Cannabis Vaporizer Combines Efficient Delivery of THC with Effective Suppression of Pyrolytic Compounds

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ABSTRACT. Cannabis vaporization is a technology designed to deliver inhaled cannabinoids while avoiding the respiratory hazards of smoking by heating cannabis to a temperature where therapeutically active cannabinoid vapors are produced, but below the point of combustion where noxious pyrolytic byproducts are formed.

This study was designed to evaluate the efficacy of an herbal vaporizer known as the Volcano®, produced by Storz & Bickel GmbH&Co. KG, Tuttlingen, Germany (http://www.storz-bickel.com). Three 200 mg samples of standard NIDA cannabis were vaporized at temperatures of 155°-218°C. For comparison, smoke from combusted samples was also tested.

The study consisted of two phases: (1) a quantitative analysis of the solid phase of the vapor using HPLC-DAD-MS (High Performance Liq-

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The authors offer thanks for insight and technical support to Jeff Jones, Elvy Musikka, Irvin Rosenfeld and Aidan Hampson.

This research was supported by a grant from the Marijuana Policy Project. Additional support provided by the NORML Foundation, the Multidisciplinary Association for Psychedelic Studies and Storz & Bickel GmbH&Co.

Journal of Cannabis Therapeutics, Vol. 4(1) 2004
http://www.haworthpress.com/web/JCANT
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Digital Object Identifier: 10.1300/J175v04n01_02

uid Chromatograph-Diode Array-Mass Spectrometry) to determine the amount of cannabinoids delivered; (2) a GC/MS (Gas Chromatograph/Mass Spectrometer) analysis of the gas phase to analyze the vapor for a wide range of toxins, focusing on pyrene and other polynuclear aromatic hydrocarbons (PAHs).

The HPLC analysis of the vapor found that the Volcano delivered 36%-61% of the THC in the sample, a delivery efficiency that compares favorably to that of marijuana cigarettes.

The GC/MS analysis showed that the gas phase of the vapor consisted overwhelmingly of cannabinoids, with trace amounts of three other compounds. In contrast, over 111 compounds were identified in the combusted smoke, including several known PAHs.

The results indicate that vaporization can deliver therapeutic doses of cannabinoids with a drastic reduction in pyrolytic smoke compounds. Vaporization therefore appears to be an attractive alternative to smoked marijuana for future medical cannabis studies. *[Article copies available for a fee from The Haworth Document Delivery Service: 1-800-HAWORTH. E-mail address: <docdelivery@haworthpress.com> Website: <http://www.HaworthPress.com> © 2004 by The Haworth Press, Inc. All rights reserved.]*

KEYWORDS. Marijuana, cannabis, vaporization, smoking, harm reduction

INTRODUCTION

Concern about the respiratory hazards of smoking has spurred the development of vaporization as an alternative method of medical cannabis administration. Cannabis vaporization is a relatively new technology aimed at suppressing respiratory toxins by heating cannabis to a temperature where cannabinoid vapors form (typically around 180-190°C), but below the point of combustion where smoke and associated toxins are produced (near 230°C). The purpose of this is to permit the inhalation of medically active cannabinoids while avoiding noxious smoke compounds that pose respiratory hazards. Of particular concern are the carcinogenic polynuclear (or "polycyclic") aromatic hydrocarbons (PAHs), known byproducts of combustion that are thought to be a major culprit in smoking-related cancers. While there exists no epidemiological evidence that marijuana smokers face a higher risk of smoking-related cancers, studies have found that they do face a higher risk of bronchitis and respiratory infections (Polen et al. 1993, Tashkin 1993). This risk is not thought to be due to cannabinoids, but rather to extraneous byproducts of pyrolysis in the smoke.

In principle, vaporization offers medical cannabis patients the advantages of inhaled routes of administration: rapid onset, direct delivery into the bloodstream, ease of self-titration and concomitant avoidance of over- and under-dosage, while avoiding the respiratory disadvantages of smoking. Compared to other proposed non-smoked delivery systems using pharmaceutical extracts and synthetics, vaporization also offers the economic advantage of allowing patients to use inexpensive, homegrown cannabis.

In practice, the major question concerning vaporization comes down to feasibility. How well can one design a vaporizer that reliably produces "smokeless," toxin-free cannabinoid vapors from crude cannabis? To address this question, we tested a device known as the Volcano®, an herbal vaporizer produced by Storz & Bickel GmbH&Co. KG, Tuttlingen, Germany (http://www.storz-bickel.com). The study was designed to measure how efficiently the device delivered delta-9-tetrahydrocannabinol (THC) and other cannabinoids, and how effectively it suppressed other, non-cannabinoid compounds from the vapor.

The study consisted of two phases: (1) a quantitative analysis of the solid phase of the vapor using HPLC-DAD-MS (High Performance Liquid Chromatograph-Diode Array-Mass Spectrometry) to determine the amount of cannabinoids delivered; (2) a GC/MS (Gas Chromatograph/Mass Spectrometry) analysis of the gas phase to analyze the vapor for a wide range of toxins, focusing on pyrene and other polynuculear aromatic hydocarbons. Vapor was generated by loading the Volcano with 200 mg samples of NIDA cannabis. For comparison, a combusted control using 200 mg of cannabis burned in a glass pipe bowl was also tested.

Upon analysis, the Volcano vapors were found to consist overwhelmingly of cannabinoids, while the combusted control contained over one hundred additional chemicals, including several known PAHs. The results, which are discussed below, provide encouraging confirmation of the feasibility and efficacy of vaporization.

This study was the third in a series of cannabis smoke harm reduction studies sponsored by California NORML (National Organization for the Reform of Marijuana Laws, www.canorml.org) and MAPS (Multidisciplinary Association for Psychedelic Studies, www.maps.org) (Gieringer 2001). The first study tested a variety of smoking devices, including two crude homemade vaporizers along with several waterpipes and other devices, specifically examining THC and solid smoke tars (Gieringer 1996). It indicated that only vaporizers were capable of achieving reductions in tar relative to THC. The second study (Chemic 2000) was a

"proof of concept" study of an electric radiant heat vaporizer known as the M-1 Volatizer® (http://www.volatizer.com). The M-1 was found to deliver THC while completely eliminating three specific toxins (naphthalene, benzene and toluene) in the solid phase of the vapor. The study also detected a $\geq$ 56% reduction in tars and a qualitative reduction in carbon monoxide, but did not test for any other chemicals (Gieringer 2001). The present study (Chemic 2003) is the first to use a GC/MS to analyze the gas phase of vaporized cannabis for a wide range of toxins, concentrating on the highly carcinogenic PAHs.

