



New trends in cannabis potency in USA and Europe during the last decade (2008–2017)

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Abstract

Through the potency monitoring program at the University of Mississippi supported by National Institute on Drug Abuse (NIDA), a total of 18108 samples of cannabis preparations have been analyzed over the last decade, using a validated GC/FID method. The samples are classified as sinsemilla, marijuana, ditchweed, hashish, and hash oil (now referred to as cannabis concentrate). The number of samples received over the last 5 years has decreased dramatically due to the legalization of marijuana either for medical or for recreational purposes in many US states. The results showed that the mean Δ^9 -THC concentration has increased dramatically over the last 10 years, from 8.9% in 2008 to 17.1% in 2017. The mean Δ^9 -THC:CBD ratio also rose substantially from 23 in 2008 to 104 in 2017. There was also marked increase in the proportion of hash oil samples (concentrates) seized (0.5–4.7%) and their mean Δ^9 -THC concentration (6.7–55.7%) from 2008 to 2017. Other potency monitoring programs are also present in several European countries such as The Netherlands, United Kingdom, France, and Italy. These programs have also documented increases in Δ^9 -THC concentrations and Δ^9 -THC:CBD ratios in cannabis. These trends in the last decade suggest that cannabis is becoming an increasingly harmful product in the USA and Europe.

Keywords Cannabis · Potency monitoring · Sinsemilla · Marijuana · Hashish · Hash oil · Concentrates · Δ^9 -THC · CBD · CBN · CBG

Introduction

The use of psychoactive substances by humans can be traced back to ancient times. First documentation of cannabis use was in 2700 B.C.; however, archeological and historical data from China indicate that *Cannabis sativa* was cultivated for

fibers since 4000 B.C. in Central Asia and North-Western China [1–3]. Cannabis use, and ultimately cultivation, subsequently spread throughout the world, specifically in India (ca. 1600 B.C.), Egypt (1550 B.C.), the Near and Middle East (ca. 900 B.C.), Europe (ca. 800 B.C.), South-East Asia (100–200 A.D.), sub-Saharan Africa (1000–1100 A.D.), and the Americas (1500–1900 A.D.).

The Chinese used cannabis fibers to manufacture textiles, paper, and ropes, while the fruit was used as food. Medicinal use of cannabis started around the same time as its use as an agricultural crop, with uses that included rheumatic pain, intestinal constipation, and malaria. Reports of the medicinal uses of cannabis first appeared in the Chinese pharmacopoeia, Shen-nung Pen Ts'ao ching (Divine Husbandman's Materia Medica), in the first century A.D. [3–5]. According to the pharmacopoeia, mafen, the flowers of the female plant, provided the most medicinal value, being prescribed for menstrual fatigue, rheumatism, malaria, beriberi, constipation, and forgetfulness. The pharmacopoeia, however, warned that ingesting too many cannabis seeds “will produce visions of devils...

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over a long term, it makes one communicate with spirits and lightens one's body..." [6]. This is the first known documented reference to the psychoactive properties of cannabis.

In India, cannabis was widely used as a medicine and a recreational drug; however, authorities differ on the exact date of its introduction into the sub-continent. Cannabis use in Ancient India was claimed in the *Atharva Veda* ca. 1600 B.C. [7], while others have questioned whether references to cannabis in Indian literature are reliable prior to 1000 A.D. [2, 8]. There are three popular preparations available, each providing a range of psychoactivity. Three popular preparations are available providing a range of psychoactivity: "Bhang", prepared from dry leaves without any flowers, was the weakest preparation, followed by "Ganja", prepared from the flowers of female plants, and "Charas", made from the highly potent resin that covers female flowers. Medicinal indications included analgesic, anti-convulsant, hypnotic, tranquilizer, anesthetic, anti-inflammatory, anti-biotic, anti-parasitic, anti-spasmodic, digestive, appetite stimulant, diuretic, aphrodisiac or anaphrodisiac (anti-aphrodisiac), anti-tussive, and expectorant [9].

The ancient Egyptians also used cannabis as a medicine. A series of ancient writings on stone and medical papyri, including the oldest surviving original document which mentions cannabis, the *Ebers papyrus* (ca. 1550 B.C.), describe the medicinal use of cannabis for glaucoma, gynecological disorders, migraines, and anti-inflammatory and analgesic effects. However, the limited reference to cannabis and the absence of therapeutic information indicate that it was not frequently used medicinally. This is possibly due to the fact that cannabis was not native to Egypt and, therefore, only available in limited supply. In addition, these documents did not explicitly refer to the psychoactive effects of cannabis [10, 11].

The Scythians, an Ancient Iranian people who originated from Central Asia, introduced cannabis to Europe before the Christian Era (C.E.), as described by the Dorian Greek historian Herodotus of Halicarnassus (430–424 B.C.) [6, 8]. The Greeks and Romans also used medical cannabis, although it appears that they did not use the flowering tops, only the seeds and roots of the plant to treat minor ailments [12].

Cannabis has been cultivated and used in sub-Saharan Africa, especially Eastern and Southern Africa, since at least the fifteenth century, when it was probably introduced by Arab merchants establishing trading posts on the continent (1100–1200 A.D.). Research indicates that the San and Khoikhoi people, the earliest inhabitants of Southern Africa, used "dagga" (slang for cannabis in South Africa) before 1500 A.D., i.e., before the first contact between Europeans and native Africans. In Africa, the plant was used for snake bites, to facilitate childbirth, malaria, fever, blood poisoning, anthrax, asthma, and dysentery. Present-day uses include

treatment of indigestion and high blood pressure, as well as to deworm horses and donkeys [13–16].

In America, the cannabis use probably began in South America when the Spanish introduced the plant to Chile (1545 A.D.). However, bones of Peruvian mummies dated from 200 to 1500 A.D. were shown to contain cannabinoids [17], indicating contact between South America and Asia or Egypt before the arrival of Christopher Columbus (1451–1506) in 1545 A.D. [18]. It is generally accepted that cannabis was imported to Brazil in the early sixteenth century by slaves from Western African countries, particularly to Angola, Congo, Senegal, and the Guinea Coast [11, 19, 20].

Although it is not known exactly when the psychotropic properties of cannabis were discovered in North America, evidence suggests that Louis Hébert (1575–1627), the apothecary (pharmacist) of Samuel de Champlain (1580–1635), a French navigator, cartographer and explorer, introduced cannabis to American settlers in 1606. Initially, hemp was only used in the production of rope, sails, and clothing; the medicinal use of cannabis across North America started between 1840 and 1900 [21]. It was prescribed for tetanus, epilepsy, rheumatism, rabies, and as a muscle relaxant. During this time, cannabis preparations were sold freely in pharmacies of Western countries.

