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RESEARCH ARTICLE

Strong increase in total delta-THC in cannabis preparations sold in Dutch coffee shops

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Abstract

The total concentration of THC has been monitored in cannabis preparations sold in Dutch coffee shops since 1999. This annual monitoring was issued by the Ministry of Health after reports of increased potency. The level of the main psychoactive compound, Δ^9-tetrahydrocannabinol (THC), is measured in marijuana and hashish. A comparison is made between imported and Dutch preparations, and between seasons. Samples of cannabis preparations from randomly selected coffee shops were analyzed using gas chromatography (GC-FID) for THC, CBD and CBN. In 2004, the average THC level of Dutch home-grown marijuana (Nederwiet) (20.4% THC) was significantly higher than that of imported marijuana (7.0% THC). Hashish derived from Dutch marijuana (Nederhasj) contained 39.3% THC in 2004, compared with 18.2% THC in imported hashish. The average THC percentage of Dutch marijuana, Dutch hashish and imported hashish was significantly higher than in previous years. It nearly doubled over 5 years. During this period, the THC percentage in imported marijuana remained unchanged. A higher price had to be paid for cannabis with higher levels of THC. Whether the increase in THC levels causes increased health risks for users can only be concluded when more data are available on adjusted patterns of use, abuse liability, bioavailability and levels of THC in the brain.

Introduction

The cultivation of the hemp plant (*Cannabis sativa* L.) stretches back into antiquity. Originally this plant was used as a source of fibre, but it is also the source for marijuana (herbal cannabis) and hashish (cannabis resin). In modern times, marijuana and hashish are the most recreationally used illegal drugs in developed countries.

Comments in the media and elsewhere regarding a large increase in the potency of cannabis have raised concerns that the currently available drug is much stronger than in the past. A much stronger drug might have implications for the health of users. However, the information on which these claims of greatly increased cannabis potency have been based is not always convincing (Mikuriya and Aldrich, 1988; Hall and Swift, 2000; King et al., 2004).

The policy on cannabis use in the Netherlands is substantially different from that in many other countries. It is based on the idea that separating the markets for hard and soft drugs prevents soft drug users from moving on to the more harmful hard drug use. Over the years, so-called coffee shops have emerged. Coffee shops are alcohol free establishments where the selling (for consumer use) and using of soft drugs is not prosecuted, providing certain conditions are met. Most of the cannabis preparations sold in these coffee shops originate from Dutch-grown grass called ‘Nederwiet’. In the Netherlands, there has been a shift in cannabis use from hashish to marijuana and subsequently to Nederwiet.

A number of publications in the 1990s have claimed that the THC content of cannabis used in the Netherlands has increased between 10 and 30 times. The home-grown variant of herbal weed, Nederwiet, could even contain amounts of THC as high as 40% (Paris and Tran, 1998; Collins, 1999). This potency question is not new. In the beginning of the 1980s and again in the 1990s, many authors suggested

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strong increases in potency as compared with the previous decade. Mikuriya and Aldrich (1988) pointed out that the cultivation of sinsemilla (without seeds) and its superiority to other forms of cannabis was already well known in India in the nineteenth century. They concluded that the range of potencies available in the 1980s was the same as in the 1970s, with certain sinsemilla varieties ranging from 5 to 14% (Perry, 1977).

In the Netherlands, the recreational use of cannabis started in the 1950s. At first, virtually all cannabis was imported from countries outside Europe. In the last decades of the twentieth century, as in the rest of Europe, interest in cannabis expanded considerably in the Netherlands. This led to the production of home-grown cannabis, which in turn led to new intensive methods of cultivation. In parallel with this, there has been a greater focus on the constituents of cannabis, and in particular the principle psychoactive substance: Δ^{-9}-tetrahydrocannabinol (THC).

Although cannabis has been the most used illegal recreational drug for decades, efforts to evaluate the health problems associated with its use still produce conflicting results (Hall and Solowij, 1998; Ashton, 2001; Schwartz, 2002; Smit et al., 2004).

The cannabis plant contains over 400 unique chemical compounds. Approximately 60 of these compounds are cannabinoids and belong to the terpenophenolic chemical class. Δ^{-9}-tetrahydrocannabinol (THC), cannabidiol (CBD) and cannabinol (CBN) are the major cannabinoids present in the cannabis plant.

The isolation of cannabinol and cannabidiol in the 1940s provided the general structure of the active principle of cannabis, but neither of these compounds had significant psychotomimetic activity (Adams et al., 1940a; Adams et al., 1940b). Mechoulam and his colleagues, in the 1960s, first isolated Δ^{-9}-tetrahydrocannabinol (Δ^{-9}-THC or THC), which was later found to be primarily responsible for the psychoactive properties of the plant (Gaoni and Mechoulam, 1964). However, its acid precursors, the form in which THC is actually present in the plant, are not psychologically active.

