

PAPER**CRIMINALISTICS**

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Potency Trends of Δ^9 -THC and Other Cannabinoids in Confiscated Cannabis Preparations from 1993 to 2008*

ABSTRACT: The University of Mississippi has a contract with the National Institute on Drug Abuse (NIDA) to carry out a variety of research activities dealing with cannabis, including the Potency Monitoring (PM) program, which provides analytical potency data on cannabis preparations confiscated in the United States. This report provides data on 46,211 samples seized and analyzed by gas chromatography-flame ionization detection (GC-FID) during 1993–2008. The data showed an upward trend in the mean Δ^9 -tetrahydrocannabinol (Δ^9 -THC) content of all confiscated cannabis preparations, which increased from 3.4% in 1993 to 8.8% in 2008. Hashish potencies did not increase consistently during this period; however, the mean yearly potency varied from 2.5–9.2% (1993–2003) to 12.0–29.3% (2004–2008). Hash oil potencies also varied considerably during this period ($16.8 \pm 16.3\%$). The increase in cannabis preparation potency is mainly due to the increase in the potency of nondomestic versus domestic samples.

KEYWORDS: cannabichromene (CBC), cannabidiol (CBD), cannabigerol (CBG), cannabinoids, cannabinol (CBN), cannabis, criminalistics, forensic science, gas chromatography-flame ionization detection (GC-FID), marijuana, potency, tetrahydrocannabivarin (THCV), Δ^9 -tetrahydrocannabinol (Δ^9 -THC)

Marijuana, the crude drug derived from *Cannabis sativa* L. pistillate inflorescence, is the most widely cultivated and consumed illicit drug in the world despite being under international control for eight decades (1,2). The reason for this is mainly attributed to two factors; namely, relaxation of cannabis law enforcement relative to other illicit drugs and the enormous extent of cannabis production and consumption. Furthermore, cannabis is cultivated both indoors and outdoors, often on a small scale, facilitating inconspicuous trading. Hashish (hash) and hash oil are two preparations designed to minimize the volume of the drug, thereby minimizing confiscation.

The Δ^9 -tetrahydrocannabinol (Δ^9 -THC) potency (concentration or content) of cannabis depends on soil and climate conditions, variety (phenotype), and cultivation techniques, with different parts of the plant having varying concentrations of the drug (3–6). The total number of identified cannabis constituents has increased from 489 in 2005 (7) to 537 in 2009, while the number of cannabinoids has increased from 70 to 109 (8–13). The main psychoactive

ingredient in cannabis is Δ^9 -THC (14,15); however, other cannabinoids have also demonstrated pharmacological activities, e.g., the nonpsychotropic cannabinoid cannabidiol (CBD) displays antipsychotic, antihyperalgesic, anticonvulsant, neuroprotective, and antiemetic properties (16–18).

The complex political, medical, cultural, and socioeconomic issues associated with cannabis necessitates not only public and governmental scrutiny, but especially scientific inquiry (1,2,19–24). The National Institute on Drug Abuse (NIDA) Potency Monitoring (PM) program at the National Center for Natural Products Research, University of Mississippi, provides analytical potency data on cannabis preparations seized in the United States, including both domestic and nondomestic material (25–28). A survey of the literature reporting similar programs in other countries revealed a number of comprehensive studies, e.g., England (2004–2005) (29), Brazil (2006–2007) (30), Netherlands (1999–2007) (31–34), Italy (1997–2004) (35), New Zealand (1976–1996) (36), and Australia (37), as well as a number of general reviews pertaining to cannabis potency trends (1,2,21,22,32,38,39).

This report covers 46,211 cannabis preparations confiscated and analyzed by gas chromatography-flame ionization detection (GC-FID) in the United States during 1993–2008, following on previous reports covering 1972–1997 (36,297 samples) (25–28). The total number of samples received during this period (1993–2008) was 47,583 as of 30 March 2009. The number of samples analyzed was 46,211, with 1,372 samples not analyzed for a variety of reasons, including insufficient material, wet material, and material containing only seeds and stems. Statistical analysis on the mean yearly Δ^9 -THC concentration is included to establish the potency trend over time. Data on hashish, hash oil, and the potencies of

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cannabichromene (CBC), cannabidiol (CBD), cannabinol (CBN), cannabigerol (CBG), and tetrahydrocannabivarin (THCV) are also presented.

Materials and Methods

Sample Acquisition

All samples analyzed in this investigation were confiscated during 1993 through 2008 by United States Federal and State law enforcement agencies.

Sample Identification

Sample classification is based on physical characteristics according to the following guidelines:

Cannabis Samples—All samples were received as raw plant material. These samples were further categorized as follows:

- *Marijuana* (known as herbal cannabis in Europe): usually found in four forms: (i) loose material - loose cannabis plant material with leaves, stems, and seeds; (ii) leaves - cannabis plant material consisting primarily of leaves; (iii) kilo bricks - compressed cannabis with leaves, stems, and seeds (typical Mexican packaging); and (iv) buds - flowering tops of female plants with seeds.
- *Sinsemilla*: flowering tops of unfertilized female plants with no seeds (subdivided as for marijuana with most samples being classified as buds).
- *Thai sticks*: leafy material tied around a small stem (typical Thailand packaging).
- *Ditchweed*: fiber type wild cannabis found in the Midwestern region of the United States (subdivided as for marijuana).

Hashish Samples—Hashish (known as cannabis resin in Europe) is composed of the resinous parts of the flowering tops of cannabis, mixed with some plant particles and shaped into a variety of forms, e.g., balls, sticks, or slabs. It is generally very hard with a dark green or brownish color.

Hash Oil Samples—Hash oil is a liquid or semi-solid concentrated extract of cannabis plant material. Depending on the process used to prepare hash oil, it is usually dark green, amber, or brownish.

Sample Storage

All samples are stored in a vault at controlled room temperature ($17 \pm 4^\circ\text{C}$).

Domestically Cultivated Cannabis

Cannabis preparations that have been verified as being produced from plants grown in the United States are classified as domestic samples, whereas all other samples are classified as nondomestic.

Sample Preparation

Cannabis—The samples were manicured in a 14 mesh metal sieve to remove seeds and stems. Duplicate samples (2×0.1 g) were extracted with internal standard solution (ISTD) [3 mL, 4-androstene-3,17-dione (100 mg) (Sigma Aldrich, St. Louis, MO) in chloroform/methanol (100 mL, 1:9, v/v), 1 mg/mL] at room temperature

for 1 h. The extracts were transferred to GC vials via filtration through sterile cotton plugs, followed by capping of the vials (25).