The American market produced numerous cannabis-containing home remedies in the late nineteenth and early twentieth centuries [9, 22]. Companies such as Merck, Burroughs-Wellcome, Bristol-Meyers Squibb, Parke-Davis, and Eli Lilly marketed various cannabis extracts and tinctures. However, cannabis was dropped from the British Pharmacopoeia in 1932 and from the United States Pharmacopoeia in 1941 [23]. Reasons for this decline included variable repeatability, efficacy and potency, short and unpredictable shelf-life, irregular response to oral administration, availability of potent opiates and synthetic alternatives, popularity of parenteral medicines, commercial pressures, and concern about recreational use. These concerns led to national and international laws restricting the medicinal use and research of cannabis. Currently, cannabis is highly regulated in the USA at the federal level.

In spite of strict laws, cannabis use is still prevailing in the United States and marijuana is the most widely used illicit drug. At the time of writing this manuscript, cannabis has been legalized for recreational use in 9 US states and as a medicine in 31 US states. It is probably too early to predict the long-term public health implications of these changes [24]. However, one key aspect of cannabis use that can be regularly monitored is the potency of cannabis preparations. The cannabis plant bio-synthesizes at least 144 cannabinoids [25], and the most abundant of these is Δ^9 -tetrahydrocannabinoid (Δ^9 -THC) and cannabidiol (CBD). Δ^9 -THC is responsible for the intoxicating effects

of cannabis, and experimental studies show that it can cause memory impairment, anxiety, and transient psychotic-like symptoms in a dose-dependent manner [26]. CBD is non-intoxicating and has been found to offset several, harmful effects of Δ^9 -THC, including memory impairment and psychotic-like symptoms [27–29]. As a result, the doses of Δ^9 -THC and CBD, and their relative ratio, are important factors in determining the level of harm an individual may experience [30–32]. Data from naturalistic studies show that cannabis users only partially adapt their smoking behavior to variation in Δ^9 -THC concentrations, implying that higher potency cannabis preparations will deliver larger doses of Δ^9 -THC [33, 34]. Moreover, a growing number of studies report that higher potency cannabis preparations are associated with adverse health outcomes, including elevated symptoms of cannabis use disorder [35–37], increased treatment admissions for cannabis problems [38], higher risk of developing psychosis [39], and increased risk of relapse to psychosis [40]. Increases in cannabis potency could, therefore, have important implications for the health effects of cannabis use, especially among adolescents who may be more vulnerable to cannabis harms [41].

In the United States, early evidence suggests that extremely potent cannabis concentrates (such as Butane Hash Oil) have risen in popularity in recent years. Within 2 years of legal sale in Washington State (2014–2016), these were estimated to account for 21% of the entire retail market and had a mean potency of 69% Δ^9 -THC [42]. However, the extent to which these products are available in illicit markets across the United States is currently unknown. It is very important to monitor the potency of the confiscated biomass and cannabis products as a measure of what is actually being sold and consumed on the illicit market [43]. We previously reported that cannabis potency in the United States increased from ~4% in 1996 to ~12% in the year 2014 [44]. In this article, we report new trends in cannabis potency in the United States over the last decade (2008 to 2017) and provide an overview of recent trends in cannabis potency in Europe.

Potency monitoring program in the US

Materials and methods

Sample acquisition and identification

Our laboratories at the University of Mississippi receive confiscated samples from the Drug Enforcement Administration (DEA) laboratories under agreement with the National Institute on Drug Abuse (NIDA). These DEA laboratories include Special Testing Research Laboratory (STRL), Northeast Regional Laboratory (NRL), Mid-Atlantic

Regional Laboratory (MARL), North Central Regional Laboratory (NCRL), South Central Regional Laboratory (SCRL), Southwest Regional Laboratory (SWRL), and Western Regional Laboratory (WRL). The received samples can be classified into three categories: cannabis, hashish, and hash oil. Cannabis samples are further classified into two categories, based on their physical characteristics: marijuana or sinsemilla. Marijuana is the dried buds with leaves, stems, and seeds typically grown outdoors for illicit drug use, mainly of female cannabis plants.

Sinsemilla consists of buds of unfertilized female plants, typically without seeds, mainly grown indoors. Ditchweed consists of a mixture of a fiber-type male and female wild cannabis grown in the Midwestern states. Hashish is a black, green, or golden colored resin (based on the purity and method of preparation) obtained from the buds of the female plants and shaped as balls, sticks, or slabs. Hash oil (referred to as concentrates) is a liquid or semi-solid cannabis product obtained by the solvent extraction of cannabis biomass (usually from the intermediate-type). It is black to dark green in color with a strong marijuana smell. All samples received are stored at room temperature ($17 \pm 4^\circ\text{C}$) and are analyzed shortly after receipt.

Sample preparation

Cannabis (Marijuana, sinsemilla, or ditchweed) Samples were manicured by sieving for the removal of the stems and seeds. Each of the two 100.0 mg portions of the manicured material were each extracted with 3 mL of the internal standard solution [4-androstene-3,17-dione (IS), at 1 mg/mL in $\text{CHCl}_3/\text{MeOH}$ (1:9)] at room temperature for 1 h. The extract was filtered and the filtrate analyzed by gas chromatography with flame ionization detection (GC/FID).

Hashish A single-edge razor blade was used to scrape 100 mg (in duplicate) from the block of hashish and extracted following the above procedure for cannabis preparations.

Hash oil (concentrates) Two 100 mg aliquots were extracted with 4.0 mL of IS (1.0 mg/mL ethanol) at room temperature for 2 h and sonicated for 5 min. Then, 20 mL of ethanol was added to each sample and sonicated briefly. The extract was filtered and transferred to GC vials for analysis.

GC-FID analysis

All samples were analyzed using a Varian 3380 gas chromatograph equipped with a Varian CP-8400 automatic liquid sampler, dual capillary injectors, and dual flame ionization detectors (GC/FID). The column was a 15 m $\times$ 0.25 mm DB-1, 0.25 μ film. Data were recorded with a Dell Optiplex GX1 computer with Microsoft Windows 98 and Varian Star (version 5.31) workstation software. Technical grade

helium was used as the carrier gas. A high capacity oxygen trap was located in the helium line. Helium was used as the detector make-up gas. Hydrogen and compressed air were used as the combustion gases. The method was previously reported [45] and used for the quantitative analysis of seven main cannabinoids in the received samples, namely, Δ^9 -tetrahydrocannabinol (Δ^9 -THC), cannabidiol (CBD), cannabinol (CBN), cannabichromen (CBC), Δ^8 -tetrahydrocannabinol (Δ^8 -THC), cannabigerol (CBG), and Δ^9 -tetrahydrocannabivarin (Δ^9 -THCV). This analytical method is fast (12 min/run), accurate, and precise using a single column. Direct injection of cannabis extract into the GC results in decarboxylation of the cannabinoid acids, therefore, measuring the concentration of the total cannabinoids (free and acids). Quantitative values are based on peak area ratios relative to the area of the internal standard peak (4-androstene-3,17-dione) contained in the extraction solvent.

Calculation of cannabinoid concentration

Quantitative values of potency (% dry weight) are computer-generated based on the analyte/internal standard area ratio, with each cannabinoid having a response factor of 1.0. The concentration of each cannabinoid in the samples is calculated from the following equation:

$$\% \text{ Analyte} = (\text{area analyte/area internal standard}) \times (\text{amount of IS}^*/100 \text{ mg}) \times 100,$$

* The amount of IS is 3 mg in cannabis and hashish samples and 4 mg in hash oil.

