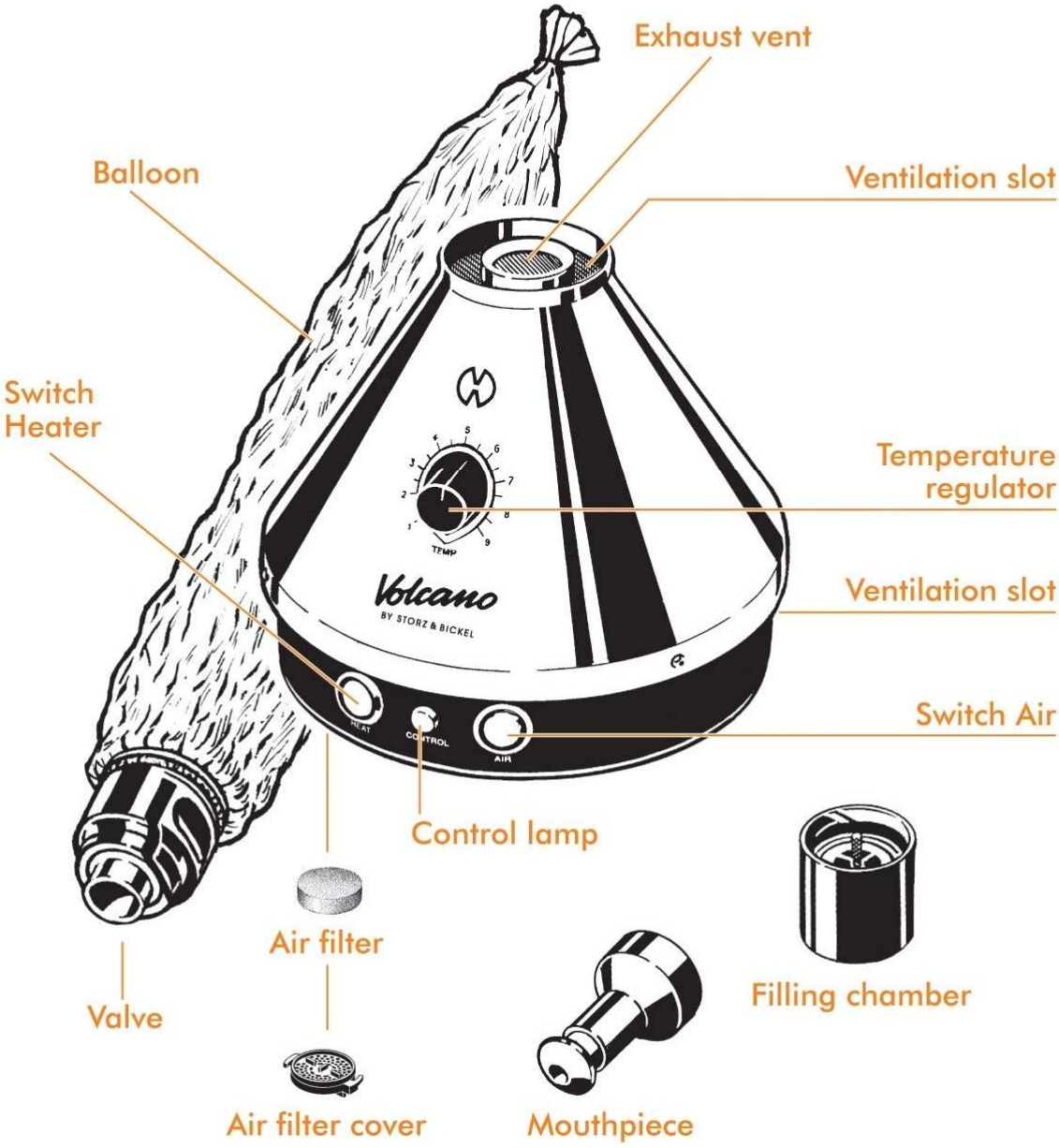


Figure 2: Consort Diagram