DESCRIPTION OF THE VOLCANO®

The Volcano, as its name suggests, consists of a conical body containing a ceramic heater with a heat vent on top (Figure 1). Above the vent sits a removable chamber that is loaded with sample material. Hot air is blown from below through the sample to produce vapor, which is collected in a detachable plastic balloon. After the balloon has been filled, it can be removed and fitted with a mouthpiece, through which the vapors can be inhaled. The balloon is a unique feature of the Volcano. It has the advantages of preventing loss of sidestream vapor and providing a uniform, consistent dosage volume. This renders it an ideal instrument for controlled dosage studies.

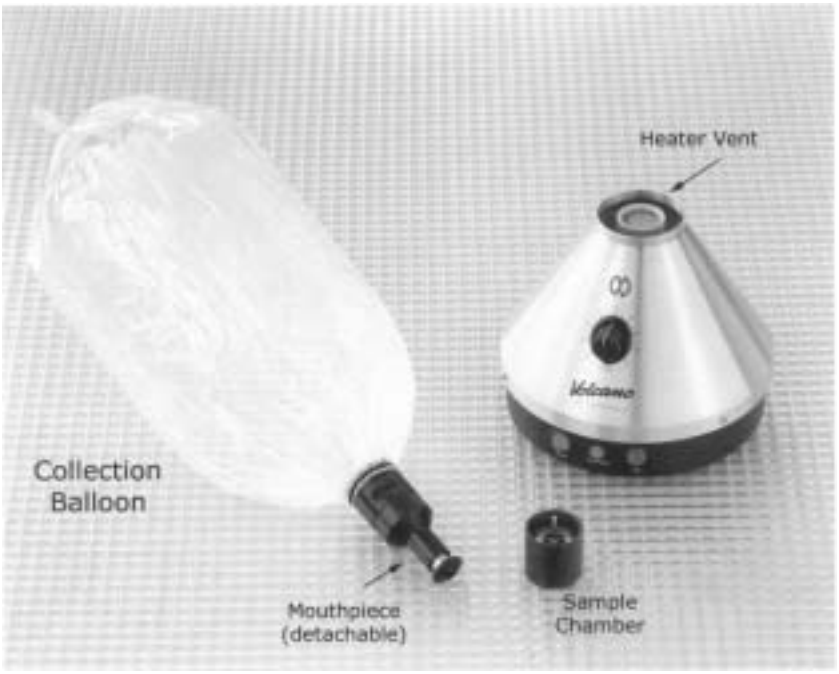
The temperature control ranges from 1 to 9, corresponding to temperatures of 130° to 226°C. The manufacturer suggests using a temperature setting of 7, corresponding to a nominal 202°C. Our previous study using the M-1® found that sample temperatures around 185°C were optimal for vaporization, with toxins beginning to appear above 200°C (Chemic 2000, Gieringer 2001). As a worst-case test of the Volcano's safety, we set it at its highest setting to ascertain whether pyrolytic byproducts might result. Two thermocouples were placed in the vaporizer above and below the sample to determine the actual operating temperature. The temperature was found to be stable, measuring 155°C on the top surface of the sample and 218°C on the screen closest to the heater.

THE SAMPLE

The sample consisted of standard NIDA cannabis supplied through an independent laboratory. Portions were prepared in 1.7 gram batches by gently sifting through a 2 mm sieve screen and mixing.

The baseline concentrations of cannabinoids in the sample were ana-

FIGURE 1. The Volcano® Vaporizer



Photograph courtesy of Storz & Bickel.

lyzed by Soxhlet extraction for THC, cannabidiol (CBD) and cannabinol (CBN). Three separate samples of 200 mg were extracted in 250 ml ethanol under heat for 2 hours, concentrated by rotary evaporation, and analyzed by HPLC-DAD-MS. The mean concentration of THC was 4.15% (range 4.0%-4.3%), consistent with NIDA standards. CBD and CBN were detected in only trace amounts, with the CBD showing a wide range of variance: 0.0428%-0.128% (mean 0.075%). CBN ranged more tightly from 0.086% to 0.10% (mean 0.094%).

The water content of the sample was measured by heating a prepared 0.56 gram sample for 30 minutes at 140°C and measuring the weight loss. The water content was found to be 11.9% by weight.

PHASE ONE: CANNABINOID RECOVERY ANALYSIS

Vapor from the Volcano was analyzed to determine the cannabinoid delivery efficiency of the vaporizer. A 200 mg sample was loaded into

the Volcano and exposed to heat for 45 seconds, enough to fill the collection balloon. The vapor was then transferred from the balloon over a period of approximately 15 minutes by a vacuum pump into a solvent reservoir containing 50 ml of methanol.

Three balloons were collected from each sample. The three balloon quota was based on preliminary tests, which found that most of the cannabinoids were delivered in the first two balloons, with just trace amounts in the third. The vapor is typically visible as a light gray wispy haze and has a distinct cannabis terpene odor. In practice, Volcano users report inhaling anywhere from two to six balloons from a given sample. However, most load the chamber with a half gram or more, over twice the sample size in our tests. The more cannabis that is loaded, the more balloons of vapor that can be drawn. According to the manufacturer, up to ten balloons can be drawn from a one-gram sample (Russo 2003). In order to facilitate maximal vaporization, the manufacturer recommends stirring the sample around after inhaling a few balloons, then repeating. However, this procedure was not followed in our tests since we used relatively small amounts of sieved material.

The dissolved vapor from the Volcano was subjected to quantitative analysis on the HPLC-DAD. Two separate samples of 1.5 ml were tested from each dissolved sample as a consistency check. The entire process was repeated for three different 200 mg samples of cannabis. Results are shown in Table 1. On average, the recovered THC amounted to 1.95% of the original weight of the sample, or 47% of the original THC in the crude sample. There was a large variance in the percentage of THC recovered in the three different vaporizer test runs, ranging from 36% to 61%. This suggests that the efficiency of vaporization is highly sensitive to variations in the sample and micro-conditions in its environment.