Results and discussion

There were a total of 18,674 samples seized between January 1, 2008 and June 31, 2018 by DEA regional laboratories, out of which 18,108 samples (96.9%) were analyzed in our laboratory (Table 1). As shown in Table 1, the number of seized samples decreased dramatically from 2882 in 2008 to 642 samples in 2017. Confiscated samples are classified as cannabis, hashish, or hash oil (concentrates). Cannabis is plant material which is further classified into sinsemilla, marijuana, and ditch weed. Table 1 and Fig. 1 show the number of samples analyzed by category for each year from

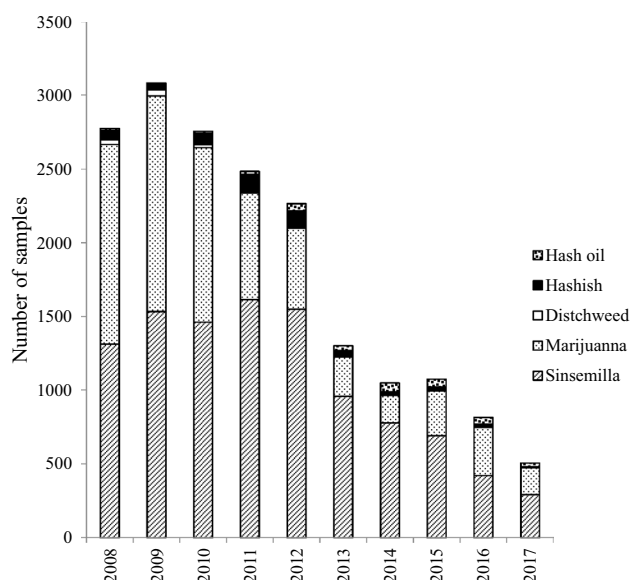


Fig. 1 Number of cannabis seizures by type and years 2008–2017

Table 1 Number of analyzed samples (*n*) per year

Year Seized	Total number Seized	Total number Analyzed	Number of cannabis samples analyzed						Number of ana-lyzed Hashish samples		Number of ana-lyzed Hash oil samples	
			Sinsemilla		Marijuana		Ditch-weed					
			<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%
2008	2882	2776	1313	47.3	1354	48.8	33	1.2	62	2.2	14	0.5
2009	3159	3083	1533	49.7	1462	47.4	40	1.3	42	1.4	6	0.2
2010	2812	2756	1462	53	1183	42.9	21	0.8	79	2.9	11	0.4
2011	2540	2484	1615	65.0	722	29.1	6	0.2	120	4.8	21	0.9
2012	2326	2264	1550	68.5	548	24.2	2	0.1	116	5.1	48	2.2
2013	1329	1302	958	73.4	269	20.7	2	0.1	41	3.1	32	2.5
2014	1058	1049	777	74.1	187	17.8	1	0.1	23	2.2	61	5.8
2015	1086	1074	690	64.3	303	28.2	5	0.5	23	2.1	53	4.9
2016	840	814	421	51.7	326	40.1	2	0.2	18	2.2	47	5.8
2017	642	506	292	57.7	183	36.2	0	0	7	1.4	24	4.7
2008–2017	18,674	18,108	10,611	58.6	6537	36.1	112	0.6	531	2.9	317	1.8

2008 to 2017, with cannabis representing more than 95.0% of the samples analyzed. As can be seen in Table 1, the most predominant type of seized cannabis is the sinsemilla form, representing 58.6% of all seizures, followed by marijuana (36.1%), and ditch weed (0.6%). Hash oil (concentrates) seizures gradually increased from 0.5% in 2008 to 4.7% in 2017 with the highest number in 2016 (5.8%). The number of hashish samples represented 1.4–5.1% of seizures with no observable trend over time.

The mean concentration of Δ^9 -THC of all the analyzed samples increased from 8.9% in 2008 to 17.1% in 2017 (Table 2; Fig. 2). The highest mean concentration was recorded in 2017 (17.1%), with no change between 2012 and 2016. Sinsemilla and marijuana showed the same trend of increasing potency over the last 10 years. The highest Δ^9 -THC content was achieved in 2017 for both sinsemilla and marijuana with potencies of 17.8% and 9.4% Δ^9 -THC, respectively (Table 2; Fig. 3). The marijuana mean Δ^9 -THC concentration showed a slight increase in the last decade from 6.0% in 2008 to 7.3% in 2016. Since ditch weed represents only 0.6% of the analyzed samples and the average THC content is $0.4\% \pm 0.2\%$, the potency of both sinsemilla and marijuana largely determines the overall potency of confiscated cannabis over the last decade (Table 2; Figs. 2, 3). Sinsemilla samples showed much higher potency than marijuana, which is in agreement with previously published data [44–48]. The Δ^9 -THC/CBD ratio across all samples tested during the period of this report increased dramatically from 23 in 2008 to 104 in 2017 (Fig. 4), which reflects an increasing trend of the growth and consumption of high Δ^9 -THC/low CBD cannabis material over the last decade.

Trends in the Δ^9 -THC content of hash and hash oil over time are shown in Table 2 and Fig. 5. The mean Δ^9 -THC concentration in confiscated hashish samples between 2008 and 2014 increased from 22.8% to 30.3%, dropped in 2015 (17.6%) and 2016 (15.5%), and achieved the maximum

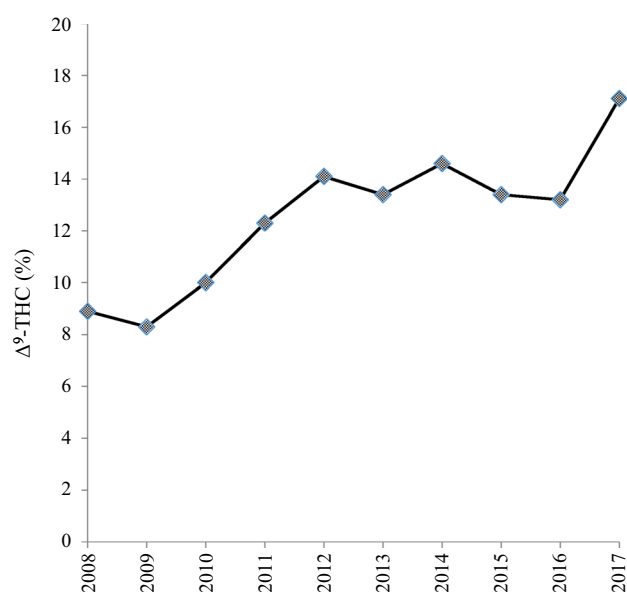


Fig. 2 Mean Δ^9 -THC concentration for all samples seized from 2008 to 2017

concentration in 2017 (45.9%). The hash oil (concentrates) mean Δ^9 -THC content showed a substantial increase in the last decade. It increased from 6.7% in 2008 to 53.5% in 2012, stabilized at 50% in 2013 and 2014, then dropped significantly in 2016 (37.9%), and sharply increased to 55.7% in 2017 (Table 2; Fig. 5).

