SOME SMOKING CHARACTERISTICS OF MARIJUANA CIGARETTES*

K. H. Davis, Jr., I. A. McDaniel, Jr.
L. W Cadwell, P. L. Moody

Research Triangle Institute
Research Triangle Park, North Carolina

I. INTRODUCTION

The primary route of illicit consumption of Cannabis sativa L. is through the smoking of cigarettes made from the leaves and "tops" of the plant, which are commonly known as "marijuana". Marijuana cigarette smoking has been the subject of a number of research studies, and in recent times has received limited medical use for the relief of nausea associated with cancer chemotherapy and for the treatment of elevated intraoptic pressure associated with glaucoma.

We have been involved since 1974 in the manufacture, analysis and distribution of standardized machine-made marijuana cigarettes to clinical and basic research programs, and in the identification of factors affecting patient acceptability of these cigarettes. Lately, we have been particularly concerned with quantitating the cigarette smoking process with respect to delivery of delta-9-tetrahydrocannabinol (THC) in mainstream smoke, and with the determination of the effect on cannabinoid delivery of various measures employed to increase patient acceptability.

In earlier unpublished studies, we found that burning temperatures in two different potencies of standard marijuana cigarettes when smoked by human subjects were about 800°C. We also found that puffing conditions (40 mL/2-sec puff), approximating the standard puffing conditions established foruse with cigarette smoking machines in tobacco cigarette testing laboratories, would produce burning temperatures of about

*Supported by NIDA contract No. 271-81-3802.

800°C (1). Among other researchers Perez-Reyes et al. (2) and Kinzer et al. (3) measured similar puff volumes and puff durations in human subjects smoking marijuana cigarettes, although the puff frequencies measured by these researchers (approximately three puffs/min) were different from the one puff/min puff frequency built into most cigarette smoking machines. While such smoking conditions may not represent the smoking parameters of heavy marijuana smokers, they are representative of light to moderate smokers. Thus, smoke condensate collected from the smoking of standard marijuana cigarettes on a cigarette smoking machine should be representative of that ingested by light to moderate smokers, with respect to the cannabinoid profile, but not in quantitative terms. All except inexperienced smokers should receive heavier cannabinoid doses through cigarette smoking than are contained in these smoke condensates.

Investigational use of marijuana cigarettes has been complicated by lack of quantitative information about the delivery of THC in the mainstream smoke under various smoking conditions. In this study, a cigarette smoking machine was used to obtain mainstream smoke condensates in which the THC content was quantitated by use of GLC methodology with an internal standard. The data obtained provide an estimate of the lower limit of THC ingestion by marijuana smokers, as well as a measure of the total amount of THC produced in the smoke of marijuana cigarettes and the degree of destructive pyrolysis of THC. Changes in the rate of delivery of THC in the mainstream smoke of marijuana cigarettes with progressive burning were found and quantitated. The degrees of translation of THC into mainstream smoke for marijuana cigarettes of two different potencies were compared.

The popular cigarette rolling papers employed in "street" use of marijuana are less porous than the standard cigarette papers used in the manufacture of marijuana cigarettes. Possible differences in the performance of machine-made cigarettes rolled with standard papers as compared to those rolled with "street" papers in production of THC in the smoke were investigated.

Humidification of marijuana cigarettes prior to smoking is commonly used as a means of moderating their "harshness", as perceived by patients and research subjects. The effect of humidification on the production of THC into mainstream smoke was determined.

II. MATERIALS AND METHODS

A. Marijuana Cigarettes, 3.10% THC

Marijuana (leaf material and tops) grown by the University of Mississippi in 1980 were blended and treated with amounts of water calculated to raise the moisture content to ca. 18%. Cigarettes were manufactured on an AMF cigarette machine following removal of seeds, stems, and fines by sieving. Cigarettes were dried, analyzed for cannabinoid content, graded by hand, packed in metal cans, and stored at -20°C until needed. THC analysis values were obtained on a dry-weight basis.

