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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 recreational purposes in many US states. The results showed that the mean Δ^9 -THC concentration has increased dramatically over the last ten 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% to 4.7%) and their mean Δ^9 -THC concentration (6.7% to 55.7%) from 2008-2017. 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.

Key Words Cannabis. Potency Monitoring. Sinsemilla. Marijunna. 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 2,700 B.C.; however, archeological and historical data from China indicate that *Cannabis sativa* was cultivated for fibers since 4,000 B.C. in Central Asia and North-Western China [44, 51, 60]. Cannabis use, and ultimately cultivation, subsequently spread throughout the world, specifically in India (*ca.* 1,600 B.C.), Egypt (1,550 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 (1,000–1,100 A.D.), and the Americas (1,500–1,900 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. [1, 36, 60]. According to the pharmacopoeia, ma-fen, 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... over a long term, it makes one communicate with spirits and lightens one's body..." [32]. 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. 1,600 B.C. [53], while others have questioned whether references to cannabis in Indian literature are reliable prior to 1,000 A.D. [39, 51]. 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 [25].

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. 1,550 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. Also, these documents did not explicitly refer to the psychoactive effects of cannabis [45, 56].

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.) [32, 39]. 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 [7].

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 (1,100–1,200 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 1,500 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 [15-17, 37].

In America, the cannabis use probably began in South America when the Spanish introduced the plant to Chile (1,545 A.D.). However, bones of Peruvian mummies dated from 200 to 1,500 A.D. were shown to contain cannabinoids [46], indicating contact between South America and Asia or Egypt before the arrival of Christopher Columbus (1451–1506) in 1,545 A.D.[42]. 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 Coas [3, 38, 56].

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 [12]. 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 [2, 25]. 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 Pharmacopeia in 1932 and from the United States Pharmacopeia in 1941 [8]. 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 nine 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 [31]. 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 [33], and the most abundant of these are Δ^9 -tetrahydrocannabinoid $(\Delta^9$ -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 [13]. CBD is nonintoxicating and has been found to offset several, harmful effects of Δ^9 -THC, including memory impairment and psychotic-like symptoms [4, 24, 43]. 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 [6, 11, 23]. 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 [28, 55]. 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 [5, 30, 41], increased treatment admissions for cannabis problems [29], higher risk of developing psychosis [14], and increased risk of relapse to psychosis [52]. 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 [57].

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 two 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 [54]. 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 [26]. We previously reported that cannabis potency in the United States increased from ~4% in 1996 to ~12% in the year 2014 [22]. 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 $(17\pm4~^{\circ}\text{C})$ 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 CHCl₃/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 X 0.25 mm DB-1, 0.25 μ film. Data was 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 [40] 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:

% Analyte = (Area Analyte/Area Internal Standard) x (amount of IS*/100 mg) x 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 seen 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 2008-2017, 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 2012-2016. 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, Figure 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 analysed samples and the average THC content is 0.4% \pm 0.2%, the potency of both sinsemilla and marijuana largely determine the overall potency of confiscated cannabis over the last decade (Table 2, Fig. 2-3). Sinsemilla samples showed much higher potency than marijuana, which is in agreement with previously published data [19-22, 40]. 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 Figure 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 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 and Figure 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 3-6. 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 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 every year (Tables 5 and 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 [50]. 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% to 3%, while the CBG concentration ranged from approximately 0.15% to 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 [9]. More recently, the data collected and submitted between 2006-2016 from the 28 European Union Member States, Norway, and Turkey to the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) was analyzed [27]. 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 quadratic time trend in which there was minimal change from 2006-2011, followed by rapid increase in Δ^9 -THC from 2011-2016 [27]. 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 [10]. 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 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]. Additionally, hashish made from domestically grown herbal cannabis (Nederhasj) contained an increasing content of Δ^9 -THC from a mean of 20.7% to 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% [47].

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 2005-2015, 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% to 15.3%, and imported herbal cannabis decreased from a mean of 6.7% to 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% to 31.6%. As in the previous study [47], imported hashish was the only type of cannabis with significant levels of CBD, and these did not change from 2005-2015.

