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A preliminary investigation of lung availability of cannabinoids by smoking marijuana or dabbing BHO and decarboxylation rate of THC- and CBD-acids

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ABSTRACT

Highly potent cannabis concentrates obtained by butane or by supercritical carbon dioxide-extraction are gaining popularity. These extracts called butane hash oil (BHO) with Δ^9-tetrahydrocannabinolic acid A (THCA) contents above 60% are consumed by flash vaporization on a glowing titanium nail, followed by inhalation of the resulting vapor through a water pipe in a single puff — a technique referred to as "dabbing". We herein investigated the decarboxylation rate of THCA during artificial smoking of cannabis plant material and simulated dabbing, and the lung availability of Δ^9-tetrahydrocannabinol (THC) which we define as the recovery of THC in the smoke and vapor condensates. Preliminary smoking and dabbing experiments were performed using an apparatus built in-house. Due to availability of cannabidiol (CBD)-rich hemp in Switzerland, we included a sample of CBD flowers in our experiments and investigated the decarboxylation and recovery of cannabidiolic acid (CBDA) and CBD, respectively. Decarboxylation of THCA and CBDA during combustion of the plant material and vaporization of the BHO, respectively, was complete. The high recovery of total THC (75.5%) by dabbing cannot be achieved by smoking marijuana. Lung availability ranged from 12% for mixed cannabis material with a rather low THC content, to approximately 19–27% for marijuana flowers, similar for THC in marijuana as for CBD in CBD-rich marijuana. In reality, when smoking a joint, further losses in recovery must be assumed by additional sidestream smoke. The rather high lung availability of THC via dabbing can explain the increased psychoactive and adverse effects associated with this new trend of cannabis consumption.

1. Introduction

Nowadays, there is a tendency among cannabis users to consume more potent products [1–3]. New strains of highly potent cannabis plants have been developed and concentration of cannabinoids by means of extraction has also been used to produce extracts with very high Δ^9-tetrahydrocannabinol (THC) content: classical hash oil is extracted with solvents, and after solvent evaporation, residues are mixed with a vegetable oil. Seized drugs include butane hash oil (BHO) or extracts of cannabis with other evaporable solvents, such as pressurized liquid carbon dioxide — which have a total THC concentration of more than 60%. A new form of application for these extracts is the use of a titanium nail mounted on a water pipe. The nail is usually heated by a gas torch until glowing red and then allowed to cool down for a few seconds before a small amount of the cannabis concentrate, called dab, is placed on the hot surface. The dab evaporates quickly and the resulting vapor is inhaled in one single puff through the water pipe. In a previous study, up to 60% of the theoretically available THC could be recovered in the vapor condensates of dabs. Efficiency of THC transfer from the concentrate to the vapor varied only slightly among concentrates of different consistencies and qualities [4]. This new method of cannabis consumption called dabbing has been imported from the USA to Europe. Its rise in popularity seems to be a consequence of the legalization of medicinal or recreational cannabis in some states in the USA. The first seized dabs sent to the Landeskriminalamt Nordrhein-Westfalen, Germany, were concentrates of butane hash oil that had a total THC content of 56–68%, as determined by gas chromatographic analysis. According to the labelling, the origin of these products was Washington State (USA). In Switzerland, cannabis is only considered illegal by

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the narcotics legislation if the total THC content exceeds 1%. CBD-rich hemp with a total THC content below 1% can be legally obtained as a tobacco substitute product in supermarkets or from CBD-hemp shops and has become very popular since the beginning of 2017 [5,6].

The aim of our preliminary study was to investigate the decarboxylation of precursor acids of THC and CBD by dabbing and by smoking, respectively. Furthermore, we wanted to determine the recovery of THC in the condensate by dabbing in comparison to smoking marijuana by use of two different setups of the smoking device for simulation of the different methods of consumption. Due to availability of CBD-rich hemp in Switzerland, we included this material in our study.