Hashish—Samples were powdered using a mortar and pestle or an electric blender. Duplicate samples (2×0.1 g) were extracted following the procedure outlined for cannabis samples (*vide supra*).

Hash Oil—Duplicate samples (2×0.1 g) were extracted with ISTD [4 mL, 4-androstene-3,17-dione (50 mg) in absolute ethanol (50 mL), 1 mg/mL] as follows: maceration at room temperature for 2–4 h, sonication for 5 min, addition of absolute ethanol (20 mL), and sonication for 5 min. The extracts were transferred to GC vials as described earlier.

Chromatographic Analysis

GC analyses were performed using Varian CP-3380 gas chromatographs, equipped with Varian CP-8400 automatic liquid samplers, capillary injectors, dual flame ionization detectors, and DB-1MS columns (15 m \times 0.25 mm \times 0.25 μm) (J&W Scientific, Folsom, CA). Data were recorded using a Dell Optiplex GX1 computer and Varian Star workstation software (version 6.1). Helium was used as carrier and detector makeup gas with an upstream indicating moisture trap and a downstream indicating oxygen trap. Hydrogen and compressed air were used as the combustion gases. The following instrument parameters were employed: air, 30 psi (300 mL/min); hydrogen, 30 psi (30 mL/min); column head pressure, 14 psi (1.0 mL/min); split flow rate, 100 mL/min; split ratio, 50:1; septum purge flow rate: 5 mL/min; makeup gas pressure, 20 psi (30 mL/min); injector temperature, 240°C; detector temperature, 270°C; oven program, 170°C (hold 1 min) to 250°C at 10°C/min (hold 3 min); run time, 12 min; injection volume, 1 μL . The instruments are daily maintained and calibrated to ensure a Δ^9 -THC/internal standard response factor ratio of one.

Calculation of Concentrations

The concentration of a specific cannabinoid is calculated as follows:

$$\text{cannabinoid}\% = \frac{GC[\text{area}](\text{cannabinoid})}{GC[\text{area}](\text{ISTD})} \times \frac{\text{amount}(\text{ISTD})}{\text{amount}(\text{sample})} \times 100$$

Statistical Analysis

The mean and standard deviation (SD) of the sample concentrations were calculated for the combined data set, by year and sample type, and for domestic and nondomestic samples. Normal and outlier cannabis samples were determined based on the mean and SD of the Δ^9 -THC concentration for each year and sample type (40). Normal samples are defined as samples with potencies in the range: mean $\pm 2.5 \times$ SD. Outlier samples are defined as samples with potencies that fall outside this range. The precision of the mean was determined through 95% confidence intervals (CIs). The CI was calculated using the Excel function TINV(probability, degrees of freedom), which returns the inverse or t-value of the Student's t-distribution as a function of the probability associated with the two-tailed Student's t-distribution and the degrees of freedom [number of samples (n) - 1]. The CI range is subsequently calculated as the mean \pm the product of the TINV value and the standard error of the mean (SEM), i.e., the SD divided by the square root of the number of samples, thus mean \pm SEM \times TINV

[$SEM = SD/\sqrt{n}$, $TINV = TINV(0.05, n - 1)$]. A 95% CI is a range of values that contains the true mean of the population with 95% certainty. The Pearson product-moment correlation coefficient (r) was calculated using the Excel PEARSON function, and the standard error for the predicted mean values for each year in the regression was calculated using the Excel STEYX function.

Results and Discussion

During the past 16 years (1993–2008), 46,211 samples of cannabis preparations confiscated in the United States, representing c. 8,321 tons, were analyzed at the University of Mississippi PM laboratory (Table 1). The PM program has analyzed 67,227 samples to date since 1968 (25–28). Samples classification is performed by the submitting agency and verified by the PM laboratory. Prior to 1995, there was no classification in the database for ditchweed; therefore, all ditchweed samples were classified as marijuana.

However, interest in monitoring ditchweed samples and its effect on the overall potency of confiscated marijuana necessitated this category on the sample report form since 1995. The data presented in this report on ditchweed samples prior to 1995 were generated by retrospective review of the PM data. Marijuana samples with Δ^9 -THC <1% and CBD > Δ^9 -THC were classified as ditchweed. Cannabis, i.e., marijuana, sinsemilla, Thai sticks, and ditchweed, represents the overwhelming majority of the samples confiscated in the United States (98.7%), while the hashish and hash oil combined contribution is <1.5% (Table 1). Marijuana typically represents at least 50% of the samples. Sinsemilla samples gradually increased from 2002, with a concurrent decrease in the number of marijuana samples.

The yearly arithmetic mean Δ^9 -THC concentration for the different types of cannabis samples shows large variation within categories and over time, with only the ditchweed samples being relatively constant (Table 2). Hashish and hash oil sample potencies

TABLE 1—Number of samples (n) analyzed by type and year.

Year	All		Marijuana*		Sinsemilla*		Thai sticks*		Ditchweed*		Hashish [†]		Hash oil [†]	
	n		n	%	n	%	n	%	n	%	n	%	n	%
1993	3412		3033	88.9	123	3.6	0	0.0	200	5.9	39	1.1	17	0.5
1994	3327		3032	91.1	104	3.1	0	0.0	148	4.4	29	0.9	14	0.4
1995	4791		4430	92.5	164	3.4	2	0.04	163	3.4	19	0.4	13	0.3
1996	2455		2148	87.5	169	6.9	0	0.0	118	4.8	12	0.5	8	0.3
1997	2495		2273	91.1	121	4.8	0	0.0	60	2.4	31	1.2	10	0.4
1998	2283		2075	90.9	101	4.4	0	0.0	87	3.8	15	0.7	5	0.2
1999	2692		2450	91.0	136	5.1	0	0.0	72	2.7	23	0.9	11	0.4
2000	3148		2928	93.0	113	3.6	0	0.0	73	2.3	27	0.9	7	0.2
2001	2716		2398	88.3	235	8.7	0	0.0	63	2.3	13	0.5	7	0.3
2002	2413		1789	74.1	528	21.9	0	0.0	75	3.1	16	0.7	5	0.2
2003	2517		1893	75.2	538	21.4	0	0.0	66	2.6	16	0.6	4	0.2
2004	2637		1815	68.8	731	27.7	0	0.0	62	2.4	25	0.9	4	0.2
2005	3004		1964	65.4	931	31.0	0	0.0	56	1.9	47	1.6	6	0.2
2006	2890		1770	61.2	1032	35.7	0	0.0	53	1.8	32	1.1	3	0.1
2007	3097		1635	52.8	1327	42.8	0	0.0	47	1.5	70	2.3	18	0.6
2008	2334		1151	49.3	1093	46.8	0	0.0	28	1.2	50	2.1	12	0.5
1993–2008	46,211		36,784	79.6	7446	16.1	2	0.0	1371	3.0	464	1.0	144	0.3

*Total cannabis: 45,603 samples (98.7%).

