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RESEARCH ARTICLE

Cannabis smoke condensate III: The cannabinoid content of vaporised *Cannabis sativa*

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Abstract

Cannabis sativa is a well-known recreational drug and, as such, a controlled substance of which possession and use are illegal in most countries of the world. Due to the legal constraints on the possession and use of *C. sativa*, relatively little research on the medicinal qualities of this plant has been conducted. Interest in the medicinal uses of this plant has, however, increased in the last decades. The methods of administration for medicinal purposes are mainly through oral ingestion, smoking, and nowadays also inhalation through vaporization. During this study the commercially available Volcano vaporizing device was compared with cannabis cigarette smoke. The cannabis smoke and vapor (obtained at different temperatures) were quantitatively analyzed by high-performance liquid chromatography (HPLC). In addition, different quantities of cannabis material were also tested with the vaporizer. The cannabinoids:by-products ratio in the vapor obtained at 200°C and 230°C was significantly higher than in the cigarette smoke. The worst ratio of cannabinoids:by-products was obtained from the vaporized cannabis sample at 170°C.

Keywords: *Cannabinoids;* Cannabis sativa*; tetrahydrocannabinol; vaporiser*

Introduction

Cannabis sativa L. (*Cannabaceae*) played an important role in various cultures for millenia. Renewed interest into cannabis in the last few decades balanced between excitement from all kinds of newly discovered pharmacologically desirable effects and fear from abuse and risky behavior in society. However, no matter what politicians and regulatory bodies decide or in future might decide, cannabis use has its place in the society (Reinarman et al., 2004). The proper use of cannabis as a medicine has recently become a matter of debate. The positive effects of cannabis use in treatment of multiple sclerosis, HIV/AIDS, cancer, pain, etc. were recently reviewed (Smith, 2007; McCarberg, 2007; Engels et al., 2007). However, because of the limitations such as legislation and the method of administration, cannabis is today still generally better known as a recreational drug. Many patients also resort to unprescribed self-medication to treat their symptoms. The most popular way of administration in this case is smoking of cannabis cigarettes. Smoking is, however, not recommended because of the high number of undesired products produced during combustion of the plant material (Gieringer, 2001; Russo, 2003). These toxic pyrolytic compounds are produced when the temperature in the plant material exceeds 200°C (Chemic, 2000; Gieringer, 2001), which happens during smoking. The ratio between the desired (cannabinoids) and undesired (carcinogenic) compounds in administered smoke of cannabis is hence grossly influenced by the temperature of vaporization or combustion. In several publications scientists are exploring smokeless inhalation devices, which can reduce the potential harm from smoking cannabis (Gieringer, 2004; Hazekamp, 2006; Abrams, 2007; Bloor et al., 2008).

Vaporizing cannabis is a promising alternative to smoking cannabis. Vaporizing the plant material seems to have a number of advantages over smoking cannabis, including formation of a smaller quantity of toxic by-products and a more efficient extraction of tetrahydrocannabinol (THC) from the cannabis material. With the use of the commercially available Volcano vaporizer the temperature of vaporization of the plant material can be controlled and combustion avoided. In a certain range of temperatures, the

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cannabinoids can be vaporized by hot air without any "burning" of the plant material. The body of evidence to support this advantage in vaporizing the plant sample in comparison with common smoking is growing rapidly (Gieringer, 1996, 2001, 2004; Hazekamp, 2006; Abrams, 2007).

The main objectives of this study was to compare the amount of cannabinoids and by-products present in the vapor produced at different temperatures in comparison with cannabis cigarette smoke. The second objective was to study the effect of the amount of plant material vaporized and its effect on the cannabinoids versus by-products ratio. Because of the fact that users tend to alter the prescribed method or customize the administration to suit their specific medicinal need, we find it important to test various settings in order to study the effect that this will have on the cannabinoid content as well as the amount of by-products produced.