B. Marijuana Cigarettes, 1.60% THC

Marijuana (leaf material) of 1978 and 1979 crop years, furnished by the University of Mississippi, was made into cigarettes as described above for 3.10% THC cigarettes.

C. Preparation of Cigarettes for Smoking Studies

In order to accommodate 70 mm "street" rolling papers, all cigarettes were cut from their original 85 mm length to 70 mm. For those cigarettes to be smoked with "street" papers, the original cigarette paper was removed without disturbing the plant material "rod" formed in manufacturing. The "street" paper was then put in place with the aid of a hand-held cigarette rolling device. Prior to smoking, all cigarettes were brought to 15-16% moisture content by humidification in a closed container over saturated aqueous sodium chloride solution for 16 hr. at room temperature.

D. Smoking Studies

A 15-port cigarette-smoking machine (non-commercial Liggett and Myers Tobacco Co., Inc. design, modification no. 4) was used for these studies. The smoke-condensate collection train consisted of a solvent bubbler trap charged with absolute ethanol upstream of a cylindrical smoke trap packed with sea sand (Fisher Chemical Co., Raleigh, NC). Prior to use, the sea sand was washed with organic solvents and water, then dried at 105°C. A flowmeter was placed in the suction line between the collection train and a small vacuum pump. This apparatus was operated with smoking parameters of 40 mL/2-sec puff, two puff/min/cigarette. In constant draft smoking

machine runs, each cigarette was burned in a single, uninterrupted draft at a flow rate of 20 mL/sec.

For each smoking condition, at least four replicate 15-cigarette runs on the smoking machine were carried out. Cigarettes were ignited with a small Bunsen burner and extinguished in a container of dry ice at the end of smoking or after a predetermined number of puffs. The smoke condensate was collected from each run by washing the sand trap with absolute ethanol and combining the washings with the ethanol from the bubbler trap. Smoke condensate and cigarette butt fractions were preserved at -20°C for analysis.

E. GLC Analysis Procedures

Aliquots of smoke condensate solutions equivalent to about 2 mg THC were treated with 1 ml of a 3 mg/ml solution of

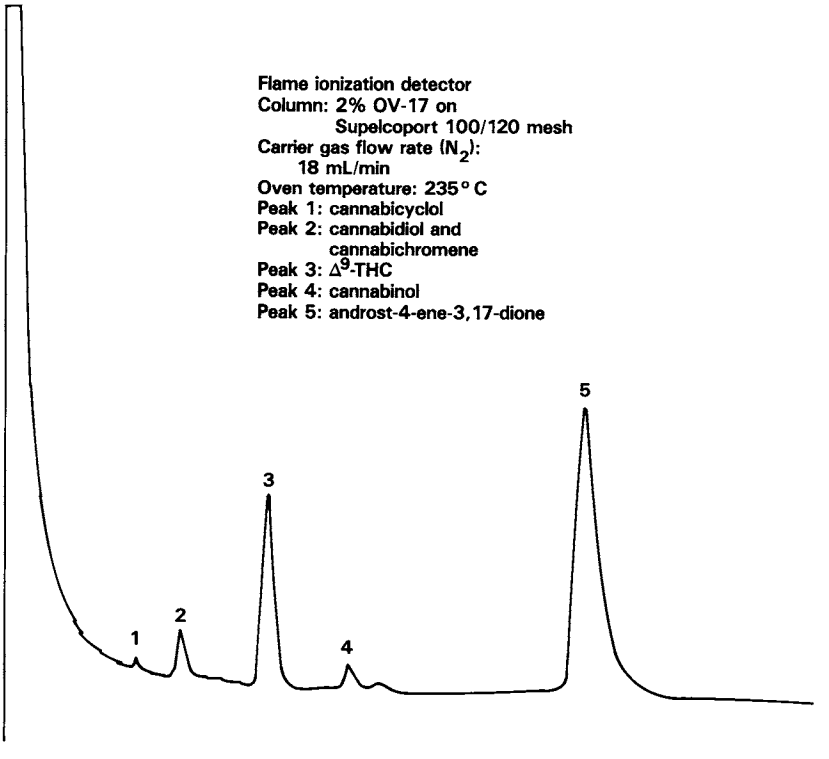

FIGURE 1. Gas-liquid chromatogram of marijuana smoke condensate.