2. Material and methods

2.1. Chemicals

Methanol (CHROMASOLV™, for HPLC, ≥99.9%) was purchased from Honeywell Riedel-de-Haën (Seelze, Germany), hexane (EMSURE®) from Merck (Darmstadt, Germany) and acetonitrile (HPLC gradient grade, 99.9%) from Acros Organics (Geel, Belgium). Formic acid solution (puriss p.a., 50% in water) was obtained from Sigma-Aldrich (Buchs, Switzerland). Ultrapure water was produced in-house with a Direct-Q water purification system from Millipore (Zug, Switzerland). THCA, THC, CBDA, CBD and cannabinol (CBN) reference standards were acquired from Lipomed (Arlesheim, Switzerland).

2.2. Cannabis products

The cannabis plant material (mainly flowers — marijuana, or mixed material consisting of leaves and stems) and cannabis concentrate (BHO) used in this study had been confiscated by the police and had been submitted to the Landeskriminalamt Nordrhein-Westfalen, Germany, for routine determination of the total THC, CBD and CBN content by a validated gas chromatographic method with flame-ionization detection (GC-FID). For the present study, samples were re-analyzed by HPLC-DAD as described below to quantify the neutral cannabinoids and their carboxylic acid precursors separately and thus to determine the original cannabinoid composition of the samples. CBD-rich hemp (Cannabis Sativa L.) was obtained from Swiss Cannabis SA (Härkingen, Switzerland).

2.3. Apparatus and method for condensation and recovery of cannabinoids in smoke stream and dab vapor

A representation of the apparatus used for the smoking experiments can be found in Fig. 1. One-gram aliquots of the dry cannabis material (flowers and mixed material) were pressed into a glass frit which was connected by a short tube to two gas washing bottles in series (Fig. 1). A platinum resistance thermometer was inserted through a hole in the tube to monitor the temperature at the inlet of the first gas washing bottle. The bottles were filled up to about one-fifth of their volume with 3-mm-diameter glass boiling chip granules and were cooled in an ice bath and by liquid nitrogen, respectively, to capture the smoke. The exit tube of the second gas washing bottle was connected via a three-way valve to a water jet pump generating a vacuum. The cannabis material was ignited with a gas torch and the smoke was sucked through the two bottles. Marijuana was burnt in approximately 2.2 min, for the mixed material the time was 3.5–4.2 min. Smoke temperatures measured at the inlet of the gas washing bottle were between 60 and 92 °C for marijuana and 47–80 °C for mixed material.

To simulate the process of dabbing, the glass frit was replaced by glass reducing/enlarging adapters equipped with a titanium dab nail and the water jet pump was replaced by an oil pump for faster suction (Fig. 2). Furthermore, the three-way valve was removed. The titanium nail was heated with a gas torch until glowing red-hot, allowed to cool down for a few seconds, and then 160–230 mg of cannabis concentrate were placed on the nail using a weighing boat. The evaporation of the concentrate and suction of the vapors through the apparatus occurred in less than 5 s for simulating the consumption of a dab. Measured temperature in the connecting tube in front of the first washing bottle during suction was on average 44 °C (n = 12, min. 36 °C–max. 50 °C).

After combustion of the applied plant material and vaporization of the concentrate, respectively, the condensate was collected by washing the boiling chip granules and gas washing bottles with approximately 350 mL of methanol each. The obtained methanolic solutions were combined and the solvent was removed under reduced pressure using a rotary evaporator and the residue was reconstituted in 50 mL of methanol.