Cannabis smoke was produced using a small-scale smoking machine as previously described (Van der Kooy et al., 2008a). It consisted of two gas traps connected in series, a regulator for controlling suction length and frequency, and a controlled vacuum pump to generate the correct suction volume. Cannabis vapor was produced according to the manufacturer's recommendations with the use of the commercially available Volcano device. It is, however, important to note that the identification of the by-products was not investigated during our current studies. It is therefore not claimed or suggested that the by-products produced by smoking cannabis are similar to those formed during vaporization of cannabis. The identification of the by-products produced by combustion and vaporization and their classification as harmful or toxic will be investigated during future research. It is, however, envisaged that the vaporizer will produce nontoxic by-products while the combusted cannabis material will consist of toxic by-products due to the significantly higher temperature reached during smoking, as this is known to occur in tobacco.

Materials and methods

Plant material and chemicals

Cannabis plant material was obtained from the Office of Medicinal Cannabis and grown by Bedrocan BV (Veendam, The Netherlands) and was of the "Bedrocan" variety. Only the female flower tops were used. This cultivar had at the time of use a tetrahydrocannabinolic acid (THCA) content of 142 mg/g (14.2%) of dry weight plant material. The THC content in the plant material was determined to be 2.7%. All chemicals used were of AR purity, and the high-performance liquid chromatography (HPLC) solvents were of HPLC grade. THC, THCA, cannabigerol (CBG), and cannabinol (CBN) standards were purchased from Farmalyse (Zaandam, the Netherlands).

Quantification of cannabinoids

An adapted HPLC method of Hazekamp et al. (2004) was used to quantify the amount of cannabinoids present in the smoke condensate by using a five-point standard curve of each cannabinoid standard. The HPLC system and conditions are described by Van der Kooy et al. (2008a).

Smoking and vaporization experiments

The small-scale smoking machine used during these experiments is described by Van der Kooy et al. (2008a, 2008b). A Volcano device with digital temperature settings was obtained from Storz & Bickel GmbH & Co. (Tuttlingen, Germany) and is depicted in Figure 1.

The cigarettes were smoked using the conditions described by Van der Kooy et al. (2008a). Three samples of cigarettes were tested using the following conditions: a total puff volume of 35 ml, a puff length of 3 s, and a puff frequency of 30 s. We have found that under these conditions the most reproducible cannabis smoke condensate could be produced and that the burning efficiency was acceptable. The cigarettes were manually lit and the resulting smoke was trapped in a 1:1 mixture of ethanol and hexane (80 ml) at room temperature. The solvents were evaporated with a rotary evaporator at 40°C and the solid material was weighed in order to determine the total yield of each sample. The experiment was performed in triplicate. For the production of the vapor a Volcano device was used according to the recommendations of the manufacturer. During the first test approximately 500 mg of ground, dried cannabis was vaporized at 170°C, 200°C, and 230°C. (In comparison, a cigarette is known to burn at a temperature of around 500–600°C.)

The exact weight of each sample was noted. One balloon of 56 cm (about 8 L) of the vapor was collected and extracted with the use of a vacuum pump in a 1:1 mixture of ethanol and hexane (80 ml) at room temp. The average time for the balloon to fill was 35 ± 5 s. The vapor condensates trapped in the organic solvent were treated in exactly the same way as for the cigarette smoke condensate.

A second experiment was performed testing the vaporizer at 5 different temperature settings, 170, 185, 200,

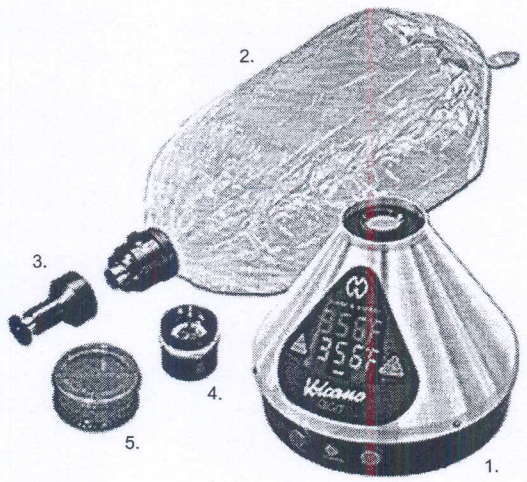

Figure 1. The commercial available Volcano vaporizer, consisting of (1) temperature-controlled vaporizer, (2) vapor collection balloon, (3) mouthpiece, (4) filling chamber, and (5) material grinder.