The average concentration of cannabinoids other than Δ^9 -THC in all of the confiscated samples (cannabis, hashish, and hash oil) from 2008 to 2017 is presented in Tables 3, 4, 5, and 6. These cannabinoids include cannabichromene (CBC), cannabidiol (CBD), Δ^8 -tetrahydrocannabinol (Δ^8 -THC), cannabinol (CBN), cannabigerol (CBG), and Δ^9 -tetrahydrocannabivarin. The mean concentration of these minor cannabinoids is relatively higher in hash and hash

Table 2 Mean and SD of Δ^9 -THC concentration (%) by type of sample and year

Year	All		Cannabis							All can- nabis		Hashish		Hash oil	
			Sinsemilla		Marijuana		Ditchweed								
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
2008	8.9	6.7	11.5	6.1	6.0	3.9	0.4	0.3	6.0	3.4	22.8	19.3	6.7	9.3	
2009	8.3	6.2	10.8	6.1	5.7	4.2	0.4	0.3	5.6	3.5	21.3	15.3	8.9	9.6	
2010	10.0	7.7	12.7	6.1	5.7	4.4	0.5	0.3	6.3	3.6	22.8	16.5	38.3	30.1	
2011	12.3	8.9	13.6	6.2	5.6	3.1	0.5	0.2	6.6	3.2	30.0	15.1	37.0	26.2	
2012	14.1	11.3	14.5	6.4	6.1	3.7	0.65	0.1	7.1	3.4	31.7	19.1	53.5	25.5	
2013	13.4	10.2	13.6	5.9	6.3	3.1	0.5	0.1	6.8	3.0	29.3	16.4	50.0	26.6	
2014	14.6	13.5	13.5	6.4	5.8	3.7	0.2	–	6.5	5.1	30.3	23.7	50.8	27.3	
2015	13.4	13.2	12.7	6.1	6.8	3.2	0.4	0.3	6.6	3.2	17.6	20.1	56.3	24.9	
2016	13.2	10.8	15.0	5.6	7.3	3.4	0.8	0.1	7.7	3.0	15.5	14.3	37.9	26.6	
2017	17.1	12.9	17.8	5.1	9.4	4.7	0	0	13.6	4.9	45.9	26.6	55.7	24.7	

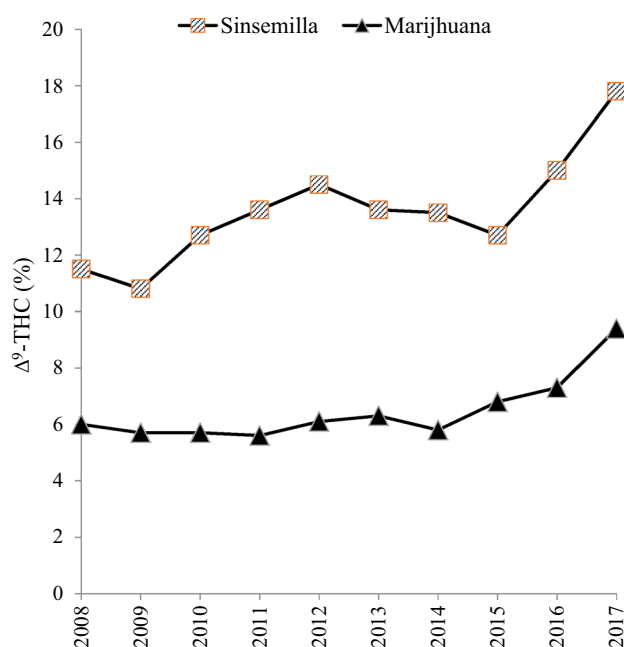


Fig. 3 Mean Δ^9 -THC concentration for sinsemilla and marijuana samples seized from 2008 to 2017

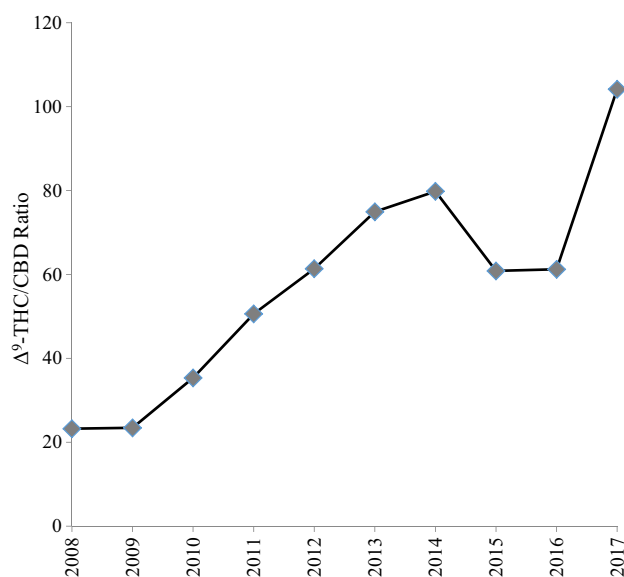


Fig. 4 Ratio of the mean concentration of Δ^9 -THC to CBD in across all samples by year

oil compared to the cannabis samples. CBD is the major cannabinoid in ditch weed and in the intermediate-type, which contains both THC and CBD in moderate level, cannabis plant material, from which hashish is made. Hash oil is predominantly made from high-potency (high Δ^9 -THC) cannabis plant material. The average concentration of CBD in hash and hash oil in the last decade showed significant fluctuation with a high Standard Deviation (SD) almost

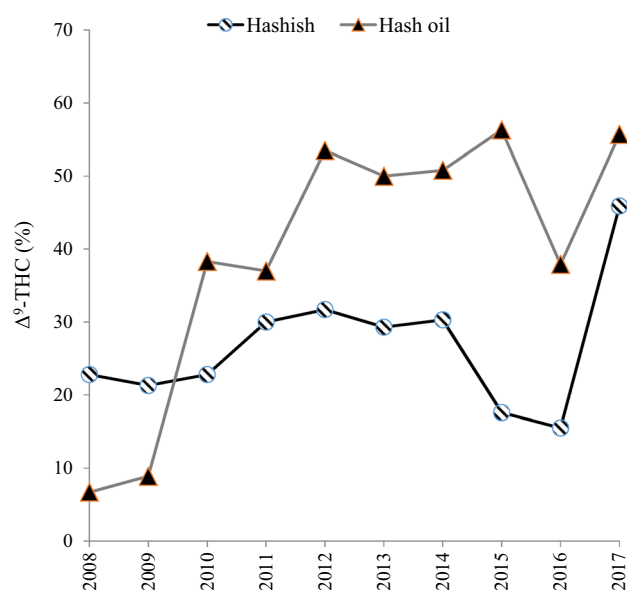


Fig. 5 Mean Δ^9 -THC concentration for hashish and hash oil (concentrates) samples seized from 2008 to 2017

every year (Tables 5, 6). After Δ^9 -THC and CBD, the most prevalent cannabinoids were identified to be CBN and CBG. The ratio of CBN concentration to Δ^9 -THC reflects, to a certain degree, the age of the sample, with higher concentrations of CBN indicating older material [49]. The concentrations of both CBN and CBG are higher in hashish and hash oil than in cannabis. The mean concentration of CBN in hash oil ranged from approximately 1.5–3%, while the CBG concentration ranged from approximately 0.15–1.7%, with substantial fluctuation. The CBN concentration in hashish was higher than hash oil, reaching almost 6% in 2016, but generally around 2–3%. The CBG concentration, on the other hand, was generally less than 1% in hashish.