androst-4-ene-3,17-dione (internal standard for GLC) in ethanol, evaporated nearly to dryness *in vacuo* at room temperature, and restored with absolute ethanol to an approximate concentration of 0.3 mg/ml with respect to THC. Entire cigarette butt fractions from each smoking run were extracted for analysis by a modification of the procedure of Fetterman et al. (4). Each extract was treated with an amount of a 10 mg/ml solution of androst-4-ene-3,17-dione in ethanol equivalent to about 1.5 mg of the internal standard per 1 mg of THC present, evaporated nearly to dryness, and restored to a concentration of about 0.3 mg/ml with respect to THC. Marijuana cigarettes were extracted for analysis using both the Soxhlet extraction procedure of Davis et al. (5) and a modification of the procedure of Fetterman et al. (4).

Essentially the GLC procedure of Davis et al. (5) was used to analyze samples, prepared as described above, of smoke condensates, butt fractions and cigarettes on an automated GLC apparatus consisting of a Varian 2440 gas chromatograph (Walnut Creek, CA) with flame ionization detectors coupled to a Varian 8000 autosampler and a Spectraphysics 4100 computing integrator (Santa Clara, CA). A 1.83 m x 2 mm ID 2% OV-17 on Supelcoport 100/120 mesh (Supelco Inc., Bellefonte, PA) glass GLC column, operated at 225°C with a carrier gas (N_2) flow rate of 25 ml/min, was used. Samples for analysis were run *vs.* a calibration standard containing 0.3 mg/ml of THC and 0.45 mg/ml of androst-4-ene-3,17-dione, and all assay results were corrected for calibration changes. Volumes of 1 mclof each sample were injected for analysis.

F. Moisture Content Determinations

Cigarette moisture contents were determined from the weight loss ofcigarette samples dried at 105-112°C ina forced draft oven.

III. RESULTS

Smoke condensates from marijuana cigarette smoking studies were analyzed for THC content by use of automated GLC technology (see Figure 1). In a comparison of low porosity "street" cigarette papers with the medium porosity papers used in the manufacture of the standard cigarettes, six replicate smoking runs were made with each of the paper types. The amount of THC produced with each paper type, expressed as percent of the total THC present in the marijuana smoked, is shown in Table I. Popular low porosity "street" cigarette papers provide a

TABLE I. Effect of Low and Medium Porosity Papers on THC Production in Mainstream Smoke Condensate from Marijuana Cigarettes[1]

	Combustion replicates, % translation of Δ^9-THC into mainstream smoke						
	1	2	3	4	5	6	Mean ± S.E.[2]
	Intermittent Puff Mode[3]						
Medium porosity paper CORESTA value = ~ 50	16.4	19.2	15.3	17.6	12.1	21.7	17.0 ± 1.4
Low porosity paper CORESTA value = ~ 10	10.8	18.6	16.8	14.6	24.7	22.3	19.6 ± 1.5

[1]Marijuana cigarettes contained 1.60% Δ^9-THC (dry weight basis).

[2]Standard error.

[3]One 2 second puff per minute, 40 mL per puff, 15 cigarettes per replicate.

slight increase in the degree of translation of THC to mainstream smoke as compared with the standard medium porosity papers used in cigarette manufacturing. This difference was statistically insignificant.

In determining the effect of high and low moisture content on the delivery of THC, four replicate smoking runs were carried out with each of two batches of cigarettes, one at 8% moisture and one at 16% moisture. The results are shown in Table II. No difference was found in the THC content of the mainstream smoke of marijuana cigarettes burned at high moisture content or at low moisture content.

Cigarettes of 1.60 and 3.10% THC content were compared with respect to delivery of THC in the mainstream smoke. For each potency, the results from four replicate smoking runs are reported in Table III. No statistically significant difference was observed between the two cigarette potencies, which yielded in the mainstream smoke 19 and 16% respectively of the THC contained in the marijuana actually combusted.