2.4. Quantification of cannabinoids by HPLD-DAD analysis

Quantification of cannabinoids of plant material extracts and condensates collected in the gas-washing bottles was performed

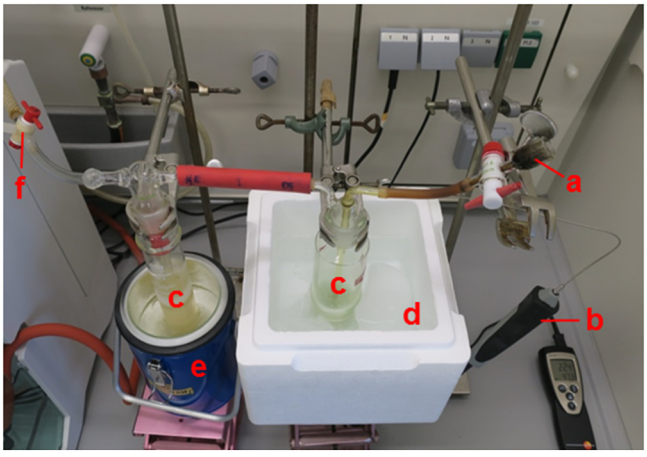

Fig. 1. The apparatus for collecting cannabis smoke condensates. Components: **a** glass frit, **b** thermometer, **c** gas washing bottle, **d** ice bath, **e** liquid nitrogen flask, **f** connection to water jet pump.

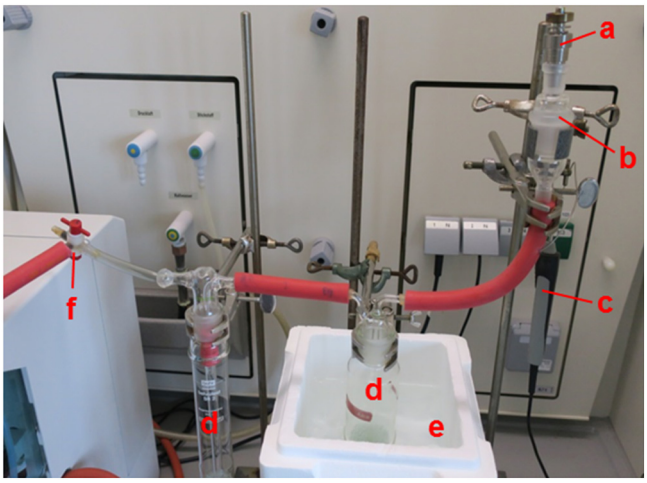

Fig. 2. Apparatus for collecting vapor condensates of dabbed cannabis concentrates. Components: **a** titanium nail, **b** glass reducing/enlarging adapters, **c** thermometer, **d** gas washing bottle, **e** ice bath, **f** connection to oil pump.

by HPLC-DAD for THCA, THC, CBD, CBDA and CBN (without decarboxylation). Aliquots of the dry, finely ground plant material and the cannabis concentrate (BHO) were extracted with a mixture of methanol/hexane 9:1 (v/v) by ultrasonication for 20 min (flowers: 75 mg/5 mL; mixed plant material: 50 mg/2.5 mL; concentrate: 75 mg/10 mL) and the extracts were then diluted 20- to 80-fold with extraction solvent for subsequent HPLC-DAD analysis. The methanolic solutions (50 mL) of the smoke and vapor condensates were analyzed undiluted and after 10- or 20-fold dilution with extraction solvent to bring the cannabinoid concentrations into the calibration range.

HPLC-DAD analysis was performed using a fully validated in-house method, with an UltiMate 3000 HPLC system (Dionex, Olten, Switzerland) and a Kinetex 2.6 μm C8, 100 × 2.1 mm column (Phenomenex, Aschaffenburg, Germany). Chromatographic separation was achieved using gradient elution with 0.1% formic acid in water as mobile phase A and 0.1% formic acid in acetonitrile as mobile phase B. The flow rate was 0.6 mL/min and the gradient program was as follows: 0–2 min, 50% B; 2–9 min, 50–65% B; 9–10 min, 65% B; 10–10.1 min, 65–50% B; 10.1–13 min, 50% B. The injection volume was 5 μL and the detection wavelength was set at 210 nm. Linearity ranged from 1 to 100 μg/mL for THC, CBD and CBN, and from 10 to 500 μg/mL for THCA and CBDA, with the lowest calibrator being the lower limit of quantification (LLOQ). Limits of detection (LODs) were 0.3 μg/mL for THC, CBD and CBN, and 0.5 μg/mL for THCA and CBDA, with signal-to-noise ratios (S/N) of >3, tested with methanolic solutions containing decreasing concentrations of cannabinoid reference standards.