Potency monitoring programs in Europe

Consistent with our findings in the USA, a meta-analysis performed on 21 different studies worldwide, containing 75 observations from 1979 to 2009 on mean Δ^9 -THC levels in herbal cannabis samples, revealed a consistent increase in cannabis potency worldwide, with a mean increase of 0.21% Δ^9 -THC each year [50]. More recently, the data collected and submitted between 2006 and 2016 from the 28 European Union Member States, Norway, and Turkey to the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) were analyzed [51]. Mean Δ^9 -THC concentrations increased from 5.00 to 10.22% in herbal cannabis. Cannabis resin increased in mean Δ^9 -THC concentration from 8.14 to 17.22%. Moreover, the increase in the potency of cannabis resin was characterized by a

Table 3 Mean and SD of CBD concentration (%) by type of sample and year

Year	All samples		Cannabis		Hashish		Hash oil	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
2008	0.41	1.08	0.37	0.96	2.22	2.97	0.20	0.40
2009	0.33	0.90	0.35	0.86	1.26	2.10	0.34	0.56
2010	0.28	0.69	0.27	0.66	0.25	0.60	0.65	1.24
2011	0.23	0.59	0.22	0.56	0.49	0.98	0.44	1.02
2012	0.22	0.71	0.20	0.56	0.53	1.41	0.66	2.36
2013	0.18	0.59	0.16	0.56	0.36	0.56	0.46	1.33
2014	0.23	0.99	0.15	0.61	1.38	2.58	1.13	2.70
2015	0.21	0.70	0.18	0.50	0.95	1.78	0.57	1.84
2016	0.35	2.37	0.19	0.77	0.64	0.66	2.82	9.11
2017	0.15	0.66	0.14	0.66	0.39	0.57	0.39	0.78

Table 4 Mean cannabinoid concentration in cannabis samples by year

Year	CBC	CBD	Δ^9 -THC	Δ^8 -THC	CBN	CBG	THCV
2008	0.26±0.18	0.37±0.96	6.0±3.4	0.00	0.32±0.42	0.32±0.35	0.09±0.14
2009	0.26±0.25	0.35±0.86	5.6±3.5	0.01±0.04	0.37±0.44	0.28±0.35	0.08±0.11
2010	0.26±0.20	0.27±0.66	6.3±3.6	0.05±0.25	0.43±0.43	0.31±0.33	0.08±0.10
2011	0.25±0.24	0.22±0.56	6.6±3.2	0.06±0.10	0.45±0.45	0.42±0.96	0.09±0.13
2012	0.24±0.14	0.20±0.56	7.1±3.4	0.08±0.11	0.56±0.46	0.43±0.34	0.09±0.10
2013	0.26±0.15	0.16±0.56	6.8±3.0	0.08±0.12	0.63±0.49	0.46±0.36	0.10±0.15
2014	0.22±0.12	0.15±0.61	6.5±5.1	0.07±0.12	0.65±0.57	0.43±0.32	0.08±0.12
2015	0.22±0.11	0.18±0.50	6.6±3.2	0.07±0.11	0.75±0.57	0.47±0.32	0.08±0.10
2016	0.23±0.14	0.19±0.77	7.7±3.0	0.08±0.12	0.73±0.53	0.46±0.32	0.08±0.11
2017	0.28±0.19	0.14±0.66	13.6±4.9	0.13±0.16	0.62±0.44	0.54±0.37	0.09±0.08

Table 5 Mean cannabinoid concentration in hashish samples by year

Year	CBC	CBD	Δ^9 -THC	Δ^8 -THC	CBN	CBG	THCV
2008	0.91±0.62	2.22±2.97	22.8±19.3	0.00	2.19±1.69	0.76±0.67	0.37±0.59
2009	0.92±0.89	1.26±2.10	21.3±15.3	0.06±0.13	2.94±2.92	0.41±0.44	0.17±0.13
2010	0.73±0.63	0.25±0.60	22.8±16.5	0.41±0.39	2.28±1.99	0.62±0.69	0.36±0.27
2011	1.12±0.70	0.49±0.98	30.0±15.1	0.24±0.20	2.90±2.23	0.70±0.58	0.23±0.16
2012	0.82±0.51	0.53±1.41	31.7±19.1	0.33±0.27	2.79±2.37	0.71±0.66	0.21±0.16
2013	0.72±0.31	0.36±0.56	29.3±16.4	0.28±0.24	2.44±1.92	0.83±0.72	0.21±0.18
2014	0.97±0.59	1.38±2.58	30.3±23.7	0.33±0.29	3.05±3.06	0.90±0.70	0.24±0.20
2015	0.51±0.28	0.95±1.78	17.6±20.1	0.15±0.10	2.60±2.30	0.56±0.60	0.14±0.17
2016	0.72±0.45	0.64±0.66	15.5±14.3	0.14±0.16	5.70±3.99	0.85±2.26	0.07±0.07
2017	0.99±0.57	0.39±0.57	45.9±26.6	0.80±0.23	2.88±1.91	1.66±1.16	0.36±0.17

quadratic time trend in which there was minimal change from 2006 to 2011, followed by rapid increase in Δ^9 -THC from 2011 to 2016 [51]. The recent increase in European resin potency has been attributed to a new form of resin produced from cannabis-containing high Δ^9 -THC and little CBD, which may be due to the replacement of landrace crops by newer high Δ^9 -THC strains in Morocco [52]. Findings in specific European countries are given below.