United Kingdom

A study in England assessed the potency of 451 cannabis samples seized during 2004-2005 by police from five different constabularies [48]. The median Δ^9 -THC content of imported herbal cannabis, sinsemilla and resin (hashish) samples were reported to be 2.1%, 13.9% and 3.5%, respectively. A subsequent study of 2,921 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 were 9.0%, 15.0%, and 5.0%, respectively [34]. More recently, a study of 995 cannabis samples [49] from the same five constabularies as the 2004-2005 study [48] 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 73-83% 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 time points, 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. (2014) [59] 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 4,962 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 [18]. 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 1995-2016), 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 [35], 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 [50]. 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 to 2 years old. Whereas, this ratio was found to be lower in the samples from 2009 till 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 [18]. 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 2001-2010, and then increased two-fold to 18.2% from 2011-2016. 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 2011-2016; almost 75% of all resin samples in 2016 were in this category. Across all resin samples, CBD concentrations remained relatively stable from 1992-2016, 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 indicates 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 previous years.

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Compliance with Ethical Standards

Conflict of interest - none.

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 Table 1 Number of analyzed samples (n) per year

	Total number	Total number		Number o	of Cannabi.	s samples an	alyzed		Number o	f analyzed		
Year Seized	Seized	Analysed	<u>Sinsemilla</u>		<u>Marijuana</u>		<u>Ditchweed</u>		Hashish samples		Number of analyzed	
											Hash o	oil samples
			n	%	n	%	n	%	n	%	n	%
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	18674	18108	10611	58.6%	6537	36.1%	112	0.6%	531	2.9%	317	1.8%

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

	A	11			Canno	abis								
Year			Sinsen	<u>ıilla</u>	<u>Marij</u>	<u>uana</u>	<u>Ditch</u>	<u>weed</u>	All Can	<u>nabis</u>	Has	<u>shish</u>	Hasi	h oil
	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

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

Year	Year All samples		<u>Can</u>	<u>Hashi</u>	<u>sh</u>	<u>Hash oil</u>		
	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 ± 057	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

Year	СВС	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	$0.49{\pm}0.98$	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	$0.53{\pm}1.41$	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	$0.95{\pm}1.78$	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

Table 5 Mean cannabinoid concentration in hashish samples by year

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	$0.44{\pm}1.02$	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	$0.46{\pm}1.33$	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	$0.57{\pm}1.84$	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	$1.29{\pm}1.05$	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

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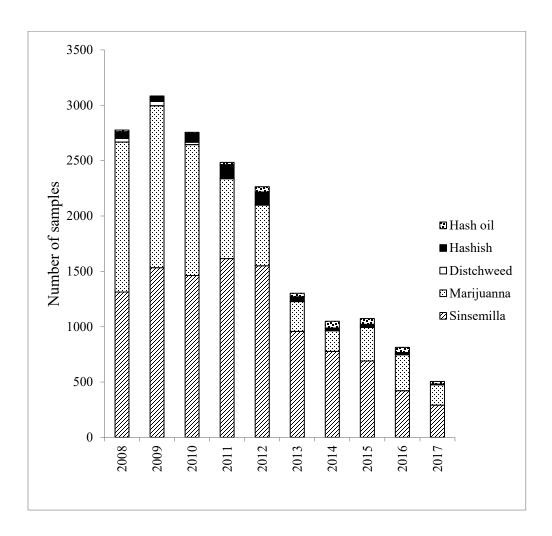


Fig 1 Number of cannabis seizures by type and year (2008-2017)