[†]Total hashish + hash oil: 608 samples (1.3%).

TABLE 2—Mean and SD Δ^9 -THC concentration by type of sample and year.

Year	All		Marijuana		Sinsemilla		Thai sticks		Ditchweed		Hashish		Hash oil	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
1993	3.4	2.9	3.4	2.4	5.8	3.8	0.0	0.0	0.4	0.3	6.6	6.7	16.5	11.7
1994	3.5	2.5	3.5	2.1	7.5	4.8	0.0	0.0	0.4	0.3	4.6	3.6	11.6	7.9
1995	3.8	2.3	3.7	1.8	7.5	4.4	4.5	0.8	0.4	0.4	3.6	3.7	13.2	8.9
1996	4.1	3.0	3.9	2.2	9.2	4.7	0.0	0.0	0.4	0.3	2.5	1.4	12.8	9.5
1997	4.6	3.7	4.3	2.7	11.6	5.9	0.0	0.0	0.5	0.3	8.9	9.3	18.2	9.0
1998	4.5	3.6	4.2	2.9	12.3	5.2	0.0	0.0	0.4	0.3	5.9	5.2	15.8	9.9
1999	4.6	4.0	4.2	3.2	13.4	4.7	0.0	0.0	0.4	0.3	4.9	4.2	16.2	10.7
2000	4.9	4.0	4.7	3.4	12.8	4.4	0.0	0.0	0.4	0.3	4.2	4.2	28.6	11.6
2001	5.4	4.1	5.0	3.5	9.6	5.4	0.0	0.0	0.4	0.3	8.5	5.9	19.4	8.1
2002	6.4	5.1	5.1	3.4	11.4	5.7	0.0	0.0	0.4	0.3	9.1	8.5	22.5	28.3
2003	6.3	4.8	5.0	3.1	11.6	5.7	0.0	0.0	0.3	0.3	9.2	7.6	15.5	6.9
2004	7.2	5.8	5.4	3.6	11.9	6.0	0.0	0.0	0.4	0.3	18.9	15.1	31.3	34.6
2005	7.2	5.3	5.2	3.2	11.6	5.7	0.0	0.0	0.4	0.3	12.0	10.3	6.4	2.8
2006	7.8	6.5	5.6	4.0	11.2	6.5	0.0	0.0	0.3	0.2	29.3	19.7	18.7	26.1
2007	8.8	7.4	6.1	3.7	11.1	6.6	0.0	0.0	0.4	0.3	27.7	18.4	24.9	29.6
2008	8.8	6.9	5.8	3.9	11.5	6.2	0.0	0.0	0.4	0.3	23.1	19.6	6.5	9.7
1993–2008	5.6	5.0	4.5	3.1	11.1	6.1	4.5	0.8	0.4	0.3	14.1	15.7	16.8	16.3
95% CI range*	5.53–5.62		4.46–4.53		11.01–11.28		0.00–11.69		0.37–0.40		12.69–15.56		14.07–19.45	

SD, Standard deviation.

*95% CI range: range of values that contains the true mean with 95% certainty.

showed the most variability over the 16-year period. The mean and SD for these categories were $14.1\% \pm 15.7\%$ and $16.8\% \pm 16.3\%$, respectively. The marijuana Δ^9 -THC concentration appeared to gradually increase from 1993 to 2008, with a Pearson product-moment correlation coefficient (r) of 0.982 and a standard error for the predicted mean values of 0.17 (Fig. 1). The mean Δ^9 -THC concentration for sinsemilla fluctuated considerably, ranging from a minimum in 1993 ($5.8\% \pm 3.8\%$) to a maximum in 1999 ($13.4\% \pm 4.7\%$) (Table 2, Fig. 1). Other than the expected finding that the yearly mean potencies of sinsemilla samples were much higher than that for marijuana samples, there did not appear to be any meaningful trend in the mean potency of the sinsemilla samples. The mean Δ^9 -THC concentration of sinsemilla samples

between 1993 and 2000 increased from 5.8% to 12.8% (121.8% increase), dropping slightly in 2001 (9.6%), and stabilizing between 2002 and 2008 ($11.5\% \pm 0.3\%$) (Fig. 1).

The change in cannabis potency over the past 40 years has been the subject of much debate and controversy. This report investigates the influence of outlier samples on the overall mean concentration of Δ^9 -THC for the time period studied in an attempt to clarify this issue. Normal and outlier cannabis preparations are samples with Δ^9 -THC concentrations that fall within and outside the range $\text{mean} \pm 2.5 \times \text{SD}$, respectively.

The outlier samples for marijuana and sinsemilla represent 2.4% and 0.5%, respectively, of the total samples for each type (Table 3). The distribution of Δ^9 -THC concentrations is positively skewed,

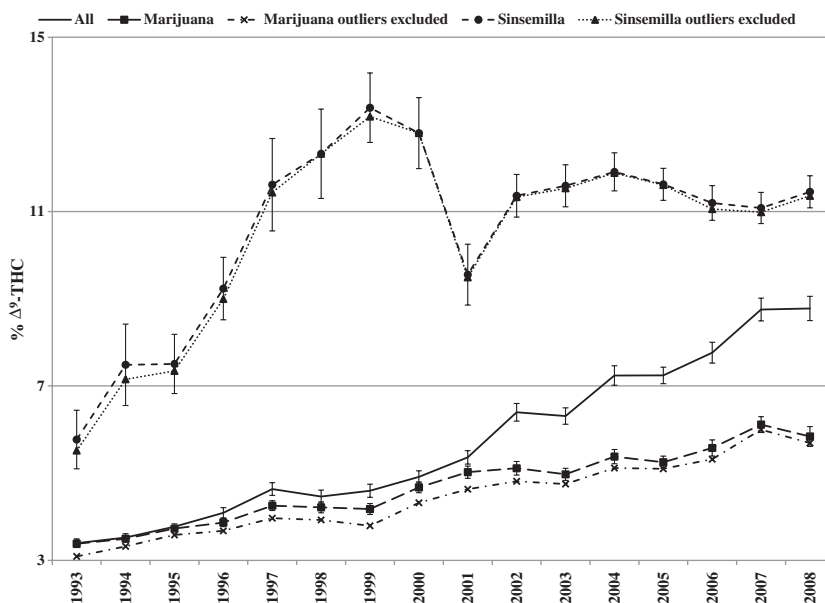


FIG. 1—Mean Δ^9 -THC concentration with 95% confidence intervals for all samples, marijuana and sinsemilla samples, and marijuana and sinsemilla samples with outliers excluded.