The Netherlands

The Netherlands has the most comprehensive cannabis monitoring program in Europe, conducted by the Trimbos Institute. Each year, at least 50 retail outlets ('coffee shops') are visited at a fixed time of year, to control for seasonal variation in potency. Test purchases are made for a range of different products using a standardized protocol. The retail

Table 6 Mean cannabinoid concentration in hash oil (concentrates) samples by year

Year	CBC	CBD	Δ^9 -THC	Δ^8 -THC	CBN	CBG	THCV
2008	0.33 ± 0.53	0.20 ± 0.40	6.7 ± 9.3	0.00	1.41 ± 3.06	0.14 ± 0.21	0.13 ± 0.19
2009	0.21 ± 0.34	0.34 ± 0.56	8.9 ± 9.6	0.08 ± 0.20	3.28 ± 5.82	0.26 ± 0.33	0.24 ± 0.29
2010	0.86 ± 0.63	0.65 ± 1.24	38.3 ± 30.1	0.24 ± 0.20	2.96 ± 2.58	0.51 ± 0.51	0.21 ± 0.37
2011	0.95 ± 0.65	0.44 ± 1.02	37.0 ± 26.2	0.22 ± 0.17	2.52 ± 3.34	0.86 ± 0.80	0.32 ± 0.53
2012	0.96 ± 0.66	0.66 ± 2.36	53.5 ± 25.5	0.50 ± 0.34	2.73 ± 2.24	1.05 ± 0.67	0.33 ± 0.29
2013	1.06 ± 0.75	0.46 ± 1.33	50.0 ± 26.6	0.37 ± 0.28	2.18 ± 1.51	1.05 ± 0.72	0.27 ± 0.16
2014	0.92 ± 0.65	1.13 ± 2.70	50.8 ± 27.3	0.33 ± 0.37	2.17 ± 2.06	1.29 ± 1.09	0.43 ± 0.62
2015	1.14 ± 0.76	0.57 ± 1.84	56.3 ± 24.9	0.53 ± 0.35	2.84 ± 2.90	1.60 ± 1.13	0.29 ± 0.15
2016	1.02 ± 0.66	2.82 ± 9.11	37.9 ± 26.6	0.48 ± 0.48	3.01 ± 3.18	1.29 ± 1.05	0.25 ± 0.23
2017	1.13 ± 0.65	0.39 ± 0.78	55.7 ± 24.7	0.80 ± 1.17	2.88 ± 2.50	1.66 ± 0.86	0.36 ± 0.44

outlets are selected from a national list each year using randomized sampling. A study reveals that the mean percentage of Δ^9 -THC in domestically grown herbal cannabis (Nederwiet) increased from 8.6 to 20.4% from 2000 to 2004 [51]. In addition, hashish made from domestically grown herbal cannabis (Nederhasj) contained an increasing content of Δ^9 -THC from a mean of 20.7–39.3%; the mean Δ^9 -THC content in imported hashish rose from 11.0 to 18.2%. The mean Δ^9 -THC content for imported herbal cannabis rose at a smaller rate, from 5.0% in 2000 to 7.0% in 2004. Only imported hashish contained significant CBD, ranging from 3.7 to 13.5% [53].

In a more recent study from 2005 to 2015, the mean Δ^9 -THC content of cannabis products in The Netherlands has decreased slightly from 2005 to 2015, with an overall decline of 0.22% each year. The most popular form of Nederwiet decreased from a mean Δ^9 -THC concentration of 17.8–15.3%, and imported herbal cannabis decreased from a mean of 6.7–4.8% Δ^9 -THC. However, the content of Δ^9 -THC in imported hashish remained relatively stable, starting from 16.9% and ending at 17.8%; Nederhasj increased from a mean of 20.0–31.6%. As in the previous study [53], imported hashish was the only type of cannabis with significant levels of CBD, and these did not change from 2005 to 2015.

United Kingdom

A study in England assessed the potency of 451 cannabis samples seized during 2004–2005 by police from five different constabularies [54]. The median Δ^9 -THC content of imported herbal cannabis, sinsemilla, and resin (hashish) samples was reported to be 2.1%, 13.9%, and 3.5%, respectively. A subsequent study of 2921 cannabis samples from 23 constabularies across England and Wales in 2008 found that the median Δ^9 -THC content of imported herbal, sinsemilla, and resin was 9.0%, 15.0%, and 5.0%, respectively [55]. More recently, a study of 995 cannabis samples [56] from the same five constabularies as the 2004–2005 study

[54] found similar potencies to those in the original study for herbal forms of cannabis, with median Δ^9 -THC concentrations of 3.5% (imported herbal) and 14.2% (sinsemilla). However, cannabis resin had increased in potency from a mean Δ^9 -THC concentration of 3.7% in 2005 to 6.3% in 2016. Two samples of hash oil (51% Δ^9 -THC and < 1% CBD) and a small number of butane hash oil samples (ranging from 73 to 83% Δ^9 -THC, with < 1% CBD) were also provided by constabularies, showing that cannabis concentrates may be emerging in the illicit UK market. Cannabis resin was the only preparation to contain significant levels of CBD in England and Wales. However, CBD concentrations in resin dropped from a mean of 4.3% in 2004–2005 to 2.3% in 2016. The most substantial changes occurring in the UK cannabis market have been the increase in the market share of sinsemilla. Within the five constabularies sampled in England at three recent timepoints, the market share of sinsemilla increased from 50.6% in 2005 to 84.5% in 2008, and 93.6% in 2016. As a result, the Δ^9 -THC:CBD ratio of all samples increased during this time, consistent with recent trends in the USA.

Italy

A study published by Zamengo et al. [57] and an update by the same authors in 2015 [58] provide information on trends of cannabinoid concentrations in the Venice area based on a total of 4962 samples. Among all of the samples, the mean Δ^9 -THC increased over time from 6.84% in 2010, 6.87% in 2011, 8.53% in 2012, and 9.57% in 2013. For all of the herbal preparations, the mean Δ^9 -THC increased from 6.17% in 2010, 5.75% in 2011, 7.51% in 2012, and 9.07% in 2013. There was also evidence for an increasing Δ^9 -THC concentration in resin, from 7.58% in 2010, 7.89% in 2011, 10.31% in 2012, and 10.69% in 2013. Across all of the cannabis preparations, there were decreases in the ratio of CBD: Δ^9 -THC and in CBN: Δ^9 -THC. The mean CBD: Δ^9 -THC ratios were 0.458 in 2010, 0.401 in 2011, 0.317 in 2012, and 0.273 in 2013. The

mean CBN: Δ^9 -THC ratios were 0.115 in 2010, 0.192 in 2011, 0.085 in 2012, and 0.069 in 2013. These changes were attributed to an increase in the market share of cannabis preparations from indoor and domestic cultivation (e.g., sinsemilla and new methods of resin production using high Δ^9 -THC/low CBD plant material) [58].

France

In France, a major study published by Dujourdy and Besacier presented trends in cannabis potency over the last 25 years, from 1992 to 2016, from five French forensic police laboratories [59]. For herbal cannabis, the authors identified three different time periods based on the data collected. From 1995 to 2002, Δ^9 -THC concentrations remained below 7.6% (the overall mean from 1995 to 2016), from 2003 to 2009, they fluctuated around 7.6%, and from 2010 to 2016, they reached a peak of 13%. The authors also reported an increase in the Δ^9 -THC:CBD ratios according to the classification system of Hillig and Mahlberg [60], with evidence that from 2010, plants with the ‘chemotype 1’ (log Δ^9 -THC:CBD ratio > 1) were predominant over ‘chemotype 2’ (log Δ^9 -THC:CBD ratio between –0.6 and 1). According to Ross and ElSohly, the CBN: Δ^9 -THC ratio is an indicator of freshness of the sample [49]. In this study, the overall mean of CBN: Δ^9 -THC ratio in herbal cannabis was reported to be 0.06 which suggests that the material was 1–2 years. Whereas, this ratio was found to be lower in the samples from 2009 until mid-2016, showing that these samples were relatively fresher (less than 1 year).