In contrast to what was previously postulated, cannabidiol (CBD) is not a precursor of THC (Giroud, 2002). CBD itself does not seem to have psychoactive effects, although it probably influences the effects of THC (Jaeger et al., 1996; Zuardi et al., 1981). CBN is the fully aromatized derivative of THC. It is thought to be an artefact resulting from air oxidation of THC. Ross and Elsohly (1998) used an empirical formula based on the concentration of CBN relative to THC to determine the freshness of plant material. Notwithstanding the psychophysical effects of other cannabinoids present in cannabis, the amount of THC is believed to determine the drug's potency. Therefore, potency is usually expressed in percent THC by weight.

The THC content of cannabis preparations as sold in the coffee shops has not systematically been tested. At the request of the Dutch government, the potency of cannabis products as sold in coffee shops in the Netherlands has been monitored since 1999. The aim of this study was to investigate the concentration of THC in marijuana and hashish as sold in Dutch coffee shops. In addition, the differences between home-grown and imported cannabis were also studied.

This report covers the period between 1999 and 2004 when analysis of a total of 2021 cannabis preparations bought in Dutch coffee shops was carried out. Statistical analysis of the differences in the mean Δ^{-9}-THC concentrations from year to year was carried out to ascertain the trend in the change in marijuana potency over time. The other major cannabinoids present in the cannabis, CBN and CBD, were also studied. Additionally, seasonal variation in THC and the price of the cannabis preparations were examined.

Materials and methods

Samples

Each year, samples were gathered using a standardized protocol. Prior to the first measurement in 2000, a power analysis was performed to determine the number of samples necessary for statistical analysis. The assumptions for the power analysis were based on pilot studies of the DeltaLab and on studies from the Dutch National Forensic Institute. Over 1994, 1995, 1996 and 1997, the National Forensic Institute reported average concentrations of THC in Nederwiet of 8.5, 8.5, 8.9 and 8.6% respectively. For imported hemp, THC concentrations of 6 and 5% were reported for 1995 and 1996, respectively. An experiment on the average THC content in Nederwiet by the DeltaLab in the early 1990s revealed a standard deviation of almost 40%. The number of samples of home-grown marijuana, Nederwiet, and imported marijuana was therefore calculated to detect a difference in Δ^9-THC levels of 3.5% ($\alpha = 0.05$ one-sided; $(1-\beta) = 0.80$). Nederwiet was thought to contain approximately 8.5% Δ^9-THC, compared with imported marijuana at 5.0% Δ^9-THC, which would result in a difference of 3.5%, with a standard deviation of 3.25 (40%). A minimum of 19 samples was required to detect this difference. However, since not all shops will carry both Nederwiet and imported marijuana and samples should be collected in a limited time frame, it was decided to visit 50 coffee shops.

Sampling was performed by employees of the Drugs Information and Monitoring System (DIMS) of the Trimbos-Institute. Each year, 50 randomly selected coffee shops were anonymously visited in January. From 2001 onwards, the same coffee shops were also visited at the end of the summer season in September, when only home-grown marijuana samples from identical varieties to those bought in January were purchased. Imported and home-grown marijuana (Nederwiet) as well as hashish samples were bought. Nederwiet appears in a number of varieties; some of the most familiar are 'Skunk', 'Super Skunk', 'White Widow' and 'Northern Light'. Examples of imported marijuana samples are 'Thai', 'Maroc', 'Jamaica' and 'Colombia'. The major cannabis preparations sold in coffee shops are hashish and marihuana. Hashish is the material produced by sieving the resinous parts of the flowering tops of *Cannabis sativa* from other vegetable matter, and is also known as cannabis resin.

Marihuana, or marijuana, consists of fresh or dried leaves and flowering tops, but excluding stalk, roots and seeds of *Cannabis sativa*. The cannabis preparations are either imported from outside Europe or home grown.

The following cannabis preparations were bought:

1. Home-grown marijuana (Nederwiet); the coffee shop was asked for the 'most popular' type, i.e. the variety that was most often sold,
2. Hashish made from home-grown marijuana (Nederhasj),
3. Imported marijuana,
4. Imported hashish.

After the purchase, the employee of the coffee shop was informed about the scientific purposes of the sampling and additional information on the products was asked for. Information was obtained on the variety of the cannabis samples, price per gram, origin of the sample and conditions of growing (indoor/outdoor, hydroculture, biological growth). The samplers bought standard pre-packed consumer units (usually 5 or 10 euro per unit), which were sealed in a bag and labelled. Samplers registered all purchases for the opium permit and provided a certificate of purchase.

At the Trimbos-Institute, the cannabis samples were registered, weighed, sealed in plastic and stored in a dry dark place at room temperature until further analysis was performed. Within 3 weeks, the samples were sent to the laboratory for analysis without reference to the origin of samples.

Chemical analysis

Capillary gas chromatography analysis with flame ionisation detection (GC-FID) was performed at the DeltaLab in Poortugaal, the Netherlands. In the laboratory, marijuana samples were cut into smaller parts and reduced to powder by mortar, and seeds and woody parts were removed. Duplicate 0.100 g samples were each dissolved in a methanol/chloroform (4:1) solution. For the hashish, a piece of fresh material from the inside of the block was cut and duplicate 0.100 g samples were each dissolved in the methanol/chloroform (4:1) extraction solution. Hashish and marijuana samples were ultrasonely extracted in a two-step procedure and centrifuged. The extracts obtained were immediately analyzed.