These results compare favorably to the delivery efficiencies of marijuana cigarettes as measured in other studies. THC efficiencies of 34% to 61% were reported in studies of marijuana cigarettes smoked via a smoking machine under varying conditions of puff duration and air speed (Fehr and Kalant 1971). Efficiencies of 50% were obtained using a machine designed to mimic human marijuana cigarette smoking (Manno 1970) and in an unpublished study at Battelle by Foltz et al. (cited in Truitt 1971). It has been estimated that 23-30% of the THC in combusted cannabis is destroyed by pyrolysis, while as much as 40-50% can be lost in sidestream smoke (Perez-Reyes 1990). Efficiencies as low as 16%-19% were reported in tests of cigarettes smoked intermit-

TABLE 1. Cannabinoid Recovery Efficiencies

(A) CRUDE CANNABIS (Soxhlet Extraction)

Sample	THC (%)	CBD (%)	CBN (%)
Crude 1	4.3	0.044	0.10
Crude 2	4.1	0.055	0.0925
Crude 3	4.0	0.127	0.0975
Mean (Std.Dev)	4.15 (0.17)	0.075 (0.044)	0.094 (0.007)

(B) VOLCANO VAPOR

Sample	THC (%)	CBD (%)	CBN (%)
Volcano 1	2.55	0.12	0.11
Volcano 2	1.50	0.068	0.0595
Volcano 3	1.80	0.081	0.070
Mean	1.95 (0.49)	0.091 (0.026)	0.081 (0.025)

(C) COMBUSTED SMOKE

Sample	THC (%)	CBD (%)	CBN (%)
Combustion 1	3.4	0.155	0.19
Combustion 2	3.2	0.16	0.185
Combustion 3	3.1	0.13	0.18
Mean	3.24 (0.11)	0.15 (0.016)	0.19 (0.005)

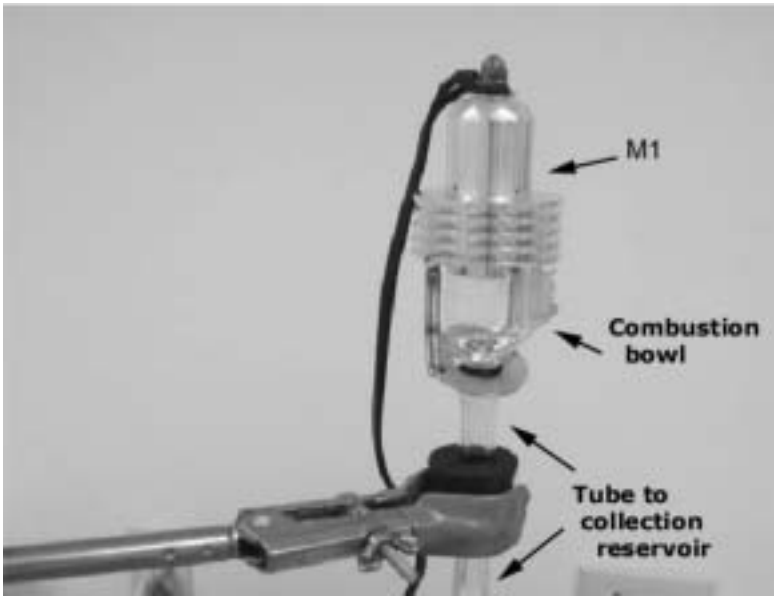
Note: Each sample was tested twice; in each case, results were consistent within 3%. Data above reflect the average of the two test results.

tently on smoking machines (Davis et al. 1984). In contrast, continuous smoking on a smoking machine yielded efficiencies of 69%.

The THC delivery of combusted cannabis was measured in our study by repeating the experiment with three more 200 mg samples. The samples were not rolled into cigarettes, but combusted in a glass pipe bowl like that of a marijuana bong. Each sample was ignited by exposure to an electric radiant heater placed over the bowl, and the smoke was drawn through a tube directly into the methanol (Figure 2). The dissolved smoke was assayed for cannabinoids as previously described.

The combusted sample registered a relatively high THC delivery efficiency of 78%. The variance was low for the three different test runs. The high efficiency may be explained by the fact that the laboratory conditions minimized loss of sidestream smoke; the sample was completely consumed with no "butt" remaining; and the pipestem led directly into the solvent so as not to cause excessive loss by adhesion to

FIGURE 2. Combustion Setup. Electric heater (MI) radiates down into bowl, igniting sample below. Smoke is drawn by vacuum through tube to solvent reservoir (below, not shown).



the walls. The amount of THC lost (22%) in combustion was consistent with the losses attributed to pyrolysis in other studies.

Theoretically, the vaporizer might have been expected to realize a higher THC delivery efficiency than combustion, since it should have avoided loss of THC by pyrolysis. That this was not observed indicates that there were other inefficiencies in the vaporization process. The most likely explanation would seem to be incomplete vaporization, due to lack of uniform thorough heating and ventilation of the sample. It is certainly possible that higher efficiencies might have been achieved by stirring the sample and drawing another balloon from the vaporizer, as recommended by the manufacturer.

All of the vaporized and combusted samples were also assayed for CBD and CBN. The amount of CBD delivered was unexpectedly somewhat higher for both the vaporized and combusted samples. At first glance, this result is not easy to explain. However, given the unusually high variance of CBD measured in the crude samples and the minimal levels of CBD detected, the results do not seem to be significant.

For CBN, there was no significant change under vaporization. In contrast, the level of CBN was twice as high in all three combusted samples, with little variance. This result may be explained by the oxidation of THC under heat (El Sohly 2002). However, it should be noted that the amounts of CBN observed were still quite low (0.19%), two orders of magnitude less than the loss of THC observed under combustion.

PHASE 2: GAS PHASE GC/MS ANALYSIS

The second phase of the study analyzed the gas phase of the vapor for a broad spectrum of compounds via GC/MS. The GC/MS was outfitted with a DB-XLB analytical separation column (DB-xtra low bleed, 30 M × 0.25 mm, 0.25 µm film), which is especially suited for the detection of polynuclear aromatic hydrocarbons.