3. Results

Table 1 displays the cannabinoid profiles of the cannabis samples. In the cannabis plant, THC and CBD are synthesized as pharmacologically inactive carboxylic acids, THCA and CBDA, respectively. Conversion into their active neutral forms by decarboxylation occurs naturally as the plant ages, and is accelerated by light and heat (e.g. upon smoking, vaporizing or baking the plant material) [7]. Since BHO production usually involves little to no heating of the plant material [4], most of the THC present in the concentrate is still in its acidic form. THC-rich marijuana, mixed material and the BHO concentrate contained only small or even non-detectable levels of CBD, CBDA and CBN. The total contents of THC and CBD indicated in Table 1 correspond to the sum of the free cannabinoid and its respective acid precursor, corrected for weight of the carboxylic acid groups, and thus refer to the maximum amount of THC that could theoretically be present in the smoke or vapor as a results of complete decarboxylation.

The cannabinoid contents in the trapped condensates were analyzed to determine the theoretical lung availability.

Lung availability (see Tables 2 and 3) can be defined as the recovery of THC in the condensate (after burning/vaporizing the material) in relation to the total THC content of the cannabis sample (see Table 1).

$$\text{Lung availability } [\%] = \frac{\text{mean THC conc. of smoke/vapor condensate}}{\text{THC conc. of plant material}} \times 100\%$$

The analysis of the condensates by HPLC-DAD revealed that THCA and CBDA were not detectable, and thus decarboxylation of the precursors during the burning/evaporation process was complete.

Burning of marijuana took approximately 2 min, the burning of mixed material up to 4.2 min, whereas the dabbing process for simulation of inhalation “in one single puff” only took a few

Table 1
Cannabinoid content (% w/w, n = 2) of cannabis samples as determined by HPLC-DAD analysis.

Sample type	THC	THCA	Total THC[a]	CBD	CBDA	Total CBD[b]	CBN
Marijuana flowers	2.7	16.7	17.3	1.1	n.d.	1.1	n.d.
Mixed material	0.5	0.5	0.9	n.d.	n.d.	n.d.	<0.1
BHO	13.1	66.5	71.4	1.4	n.d.	1.4	0.6
CBD marijuana flowers	<0.1	<0.1	<0.1	0.3	6.8	6.3	<0.1

Uncertainty of measurement: 0.5–1%: <30% (relative), 1–10%: <(25–18)% relative, 10–25%: <(18–<14)% relative, >25%: <14% relative.
[a] Total THC is the sum of THC and THCA corrected for loss of CO_2, i.e. THC + (THCA/358.48) × 314.47.
[b] Total CBD is the sum of CBD and CBDA corrected for loss of CO_2, i.e. CBD + (CBDA/358.48) × 314.47.

Table 2
Average lung availability of decarboxylated THC in smoking or dabbing experiments.

	Marijuana flowers (n = 6)	Mixed material (n = 6)	BHO (n = 5)
Lung availability [%]	26.7	12.8	75.5
Decarboxylation rate of THCA	>99 %	>99%	>99%

Table 3
Average lung availability of decarboxylated CBD in smoking experiments.

	CBD-marijuana flowers (n = 5)
Lung availability [%]	20.0
Decarboxylation rate of CBDA	>99%

seconds (<5 s). The recovery of the cannabinoids in the vapor condensate was very high for the BHO (75%), while for marijuana flowers still 27% were recovered. For CBD, 20% were recovered when burning CBD marijuana flowers. For the mixed material, which contained leaves and stems of the hemp plant besides remains of flowers, low recovery was found in the condensate.

4. Discussion

In the present study, the transfer of cannabinoids from cannabis plant material to smoke (by burning) and from BHO to vapor (by dabbing) was investigated.