The reference standards for Δ^9-THC, CBD and CBN were obtained from Lipomed (Switzerland).

GC analyses were performed using an HP5890 series II gas chromatograph equipped with an HP7673A auto-sampler, capillary injector and HP flame ionization detector. The column was a 25 m × 0.32 mm CPsil8CB, df 0.25 μ (Varian Chrompack). Totalchrom Nelson (PE-Biosystems) software was used for data analysis. Helium was used as the carrier gas. Nitrogen was used as 'make-up' gas for the detector, and hydrogen and compressed air were used as the combustion gases.

The following instrument parameters were used for monitoring the samples: air 3.2 Bar; hydrogen 1.8 Bar; column head pressure 12 psi; split flow rate 20 ml/min; make up gas pressure 4.5 Bar; injector temperature 280°C; detection temperature 300°C; oven temperature 250°C isotherm. Runtime was 8 minutes. The instruments were calibrated each time columns were changed and routinely checked for compliance with the calibration response factor for Δ^9-THC relative to internal standard, which was constant. Introduction of cannabis extracts into the GC under the described circumstances results in decarboxylation of all non-derivatized cannabinoid acids to their neutral form. Hence the Δ^{-9}-tetrahydrocannabinol measured corresponds to native Δ^{-9}-tetrahydrocannabinol plus its acid counterparts present in the plant material (Giroud, 2002).

Control and validation of the method used

An internal laboratory audit by an independent Dutch laboratory was performed to verify the method used. To validate the method, 30 samples were also analyzed by both GC-FID and GC in combination with mass spectrometry (GC-MS). These 'duplo'-results never deviated by more than 5%. Furthermore, a number of samples were analyzed in the DeltaLab and also in two laboratories in the United Kingdom (Huntingdon Forensic Science Services in Huntingdon and Birmingham) and Switzerland (Dr. R. Brenneisen, Laboratory of Phytopharmacology, University of Bern). The results of the validation studies are shown in Tables 1a, 1b and 1c. Table 1a shows THC levels in 36 homogenized samples of Dutch cannabis (marijuana ($n = 24$) and hasj ($n = 12$)) in the DeltaLab and Huntingdon Forensic Science Service in Huntingdon. Table 1b shows THC levels in six homogenized samples of Dutch marijuana measured in three laboratories: the DeltaLab (NL), and the Huntingdon Forensic Science Services in Huntingdon (UK) and Birmingham (UK), respectively. Table 1c shows the THC levels in marijuana measured in two laboratories, the DeltaLab (NL) and the Laboratory of Phytopharmacology of the University of Bern (CH). For this study, both Swiss and Dutch marijuana samples were analyzed. These samples were not homogenized before they were split in two. To compare the results from the different laboratories, a Bablok-Passing analysis for linear regression was performed (Passing and Bablok, 1983).

Statistical analyses

Usually, two samples of a preparation were bought, although this was not always possible. Furthermore, each sample was chemically analyzed in duplicate. For further analyses, the mean value of the four (or two) results was used as statistical entity.

Statistical analyses were performed using SPSS with a two-sided $\alpha = 0.05$, unless specified otherwise. Differences between cannabis preparations were analyzed for:

1. All separate preparations,
2. Marijuana and hashish (Dutch and imported) separately,
3. Cannabis in general: marijuana and hashish together (Dutch and imported).

Means and standard error of the means (SEM) were calculated for percentage Δ^9-tetrahydrocannabinol and price. Significance of differences for separate preparation was calculated using a two-sample Student *t*-test; a one-way analysis of variance (ANOVA) with a *post hoc* Student Newman Keuls (SNK) test was used to investigate group effects.

Table 1a. *THC levels (mean ± SD) in 36 samples of Dutch marijuana and hasj analyzed in two laboratories, the DeltaLab and the Huntingdon FSS at Huntingdon. Samples were homogenized at the DeltaLab. Minimum and maximum values of the study and results from Bablok-Passing analysis for linear regression are given.*

Laboratory	N	Mean THC % ± SD	Median	Min. %	Max. %
Deltalaboratory (NL) (= X)	36	12.5 ± 6.4	14.1	0.6	20.2
Huntingdon (Huntingdon FSS, UK) (= Y_1)	36	11.8 ± 6.1	13.9	0.3	20.0
Bablok-Passing for linear regression:	*Slope* (95% Confidence limits)		*Intercept* (95% confidence limits)		*n*
Δ^9-THC	0.996 (0.906 to 1.052)		-0.296 (-0.749 to 0.611)		36

Table 1b. *THC levels (mean ± SD) in six samples of Dutch marijuana measured in three laboratories: the DeltaLab, Huntingdon FSS at Huntingdon and Huntingdon FSS at Birmingham. Samples were homogenized at the DeltaLab. Minimum and maximum values of the study and results from Bablok-Passing analysis for linear regression are given.*