TABLE 3—Mean and SD Δ^9 -THC concentration for marijuana and sinsemilla samples with outliers* excluded.

Year	Marijuana					Sinsemilla				
	Outliers %	All samples		Outliers excluded		Outliers %	All samples		Outliers excluded	
		Mean	SD	Mean	SD		Mean	SD	Mean	SD
1993	2.9	3.4	2.4	3.1	1.7	2.4	5.8	3.8	5.5	3.4
1994	2.3	3.5	2.1	3.3	1.7	1.9	7.5	4.8	7.2	4.2
1995	2.0	3.7	1.8	3.6	1.5	1.2	7.5	4.4	7.3	4.2
1996	2.3	3.9	2.2	3.7	1.8	1.8	9.2	4.7	9.0	4.4
1997	3.1	4.3	2.7	4.0	2.2	0.8	11.6	5.9	11.4	5.6
1998	2.7	4.2	2.9	3.9	2.3	0.0	12.3	5.2	12.3	5.2
1999	3.5	4.2	3.2	3.8	2.4	1.5	13.4	4.7	13.2	4.4
2000	3.2	4.7	3.4	4.3	2.8	0.0	12.8	4.4	12.8	4.4
2001	3.4	5.0	3.5	4.6	2.8	0.4	9.6	5.4	9.5	5.4
2002	2.5	5.1	3.4	4.8	2.8	0.2	11.4	5.7	11.3	5.7
2003	2.1	5.0	3.1	4.8	2.7	0.4	11.6	5.7	11.5	5.6
2004	2.1	5.4	3.6	5.1	3.1	0.1	11.9	6.0	11.9	6.0
2005	1.5	5.2	3.2	5.1	3.0	0.1	11.6	5.7	11.6	5.7
2006	2.0	5.6	4.0	5.3	3.5	0.8	11.2	6.5	11.1	6.3
2007	0.9	6.1	3.7	6.0	3.5	0.5	11.1	6.6	11.0	6.5
2008	1.1	5.8	3.9	5.7	3.7	0.5	11.5	6.2	11.4	6.1
1993–2008	2.4	4.5	3.1	4.2	2.7	0.5	11.1	6.1	11.1	6.0
95% CI range [†]	–	4.46–4.53		4.22–4.27		–	11.01–11.28		10.92–11.20	

SD, Standard deviation.

*Mean $- 2.5 \times \text{SD} > \text{Outlier} > \text{Mean} + 2.5 \times \text{SD}$.

[†]95% CI range: range of values that contains the true mean with 95% certainty.

i.e., all outliers are samples with potencies higher than the mean potency. It is therefore important that the potential effect of the outliers is examined to determine whether the apparent trend of increasing potency is real or simply a statistical artifact. A comparison of the mean potency of marijuana and sinsemilla samples calculated for all samples versus for samples with outliers excluded indicates that the mean Δ^9 -THC concentration decreases for each year when the outliers are excluded (Table 3, Fig. 1). However, the general pattern of increasing potency of marijuana samples since 1993 appears to exist even when outliers are excluded. The Pearson product-moment correlation coefficient (r) and standard error for the predicted mean values after exclusion of marijuana sample outliers were 0.981 and 0.18, respectively. Because of the greater variability found in the potency of sinsemilla samples, fewer cases

were excluded as outliers and thus there was little effect on the mean potency for each of the years reported (Table 3, Fig. 1). The mean Δ^9 -THC concentration for marijuana and sinsemilla samples decreased by 0.24% and 0.08%, respectively, after exclusion of the outliers.

Further evidence that the mean Δ^9 -THC concentration for marijuana may be increasing is inferred by the analysis of the percentage of samples each year with Δ^9 -THC concentration more than 3%, 5%, and 9%. Marijuana samples with Δ^9 -THC >9% increased from 3.23% (1993) to a maximum 21.47% (2007). Conversely, the number of marijuana sample containing Δ^9 -THC <3% decreased between 1993 and 2007, with a slight increase in 2008 (Fig. 2). The trend for sinsemilla samples with Δ^9 -THC >9% followed a similar pattern to the overall trend for the yearly mean potencies

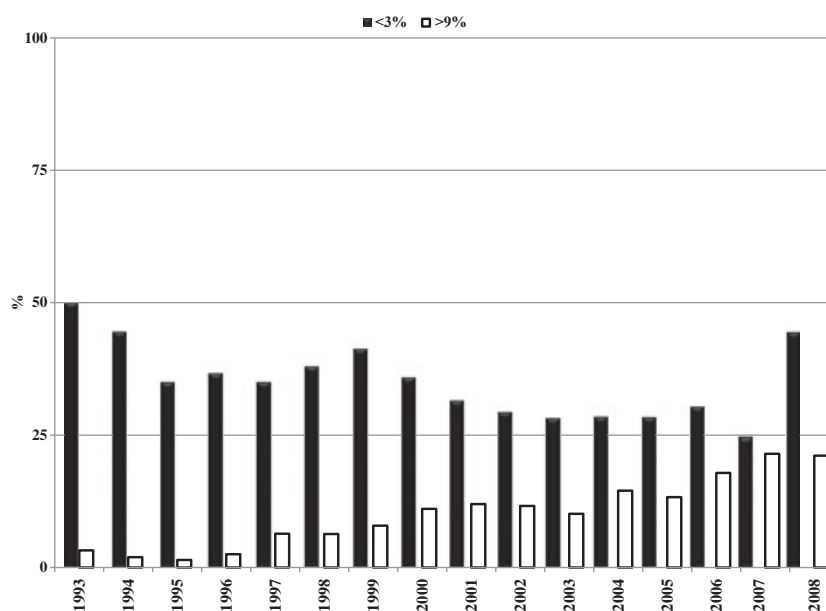


FIG. 2—Prevalence of low (<3%) and high (>9%) potency marijuana samples.