In order to obtain an estimate of the total amount of THC produced by standard marijuana cigarettes, four replicate constant-draft smoking runs were carried out with each potency (1.60 and 3.10% THC). As shown in Table III, 69% of the THC present in the marijuana combusted was found in the smoke condensate.

An investigation into the rate with which THC was delivered into the mainstream smoke with progressive burning of the cigarette was carried out. Individual studies were done (four replicates each) in which smoking was terminated after 2, 5, 7 and 9 puffs respectively. The THC contents of the resulting smoke condensates are given in Table IV, and presented graphically in Figures 2 and 3. These data indicate an increasing

TABLE II. Effect of Low and High Moisture Content on THC Production in Mainstream Smoke Condensate from Marijuana Cigarettes[1]

	Combustion replicates, % translation of Δ^9-THC into mainstream smoke				
	1	2	3	4	Mean ± S.E.[2]
	Intermittent Puff Mode[3]				
Marijuana cigarettes, 15.5% moisture content	16.7	18.4	18.2	14.7	17.0 ± 0.9
Marijuana cigarettes, 8.2% moisture content	16.3	18.2	19.7	16.4	17.6 ± 0.8

[1]Marijuana cigarettes contained 1.60% Δ^9-THC (dry weight basis).

[2]Standard error.

[3]One 2 second puff per minute, 40 mL per puff, 15 cigarettes per replicate.

TABLE III. Comparison of THC Production in Smoke Condensate from Two Potencies of Marijuana Cigarettes

	Combustion replicates, % translation of Δ^9-THC into smoke						
	1	2	3	4	5	6	Mean ± S.E.[1]
	Constant Draft Mode[2]						
1.60% Δ^9-THC cigarettes	66.2	64.2	70.0	72.7	72.5	70.9	69.4 ± 1.4
3.10% Δ^9-THC cigarettes	71.2	67.9	71.1	66.3	–	–	69.1 ± 1.2
	Intermittent Puff Mode[3]						
1.60% Δ^9-THC cigarettes	16.2	21.8	19.5	18.4	–	–	19.0 ± 1.2
3.10% Δ^9-THC cigarettes	17.7	15.5	14.7	16.5	–	–	16.1 ± 0.6

[1]Standard error.

[2]Constant burn at flow rate of 1,200 mL per minute, 15 cigarettes per replicate.

[3]One 2 second puff per minute, 40 mL per puff, 15 cigarettes per replicate.

rate of production of THC with progressive smoking. The increase appears to be linear. The butt fractions from these smoking runs also were analyzed for THC content, with results as shown in Table IV and Figure 4. As compared to the calculated THC content based on the weight of the butt fractions, the THC assay values were lower than expected after 2 and 5 puffs (18.7 and 39.3% burned). However, after 7 and 9 puffs (67.6 and 80.3% burned), no difference was observed.

TABLE IV. Differential Production of THC in Mainstream Smoke Condensate for Marijuana Cigarettes[1]

Amount of cigarette burned (%)	Combustion replicates, Δ^9-THC content of butt fractions (mg)					Combustion replicates, translation into mainstream smoke, Δ^9-THC per gram burned (mg)				
	1	2	3	4	Mean ± S.E.[2]	1	2	3	4	Mean ± S.E.[2]
					Intermittent Puff Mode[3]					
18.7	89	80	95	99	90.8 ± 4.1	1.7	2.0	1.5	1.6	1.7 ± 0.1
39.3	68	70	77	82	74.2 ± 3.2	2.8	2.4	2.0	2.3	2.4 ± 0.2
67.6	36	41	50	46	43.2 ± 3.0	3.4	2.3	2.6	2.6	2.7 ± 0.2
80.3	23	24	23	30	25.0 ± 1.7	2.6	3.5	3.2	2.9	3.0 ± 0.2

[1]Marijuana cigarettes contained 1.60% Δ^9-THC (dry weight basis).

[2]Standard error.