A PAH reference stock solution was used that included analytes for naphthalene, acenaphthalene, anthracene, chrysense, benzo(a)pyrene, benzo(k)fluoranthene, 1,1,2-benzoperylene, indeno(1,2,3-c,d)pyrene, ancenaphthylene, fluorene, phenanthrene, pyrene, 1,2-benzanthracene, benzo(b)fluroanthene, and 1,2,4,6-dibenzanthrancene. Pyrene was used as a reference standard.

The evolved vapor from the Volcano was transferred from the collection balloon via vacuum directly to a 250 ml volatile gas trap. A 2.0 ml portion of the gaseous sample was then transferred using a headspace syringe directly onto the chromatographic system and assayed. In addition, the condensed residue that had adhered to the gas trap was analyzed by adding 2.0 ml of methanol to the trap to dissolve it. Subsequently, 1 µl of the solution was injected directly into the GC/MS. This process was repeated for three samples with three balloons from each sample, making a total of nine runs with gas samples and nine more with the condensed residue.

The gas was analyzed qualitatively and semi-quantitatively for polynuclear aromatic hydrocarbons at sample concentrations of 2.25-125 µg/ml. The GC/MS operated at a thermal gradient of 110°-320°C over 53 min. Different compounds were qualitatively identified by comparing their response peaks with an NBS reference library. Compounds that demonstrated greater than 70% match quality in comparison to the NBS mass spectral standard were reported as identified isolated compounds. Their mass concentrations were estimated from the response peak area in terms of the calibrated reference standard for pyrene. This yielded approximate, semi-quantitative mass determinations.

A review of the data showed that the Volcano vapor was overwhelmingly dominated by THC, with trace amounts of a handful of other compounds.

Representative data for the vapor gas and solvated condensate are shown in Tables 2 and 3 (from the first balloon of one of the samples).

Aside from THC, one other cannabinoid, CBN, was detected. No CBD was detected. This was not unexpected, since the GC/MS analysis was much less sensitive to cannabinoids than to PAHs. In general, the

TABLE 2. GC-MS Semi-Quantitative Results: Gaseous Headspace Analysis; Vaporized Sample

Retention time (min)	Response (area)	Best match	NBS Library match quality	Recovered conc. as pyrene (mg/g)	Recovered % of total
9.33	1221726	Caryophyllene[1]	78	0.0010	1.3
30.62	2417494	2-Methyl-2, 4 (2H-1-benzopyran-5-ol)	81	0.0020	2.5
32.56	85295887	Dronabinol (THC)	99	0.070	89.1
33.62	5487650	Cannabinol (CBN)	81	0.0045	5.7
42.97	1289703	5-[(Acetyl benz [e] azulene-3,8-dione	86	0.0011	1.3

Total recovered mass
as Pyrene (mg): 0.079**
Weight extracted (mg): 200
% recovered: 0.04**
** (Nominal semi-quantitative figures)

[1] "Sesquiterpinoid essential oil commonly found in cannabis." Ethan Russo, MD, Montana Neurobehavioral Specialists, Missoula, MT 59802.

TABLE 3. GC/MS Semi-Quantitative Results: Solvated Extract Analysis; Vaporized Sample

Retention time (min)	Response (area)	Best match	NBS Library match quality	Recovered conc. as pyrene (mg/g)	Recovered % of total
30.62	4961669	2-Methyl-2, 4 (2H-1-benzopyran-5-ol)	81	0.065	1.90
32.55	246510987	Dronabinol (THC)	99	3.2	94.3
33.62	9875017	Cannabinol (CBN)	94	0.13	3.78

Total recovered mass
as Pyrene (mg): 3.4**
Weight extracted (mg): 200
% recovered: 1.7**
** (Nominal semi-quantitative figures)

GC/MS analysis was intended to measure PAHs but did not provide an accurate measure of cannabinoids. For the latter, it was necessary to use the HPLC.

Aside from the cannabinoids, only three other compounds were tentatively identified in the vapor gas, and one in the solvated condensate. The three were caryophyllene (an aromatic terpene found in cannabis and other plants) plus two other compounds of undetermined origin, one of which also appeared in the condensate.

An estimated 1.7% of the weight of the 200 mg sample was recovered in the solvated condensate, as approximately quantified in terms of the pyrene standard. THC accounted for a nominal 94.3% of the inferred estimated mass. That the apparent concentration of THC inferred in the GC/MS analysis (3.2 mg/gm) was much lower than in the HPLC (19.5 mg/gm), was partly an artifact of the mathematical representation of THC in terms of pyrene, and partly due to the lack of applicability of the GC/MS system to THC due to low volatility and to sorbation characteristics of the analytic column.

The gaseous headspace was more tenuous, yielding an estimated recovered mass of just 0.04% of the sample weight. Once again, the sample was overwhelmingly dominated by THC.

A striking result in both analyses was a lack of significant quantities of pyrolytic-induced analytes in the vapor.

Comparison runs using combusted cannabis presented a strikingly different picture. As in the previous experiment, smoke produced by 200 mg of cannabis combusted under the M-1 was drawn into a 250 ml volatile gas trap. A 2 ml gaseous sample was injected into the GC/MS; 2.0 ml of methanol was added to the trap to dissolve the condensed, and another 1 µl sample was injected into the GC/MS for a second analysis. This process was repeated for three separate samples.

Representative results for the gas and solvated condensate are presented in Tables 4 and 5, respectively (data taken from first run).

Review of the data from the gaseous headspace detected 111 tentatively identified compounds, including THC and CBN. Included were five known PAHs. Cannabinoids represented only 12% of the inferred recovered mass; the remaining 88% consisted of extraneous products of combustion.