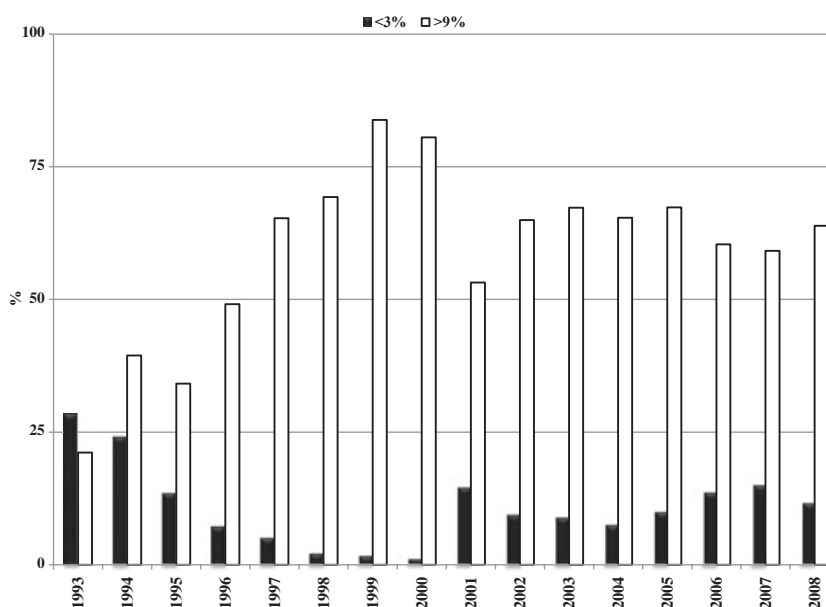


FIG. 3—Prevalence of low (<3%) and high (>9%) potency sinsemilla samples.

(Figs 1 and 3). Considering the large number of cannabis samples analyzed each year, it is doubtful that these observations are statistical artifacts.

The overall number of samples, mean, SD, maximum and minimum concentrations of Δ^9 -THC for the different types of samples categorized by origin, i.e., domestic or nondomestic, indicates that ditchweed is mainly a domestic product, whereas Thai sticks, hashish, and hash oil are nondomestic products (Table 4). Marijuana and sinsemilla samples represent more than 95% of all seizures. It is important to mention that samples are classified as being of domestic origin only if the seizure is made from a growing operation (indoor or outdoor) within the United States. All other samples are classified as being nondomestic, although they could possibly have been produced in the United States prior to seizure. It is also important to note that all nondomestic sample seizures made by the

DEA are of final products produced from mature plant material. In contrast, the domestic samples provided by the state eradication programs are seized at different stages of plant maturity. Overall, the number of samples of known domestic origin represents approximately one-third of all samples confiscated. The number of nondomestic seizures was consistently higher when compared to that of domestic seizures (Fig. 4). The mean Δ^9 -THC concentration for nondomestic cannabis samples showed a gradual increase, while domestic samples had little fluctuation (Fig. 5).

The mean concentration of the minor cannabinoids CBC, CBD, CBN, CBG, and THCV were also monitored (Table 5). CBD is the major cannabinoid found in ditchweed and is present in elevated amounts in intermediate type cannabis (moderate levels of both Δ^9 -THC and CBD) used to make hashish. The cannabinoid content of hashish and hash oil samples shows that, while hashish

TABLE 4—Number of samples (n), mean, SD, maximum and minimum Δ^9 -THC concentration by origin and type of sample.

Origin	Type	n	Mean	SD	Maximum	Minimum
Domestic	Marijuana	10,308	3.0	2.8	24.7	<0.01
	Sinsemilla	3067	7.9	5.5	33.1	0.1
	Thai sticks	0	—	—	—	—
	Ditchweed	1257	0.4	0.3	2.4	<0.01
	Hashish	3	34.0	25.4	52.9	5.1
	Hash oil	2	0.2	0.01	0.23	0.21
Nondomestic	1993–2008	14,637	3.8	4.1	52.9	<0.01
	Marijuana	26,476	5.1	3.0	37.2	<0.01
	Sinsemilla	4379	13.4	5.4	32.3	0.5
	Thai sticks	2	4.5	0.8	5.1	4.0
	Ditchweed	114	0.4	0.3	1.2	0.1
	Hashish	461	14.0	15.6	66.3	<0.01
	Hash oil	142	17.0	16.3	81.7	<0.01
	1993–2008	31,574	6.4	5.1	81.7	<0.01
All Samples	Marijuana	36,784	4.5	3.1	37.2	<0.01
	Sinsemilla	7446	11.1	6.1	33.1	0.1
	Thai sticks	2	4.5	0.8	5.1	4.0
	Ditchweed	1371	0.4	0.3	2.4	<0.01
	Hashish	464	14.1	15.7	66.3	<0.01
	Hash oil	144	16.8	16.3	81.7	<0.01
	1993–2008	46,211	5.6	5.0	81.7	<0.01

SD, Standard deviation.

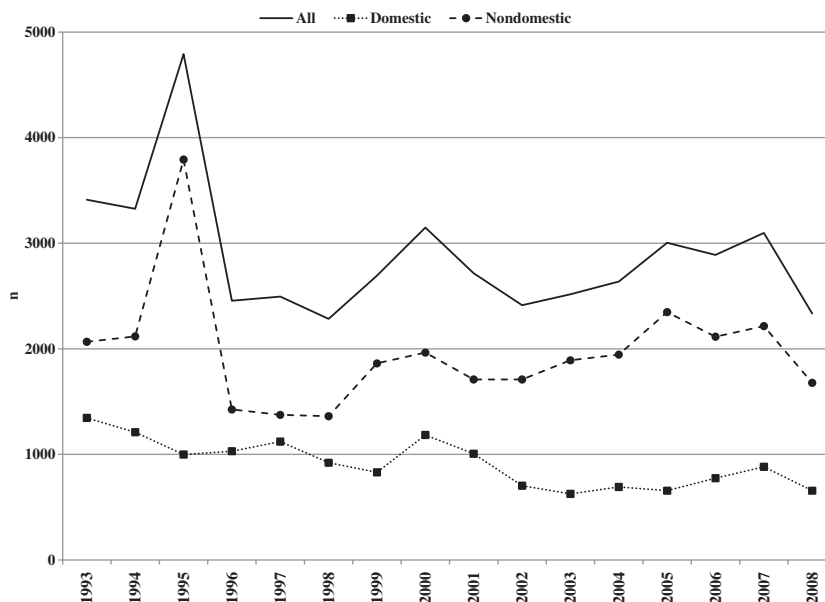


FIG. 4—Number (n) of domestic and nondomestic samples.