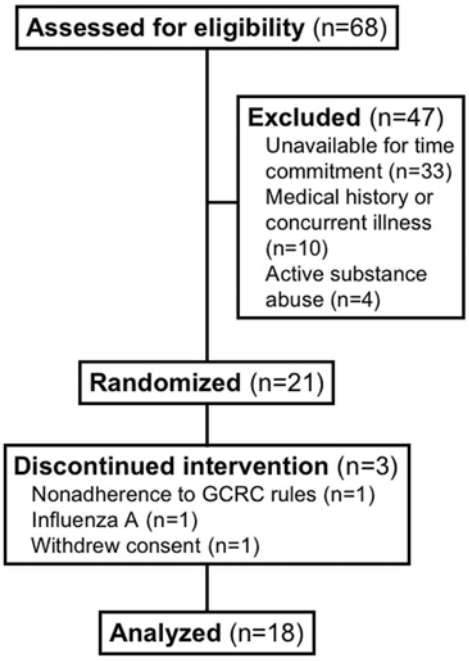
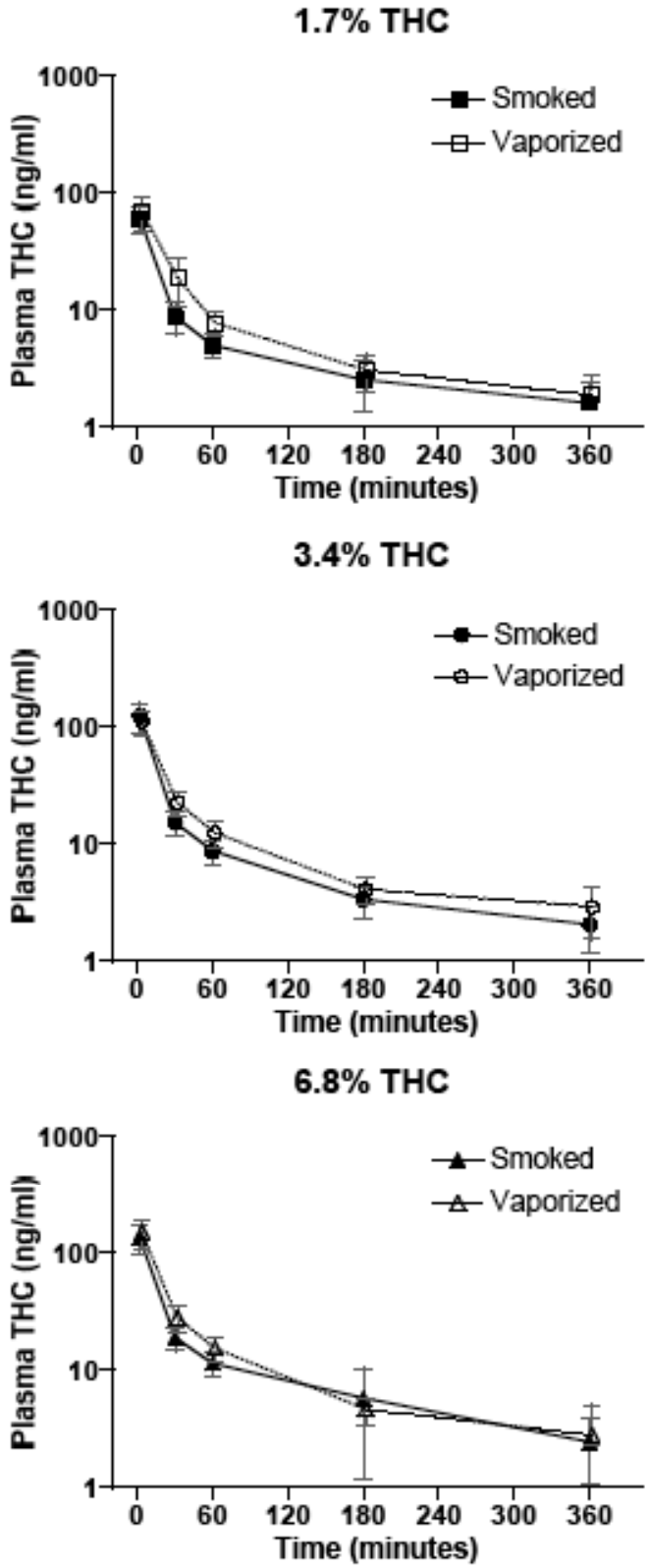