215, and 230°C, after a period of about 2 months after the initial tests. This test was performed in order to establish the reproducibility of the vaporization process. In addition, a third test was performed to test the effect of different amounts of cannabis samples on the THC content in the produced vapor. The samples were vaporized at 230°C to determine the effect on the THC content in the produced vapors and to correlate the variation to be expected when consumers uses the Vaporiser. The following amounts of dried cannabis were tested: 50, 100, 250, 500, and 1000 mg. Each amount was prepared and tested in triplicate as described earlier.

Sample preparation and HPLC analysis

All the produced samples were dried on a rotary evaporator at 40°C, after which a 1-mg/ml solution of each sample was prepared in ethanol. Five microleters of each was injected into the HPLC system. From the standard curves of the five-point standards the concentrations of cannabinoids in the samples were calculated.

Results and discussion

The results obtained from the first experiment are given in Figure 2. This comparative experiment gives the total yield, total cannabinoids, total THC, and the amount of by-products in milligrams per gram of cannabis obtained from the vapor and the cigarette smoke. The total yield obtained from the vapor gradually increased with an increase in temperature. The highest amount of material was obtained from the cigarette smoke, while the lowest amount was obtained from the vapor produced at 170°C. As was expected, the level of total cannabinoids also followed this trend and the highest amount

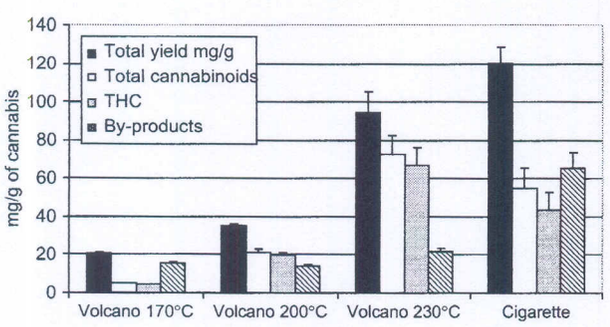

Figure 2. Experiment conducted in order to compare cannabis cigarette smoke with the vapor produced at different temperatures. For all the samples the total yield (dried condensate), total cannabinoids, THC, and total by-products are given in mg/g of cannabis plant material.

was obtained from the vapor produced at 230°C. The exception was that the cigarette produced a lower amount of total cannabinoids if compared to the vapor produced at 230°C. Table 1 includes the results of the four major cannabinoids found in the smoke condensates tested under the different conditions.

The levels of all cannabinoids increased with the temperature of vaporisation. In particular, the amount of CBG increased by as much as 90% between 200 and 230°C of the vaporization temperature. All of the cannabinoids obtained from the 230°C vapor were found in amounts higher in comparison with the smoke condensate. The vapor temperature of 200°C produced a higher yield only of THCA (0.57 ± 0.04 mg/g vs. 0.46 ± 0.10 mg/g in the cigarette smoke). This is mainly due to the reduced decarboxylation of THCA to THC at lower temperature. However the total cannabinoid production at 200°C is still 17.11% higher compared to the cigarette smoke (calculated to the total yield). The lowest vaporizing temperature, 170°C, produced only 56.75% of the total cannabinoids compared to the cigarette smoke condensate.

The THC level in the cannabis smoke was found to be lower than in the 230°C vaporized samples. The THC in the smoke condensate comprised 36.2 ± 7.9% of the total yield, while THC levels in the vaporized samples were found to be 71.2 ± 9.6% (230°C) and the lower vaporizing temperatures yielded only 56.3 ± 4.4% (200°C sample) and 21.6 ± 1.3% (170°C) of THC, respectively.