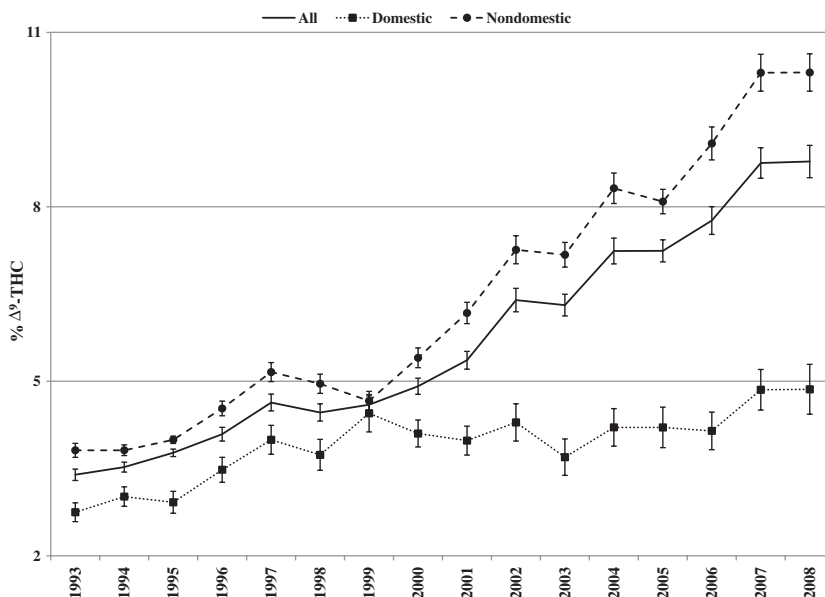


FIG. 5— Δ^9 -THC concentration of domestic and nondomestic samples with 95% confidence intervals.

TABLE 5—Mean concentration of minor cannabinoids by type and year.

Year	All						Marijuana						Sinsemilla					
	THC	CBC	CBD	CBN	CBG	THCV	THC	CBC	CBD	CBN	CBG	THCV	THC	CBC	CBD	CBN	CBG	THCV
1993	3.4	0.2	0.3	0.3	0.0	0.0	3.4	0.2	0.2	0.3	0.0	0.0	5.8	0.2	0.2	0.0	0.1	0.0
1994	3.5	0.2	0.4	0.2	0.1	0.1	3.5	0.2	0.3	0.2	0.1	0.1	7.5	0.2	0.5	0.1	0.3	0.1
1995	3.8	0.2	0.3	0.3	0.1	0.0	3.7	0.2	0.3	0.3	0.1	0.0	7.5	0.3	0.3	0.1	0.3	0.1
1996	4.1	0.2	0.4	0.3	0.2	0.1	3.9	0.2	0.3	0.2	0.1	0.1	9.2	0.3	0.5	0.1	0.4	0.1
1997	4.6	0.3	0.4	0.2	0.2	0.1	4.3	0.3	0.4	0.2	0.2	0.1	11.6	0.3	0.4	0.1	0.5	0.1
1998	4.5	0.2	0.4	0.3	0.2	0.1	4.2	0.2	0.3	0.2	0.1	0.1	12.3	0.4	0.4	0.2	0.5	0.1
1999	4.6	0.2	0.4	0.4	0.2	0.0	4.2	0.2	0.4	0.4	0.2	0.0	13.4	0.3	0.3	0.2	0.5	0.1
2000	4.9	0.2	0.5	0.4	0.2	0.1	4.7	0.2	0.4	0.4	0.2	0.1	12.8	0.2	0.3	0.2	0.4	0.1
2001	5.4	0.2	0.5	0.3	0.3	0.1	5.0	0.2	0.5	0.3	0.2	0.1	9.6	0.2	0.3	0.2	0.4	0.1
2002	6.4	0.2	0.4	0.2	0.2	0.1	5.1	0.2	0.5	0.2	0.2	0.1	11.4	0.3	0.2	0.2	0.3	0.1
2003	6.3	0.2	0.5	0.2	0.3	0.1	5.0	0.2	0.5	0.3	0.3	0.1	11.6	0.3	0.3	0.2	0.4	0.1
2004	7.2	0.3	0.5	0.3	0.3	0.1	5.4	0.2	0.5	0.3	0.3	0.1	11.9	0.3	0.2	0.2	0.5	0.1
2005	7.2	0.3	0.5	0.3	0.4	0.1	5.2	0.3	0.5	0.4	0.3	0.1	11.6	0.3	0.2	0.2	0.4	0.1
2006	7.8	0.2	0.4	0.3	0.3	0.1	5.6	0.2	0.5	0.3	0.3	0.1	11.2	0.3	0.2	0.2	0.4	0.1
2007	8.8	0.3	0.4	0.3	0.4	0.1	6.1	0.2	0.5	0.3	0.3	0.1	11.1	0.3	0.3	0.2	0.4	0.1
2008	8.8	0.3	0.4	0.3	0.4	0.1	5.8	0.2	0.4	0.3	0.3	0.1	11.5	0.3	0.2	0.2	0.4	0.1
1993–2008	5.6	0.2	0.4	0.3	0.2	0.1	4.5	0.2	0.4	0.3	0.2	0.1	11.1	0.3	0.2	0.2	0.4	0.1
SD	5.0	0.3	0.9	0.5	0.3	0.1	3.1	0.2	0.7	0.4	0.3	0.1	6.1	0.4	0.9	0.3	0.4	0.1