The solvated extract yielded 37 tentatively identified compounds, including five known PAHs. THC and CBN constituted 90% of the estimated recovered mass. (When combusted, the product saturated the chromatographic system, producing a distorted response; hence the apparently elevated concentration of THC (57.9 mg/gm); as noted above,

TABLE 4. GC/MS Semi-Quantitative Results: Gaseous Headspace Analysis; Combusted Sample

Retention time (min)	Response (area)	Best match[1]	NBS Library match quality	Recovered conc. as pyrene (mg/g)	Recovered % of total
4.30	32935726	Benzeneacetonitrile	91	0.027	0.16
4.60	2310571	1-Chloro-octadecane	91	0.002	0.01
4.99	18390657	Naphthalene	90	0.015	0.09
5.18*	69332076	2,3-Dihydro-benzofuran	86	0.057	0.34
6.21	4465468	2,6,10,14-Tetramethyl-hexadecane	90	0.004	0.02
6.91	86166759	Indole	90	0.071	0.42
7.12	7925421	1-Methyl-naphthalene	93	0.007	0.04
8.52	35115397	1,1′-Oxybis-octane	83	0.029	0.17
8.69	12256513	2,6,10-Trimethyl-tetradecane	83	0.010	0.06
9.00	23982131	3-Methyl-1H-indole	81	0.020	0.12
9.32	116897251	Caryophyllene	98	0.096	0.57
10.15	313228545	Cyclododecane	97	0.257	1.52
10.74	4799627	Pentadecane	97	0.004	0.02
10.85	146804387	Heptadecane	98	0.120	0.71
11.35	950013208	Nonadecene	86	0.780	4.60
11.95*	90056152	2,2′-Diethyl-1,1′-biphenyl	94	0.074	0.44
12.63	154063760	Hexadecanal	76	0.126	0.75
13.10	2964842	Hexadecane	90	0.002	0.01
13.50	35308265	Caryophyllene oxide	95	0.029	0.17
14.13*	33918891	2,2′-Diethyl-1,1′-biphenyl	80	0.028	0.16
14.82	296612752	Tetradecanoic acid	99	0.243	1.44
15.12	42131403	(Z)-3-Hexadecene	98	0.035	0.20
15.47	295232200	Octadecane	98	0.242	1.43
16.18	4653356	2-Dodecen-1-yl (−) succinic anhydride	89	0.004	0.02
16.28	3384476	2-Methyl-1-hexadecanol	78	0.003	0.02
16.32	5094990	1-Pentadecene	92	0.004	0.02
17.33	34270249	2-Heptadecanol	78	0.028	0.17
17.52	34215482	2-(Tetradecyloxy)-ethanol	81	0.028	0.17
17.74	13953740	Hexadecane	90	0.011	0.07
17.87	18906884	Heneicosane	87	0.016	0.09
18.08	85618813	Pentadecanoic acid	97	0.070	0.41
18.19	151994108	1,2-Benzenedicarboxylic acid, bis (2)	86	0.125	0.74
18.50	2213315118	Cyclohaxadecane	99	1.816	10.71
18.65	45837144	Nonadecane	96	0.038	0.22
18.77	42293352	1-Nonadecene	90	0.035	0.20

Retention time (min)	Response (area)	Best match[1]	NBS Library match quality	Recovered conc. as pyrene (mg/g)	Recovered % of total
19.00	199692334	2-Hexadecanol	90	0.164	0.97
19.17	76550515	2-Heptadecanone	87	0.063	0.37
19.37	103194224	Caffeine	94	0.085	0.50
19.77	14872741	Docosane	86	0.012	0.07
20.02	102125171	1-Octadecene	97	0.084	0.49
20.20	96794873	1-Hexadecanol	86	0.079	0.47
20.39	57493519	3-Eicosene	97	0.047	0.28
20.91	2933718734	Dibutyl phthalate	83	2.407	14.20
21.24	114002736	Nonadecane	90	0.094	0.55
21.49	9672077	1-Nonadecene	86	0.008	0.05
21.76	122401077	1-Octadecene	99	0.100	0.59
22.43	51345191	3,5,6,7-Tetrah-s-indacen-1(2H)-one	81	0.042	0.25
22.54	4913720	Octadecane	95	0.004	0.02
22.63	33563860	1-Nonadecene	86	0.028	0.16
23.03	32829703	N-Methyl-N-[4-[4-methoxy-acetamide	90	0.027	0.16
23.15	82313597	2,3,5,6-Tetra-s-indacene-1,7-dione	76	0.068	0.40
23.48	857664501	5-Octadecene	97	0.704	4.15
24.01	15554319	Octadecane	90	0.013	0.08
24.35	140996042	16-Methyl-, met heptadecanoic acid	96	0.116	0.68
24.52*	95037913	5-Dodecyldihydro-2 (3H)-furanone	83	0.078	0.46
24.66	32387060	1-Henricosyl formate	90	0.027	0.16
25.01	14710926	(Z)-9-Tricosene	91	0.012	0.07
25.79	32371423	2-Hexyl-1-decanol	86	0.027	0.16
25.86	200623444	Hexadecanamide	93	0.165	0.97
26.00	32616620	1-Nonadecene	99	0.027	0.16
26.33	53218271	2-Dodecen-1-yl (−) succinic anhydride	86	0.044	0.26
26.65	7339051	2-Dodecen-1-yl (−) succinic anhydride	89	0.006022	0.04
27.09	56583135	Cis-11-Hexadecen-1-yl acetate	81	0.046430	0.27
27.21	129242826	1-Phenantthrenecarboxylic acid, 7-et	96	0.106053	0.63
27.36	10625426	1-Phenantthrenecarboxylic acid, 7-et	92	0.008719	0.05
27.51	17570838	Tricosane	98	0.014418	0.09
27.58	156887637	1-Nonadecene	98	0.128737	0.76
28.37	69739203	1,2,1-Phenanthrenecarboxylic acid	92	0.057226	0.34
28.73	20887801	Hexanedioic acid dioctyl ester	90	0.017140	0.10
28.95	98593890	1-Phenantthrenecarboxylic acid, 7-et	86	0.080903	0.48
29.10	627678209	1,2,1-Phenanthrenecarboxylic acid	99	0.515053	3.04
29.26	380114163	2-[(2-bu Cyclopropanenanoic acid	92	0.311910	1.84
30.65*	70574444	2H-1-Benzopyran-5-ol, 2-methyl-2-(4	94	0.057911	0.34

TABLE 4 (continued)