[3]One 2 second puff per minute, 40 mL per puff, 15 cigarettes per replicate.

IV. DISCUSSION

Under smoking-machine conditions, which provide a reasonable approximation of the puff duration and puff volume of many marijuana cigarette smokers, the production of THC in mainstream smoke from standard marijuana cigarettes was determined. Under these puffing conditions, 16-19% of the THC contained in the marijuana actually combusted was found in the mainstream smoke condensate. This amount should be representative of the lower limit of ingestion by marijuana smokers. Under constant draft conditions in which the whole cigarette is consumed in a single puff, and under which virtually no smoke is lost as sidestream smoke, 69% translation of THC to mainstream smoke is obtained. This represents the maximum proportion of THC which could be obtained in the smoke from a marijuana cigarette. Some 31% of THC is not found upon analysis of the smoke condensate, and is presumed destroyedby pyrolysis.

In a series of progressive smoking experiments, smoking was interrupted after a certain number of puffs and the smoke condensate and butt fractions analyzed for THC. The rate of production of THC into the mainstream smoke increased in a linear fashion nearly three-fold from the beginning to the end

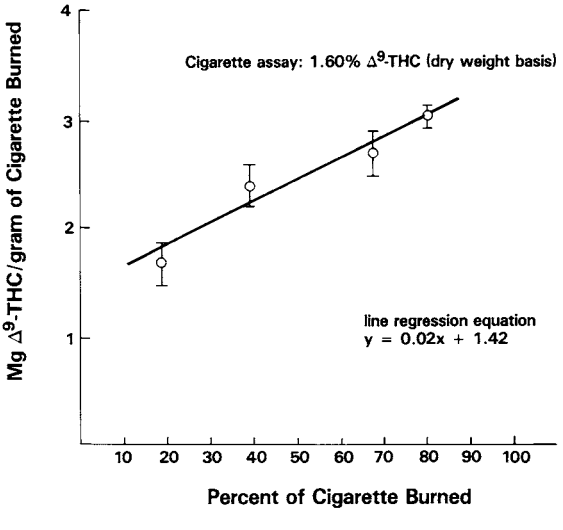

FIGURE 2. Differential production of THC: translation of THC into smoke vs. amount of cigarette (1.60% THC) burned.

of smoking. It therefore appears that smokers should receive increasingly greater amounts of THC per unit weight of marijuana burned as the cigarette is progressively consumed. The corresponding butt fractions showed a significant loss of THC during the early stages of smoking as compared to the expected THC content of the butts calculated on the basis of weight. During the latter stages of smoking, there was no significant difference between calculated and found THC contents of the butt fractions. It appears from those data that three phenomena occur in the burning marijuana cigarette which affect the initially uniform distribution of THC and its translation to smoke. First, there is initially a heavy destruction of THC by pyrolysis from the portion of the cigarette near the burning tip. Secon, the THC not destroyed by pyrolysis migrates away from the heat to concentrate in the cooler part of the cigarette. Once the initial migration has occurred and a moving equilibrium has been reached, further losses to pyrolysis are minimal. Third, there is also a continuous translation of THC to smoke, the rate of which increases sharply as cigarette. In order to verify these conclusions, the very