Laboratory	N	Mean THC % ± SD	Median	Min. %	Max. %
Deltalaboratory (NL) (= X)	6	14.1 ± 5.2	15.8	7.1	18.9
Huntingdon (Huntingdon FSS, UK) (= Y_1)	6	12.0 ± 4.8	13.8	6.4	17.8
Birmingham (Huntingdon FSS, UK) (= Y_2)	6	13.8 ± 5.3	15.4	6.9	19.4
Bablok-Passing for linear regression:	*Slope* (95% confidence limits)		*Intercept* (95 % confidence limits)		*n*
Δ^9-THC	0.846 (0.492 to 1.246)		0.162 (- 5.789 to 5.717		6
Δ^9-THC	0.994 (0.820 to 1.099)		- 0.284 (- 1.391 to 2.424)		6

Table 1c. *THC levels (mean ± SD) in 20 samples of Dutch (n = 10) and Swiss marijuana (n = 10) analyzed in the DeltaLab and the Laboratory for Phytopharmacology of the University of Bern (CH). The flower tops were split into two parts and one half was homogenized and analyzed in the Netherlands and the other half in Switzerland. Minimum and maximum values of the study and results from Bablok-Passing analysis for linear regression are given.*

Origin cannabis	Laboratory	N	mean THC % ± SD	Median	Min. %	Max. %
Dutch marijuana	Deltalaboratory (NL) (= X)	10	15.0 ± 5.5	15.7	7.4	23.3
	University Bern (CH) (= Y_1)	10	12.5 ± 5.1	11.9	5.8	19.9
Swiss marijuana	Deltalaboratory (NL) (= X)	10	10.6 ± 7.4	9.2	0.8	22.8
	University Bern (CH) (= Y_2)	10	10.1 ± 7.4	10.2	0.5	21.1
Bablok-Passing for linear regression:			*Slope* (95% confidence limits)	*Intercept* (95% confidence limits)		*n*
Δ^9-THC			1.035 (0.733 to 1.319)	- 0.064 (- 3.292 to 1.916)		10
Δ^9-THC			1.127 (0.807 to 1.594)	0.897 (- 4.649 to 4.076)		10

Kolmogorov-Smirnov testing was used to determine whether all variables showed a normal distribution. This was not the case for the level of cannabidiol (CBD) and cannabinol (CBN), and therefore the median, highest and lowest values were determined. The non-parametric Mann-Whitney *U*-test (MWU) with *Z*-value was used to investigate significant differences between variables. Some values of the level of CBD and CBN were below the 'Limit of Quantification' (0.1%), but were detected. Therefore, a fictitious value of 0.05% was assigned to these samples since the value will be between 0 and 0.1%. Correlation between price and percentage Δ^9-THC was calculated and analyzed using the Pearson correlation method.

Differences between the five different time points were analyzed using an ANOVA with the year (and cannabis product) as factor. Group differences were revealed with *post hoc* SNK analyses. Differences over time in a certain product were analyzed with an additional ANOVA with time as factor. Seasonal differences were determined with an ANOVA with season (January versus September) and year as factor. For this analysis, results from the year 2000 were excluded because in that year only one sample survey was done.

Results

Δ^9-THC concentration

Over the years, a large number of cannabis samples have been analyzed, Table 2 shows the numbers for the different preparations. Table 3 shows the mean concentration of Δ^9-THC in the cannabis products. Considering the individual cannabis preparations, it is apparent that the Δ^9-THC level in Nederwiet increased significantly year by year [$F(4,300) = 89.0$; $p < 0.001$]. Nederhasj [$F(4,50) = 5.0$; $p < 0.01$] and imported hashish [$F(4,246) = 18.7$; $p < 0.001$] only showed an increase in 2002 compared to the first 2 years and thereafter stayed at the same level. No increase in the level of Δ^9-THC was found in imported marijuana [$F(4, 114) = 1.4$; n.s.].

The percentage of Δ^9-THC in Nederwiet in the September measurement also increased over time [$F(3,183) = 13.9$; $p < 0.001$]. *Post hoc* analysis shows that Δ^9-THC levels in September 2002, 2003 and 2004 were significantly higher than in September 2001 (SNK, $p < 0.05$); however, no difference was found between 2002, 2003 and 2004. Seasonal differences became apparent by comparing Δ^9-THC levels in Nederwiet from the January and September measurement. Fig. 1 shows the level of Δ^9-THC in the marijuana samples from both imported and Dutch origin. ANOVA analysis shows a time-dependent increase in Δ^9-THC [$F(4,483) = 86.1$; $p < 0.001$], and a difference between seasons [$F(1, 483) = 39.3$; $p < 0.001$]. When the data for the year 2000 were excluded, a significant interaction was found between time and season [$F(3, 421) = 5.2$; $p < 0.001$]. The mean Δ^9-THC level in Nederwiet samples bought in September seemed to stabilize over time, while the levels in the January measurement continued to increase.