4.1. Smoking

Ideally, the method of smoke production should reflect human cannabis smoking behavior. The typical smoking cycle consists of puffing, smoke inhalation, breath-holding, smoke exhalation and rest. Compared with smoking regular tobacco, smoking cannabis was found to be associated with a two-thirds larger puff volume, a one-third greater depth of inhalation and a fourfold longer breath-holding time [8]. When cigarettes are combusted, the smoke produced is either inhaled when puffs are taken (mainstream smoke) or is released into the air when the cigarette smolders between puffs (sidestream smoke) [9]. Previous studies have attempted to simulate authentic smoking behavior by using an intermittent puff smoking system producing mainstream and sidestream smoke [10–16]. However, as highlighted by Van der Kooy et al. [17], slight differences in machine-smoking protocol (i.e. puff frequency, puff duration, puff volume) may greatly affect the amount of THC transferred to the smoke (i.e. the THC content in the smoke condensate will increase if the puff frequency is shortened and the puff duration and volume are increased). These observations are in agreement with clinical studies showing that smoking dynamics (manner in which the cannabis is smoked) influences the amount of THC reaching the systemic circulation [9,18–23]. In our study, cannabis smoke condensates were produced under constant draft conditions, i.e. the cannabis material was burned in a single, uninterrupted draft and no smoke was lost as sidestream smoke, as previously described by others [11,16,24–26]. Results thus obtained reflect the maximum proportion of THC which could be transferred from cannabis to smoke rather than a realistic estimate of the amount of THC delivered during human smoking. Cannabis smoke condensates have been collected using a variety of smoke collection devices such as solvent traps (e.g. acetone [27], ethanol [16], methanol [10,24,26], ethyl acetate [28] ethanol/hexane 1:1 (v/v) [17], cold traps [12,14], packed cold traps (e.g. sea sand [16], Pyrex beads [13], Teflon filament [13]) as well as filters [15,25]. We used cold traps partially packed with inert glass boiling chips granules to increase the surface area onto which condensates can form.

Previous studies in which cannabis cigarettes (without tobacco) were machine-smoked in intermittent puff mode reported that 16–28.9% of total THC could be recovered in the mainstream smoke condensates [12,16,29,30]. In contrast, continuous smoking on a smoking machine yielded recoveries of 69% [16] and 78% [26]. Based on these studies, it has been estimated that 22–50% of THC is destroyed by pyrolysis during smoking, while up to 40–50% may be lost in sidestream smoke. Elzinga et al. [10] recently determined the cannabinoid content in the mainstream smoke, sidestream smoke and in the ash and filter of cannabis cigarettes, thus arguably providing the most reliable data on the transfer of THC from cannabis to smoke. They reported that, on average, 36.9% (27.5–46.3%) of the theoretically available THC could be recovered in the mainstream smoke condensate, 9.2% in the sidestream smoke condensate, and 5.6% was found in the ash and filter. Additional experiments demonstrated that the incomplete mass balance could neither be explained by incomplete trapping nor by adsorption losses on the interior surfaces of the smoking apparatus, leading the authors to the conclusion that the missing THC (approximately 50%) had undergone pyrolytic degradation.

Compared to previous results obtained under constant draft conditions, our THC recoveries in the smoke condensates seem low and rather lie in the range of results obtained by intermittent puffing. This raises the question of whether the suction generated by the water jet pump was not strong enough to prevent sidestream smoke formation. Adsorption within the tubing of the smoking apparatus could have caused further loss of THC. However, as a minimal amount of tubing was used, possible adsorption losses were assumed to be minor. Since the cannabis material was not rolled into cigarettes, but placed in a glass frit, the material was completely burned to ashes, with no “butt” remaining. The residual ashes (90–150 mg) were extracted and analyzed for cannabinoid content. No cannabinoids could be found. Separate analysis of the condensates collected in the two gas washing bottles revealed that approximately 75% of recovered THC got trapped in the first bottle which was cooled in an ice bath. Since the second trap was much colder (liquid nitrogen cooling), it seems reasonable to assume that it was capable of capturing the remaining condensable material. This assumption could be tested by using a third trap. Therefore, incomplete combustion and incomplete trapping were not considered to be primary causes of the low THC recovery.