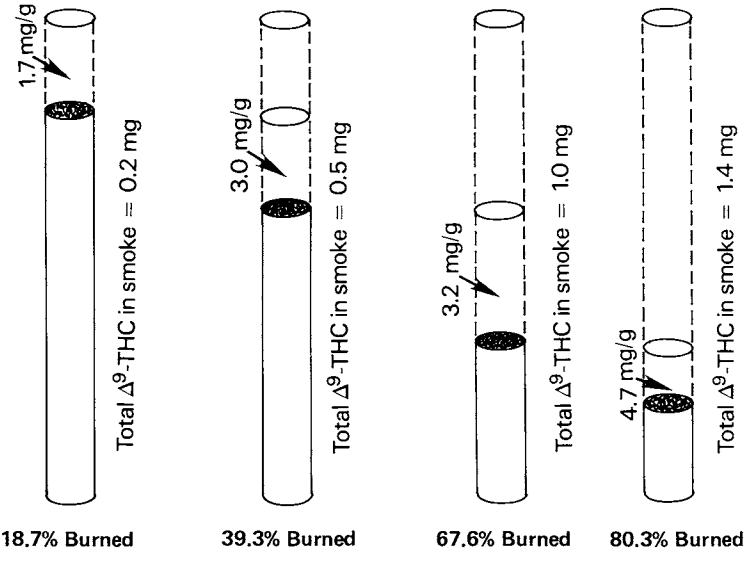

FIGURE 3. Differential production of THC in mainstream smoke condensate from marijuana cigarettes (1.60% THC) showing total THC translated to smoke and rate of production.

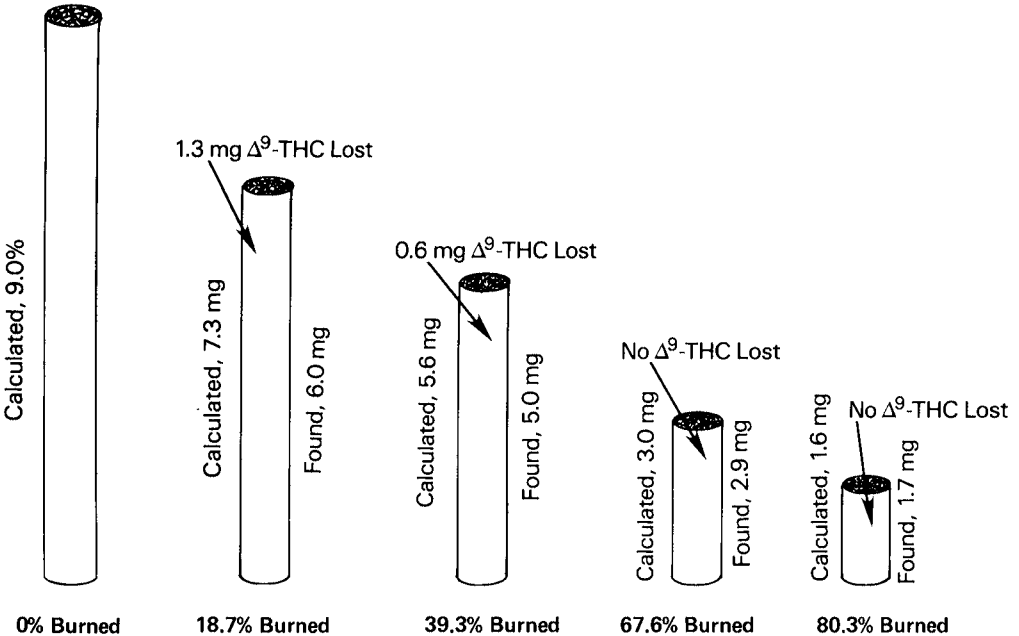

FIGURE 4. Differential loss of THC from marijuana cigarette butts showing calculated and found THC contents.

advancing heat drives the zone of THC concentration off of the interesting phenomena described herein will require more investigation.

Investigations into the effect of cigarette paper porosity on translation of THC to mainstream smoke indicate that there is no significant difference between popular "street" rolling papers of low porosity and standard medium porosity papers used in cigarette manufacture. Thus, the cigarette performance described above is representative of "street" rolling papers.

Humidification of marijuana cigarettes is a commonly used means of modifying their harshness upon smoking. The effect of high and low moisture content on the THC production of the standard cigarettes was investigated. No significant difference was found between the two conditions. Thus, neither humidification to increase acceptability to patients and research subjects nor accidental drying out of marijuana cigarettes alters their performance in the delivery of THC to mainstream smoke.

ACKNOWLEDGMENTS

We gratefully acknowledge Mr. V. L. Parker, Jr., and Mrs. B. A. Palazzolo for their assistance, and Drs. C. E. Cook, G. Barnett, R. L. Hawks and R. E. Willette for encouragement and helpful discussions.

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