Table 4 shows the variation in Δ^9-THC levels in the different products of the January 2004 measurement. The percentage Δ^9-THC was significantly different in the cannabis

Table 2. *Number of samples of the different cannabis preparations over the years in the January and September measurements.*

Product	Jan. 2000	Jan. 2001	Jan. 2002	Jan. 2003	Jan. 2004
Nederwiet	63	66	59	55	62
Imported marijuana	28	26	21	27	17
Nederhasj	9	10	12	12	12
Imported hashish	45	51	54	48	53
		Sept. 2001	Sept. 2002	Sept. 2003	Sept 2004
Nederwiet		39	50	49	49

Table 3. *Mean (± SEM) Δ^9-THC concentrations (in %) of the different cannabis preparations over the years of the January and September measurements.*

	Time period					Difference over time	
Product	Jan. 2000	Jan. 2001	Jan. 2002	Jan. 2003	Jan. 2004	F (df)	p [1]
Nederwiet	8.6 ± 0.3	11.3 ± 0.3↑	15.1 ± 0.7↑	18.1 ± 0.6↑	20.4 ± 0.6↑	89.0 (4,300)	< 0.001
Imported marijuana	5.0 ± 0.5	5.3 ± 0.4	6.6 ± 1.1	6.2 ± 0.7	7.0 ± 0.8	1.4 (4,114)	n.s.
Nederhasj	20.7 ± 1.6	15.7 ± 1.8	33.0 ± 5.9↑	35.8 ± 5.2*	39.3 ± 4.1**	5.0 (4,50)	< 0.01
Imported hashish	11.0 ± 0.6	12.1 ± 0.6	17.5 ± 0.8↑	16.6 ± 0.9**	18.2 ± 0.8**	18.7 (4,246)	< 0.001
		Sept. 2001	Sept. 2002	Sept. 2003	Sept. 2003		
Nederwiet		10.3 ± 0.7	14.4 ± 0.7↑	14.9 ± 0.6*	15.5 ± 0.5*	13.9 (3,183)	< 0.001

[1] p-value ANOVA ; ↑ = significantly different from previous year; * significantly different from 2001; ** significantly different from 2000 and 2001; n.s. = not significant.

products (F (3, 140) = 62.1; p < 0.001). The Nederwiet samples contained on average 13.6% more Δ^9-THC than the imported marijuana (SNK: p < 0.001). Nederhasj contained on average 21.1 % more Δ^9-THC than the imported hashish (SNK: p < 0.001).

Levels of cannabidiol and cannabinol

Table 5 shows the levels of the cannabinoids cannabidiol (CBD) and cannabinol (CBN) and the CBN to THC ratio in the preparations bought in January 2004. The ratio between CBN and THC can give an indication of the freshness of the preparation (Ross and Elsohly, 1997). Percentages of CBD and CBN were significantly different between the products ($\chi^2 = 107.3$ ($df = 3$) and 110.2 ($df = 3$) respectively; p < 0.001). The levels of CBD and CBN were higher in imported products (MWU: Z = 7.9 and 9.5 respectively: p < 0.001). The difference in CBD between imported and home-grown products is due to the difference in CBD content in imported hashish versus Nederhasj, because there was no significant difference between CBD content in Nederwiet as compared to imported marijuana. The ratio of CBN/THC was significantly higher in imported products (MWU: Z = 10.2; p < 0.001). The ratio was higher in imported marijuana

Table 4. *Mean (± SEM) THC levels in the different cannabis preparations in 2004. Also shown are median, lowest and highest measurement of a specific preparation.*

Product	THC concentration (%)			
	Mean ± SEM	Median	Lowest value	Highest value
Nederwiet	20.4 ± 0.6	21.5	8.1	29.4
Imported marijuana	7.0 ± 0.8	7.2	2.3	12.6
Nederhasj	39.3 ± 4.1	39.8	18.0	62.8
Imported hashish	18.2 ± 0.8	18.5	4.8	29.0

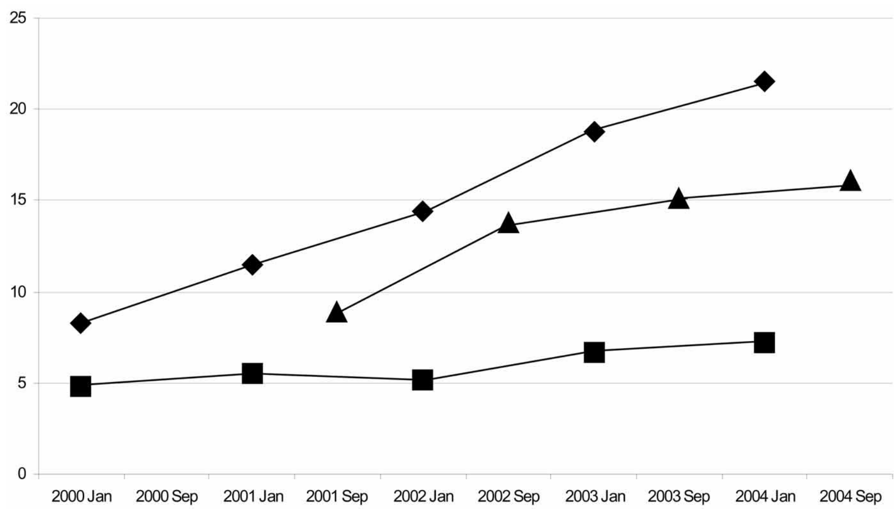

Figure 1. *Median THC concentrations (%) in Nederwiet and imported marijuana from the January measurements over 5 years and in Nederwiet from the four September measurements.* ◆ *Nederwiet January,* ■ *imported marijuana January,* ▲*Nederwiet September*