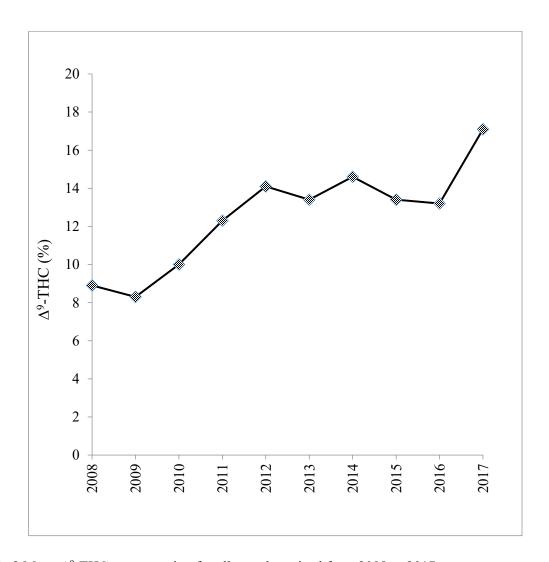


Fig 2 Mean Δ^9 -THC concentration for all samples seized from 2008 to 2017

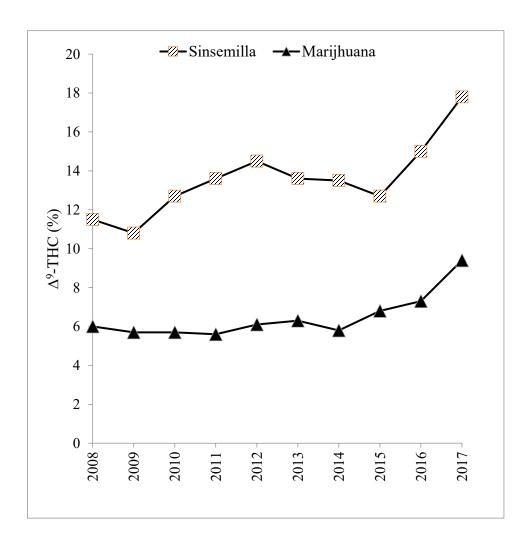


Fig. 3 Mean Δ^9 -THC concentration for sinsemilla and marijuana samples seized from 2008 to 2017

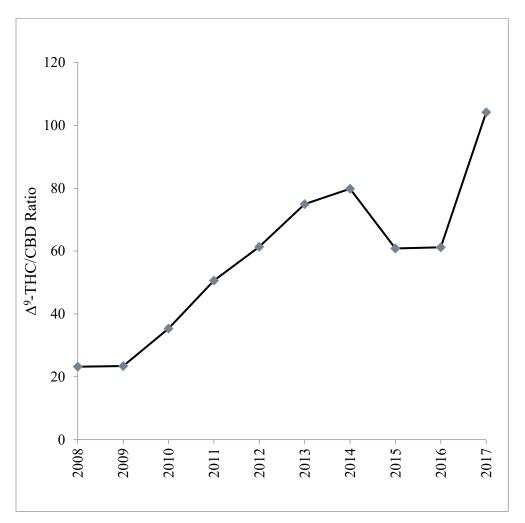


Fig. 4 Ratio of the mean concentration of Δ^9 -THC to CBD in across all samples by year

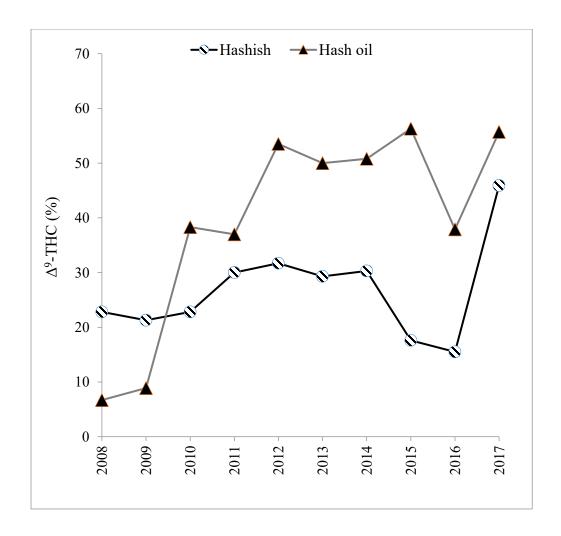


Fig 5 Mean Δ^9 -THC concentration for hashish and hash oil (concentrates) samples seized from 2008 to 2017