Year	Ditchweed						Hashish						Hash oil					
	THC	CBC	CBD	CBN	CBG	THCV	THC	CBC	CBD	CBN	CBG	THCV	THC	CBC	CBD	CBN	CBG	THCV
1993	0.4	0.1	1.7	0.0	0.0	0.0	6.6	0.7	3.8	2.3	0.5	0.3	16.5	0.7	0.1	7.7	0.3	0.5
1994	0.4	0.1	2.0	0.0	0.0	0.0	4.6	0.5	3.5	1.7	0.5	0.2	11.6	0.6	0.2	3.1	0.4	0.5
1995	0.4	0.1	1.6	0.0	0.1	0.0	3.6	0.5	3.3	1.7	0.3	0.1	13.2	1.0	0.7	4.2	0.5	0.3
1996	0.4	0.1	2.1	0.0	0.1	0.0	2.5	0.7	4.5	2.4	0.3	0.1	12.8	1.1	1.3	4.0	0.5	0.5
1997	0.5	0.1	1.9	0.0	0.0	0.0	8.9	0.7	4.0	2.1	0.5	0.3	18.2	1.0	0.3	3.5	0.3	0.6
1998	0.4	0.2	2.0	0.0	0.0	0.0	5.9	0.8	1.7	2.0	0.3	0.2	15.8	0.8	0.2	3.6	0.2	0.5
1999	0.4	0.1	1.8	0.1	0.1	0.0	4.9	0.6	1.8	2.1	0.5	0.3	16.2	1.3	0.4	4.8	0.3	0.4
2000	0.4	0.1	2.0	0.0	0.0	0.0	4.2	0.6	4.9	2.3	0.4	0.1	28.6	1.6	0.5	1.7	0.9	0.7
2001	0.4	0.1	1.8	0.0	0.1	0.0	8.5	0.6	2.7	1.5	0.6	0.3	19.4	1.2	1.3	4.4	0.9	0.6
2002	0.4	0.1	1.5	0.0	0.0	0.0	9.1	0.6	2.5	1.4	0.4	0.2	22.5	0.5	0.3	1.7	1.2	0.3
2003	0.3	0.1	1.8	0.1	0.1	0.0	9.2	0.7	3.9	1.8	0.4	0.2	15.5	0.8	0.2	1.3	0.3	0.4
2004	0.4	0.1	1.5	0.1	0.1	0.0	18.9	0.7	0.8	1.4	0.7	0.2	31.3	1.1	1.1	2.2	1.2	0.4
2005	0.4	0.1	1.9	0.1	0.1	0.0	12.0	0.9	1.7	1.9	0.4	0.2	6.4	0.2	0.3	1.1	0.2	0.2
2006	0.3	0.1	2.4	0.2	0.1	0.0	29.3	0.7	1.6	1.3	0.8	0.2	18.7	0.4	0.1	0.6	0.4	0.1
2007	0.4	0.1	2.0	0.1	0.1	0.0	27.7	0.8	1.2	1.8	1.0	0.3	24.9	0.9	0.6	1.5	0.7	0.3
2008	0.4	0.2	1.9	0.0	0.1	0.0	23.1	0.9	2.1	2.1	0.9	0.4	6.5	0.3	0.2	0.8	0.2	0.1
1993–2008	0.4	0.1	1.8	0.0	0.0	0.0	14.1	0.7	2.5	1.9	0.6	0.3	16.8	0.9	0.5	3.3	0.5	0.4
SD	0.3	0.1	1.5	0.2	0.1	0.0	15.7	0.7	2.9	1.4	0.6	0.3	16.3	0.9	0.8	3.8	0.7	0.4

CBC, cannabichromene; CBD, cannabidiol; CBG, cannabigerol; CBN, cannabinol; Δ^9 -THC, Δ^9 -tetrahydrocannabinol; THCV, tetrahydrocannabivarin.

is prepared from intermediate type cannabis, hash oil is prepared from drug-type cannabis (high Δ^9 -THC and low CBD levels) (3–6,16). CBC and CBN are usually higher in hashish and hash oil samples compared to cannabis samples. The CBN concentration relative to Δ^9 -THC reflects the age of the samples (41). CBG content is typically about 3–5% of the Δ^9 -THC content; however, in ditchweed this ratio increases to more than 10%, even though this type of cannabis preparation has the lowest overall mean CBG content. This is because ditchweed has very low Δ^9 -THC content ($0.4\% \pm 0.3\%$). THCV, an important biomarker in cannabis (42,43), is generally present at about 0.5–2.5% of the Δ^9 -THC content.

Conclusions

The question over the increase in potency of cannabis is complex and has evoked many opinions. The issue has been clouded somewhat by reports of 10- and 30-fold increases in cannabis potency since the 1970s. It is however clear that cannabis has changed during the past four decades. It is now possible to mass produce plants with potencies inconceivable when concerted monitoring efforts started 40 years ago. The PM program has strived to answer this cannabis potency question, while realizing that the data collected in this and other programs have some scientific and statistical shortcomings. These include randomness of samples, correctly identifying the various cannabis products, sampling, natural degradation of Δ^9 -THC over time, and different analytical techniques, making comparing results between countries and over time very difficult. However, analysis of the available data in conjunction with the PM program results makes a strong case that cannabis is not only more potent than in the past but also that this high-potency product's market share is also growing. This is clearly evident in the increase in sinsemilla seizures and in the increase in marijuana and sinsemilla samples with Δ^9 -THC >9%. The question now becomes: What are the effects of the availability of high-potency products on cannabis users?