Under the influence of heat and light, THCA and THC can undergo oxidative degradation to cannabinolic acid (CBNA) and CBN, respectively [31–33]. Dehydrogenation of THCA upon combustion was likely accompanied by decarboxylation thus also affording CBN. However, a reliable estimation of the percentage of theoretically available THC recovered as CBN is difficult, if not impossible to make since we cannot differentiate whether the CBN found in the condensates comes from dehydrogenation of THC and THCA upon combustion or from CBN and CBNA originally present in the plant material, especially since the CBNA content of the plant material was not determined. As, however, the amounts of CBN recovered in the smoke condensates were much lower than the amounts of THC lost during smoking, degradation of the theoretically available THC to CBN does not seem to be a major reason for the missing THC, either. This leads us to conclude that the low THC recoveries in the smoke condensates are most likely due to deficiencies in the experimental set-up (i.e. loss of sidestream smoke) and/or due to the fact that pyrolytic degradation was more extensive than previously observed.

4.2. Dabbing

The vapor of a dabbed concentrate is usually inhaled in a single breath. Therefore, in order to achieve realistic simulation of the dabbing process, the water jet pump was replaced by an oil pump which provided stronger suction. With 66.7–80.8% our recoveries of THC in the vapor condensates of dabbed BHO were significantly higher than the recoveries in the smoke condensates and were comparable to the maximal values measured by Raber et al. [4] for various types of concentrates (not only BHO). However, they observed that 18% of the potentially available THC remained within their dabbing apparatus (tubing, water pipe, dab nail) and 3.1% were found as THCA (not detectable in our study) which might explain why their THC levels in the vapor condensates were on average somewhat lower than ours. Furthermore, they suggested that the consistency of the concentrate (i.e. content of plant waxes and fats) might influence the efficiency of cannabinoid volatilization. This could complicate the comparison of THC recoveries obtained from different dabbed concentrates.

Combustion temperatures during cannabis smoking have been reported to reach 500–900 °C [16,30,34]. Dabbing, in contrast, involves vaporization rather than combustion at lower temperatures [35]. The optimum vaporizing temperature depends on the concentrate's composition and the user's preference. Low-temperature dabbing is more flavorful and tastier as terpenes are preserved, while higher temperatures assure complete vaporization without any material being wasted. "E-nails" users have reported that they prefer temperatures in the range of 340–482 °C [36]. Heating the nail (made of titanium, ceramic, or quartz) with a blow torch, which is more commonly, does not allow temperature control and can quickly result in temperatures causing combustion of the concentrate and degeneration of the cannabinoids, thus decreasing the potency of the dab. Users discussing and sharing their dabbing practices and experiences in public internet forums recommend to heat the nail until it starts to glow red-hot, then let it cool for 5–40 s before applying the dab to avoid burning [37–39].

In contrast to combustion, pyrolytic losses of THC should not occur upon vaporization of cannabis material [26]. In our study, however, 19.2–33.3% of the theoretically available THC could not be recovered in the condensate, while Raber et al. [4] found 39% to be missing after accounting for losses due to adsorption within the dabbing apparatus. As Raber et al. [4], we did not accurately control the temperature during the dabbing experiments and applied the BHO concentrates after the titanium nail had started to glow red-hot and cooled down for a few seconds. This probably resulted in temperatures at which vaporization was accompanied by combustion, causing degradation of THC to polymeric material and further unidentified degradation products, as suggested by Raber et al. [4]. As in the smoking experiments, only minor amounts of CBN could be found in the condensates, suggesting that conversion to CBN was not a major route of degradation upon dabbing.

4.3. Comparison smoking vs. dabbing

When assessing the health risks associated with dabbing, the question arises as to how much psychoactive THC is delivered by doing a dab compared to smoking a joint. Studies have estimated that the average joint contains between 0.2–0.5 g of cannabis [40,41]. In online discussion forums, however, it's not uncommon for cannabis users to report numbers between 0.5–1.0 g [42].