Table 5. *Median values of cannabidiol (CBD) and cannabinol (CBN) percentages in cannabis preparations bought in January 2004. Also shown are the lowest and highest values and the CBN/THC ratio.*

	CBD	CBN	CBN/THC
Product	Median (lowest - highest value)	Median (lowest - highest value)	x 100
Nederwiet	0.25 (0.0 - 0.7)	0.0 (0.0 - 0.2)	0.0
Imported marijuana	0.20 (0.0 - 2.0)	0.7 (0.0 - 1.9)	9.6
Nederhasj	0.60 (0.0 - 1.0)	0.6 (0.0 - 3.0)	1.4
Imported hashish	8.10 (3.7 - 13.5)	1.5 (0.6 - 5.1)	8.6
χ^2 ($df = 3$)	107.3	110.2	110.2

Table 6. *Mean prices in euro per gram (± SEM) of the different cannabis preparations over the years of the January measurement.*

	2000	2001	2002	2003	2004	Difference over years	
Product	€/g	€/g	€ /g	€/g	€/g	F	P[1]
Nederwiet	5.8 ± 0.2	5.9 ± 0.1	6.1 ± 0.2	6.4 ± 0.2	6.0 ± 0.2	2.2 (4, 299)	n.s.
Imported marijuana	3.9 ± 0.2	4.0 ± 0.3	4.2 ± 0.3	4.3 ± 0.3	4.9 ± 0.3	1.7 (4,113)	n.s.
Nederhasj	8.9 ± 0.7	7.1 ± 0.5	11.0 ± 1.5	15.0 ± 2.0*	12.5 ± 1.9	3.8 (4, 50)	< 0.01
Imported hashish	6.3 ± 0.2	6.4 ± 0.2	7.1 ± 0.3	7.6 ± 0.3*	6.6 ± 0.3	3.5 (4, 245)	< 0.01

[1] p-value of ANOVA; * significantly different from 2000 and 2001 (SNK, p < 0.01); n.s. = not significant.

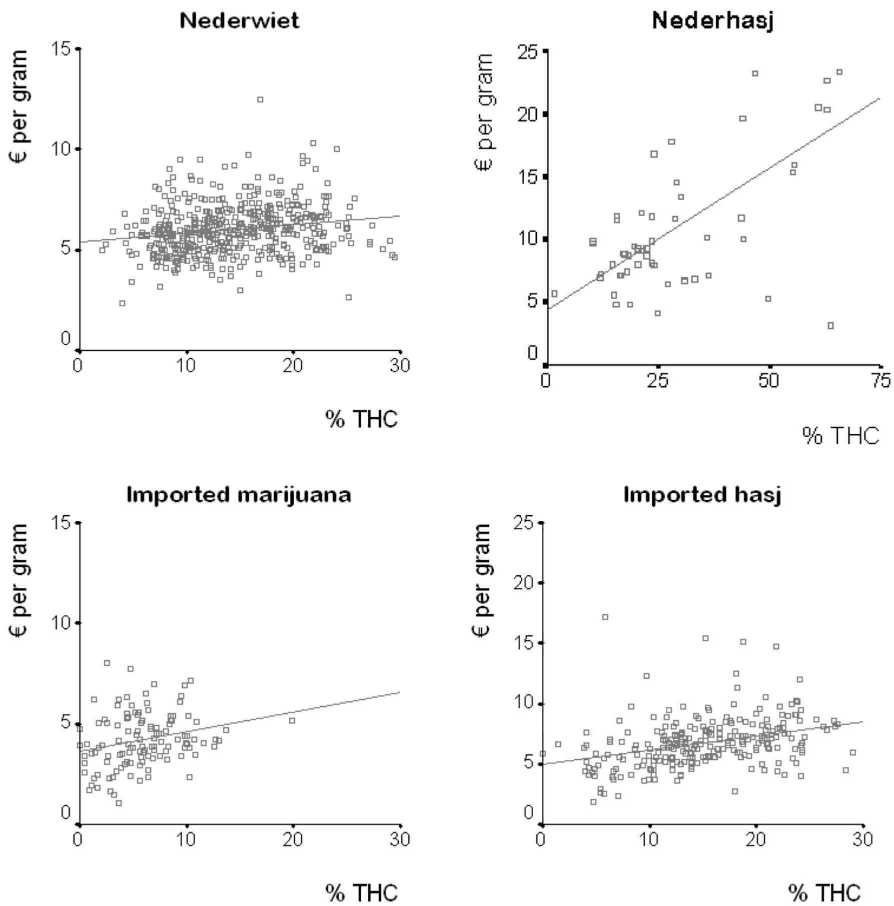

Figure 2. *Relationship between price (€/g) and mean THC content of Nederwiet (top left), Nederhasj (top right), imported marijuana (bottom left) and imported hasj (bottom right). Data relate to measurements from January 2000 to January 2004.*

compared to Nederwiet (MWU: Z = 7.1; p < 0.001) and in imported hashish as compared to Nederhasj (MWU: Z = 4.3; p < 0.001).