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References

- Leggett T. A review of the world cannabis situation. United Nations Office On Drugs and Crime (UNODC). Bull Narc 2006;58:1–155.
- UNODC World Drug Report 2008, http://www.unodc.org/documents/wdr/WDR_2008/WDR_2008_eng_web.pdf (accessed April 14, 2009).
- Pacifico D, Miselli F, Micheler M, Carboni A, Ranalli P, Mandolino G. Genetics and marker-assisted selection of the chemotype in *Cannabis sativa* L. Mol Breed 2006;17:257–68.
- Pacifico D, Miselli F, Carboni A, Moschella A, Mandolino G. Time course of cannabinoid accumulation and chemotype development during the growth of *Cannabis sativa* L. Euphytica 2008;160:231–40.
- Bócsa I, Máthé P, Hangyel L. Effect of nitrogen on tetrahydrocannabinol (THC) content in hemp (*Cannabis sativa* L.) leaves at different positions. J Int Hemp Assoc 1997;4:78–9.
- Lewis R, Ward S, Johnson R, Burns DT. Distribution of the principal cannabinoids within bars of compressed cannabis resin. Anal Chim Acta 2005;538:399–405.
- ElSohly MA, Slade D. Chemical constituents of marijuana: the complex mixture of natural cannabinoids. Life Sci 2005;78:539–48.
- Appendino G, Giana A, Gibbons S, Maffei M, Gnani G, Grassi G, et al. A polar cannabinoid from *Cannabis sativa* var. Carma. Nat Prod Commun 2008;3:1977–80.
- Radwan MM, ElSohly MA, Slade D, Ahmed SA, Wilson L, El-Alfy AT, et al. Non-cannabinoid constituents from a high potency *Cannabis sativa* variety. Phytochemistry 2008;69:2627–33.
- Ahmed SA, Ross SA, Slade D, Radwan MM, Khan IA, ElSohly MA. Structure determination and absolute configuration of cannabichromane derivatives from high potency *Cannabis sativa*. Tetrahedron Lett 2008;49:6050–3.
- Radwan MM, Ross SA, Slade D, Ahmed SA, Zulfiqar F, ElSohly MA. Isolation and characterization of new cannabis constituents from a high potency variety. Planta Med 2008;74:267–72.
- Ahmed SA, Ross SA, Slade D, Radwan MM, Zulfiqar F, ElSohly MA. Cannabinoid ester constituents from high-potency *Cannabis sativa*. J Nat Prod 2008;71:536–42.
- Radwan MM, ElSohly MA, Slade D, Ahmed SA, Khan IA, Ross SA. Biologically active cannabinoids from high potency *Cannabis sativa*. J Nat Prod 2009;72:906–11.
- Mackie K. Understanding cannabinoid psychoactivity with mouse genetic models. PLoS Biol 2007;5:2106–8.
- Mackie K. From active ingredients to the discovery of the targets: the cannabinoid receptors. Chem Biodiversity 2007;4:1693–706.
- Galal AM, Slade D, Gul W, El-Alfy AT, Ferreira D, ElSohly MA. Naturally occurring and related synthetic cannabinoids and their potential therapeutic applications. Recent Pat CNS Drug Discovery 2009;4:112–36.
- Pertwee RG. The diverse CB1 and CB2 receptor pharmacology of three plant cannabinoids: Δ^9 -tetrahydrocannabinol, cannabidiol and Δ^9 -tetrahydrocannabinol. Br J Pharmacol 2008;153:199–215.
- Mechoulam R, Peters M, Murillo-Rodriguez E, Hanus LO. Cannabidiol—recent advances. Chem Biodiversity 2007;4:1678–92.
- Ramaekers JG, Kauert G, van Ruitenbeek P, Theunissen EL, Schneider E, Moeller MR. High-potency marijuana impairs executive function and inhibitory motor control. Neuropsychopharmacology 2006;31:2296–303.
- Zuardi AW. History of cannabis as a medicine: a review. Rev Bras Psiquiatr (Braz J Psychiatry) 2006;28:153–7.
- McLaren J, Swift W, Dillon P, Allsop S. Cannabis potency and contamination: a review of the literature. Addiction 2008;103:1100–9.
- Smith N. High potency cannabis: the forgotten variable. Addiction 2005;100:1558–60.
- Carter GT, Mirken B. Medical marijuana: politics trumps science at the FDA. MedGenMed 2006;8:46.
- Swami M. Cannabis and cancer link. Nat Rev Cancer 2009;9:148.
- ElSohly MA, Ross SA, Mehmedic Z, Ararat R, Yi B, Banahan BF. Potency trends of Δ^9 -THC and other cannabinoids in confiscated marijuana from 1980–1997. J Forensic Sci 2000;45:24–30.
- ElSohly MA. Marijuana: constituents and potency trends. 219th ACS National Meeting, Book of Abstracts 2000;TOXI:006.
- ElSohly MA, Holley JH, Turner CE. Constituents of *Cannabis sativa* L. XXVI. The Δ^9 -tetrahydrocannabinol content of confiscated marijuana, 1974–1983. In: Harvey DJ, Paton W, Nahas GG, editors. Marijuana '84: proceedings of the Oxford symposium on cannabis. England: IRL Press, 1985;37–42.
- ElSohly MA, Holley JH, Lewis GS, Russell MH, Turner CE. Constituents of *Cannabis sativa* L. XXIV: the potency of confiscated marijuana, hashish, and hash oil over a ten-year period. J Forensic Sci 1984;29:500–14.
- Potter DJ, Clark P, Brown MB. Potency of Δ^9 -THC and other cannabinoids in cannabis in England in 2005: implications for psychoactivity and pharmacology. J Forensic Sci 2008;53:90–4.
- Lopes de Oliveira G, Voloch MH, Sztulman GB, Negrini Neto O, Yonamine M. Cannabinoid contents in cannabis products seized in São Paulo, Brazil, 2006–2007. Forensic Toxicol 2008;26:31–5.
- Pijlman FTA, Rigter SM, Hoek J, Goldschmidt HJM, Niesink RJM. Strong increase in total Δ^9 -THC in cannabis preparations sold in Dutch coffee shops. Addict Biol 2005;10:171–80.
- King LA, Carpentier C, Griffiths P. An overview of cannabis potency in Europe. Luxembourg, Belgium. European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) 2004. http://www.emcdda.europa.eu/attachements.cfm/att_33985_EN_Insight6.pdf (accessed April 18, 2009).
- van Laar M, Cruts G, van Gageldonk A, Croes E, van Ooyen-Houben M, Meijer R, et al. The Netherlands drug situation 2007: report to the EMCDDA by the reitox national focal point. Utrecht, Netherlands. Trimbos Institute, Netherlands Institute of Mental Health and Addiction,

- 2008, http://english.wodc.nl/images/The%20Netherlands%20Drug%20Situation%202007_tcm45-115793.pdf (accessed April 18, 2009).
34. Niesink RJM, Rigter S, Hoek J, Goldschmidt H. THC concentrations in marijuana, nederwiet and hash in Netherlands coffee shops (2006–2007). Utrecht, The Netherlands: Trimbos Institute, Netherlands Institute of Mental Health and Addiction, 2007.
 35. Licata M, Verri P, Beduschi G. Δ^9 -THC content in illicit cannabis products over the period 1997–2004 (first four months). *Ann Ist Super Sanità* 2005;41:483–5.
 36. Poulsen HA, Sutherland GJ. The potency of cannabis in New Zealand from 1976 to 1996. *Sci Justice* 2000;40:171–6.
 37. Hall W, Swift W. The THC content of cannabis in Australia: evidence and implications. *Aust NZ J Public Health* 2000;24:503–8.
 38. Holler JM, Bosy TZ, Dunkley CS, Levine B, Past MR, Jacobs A. Δ^9 -Tetrahydrocannabinol content of commercially available hemp products. *J Anal Toxicol* 2008;32:428–32.
 39. King LA, Carpentier C, Griffiths P. Cannabis potency in Europe. *Addiction* 2005;100:884–6.
 40. Barnett V, Lewis T. *Outliers in statistical data*, 3rd edn. New York, NY: John Wiley & Sons Ltd., 1994.
 41. Ross SA, ElSohly MA. CBN and Δ^9 -THC concentration ratio as an indicator of the age of stored marijuana samples. *Bull Narc* 1997–1998;49–50:139–47.
 42. ElSohly MA, DeWit H, Wachtel SR, Feng S, Murphy TP. Δ^9 -Tetrahydrocannabivarin as a marker for the ingestion of marijuana versus Marinol: results of a clinical study. *J Anal Toxicol* 2001;25:565–71.
 43. ElSohly MA, Feng S, Murphy TP, Ross SA, Nimrod A, Mehmedic Z, et al. Δ^9 -Tetrahydrocannabivarin (Δ^9 -THCV) as a marker for the ingestion of cannabis versus Marinol. *J Anal Toxicol* 1999;23:222–4.

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