Retention time (min)	Response (area)	Best match[1]	NBS Library match quality	Recovered conc. as pyrene (mg/g)	Recovered % of total
30.75	85939990	Resocinol, 2-p-mentha-1,8-dien-3-y	98	0.0705	0.42
31.07	125006268	Tricosane	93	0.103	0.61
31.66	21935407	Acetamide, N-methyl-N-[4-[4-4methoxy	91	0.0180	0.11
31.83	432784246	Hexadecanoic acid, 2,3-dihyroxypro	74	0.355	2.10
32.46	10236345	Cyclotetradecane,1,7,11-trimethyl-	91	0.00840	0.05
32.58	2219980004	Dronabinol (THC)	99	1.82	10.75
32.72	63820716	Hexacosane	96	0.0524	0.31
33.23	27548366	1,3-Benzenediol,2-(3,7-dimethyl-2,	90	0.0226	0.13
33.43	33550885	Acetamide, N-methyl-N-[4-[4-4methoxy	94	0.0275	0.16
33.63	240628731	Cannabinol (CBN)	95	0.197	1.16
34.09	13044163	Cyclohexane, 1-(1,5-dimethylhexyl)-	86	0.0107	0.06
34.32	125757721	Heptacosane	99	0.103	0.61
34.52	197356583	1-Octdecanethiol	87	0.162	0.96
35.17	243624195	Octadecanoic acid, 2,3-dihydroxypro	86	0.200	1.18
35.86	69273621	Tricosane	92	0.0568	0.34
36.15	1676695684	Squalene	94	1.38	8.12
37.29	34686159	3-Eicosene, (E)-	91	0.0285	0.17
37.34	71189968	Heneicosane	96	0.0584	0.34
38.77	62069103	Heptacosane	95	0.0509	0.30
39.10	20150673	2-Dodecen-1-yl (−) succinic anhydride	94	0.0165	0.10
40.16	67270687	Heptacosane	97	0.0552	0.33
40.96	109391601	9-Hexadecenoic acid, eicosyl ester	76	0.0898	0.53
41.04	9230053	Cyclotetradecane, 1,7,11-trimethyl-	83	0.00757	0.04
41.50	30676052	Eicosane	91	0.0252	0.15
41.79	1169213328	Cholesterol[1]	99	0.959	5.66
42.27	45017056	9-Hexadecenoic acid, eicosyl ester	72	0.0369	0.22
42.61	16741293	Cholesteryl acetate	97	0.0137	0.08
42.69	4624026	Heneicosane, 3-methyl-	91	0.00379	0.02
42.80	36515665	Eicosane	90	0.0300	0.18
43.00	4896647	Heneicosane, 3-methyl-	91	0.00402	0.02
43.22	61362365	Cholesta-3,5-dien-7-one	96	0.0504	0.30
43.32	28641892	Cholesteryl acetate	99	0.0235	0.14
43.58	130345192	9-Hexadecenoic acid, eicosyl ester	91	0.107	0.63
43.86	206844252	Hexadecanoicacid, hexadecyl ester	95	0.170	1.00
44.15	31783685	Eicosane	83	0.0261	0.15
46.70	150517876	9-Hexadecenoic acid, eicosyl ester	83	0.124	0.73

Retention time (min)	Response (area)	Best match[1]	NBS Library match quality	Recovered conc. as pyrene (mg/g)	Recovered % of total
47.02	108047194	1-Octadecanethiol	84	0.0887	0.52
50.91	86165775	9-Hexadecenoic acid, eicosyl	83	0.0707	0.42

Total recovered (mg): 17.0**
Weight extracted (mg): 200
% recovered: 8.5**
** (Nominal semi-quantitative figures)

* Polynuclear aromatic hydrocarbons.

[1] "Best match" compounds were determined by comparing the GC/MS output to the NBS standard reference library. They do not necessarily correspond to the true compound present in every case. For instance, the entry identified as "cholesterol" at retention time 41.79 is presumably something else, since cholesterol is not produced in plants. Most likely it is a wax-like fatty acid of similar molecular weight.

TABLE 5. GC/MS Semi-Quantitative Results: Solvated Extract Analysis; Combusted Sample

Retention time (min)	Response (area)	Best match	NBS Library match quality	Recovered conc. as pyrene (mg/g)	Recovered % of total
4.27	5371404	Phenol, 4-ethyl-	91	0.071	0.10
4.46	4820930	1H-Indene, 1-methyl-	91	0.063	0.09
4.62	11975267	1,2-Benzennediol	74	0.157	0.23
5.01	28398562	Naphthalene	91	0.373	0.53
5.17*	33292637	Benzofuran, 2,3-dihydro-	72	0.437	0.63
6.91	21443444	Indole	87	0.282	0.40
7.14	5635171	Naphthalene, 2-methyl-	95	0.074	0.11
7.45	5932574	Naphthalene, 2-methyl-	93	0.078	0.11
7.72	4757806	1,4-Benzenedoil, 2-methyl-	91	0.062	0.09
8.99	11013411	1H-Indole, 4-methyl-	90	0.145	0.21
9.32	60797737	Caryophyllene	99	0.798	1.15
9.71	4674849	1,6,10-Dodetatriene, 7,11-dimethyl-	96	0.061	0.09
9.97*	2209752	Naphthalene, 1,2,3,5,6,7,8,8a-octah	89	0.029	0.04
10.20	18874442	4,7,10-Cycloundecatriene	99	0.248	0.36
11.12	2060913	1H-3a,7-Methanoazulene,octahydro-1	90	0.027	0.04
11.20	2094526	Cylohexene, 1-methyl-4-(5-methyl-1	86	0.027	0.04
12.14*	13696523	Naphthalene, decahydro-4a-methyl-1-	92	0.180	0.26
12.33*	16059454	Naphthalene, 1,2,3,5,6,7,8,8a-octah	98	0.211	0.30
13.50	17021514	Caryophyllene oxide	96	0.223	0.32
13.59	4347127	1H-Cyclopropa [a]naphthalene,1a,2,3	98	0.057	0.08
14.75	2271757	10,10-Dimethylenebicyc	89	0.030	0.04

TABLE 5 (continued)