There was also strong evidence of increasing potency of cannabis resin in France [59]. As with herbal cannabis, three distinct time periods were evident. From 1992 to 2000, the mean Δ^9 -THC concentration was 6.9%, which rose to 9.2% from 2001 to 2010, and then increased two-fold to 18.2% from 2011 to 2016. The authors reported that since 2011, two different types of resin samples have been available: “classic” resin with a mean of 13% Δ^9 -THC and a new high-potency form of resin with a mean of 26% Δ^9 -THC. This new higher potency form of resin increased from 2011 to 2016; almost 75% of all resin samples in 2016 were in this category. Across all resin samples, CBD concentrations remained relatively stable from 1992 to 2016, with a mean of 4%. However, an inspection of Δ^9 -THC/CBD ratios revealed increases over a time, rising from a median of approximately 2 in 2009 to 6 in 2016. In 2004 and 2009, these ratios (Δ^9 -THC:CBD) typically ranged from 0.5 to 5; however, in 2015, the range had extended considerably to 0.5–31, supporting the emergence of new resin products containing high Δ^9 -THC and low CBD.

Conclusion

In the last decade, cannabis potency (Δ^9 -THC) and the Δ^9 -THC:CBD ratios have continued to rise in the United States and Europe. These trends can be predominantly explained by increases in the market share of sinsemilla, the rising potency of sinsemilla and imported herbal cannabis, and new methods of resin production resulting in higher Δ^9 -THC and lower levels of CBD. New, extremely potent forms of hash oil (concentrates) are becoming more prevalent and potent in the USA, but are only just beginning to emerge in Europe. The data indicate that cannabis potency has continued to rise in Europe, in line with trends in the USA. These trends may indicate that people who use cannabis are at greater risk of harm than in the previous years.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

References

1. Mukherjee A, Roy SC, De Bera S, Jiang H-E, Li X, Li C-S, Bera S (2008) Results of molecular analysis of an archaeological hemp (*Cannabis sativa* L.) DNA sample from North West China. *Genet Resour Crop Evol* 55:481–485
2. Russo EB (2007) History of cannabis and its preparations in saga, science, and sobriquet. *Chem Biodivers* 4:1614–1648
3. Zuairi AW (2006) History of cannabis as a medicine: a review. *Revista Brasileira de Psiquiatria* 28:153–157
4. Aggarwal SK, Carter GT, Sullivan MD, ZumBrunnen C, Morrill R, Mayer JD (2009) Medicinal use of cannabis in the united states: historical perspectives, current trends, and future directions. *J Opioid Manag* 5:153–168
5. Kalant H (2001) Medicinal use of cannabis: History and current status. *Pain Res Manag* 6:80–91
6. Hanuš LO (2009) Pharmacological and therapeutic secrets of plant and brain (endo) cannabinoids. *Med Res Rev* 29:213–271
7. Sharma HK (1996) Sociocultural perspective of substance use in India. *Subst Use Misuse* 31:1689–1714
8. Mary Lynn Mathre R (2012) Cannabis in medical practice: a legal, historical and pharmacological overview of the therapeutic use of marijuana. McFarland, Jefferson
9. Fankhauser M (2002) History of cannabis in western medicine. The Haworth Integrative Healing Press, New York
10. Nunn JF (2002) Ancient Egyptian medicine. University of Oklahoma Press, Norman
11. Wills S (2003) Cannabis use and abuse by man: an historical perspective. In: Brown DT (ed) Cannabis. CRC Press, Boca Raton, pp 16–46
12. Booth M (2003) Cannabis: a history. St. Martin’s, New York