Figure 3. Plasma THC using vaporizer and smoked cannabis by THC concentration



(mean and 90% CI)

Figure 4. Expired Carbon Monoxide at each time point for each mode of administration and THC concentration (mean and 95% CI)

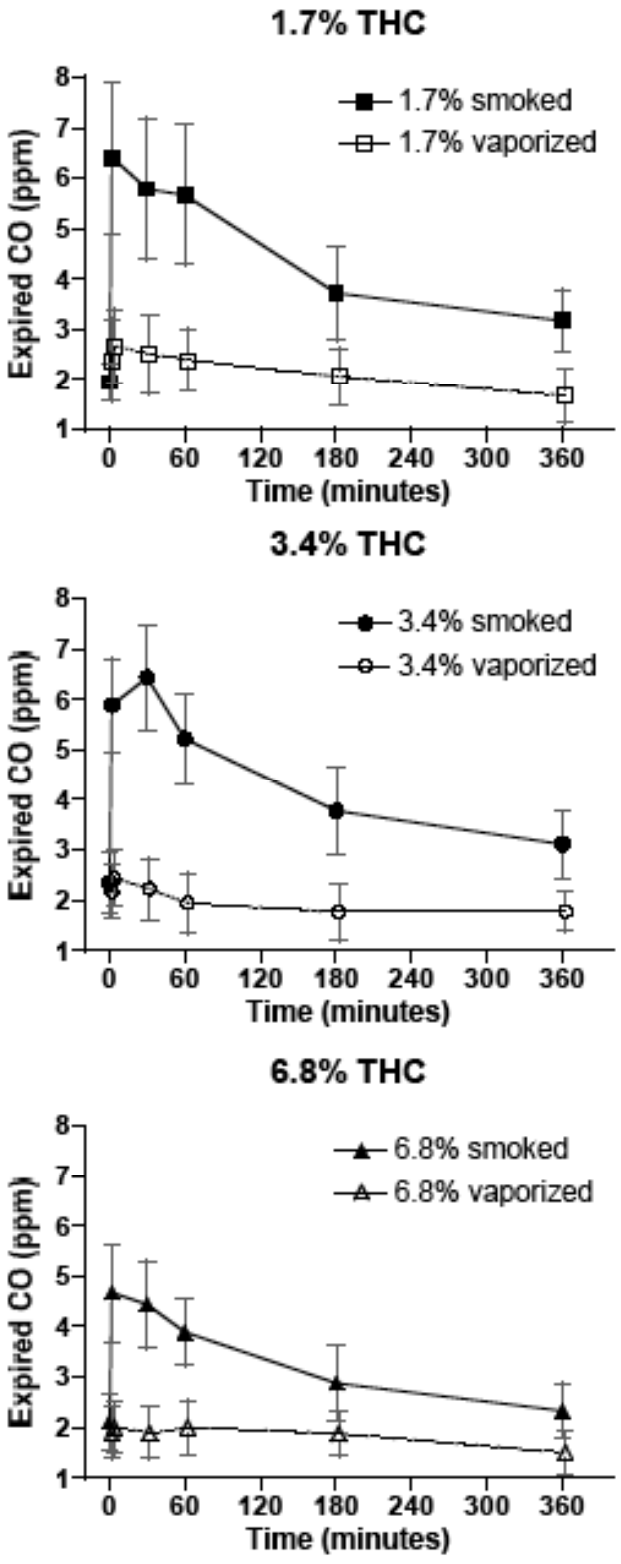


Figure 5. Self-reported "High" at each time point for each mode of administration and THC concentration (mean and 95% CI)