Retention time (min)	Response (area)	Best match	NBS Library match quality	Recovered conc. as pyrene (mg/g)	Recovered % of total
15.33	2173568	5-Azulenemethanol, 1,2,3,3a,4,5,6,7	86	0.029	0.04
15.67	26178775	.alpha.-Bisabolol	87	0.344	0.49
15.85	9580620	1-Decene	90	0.126	0.18
18.37	32298240	6-Octen-1-ol, 3,7-domethyl-, acetate	78	0.424	0.61
18.70	2422132	Diphenylethyne	90	0.032	0.05
21.24	4388527	Hexadecanoic acid	92	0.058	0.08
29.16	3509363	Glaucyl alcohol	86	0.046	0.07
30.63*	69664748	2H-1-Benzopyran-5-ol, 2-methyl-2-(4	95	0.915	1.31
30.73	75367485	Resorcinol, 2-pmemtha-1,8-dien-3-y	98	0.990	1.42
31.84	4625532	Delta.8-Tetrahydrocannabinol	91	0.061	0.09
32.59*[1]	4408666746	Dronabinol (THC)[1]	98	57.9	83.04
33.07*[1]	2029605	Dronabinol (THC)[1]	91	0.027	0.04
33.63	334263844	Cannabinol (CBN)	97	4.389	6.30
37.34	3583356	Docosane	96	0.047	0.07
41.22	25609584	Vitamine E	89	0.336	0.48
45.39	28142178	.beta.-Amyrin	95	0.369	0.53

Total recovered (mg): 69.7**
Weight extracted (mg): 200
% recovered: 35**
** (Nominal semi-quantitative figures)

* Polynuclear aromatic hydrocarbons.
[1] Significantly increased response resulting in peak splitting, thus two consecutive retention times.

the GC/MS did not provide an accurate measurement of cannabinoids.) Altogether, eight different PAHs were identified in the solvated extract and the gaseous headspace.

DISCUSSION

The major finding of this study was a drastic quantitative reduction in non-cannabinoid compounds in the vapor from the Volcano. This strongly suggests that vaporization is an effective method for delivering medically active cannabinoids while effectively suppressing other potentially deleterious compounds that are a byproduct of combustion.

Numerous outstanding questions about vaporization remain to be re-

searched. This study was not designed to measure the presence of toxic gases with low molecular weight, such as ammonia, hydrogen cyanide and carbon monoxide, which are known to be produced by marijuana cigarettes (Huber 1991; Institute of Medicine 1982). Previous studies have indicated a qualitative decrease in CO with vaporization, but this remains to be quantitatively measured. Neither did this study analyze the solid tar phase of the vapor for non-cannabinoids. However, there is sound reason to believe that the total amount of tar was drastically reduced, given the absence of detectable combustion. Unlike the combusted marijuana, which turned to ash, the vaporized sample remained greenish-brown and intact, though clearly dessicated.

Numerous unexplored variables could conceivably affect the efficiency and output of vaporization. Included are variations in temperature; differences in the density, weight, and consistency of material in the chamber; differences in the variety and potency of cannabis used; and use of different preparations such as hashish, hash oil, etc. Further research is needed to determine the extent of such effects.

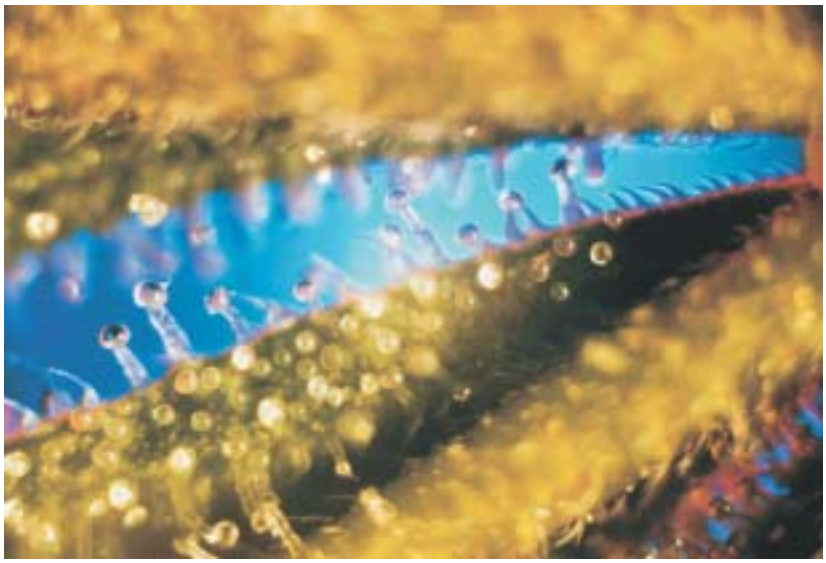
The effects of vaporization are illustrated in Figure 3 from the manufacturer. The vaporized cannabis does not turn to ash, but retains its original shape, as discussed above. A microscopic examination reveals the physical nature of the process. The cannabinoids in cannabis are borne in droplets of resin, known as glandular trichomes, which coat the exterior structures of the flowering tops, and the leaves to a lesser extent. The trichomes resemble small stalks or protuberances, appearing like dewy-capped mushrooms under a microscope. After vaporization, the resin has evaporated and trichomes have withered, while the underlying vegetative matter remains intact. This confirms that vaporization is essentially a different physical process than combustion.

The efficacy of vaporization is further attested by the growing number of patients who have taken up vaporizers instead of smoking. Many users say they have ceased smoking marijuana altogether because they find it unduly irritating to their throat and lungs. Instead, they say, vaporization gives them the same therapeutic effects without any untoward irritation or sore throat. On the other hand, a few refractory individuals say they prefer the savor of smoke or claim not to feel the same impact from vapor. It should be noted that vaporizers do not entirely eliminate respiratory irritation. A puff of strong vaporized cannabis will occasionally elicit a cough. This could be entirely due to THC itself, which is known to irritate the bronchial tract (Tashkin 1977).

In summary, there is good reason to believe that vaporization is a highly effective method of smoke harm reduction. Nonetheless, at pres-

FIGURE 3. Cannabis before and after vaporization.

(A) Macrophoto of cannabis sample prior to vaporization showing trichomes with resin.