13. Du Toit BM (1980) Cannabis in Africa: A survey of its distribution in Africa, and a study of cannabis use and users in multi-ethnic South Africa. AA Bolkema, Rotterdam
14. Du Toit BM (1975) Dagga: the history and ethnographic setting of *Cannabis sativa* in Southern Africa. In: Rubin V (ed) Cannabis and culture. Mouton Publishers, The Hague, Paris, pp 81–116
15. Du Toit BM (1976) Man and cannabis in Africa: a study of diffusion. *Afr Econ Hist* 1:17–35
16. Laniel L (2006) Producing cannabis in Africa south of the Sahara: a review of OGD findings in the 1990s. In: Paper delivered at the international workshop, drugs and alcohol in Africa: production, distribution, consumption & control, St Antony's College, University of Oxford
17. Parsche F, Balabanova S, Pirsig W (1993) Drugs in ancient populations. *Lancet* 341:503
18. Moore N, Brothwell D, Spigelman M, Parsche F (1993) Drugs in ancient populations. *Lancet* 341:1157
19. Assunção MR (1995) Popular culture and regional society in nineteenth-century Maranhão, Brazil. *Bull Latin Am Res* 14:265–286
20. Marijuana EA (1980) The first 12,000 years. Plenum Press, New York
21. Courtwright DT (2001) Forces of habit: drugs and the making of the modern world. Harvard University Press, Cambridge
22. Amar MB (2006) Cannabinoids in medicine: a review of their therapeutic potential. *J Ethnopharmacol* 105:1–25
23. Brown DT (ed) (2003) The therapeutic potential for cannabis and its derivatives. In: Cannabis. CRC Press, Boca Raton, pp 201–250
24. Hall W, Lynskey M (2016) Why it is probably too soon to assess the public health effects of legalisation of recreational cannabis use in the USA. *Lancet Psychiatry* 3:900–906
25. Hanuš LO, Meyer SM, Muñoz E, Taglialatela-Scafati O, Appendino G (2016) Phytocannabinoids: a unified critical inventory. *Nat Prod Rep* 33:1357–1392
26. Curran HV, Freeman TP, Mokrysz C, Lewis DA, Morgan CJ, Parsons LH (2016) Keep off the grass? Cannabis, cognition and addiction. *Nat Rev Neurosci* 17:293–306
27. Bhattacharyya S, Morrison PD, Fusar-Poli P, Martin-Santos R, Borgwardt S, Winton-Brown T, Nosarti C, MO'Carroll C, Seal M, Allen P (2010) Opposite effects of δ -9-tetrahydrocannabinol and cannabidiol on human brain function and psychopathology. *Neuropsychopharmacology* 35:764–774
28. Englund A, Morrison PD, Nottage J, Hague D, Kane F, Bonaccorso S, Stone JM, Reichenberg A, Brenneisen R, Holt D (2013) Cannabidiol inhibits THC-elicited paranoid symptoms and hippocampal-dependent memory impairment. *J Psychopharmacol (Oxf)* 27:19–27
29. Morgan CJ, Freeman TP, Schafer GL, Curran HV (2010) Cannabidiol attenuates the appetitive effects of δ 9-tetrahydrocannabinol in humans smoking their chosen cannabis. *Neuropsychopharmacology* 35:1879–1885
30. Boggs DL, Nguyen JD, Morgenson D, Taffe MA, Ranganathan M (2018) Clinical and preclinical evidence for functional interactions of cannabidiol and δ 9-tetrahydrocannabinol. *Neuropsychopharmacology* 43:142
31. Colizzi M, Bhattacharyya S (2017) Does cannabis composition matter? Differential effects of delta-9-tetrahydrocannabinol and cannabidiol on human cognition. *Curr Addict Rep* 4:62–74
32. Englund A, Freeman TP, Murray RM, McGuire P (2017) Can we make cannabis safer? *Lancet Psychiatry* 4:643–648
33. Freeman TP, Morgan CJA, Hindocha C, Schafer GL, Das RK, Curran HV (2014) Just say 'know': how do cannabinoid concentrations influence users' estimates of cannabis potency and the amount they roll in joints? *Addiction* 109:1686–1694
34. van der Pol P, Liebrechts N, Brunt T, Amsterdam J, Graaf R, Korf DJ, Brink W, Laar M (2014) Cross-sectional and prospective relation of cannabis potency, dosing and smoking behaviour with cannabis dependence: an ecological study. *Addiction* 109:1101–1109
35. Bidwell LC, YorkWilliams SL, Mueller R, Bryan AD, Hutchison KE (2018) Exploring cannabis concentrates on the legal market: user profiles, product strength, and health-related outcomes. *Addict Behav Rep* 8:102–106
36. Freeman TP, Winstock AR (2015) Examining the profile of high-potency cannabis and its association with severity of cannabis dependence. *Psychol Med* 45:3181–3189
37. Meier MH (2017) Associations between butane hash oil use and cannabis-related problems. *Drug Alcohol Depend* 179:25–31
38. Freeman TP, van der Pol P, Kuijpers W, Wisselink J, Das RK, Rigter S, van Laar M, Griffiths P, Swift W, Niesink R (2018) Changes in cannabis potency and first-time admissions to drug treatment: a 16-year study in The Netherlands. *Psychol Med* 48:2346–2352
39. Di Forti M, Marconi A, Carra E, Fraietta S, Trotta A, Bonomo M, Bianconi F, Gardner-Sood P, O'Connor J, Russo M (2015) Proportion of patients in south London with first-episode psychosis attributable to use of high potency cannabis: a case-control study. *Lancet Psychiatry* 2:233–238
40. Schoeler T, Petros N, Di Forti M, Klammer E, Foglia E, Ajnakina O, Gayer-Anderson C, Colizzi M, Quattrone D, Behlke I (2016) Effects of continuation, frequency, and type of cannabis use on relapse in the first 2 years after onset of psychosis: an observational study. *Lancet Psychiatry* 3:947–953
41. Wilson J, Freeman TP, Mackie CJ (2018) Effects of increasing cannabis potency on adolescent health. *Lancet Child Adolesc Health*. [https://doi.org/10.1016/S2352-4642\(1018\)30342-30340](https://doi.org/10.1016/S2352-4642(1018)30342-30340)
42. Smart R, Caulkins JP, Kilmer B, Davenport S, Midgette G (2017) Variation in cannabis potency and prices in a newly legal market: evidence from 30 million cannabis sales in Washington state. *Addiction* 112:2167–2177
43. Freeman T, Swift W (2016) Cannabis potency: the need for global monitoring. *Addiction* 111:376–377
44. ElSohly MA, Ross SA, Mehmedic Z, Arafat R, Yi B, Banahan BF 3rd (2000) Potency trends of delta9-THC and other cannabinoids in confiscated marijuana from 1980 to 1997. *J Forensic Sci* 45:24–30
45. Mehmedic Z, Chandra S, Slade D, Denham H, Foster S, Patel AS, Ross SA, Khan IA, ElSohly MA (2010) Potency trends of delta9-THC and other cannabinoids in confiscated cannabis preparations from 1993 to 2008. *J Forensic Sci* 55:1209–1217
46. Slade D, Mehmedic Z, Chandra S, ElSohly MA (2011) Is Cannabis becoming more potent? In: Castle DJ, Murray RM, D'Souza DC (eds) Marijuana and Madness, 2nd Edition. Cambridge University Press, Cambridge, pp 35–54
47. ElSohly M, Holley J, Turner C (1985) Constituents of cannabis sativa L. XXVI. The delta-9-tetrahydrocannabinol content of confiscated marijuana, 1974–1983. In: Marihuana'84: proceedings of the Oxford symposium on cannabis: 9th international congress of pharmacology, 3rd satellite symposium on cannabis/edited by D.J. Harvey; assistant editors Sir William Paton, GG Nahas. IRL Press, Oxford, c1985
48. ElSohly MA, Mehmedic Z, Foster S, Gon C, Chandra S, Church JC (2016) Changes in cannabis potency over the last 2 decades (1995–2014): analysis of current data in the united states. *Biol Psychiatry* 79:613–619
49. Ross S, ElSohly M (1997) CBN and Δ 9-THC concentration ratio as an indicator of the age of stored marijuana samples. *Bull Narc* 49:139–139
50. Cascini F, Aiello C, Di Tanna G (2012) Increasing delta-9-tetrahydrocannabinol (δ -9-THC) content in herbal cannabis over time: systematic review and meta-analysis. *Curr Drug Abuse Rev* 5:32–40
51. Freeman TP, Groshkova T, Cunningham A, Sedefov R, Griffiths P, Lynskey MT (2019) Increasing potency and price of cannabis in Europe, 2006–2016. *Addiction* (in press)

52. Chouvy P-A, Afsahi K (2014) Hashish revival in morocco. *Int J Drug Policy* 25:416–423
53. Pijlman F, Rigter S, Hoek J, Goldschmidt H, Niesink R (2005) Strong increase in total delta-THC in cannabis preparations sold in Dutch coffee shops. *Addict Biol* 10:171–180
54. Potter DJ, Clark P, Brown MB (2008) Potency of Δ^9 -THC and other cannabinoids in cannabis in England in 2005: implications for psychoactivity and pharmacology. *J Forensic Sci* 53:90–94
55. Hardwick S, King LA (2008) Home office cannabis potency study 2008. Home Office Scientific Development Branch, St Albans
56. Potter DJ, Hammond K, Tuffnell S, Walker C, Di Forti M (2018) Potency of δ^9 -tetrahydrocannabinol and other cannabinoids in cannabis in England in 2016: implications for public health and pharmacology. *Drug Test Anal* 10:628–635
57. Zamengo L, Frison G, Bettin C, Sciarrone R (2014) Understanding the risks associated with the use of new psychoactive substances (NPS): high variability of active ingredients concentration, mislabelled preparations, multiple psychoactive substances in single products. *Toxicol Lett* 229:220–228
58. Zamengo L, Frison G, Bettin C, Sciarrone R (2015) Cannabis potency in the Venice area (Italy): update 2013. *Drug Test Anal* 7:255–258
59. Dujourdy L, Besacier F (2017) A study of cannabis potency in France over a 25 years period (1992–2016). *Forensic Sc Int* 272:72–80
60. Hillig KW, Mahlberg PG (2004) A chemotaxonomic analysis of cannabinoid variation in cannabis (Cannabaceae). *Am J Bot* 91:966–975