The lower THC levels found in the cannabis cigarette are partially due to pyrolysis of THC at higher temperature and through the loss of the sidestream smoke. Gieringer et al. (2004) compared the levels of THC obtained from combusted samples, cannabis cigarettes, and vaporized cannabis at 185°C (they did, however, use the older Volcano system with manual temperature settings and cannabis sample sizes of 200 mg). The conclusion in their work is that in terms of THC, cannabis cigarettes favor delivering efficiency, while the Volcano produces a much "cleaner" cannabinoid-containing vapor. This is in part not supported by our experiments. While we have found that the Volcano does indeed produce a much cleaner cannabinoid vapor, at specific temperatures the efficiency of THC extraction was also better compared to smoking cannabis.

The following ratios of by-products to THC were achieved for the different samples: 0.3:1.0, 0.7:1.0, 1.6:1.0, and 3.5:1.0 for the Volcano at 230°C and 200°C and the cannabis cigarette and 170°C, respectively. This indicates that the Volcano sample produced at 230°C is the "cleanest" compared to the Volcano sample produced at 170°C, which is the most impure if one considers only the THC content. The amount

Table 1. Cannabinoid content of the vapor and cigarette condensates (mg/g of cannabis material).

Sample	THC	THCA	CBG	CBN	Percent cannabinoids of total yield
Volcano, 170°C	4.43 ± 0.26	0.32 ± 0.06	0.16 ± 0.02	0.06 ± 0.01	24.18 ± 1.69
Volcano, 200°C	19.79 ± 1.56	0.57 ± 0.04	0.67 ± 0.07	0.14 ± 0.01	60.17 ± 3.37
Volcano, 230°C	67.10 ± 9.07	0.91 ± 0.12	3.80 ± 0.59	0.79 ± 0.12	76.90 ± 2.01
Cigarette	43.48 ± 9.45	0.46 ± 0.10	3.06 ± 0.68	2.36 ± 0.49	43.06 ± 6.90

of by-products in the cigarette smoke was found to be the highest, reaching 65.37±8.21 mg/g of cannabis. This is nearly 70% more than is obtained from the Volcano® sample operated at 230°C.

During the second experiment vaporizing temperatures were tested at five different settings. The results (Figure 3) show a gradual increase in the total yield from 11.4±3.1 mg/g (sample at 170°C) to 75.6±14.1 mg/g (at 230°C). The results correlate well with those obtained during the first experiment except for the samples produced at the lowest temperature (170°C). The total yield differs markedly between the two sample sets, which might indicate that at lower temperatures it might be difficult to obtain reproducible results.

Besides the vaporizing temperature, the sample size considerably affects the THC:by-products ratio. Figure 4 illustrates the relationship between the amount of cannabis and the total vapor yield and THC levels after vaporizing different quantities of the cannabis material at 230°C. As the Volcano vaporizing chamber has a fixed internal diameter, it is expected that the amount (or height) of the material would strongly influence extraction factors such as temperature distribution, contact surface, and the kinetics of the air that passes through the plant material. The manufacturer's recommendation is to fill the chamber between 1 and 10 mm with finely grained plant material. In our test, 1 g dry ground cannabis comprised 10–13 mm height of the filling chamber.

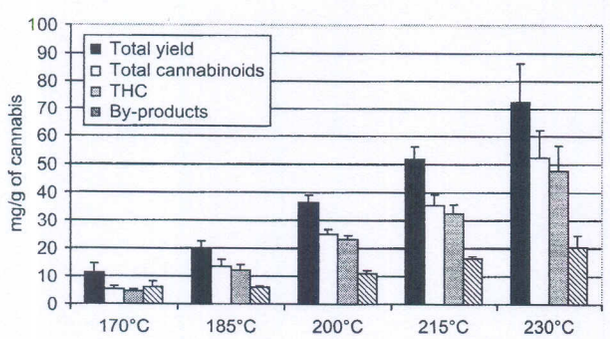

Figure 3. Analysis conducted on the Vaporiser in order to establish the differences in total yield, total cannabinoids, THC, and total by-products obtained when the samples are produced at five different temperatures.