(B) Macrophoto after the first passage of hot air flow from the Volcano. Part of the resin has vaporized, but the majority appears to be intact.

(C) Macrophoto after several passages of hot air from the Volcano. The resin has disappeared, and trichomes have withered, but non-incinerated fibrous material remains.

Figure 3 macrophotos reprinted with permission of Storz & Bickel <http://www.vapormed.de/en_anwndg.htm> 7/24/03.

ent smoked cigarettes from NIDA remain the only FDA approved method of administering cannabis to human subjects. The shortcomings of smoked marijuana have been widely viewed as an obstacle to approval of natural cannabis as a medicine. This view was expressed by the Institute of Medicine in its report on medical marijuana (IOM 1999, Executive Summary p. 8):

> Because of the health risks associated with smoking, smoked marijuana should generally not be recommended for long-term use . . .
>
> The goal of clinical trials of smoked marijuana would not be to develop marijuana as a licensed drug, but rather as a first step towards the possible development of non-smoked, rapid-onset delivery systems. However, it will likely be many years before a safe and effective cannabinoid delivery system, such as an inhaler, will be available for patients.

The IOM report failed to note that vaporizers appear to offer a feasible "non-smoked, rapid-onset delivery system."

A major goal of this study was to pave the way for vaporizers to be introduced into human studies, in particular studies of medical cannabis that are now normally conducted using NIDA cigarettes. Data from this study have been submitted to the FDA in support of an application for an investigational device exemption (IDE) to permit the Volcano to be used in a study by Dr. Donald Abrams of the University of California, San Francisco. The study, which is being supported by California's Center for Medicinal Cannabis Research, is essentially a Phase I study of vaporization. The protocol calls for testing inhaled cannabis of three different potencies in healthy test subjects. The study will compare subjective effects, cannabinoid blood levels and carbon monoxide levels in exhaled breath in subjects on six different days, three days smoking 400 mgs of NIDA marijuana of either 1.7% THC, 3.5% THC or 7% THC, and three days vaporizing identical amounts and strengths of NIDA marijuana.

The FDA currently has no criteria for evaluating vaporization devices. The only device now approved for administering marijuana to humans is NIDA pre-rolled cigarettes, which were approved before modern medical device regulations were enacted in 1976. At that time, there was no need for data on toxicity, dosage delivery, or the chemical content of the smoke delivered. Based on the evidence of this study, the Volcano should compare favorably in every respect. It remains to be seen whether the FDA will require additional pre-clinical tests before allowing the Volcano to be used in human subjects.

In any case, however, our research indicates that vaporization is a promising technology for smoke harm reduction. A growing number of vaporizers are now available through the internet (for a list, see http://www.canorml.org/healthfacts/vaporizers.html). They range from high-technology devices with medical grade components to simple hand-held glass pipes to be heated over a flame. Despite their obvious usefulness for medical cannabis patients, they have to be marketed as herbal vaporizers in order not to run afoul of federal drug paraphernalia laws. While usage of vaporizers is rapidly spreading, further testing and research are clearly needed to optimize vaporization technology.

REFERENCES

Chemic Laboratories. 2000. Proof of concept: release of chemical constituents in cannabis sativa at 170-185° versus combustion. Unpublished report to California NORML and MAPS, Nov. 17th, 2000.

Chemic Laboratories. 2003. Evaluation of Volcano® vaporizer for the efficient emission of THC, CBD, CBN and the significant reduction and/or elimination of

polynuclear-aromatic (PNA) analytes resultant of pyrolysis. Unpublished report to California NORML and MAPS, Apr 8th, 2003.

Davis, K.H. et al. 1984. Some smoking characteristics of marijuana cigarettes. In Agurell, S., Dewey, W.L. and Willette, R.E., eds. *The Cannabinoids: Chemical Pharmacologic and Therapeutic Aspects*. NY: Academic Press.

ElSohly, M. 2002. Chemical constituents of cannabis. In Grotenhermen, F. and Russo, E., eds. *Cannabis and Cannabinoids: Pharmacology, Toxicology, and Therapeutic Potential*. NY: The Haworth Press.

Fehr, K.O. and Kalant, H. 1972. Analysis of cannabis smoke obtained under different combustion conditions. *Can J Physiol Pharmacol* 50: 761-7.

Gieringer, D. 1996. Marijuana research: waterpipe study. *MAPS* (Multidisciplinary Association for Psychedelic Studies) *Bul* 6(3): 59-66.

Gieringer, D. 2001. Cannabis vaporization: a promising strategy for smoke harm reduction. *J Cannabis Therap* 1(3-4): 153-70.

Huber, G., M. First and O. Grubner. 1991. Marijuana and tobacco smoke gas-phase cytotoxins. *Pharmacol Biochem Behav* 40(3): 629-36.

Institute of Medicine. 1982. *Marijuana and Health*. Washington, DC: National Academy Press.

Institute of Medicine. 1999. *Marijuana and Medicine: Assessing the Science Base*. Washington, DC: National Academy Press.

Manno, J.E. et al. 1970. Comparative effects of smoking marihuana or placebo on human motor performance. *Clin Pharmacol Ther* 11: 808-15.

Perez-Reyes, M. 1990. Marijuana smoking: factors that influence the bioavailability of tetrahydrocannabinol. In C.N. Chiang and R.L. Hawks, eds. *Research Findings on Smoking of Abused Substances*. NIDA Research Monograph 99:42-62.

Polen, M. et al. 1993. Health care use by frequent marijuana smokers who do not smoke tobacco. *West J Med* 158(6): 596-601.

Russo, E. 2003. An interview with Markus Storz: June 19, 2002. *J Cannabis Therap* 3(1): 67-78.

Tashkin, D.P. et al. 1977. Bronchial effects of aerolized delta-9-tetrahydrocannabinol in healthy and asthmatics subjects. *Amer Rev Resp Dis* 115:57-65.

Tashkin, D. 1993. Is frequent marijuana smoking hazardous to health? *West J Med* 158(6): 635-7.

Truitt, E. 1971. Biological disposition of tetrahydrocannabinols. *Pharmacol Rev* 23(4): 273-8.

SUBMITTED: 07/09/03
ACCEPTED IN REVISED FORM: 08/02/03