Price of cannabis products

The prices of cannabis in Dutch coffee shops are shown in Table 6. Prices are given in euro per gram for each time point. The price of hashish fluctuated over the years. On average consumers had to pay more for Dutch varieties than for imported preparations (Student's *t*-test: t = 3.80, *df* = 727; p < 0.001). Fig. 2 shows the relationship between price (in euro per gram) and potency (% THC). There is a relationship between potency and price, especially for nederhasj ($r = 0.658$; $df = 53$; p < 0.01). Data for nederwiet, imported marijuana and imported hasj are ($r = 0.188$; $df = 487$; p < 0.01), ($r = 0.248$; $df = 116$; n.s.) and ($r = 0.341$; $df = 248$; p < 0.01) respectively.

Validation of analysis method
A Bablok-Passing analysis for linear regression was performed to compare results when analyses were done in different laboratories (Passing and Bablok, 1983). The results from these analyses are given in Tables 1a, 1b and 1c. None of the slopes deviates significantly from 1.0 and none of the intercepts deviates significantly from 0.0 (95% confidence limits).

Discussion

An increase in THC content of cannabis sold in the Netherlands has been frequently claimed in the literature (Paris, 1997; Paris and Tran, 1998; Collins, 1999). These statements however, have never been studied in detail. The purpose of the present study was to investigate the concentrations of Δ^9-tetrahydrocannabinol (THC) in marijuana and hashish sold in Dutch coffee shops over the years.

Since the beginning of this study, the average THC percentage of Nederwiet and of hashish made from Nederwiet has increased year by year and doubled over the 5-year period. The average potency of imported hashish has also increased over time; their levels, however, fluctuate over the years. In contrast, the THC percentage of imported marijuana has remained stable at around 6%.

During the study, the average THC content of Nederwiet sold in coffee shops was significantly higher than that of imported marijuana. In addition, hashish derived from Nederwiet, called Nederhasj, contained more THC than hashish originating from imported cannabis. The present study shows that there is substantial variation in the potency of hashish, which might be caused by the different quality of THC in the marijuana used to produce it.

Data from other European countries do not suggest a gradual increase of THC potency over the last 5 years (King et al., 2004). In the present study, the THC content of imported marijuana was higher than in other European countries, as was shown in the study of the European Monitoring Centre for Drugs and Drugs Addiction (EMCDDA) (King et al., 2004). This might be a result of the different laboratory methods used. In the present study, all available THC (neutral and THC acids) was measured, while in many other studies, part of the THC acids might have been ignored. From the results of the validation studies it can be stated that the method used in the Delta laboratory is comparable with those in 3 other laboratories that are specialized in measuring THC-potencies. So no constant or proportional difference has been found between any methods.

When comparing the THC levels from this study with previous studies, it should also be emphasized that the samples in this study were obtained from coffee shops, whereas in other studies samples are mostly derived from police and customs seizures (Pitts et al., 1990; Poulsen and Sutherland, 2000). It is very likely that there would have been different results if seized samples had been examined. However, recent data on the potency of seized cannabis are not available in the Netherlands. The portion of home-grown cannabis in other European countries is not known, which might affect the average level of THC (King et al., 2004).

Possible explanations for the increased level of THC could be growth and storage methods and genetic techniques. During the sampling of this study, it was observed that imported marijuana always contains seeds (from fertilized female flowers), while Nederwiet does not. Nederwiet is made by the sensimilla technique, using only unfertilized female cannabis flowers, which contain most THC. Furthermore, the high THC concentrations in Nederwiet are probably caused by historical developments in genetic experimentation and cross breeding, and improvements in indoor hydroponic cultivation techniques [for reviews, see (King, 2001; Rosenthal, 2001)]. In this way, high potency cannabis plants had already been developed in the early 1980s (Rosenthal, 2001). Nowadays, most Nederwiet is grown indoors and almost all growers use specific and sophisticated cultivating and harvesting techniques. This results in a more constant end-product, with a high percentage of THC. The recent increase in the average THC content of Nederwiet is probably due to the enhanced availability of the more potent breeds.

Nederwiet is sold in many different varieties. Although certain varieties stand out, the variation in THC percentage within the different varieties is much higher than that between the varieties (unpublished results). It is not possible to predict the potency of a certain variety simply on the basis of a name. Cannabis, being an illicit drug, lacks quality control. In practice, this means that it cannot be excluded that samples have been sold under incorrect names.

In the present study, the potency of Nederwiet bought at the end of the summer season was lower than that of samples previously bought in January of the same year. THC concentrations in Nederwiet bought in September 2002 were higher than in those bought in the previous year, but this increase did not persist through 2003 and 2004. This stabilization of the average potency of Nederwiet has so far only been seen in cannabis samples bought in September, and seems to be season-dependent. Additional measurements are needed to confirm the persistency of this stabilization. The seasonal variation might be explained by the fact that in the summer, relatively more cannabis is sold that is grown outdoors, while Dutch cannabis bought in the winter season is usually grown indoors. Flowers of cannabis grown indoors probably have higher THC contents than those that are grown outdoors (Kaa, 1989).