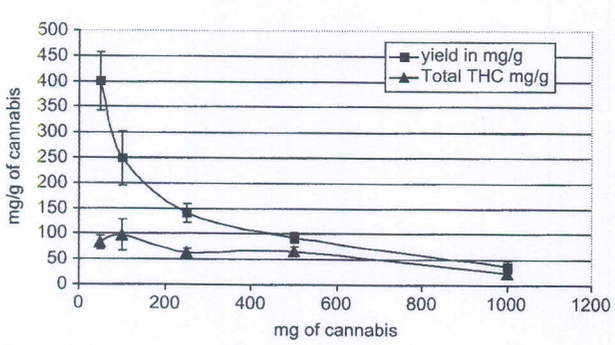

Figure 4. Total yield and total THC content of the condensates when different sample sizes were vaporised at 230°C.

Sample size corresponding to the recommendation is therefore within the interval of 50 mg to 500 mg cannabis plant material.

The lowest tested amount of cannabis, 50 mg, produced the highest total yield of vapor condensate (40% of sample). As the sample size increased, the total yield decreased considerably, while the THC levels remained relatively constant in all the samples with the only exception that of the highest amount of cannabis (1000 mg), which yielded only 23.30±6.30 mg/g of cannabis. The total yield is thus inversely proportional to the sample size. The more efficient extraction observed in the smaller sample sizes doesn't seem to influence the THC levels, so the large increase of the total yield consists mainly of additional by-products.

Conclusions

The drying methods employed during our experiments warrant some further discussion. To determine the moisture content and to dry the cannabis samples, different ways of drying could be employed. The critical point is the temperature at which this occurs. Residual water content needs to be removed either in a desiccator or in a low-temperature oven (30–40°C) for a few days. However, both these approaches produce an intense smell indicating a loss of lower terpenoids and other volatile compounds. For drying cannabis for our experiments, we placed the material in a desiccator for 5 days. The second drying step includes the drying of the smoke condensate and the vaporized condensate trapped in the organic solvent performed with a rotary evaporator at 40°C. At this temperature most of the lower terpenoids will be lost and this will lead to a lower total yield. The total yield might also be influenced by the presence of hygroscopic components in the condensates. These components might therefore cause an overall increase in the yield. The methods employed during these experiments were, however, tested for the recovery of THC and it was found that the recovery was 99.5±5.2%.

Previous experiments conducted with the cigarette smoke (Van der Kooy et al., 2008a, 2008b) gave yields of around 100 mg/g of cannabis. During our current research we found that the yields produced reached slightly higher levels, namely, about 120 mg/g. This variation indicates that slight variations in the conditions of smoke production (or during the drying of material and the smoke condensate) might result in obtaining different results. The ratio of THC to by-products did, however, remained consistent.

From the presented data it is clear that the amount of by-products in vaporized cannabis is dramatically decreased at all tested temperature settings in comparison with smoked cannabis. This finding is in agreement with Chemic (2000), Gieringer (2001), and Gieringer et al. (2004). However, the temperature and sample size effects on the production of various chemicals, desired and undesired, are undoubted. In addition, amounts of the desired products (total cannabinoids) are significantly higher at higher vaporising temperatures, showing nearly double the quantity compared to the cigarette smoke.

Although the Volcano vaporizer has several advantages compared to cannabis cigarette smoke, the proper use for the administration of medicinal cannabis has to be established in more detail. Based on our results, the amount of cannabis used plays a crucial role in the vapor quality and should thus not be left to random administration, but carefully adjusted. The vaporizing temperature is another factor to be optimized. We found the best ratio of by-product and THC at a vaporizing temperature of 230°C. Based on the results, we can conclude that with the use of the vaporizer a much "cleaner" and therefore a more healthy cannabis vapor can be produced for the medicinal use of *C. sativa,* in comparison to the administration of THC via cigarettes.

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Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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