For our calculations, we assume 0.5 g to be the standard amount per joint and the total THC content to be 15% which corresponds approximately to the average potency of today's high-potency cannabis found in several countries [43,44]. As outlined earlier, cannabis smoking is a relatively inefficient method for delivering cannabinoids, with substantial loss of THC due to pyrolysis and in sidestream smoke. Additional THC is lost in the butt. The transfer efficiency of cannabinoids from cannabis to mainstream smoke greatly depends on the smoking dynamics and machine-smoking studies have yielded somewhat different results. Based on these previous findings we consider 30% to be a good estimate for the THC transfer rate. At this rate, 22.5 mg of the theoretically available THC would actually be delivered to the smoker by consuming the standard amount mentioned above.

The amount of concentrate used for dabbing is often referred to as "small" or even "tiny", which can mean different things to different people, probably depending on their previous experience with BHO and cannabis in general (tolerant and non-tolerant users). While some users consider 25 mg a normal-sized dab and 50 mg a big dab, others say that 100 mg is normal-sized, 200 mg is medium and 500 mg is a big dab [45,46]. For the comparison with cannabis smoking, we assume that on average 50 mg of a BHO concentrate with a total THC content of 70% are dabbed. At 75.5% transfer efficiency, as determined in the present study, the user would be exposed to 26.4 mg of THC. It's important to keep in mind that the calculated values refer to the amount of THC transferred to the smoke and vapor, respectively, and not to the amount of THC actually absorbed by the body through the lungs. The amount that actually reaches the systemic circulation is smaller due to incomplete absorption in the lungs. Factors such as the lung surface area, deepness of inhalation and breath-holding time can affect the fraction being absorbed. Our estimations show that, on average, doing a dab delivers a similar amount of psychoactive THC as smoking a joint. So, in this respect, we disagree with media reports suggesting that taking a dab is equivalent to smoking five joints [47] as well as with the estimations made by Raber et al. [4] saying that a joint delivers considerably more THC than an average dab.

The major difference, however, is that delivery of THC by smoking occurs intermittently over several minutes (smoking involves repeated inhalations over time), whereas upon dabbing the available THC is inhaled in a single breath (<10 s), thus producing a euphoric high that is perceived as much more intense. The dabbing vapor is usually cooler than the smoke from a joint (in our study by about 20 °C) and contains far lower levels of irritating combustion byproducts, making it more comfortable to inhale and facilitating a longer holding time in the lungs. While several dabs could be consumed in a row within a few minutes, smoking multiple joints in the same amount of time would be much harder. Thus, compared to smoking, dabbing provides an easier way to quickly consume a massive dose of THC and is associated with a greater chance of toxic effects than concluded solely from the calculated amount of THC. Furthermore, this new trend in cannabis use is more likely to lead to tolerance and to withdrawal symptoms.

It is important to note that the presented findings are of preliminary nature and further research involving more samples will be needed to validate these results.

5. Conclusion

THCA is converted almost quantitatively to THC during the dabbing process, when applying high temperatures to a titanium nail, which has been heated until glowing with red color and cooled down only a few seconds prior to application of the concentrate.

This high recovery of total THC (75.5%) in the condensate by dabbing cannot be achieved by smoking marijuana. Lung availability ranged from 12% for mixed material with rather low content of THC, to approximately 19–27% for marijuana flowers, similar for THC as for CBD (in CBD containing marijuana). In reality, when smoking a joint, additional losses in recovery must be

assumed, e.g. by sidestream smoke. Furthermore, factors like the humidity of added tobacco or plant material itself, influences of terpenes and of smoking habits (puff volume and frequency and breath-holding time per puff) may play an additional role for the lung availability of THC, since humidity and lower temperature in a regular joint may inhibit the decarboxylation of THCA to THC. The rather high lung availability of THC via dabbing can explain the increased psychoactive and unwanted side effects associated with this route of cannabis administration.

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