Seasonal variation in THC content in marijuana sold in Dutch coffee shops was previously shown by Korf et al (1994). The potencies of marijuana and hashish in coffee shops in Amsterdam differed over 2% between seasons (8.6 %THC in winter versus 6.4% in the summer).

The physiological and pharmacological effects of marijuana are not due to THC alone (Grinspoon and Bakalar, 1997). Cannabidiol (CBD) was found to cause several pharmacological effects, some of which may modify the metabolism and effects of THC (Jaeger et al., 1996). The highest concentrations of CBD in this study were found in imported hashish; these levels were much higher than in hashish made from Nederwiet.

The relative concentration of CBN to THC reflects the freshness of cannabis samples (Ross and Elsohly, 1997). In our study, the CBN to THC ratios were significantly higher in imported hashish and imported marijuana than in the Dutch preparations. This suggests that the time-period between harvesting and selling is much longer for imported marijuana and hashish than for the home-grown products, which is to be expected.

Neither CBD nor CBN showed any significant change in concentrations over the years, as was previously found by Elsohly et al. (2000) in their cannabis monitoring study.

The chemical analysis of THC is complicated (for review see Raharjo and Verpoorte, 2004). To compare results from different studies, the analyses should have been carried out within the same laboratory using the same (type of) equipment and following the same procedures. In this study, one laboratory, using the same equipment and protocols, performed all analyses.

In cannabis plants, most THC is present as tetrahydrocannabinolic acids (Raharjo and Verpoorte, 2004). Tetrahydrocannabinolic acids themselves are not psychoactive. By heating, cannabis acids are decarboxylated into neutral THC. Recreational users also heat their cannabis by smoking or cooking, and are thus exposed to all THC present in the plant, neutral THC and tetrahydrocannabinolic acids. By using a GC technique in which cannabis is heated for analysis, the results obtained in this study represent all Δ^9-tetrahydrocannabinol, neutral as well as the decarboxylated compounds.

In this way, the maximal amount of THC present in the different samples is measured.The price of marijuana did not increase over the years. The price of Nederhasj fluctuated strongly. On average consumers had to pay more for Dutch varieties than for imported preparations. We have found a correlation between the price of cannabis products and the level of THC. People have to pay more for cannabis with a higher level of THC. This correlation is strongest for Nederhasj and less for the other varieties of marijuana.

What does an increase of THC mean for the health of recreational cannabis users? Several factors are important in formulating a health risk analysis.

It is necessary to know if an increase in THC levels changes the pattern of cannabis use (e.g. the frequency). Korf and colleagues recently interviewed a group of 400 visitors to coffee shops about the way in which they reacted to the increased potency of Nederwiet (Korf et al., 2004). Three types of consumers were found:

1. Those who stopped using Nederwiet because it was too potent,
2. Those who inhaled less from the strong marijuana than from less potent varieties, and
3. A third group, usually younger people, who liked to use very strong marijuana of which they also inhaled more.

It is clear that people from this last group are at the highest risk. Changes in patterns of cannabis use, such as earlier age of first use and more regular use, are more likely to induce health risks than the increase in the THC content of the drug (Veen et al., 2004).

The health and psychological effects and risks of cannabis with high THC concentrations are not well understood. Hardly anything is known about the dose- or time-effect relationship of high-potency cannabis. This absence of dose-effect-relationship of THC in the scientific literature is remarkable and makes a reliable risk assessment for the effects of high potency THC impossible. THC itself is not a very toxic compound in comparison with other illicit substances such as cocaine or amphetamines. Acute (oral) toxicity of THC is very low (Thompson et al., 1973) and fatal cases in humans have not been substantiated (Grotenhermen, 2004). THC may have cardiotoxic effects, but this seems to be restricted to persons who already have coronary heart disease (Bachs and Morland, 2001; Mittleman et al., 2001). Long-term use of cannabis might lead to impaired cognition, especially in those who start their use at an early age (Pope, Jr. et al., 2003). There is some epidemiological evidence that cannabis plays a role in the (early) onset of schizophrenia (Smit et al., 2004; Veen et al., 2004). These studies indicate that the age of onset of recreational cannabis use is of major importance for long-term unwanted psychological effects.

It is also important to realize that marijuana and hashish in the Netherlands are usually smoked in a mixture with cigarette tobacco. In some countries, e.g. in the USA, cannabis is smoked without tobacco. This also has implications for risk assessment. It means that there is a different amount of cannabis in a joint containing tobacco, and there are the additional risks associated with tobacco smoking.

The present study indicates that the average potency of some cannabis products has increased in the past 5 years. The data also show that the increase is not as extreme (10 – 40 times as high) as is sometimes suggested (Collins, 1999). The health effects, if any, of higher THC levels in cannabis preparations are virtually unknown. In the Netherlands, experiments are planned to compare the effects of low and high potency marijuana on the body burden of the users. Whether more potent cannabis influences the age of onset or the abuse liability for recreational users should also be further investigated.

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