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Cannabis Smoke Condensate II: Influence of Tobacco on Tetrahydrocannabinol Levels

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Medicinal cannabis has attracted a lot of attention in recent times. Various forms of administration are used, of which smoking is very common but the least desirable. Smoking cannabis generates a large amount of unwanted side products, of which carcinogenic compounds are the most dangerous. A common practice among recreational drug users, and to a lesser degree patients who uses cannabis as medicine, is to mix the cannabis material with commercially available tobacco in order to increase the burning efficiency of the cigarette and to reduce the overall costs of the cigarette. In this study cannabis material has been mixed with tobacco in order to determine whether tobacco has an influence on the amount of and ratio between tetrahydrocannabinol (THC), cannabigerol (CBG), and cannabinol (CBN) administered while smoking. A small-scale smoking machine has been used and cannabis mixed with various ratios of tobacco was smoked. The trapped smoke was quantitatively analyzed by high-performance liquid chromatography (HPLC) and the amount of THC, CBG, and CBN was determined for each cigarette. We have found that tobacco increases the amount of THC inhaled per gram of cannabis from 32.70 ± 2.29 mg/g for a 100% cannabis cigarette to 58.90 ± 2.30 mg/g for a 25% cannabis cigarette. This indicates that tobacco increases the vaporization efficiency of THC by as much as 45% under the conditions tested.

Cannabis sativa L. (Cannabaceae) is one of the oldest known medicinal plants, and its medicinal use was described in China about 2000 years ago (Formukong, 1989). Cannabis is used all over the world as a recreational drug, while renewed interest in its medicinal properties has resulted in some countries registering cannabis preparations as drugs for the treatment of mainly nausea and vomiting associated with chemotherapy. Over the last several years, cannabis-based medicines such as Sativex have been investigated for the treatment of spasticity, chronic pain, disruption of sleep, and urinary dysfunction associated with multiple sclerosis and other neurological disorders (Smith, 2007).

Although there is a long history associated with the medicinal properties of cannabis, it is today still better known as a recreational drug. According to Todd (1943), cannabis is usually smoked or eaten, with the effects, as might be expected, usually slower in developing when eaten. Other methods of ingestion are to consume a tea preparation or a milk preparation. The milk preparation increases the extraction efficiency of the active component, THC, due to its lipophilic nature (Giroud et al., 2000). The preparation of a baked product, the so-called "space cake," is also well known. A relatively new method of ingestion is to extract the active principle with heated gas. The commercially available Volcano vaporizer system performs this task as it collects the extracted smoke in a plastic bag, and this smoke is then inhaled by the user. The main active principle in *C. sativa* responsible for its psychotropic and pharmacological activity is tetrahydrocannabinol (THC). In most of the already mentioned processes, heating the material plays an important role, as each process will decarboxylate the naturally occurring inactive tetrahydrocannabinolic acid (THCA) into the active THC.

The history of smoking tobacco mixed with recreational drugs is well known and tobacco mixed with opium has been documented (Dikotter et al., 2002). Smoking cannabis causes the formation of many unwanted side products, of which tars, polyaromatic hydrocarbons (PAH), and other carcinogenic compounds are the least desirable. Smoking has, however, been one of the favored methods of ingesting cannabis for recreational drug users. The difficulties experienced with smoking cannabis are mainly the commonly experienced problem of undesirable combustion of the cannabis material. The lit cigarette tends to stop burning as soon as the user stops to puff. This causes users to

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continuously relight the cigarette or more commonly to add some commercial available tobacco to the cannabis material (Chou et al., 2007). Depending on the amount of added tobacco, the cigarette will burn just like a normal tobacco cigarette. Recreational drug users also add inexpensive tobacco to dilute the far more expensive cannabis material.

We have therefore decided to test the effects of tobacco on the THC, cannabigerol (CBG), and cannabinol (CBN) levels in cannabis smoke. Previous studies have focused on the comparison between tobacco or cannabis smoke and the effects on patients who use either cannabis or tobacco separately (Sherman et al., 1995). Analytical techniques of identifying THC from a mixture of tobacco and cannabis smoke-filled rooms have also been described (Chou et al., 2007). In the present study cannabis material has been mixed with tobacco in order to determine whether tobacco has an influence on the amount of THC inhaled while smoking. A small-scale smoking machine has been used, and cannabis mixed with various ratios of tobacco was smoked. The trapped smoke was quantitatively analyzed by high-performance liquid chromatography (HPLC), and the amounts of THC and the two minor cannabinoids, CBG and CBN, were determined for each cigarette. Throughout this article we use the term "smoke condensate" to describe the solid material that remains after the smoke has been trapped in organic solvents and subsequently dried. Strictly speaking, no condensation of the smoke occurs, but as this term is commonly used to describe the solid material obtained from cannabis smoke we have decided to use the term throughout this article.

MATERIALS AND METHODS

Plant Material and Chemicals

The *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 THCA content of 174 mg/g (17.4%) of dry weight plant material. Commercially available Drum tobacco (Joure, The Netherlands) was obtained from a local vendor. This brand of tobacco is used to prepare homemade cigarettes and is commonly used to add to cannabis cigarettes. All chemicals used were of analytical reagent (AR) purity, and the HPLC solvents were of HPLC grade. THC, THCA, CBG, and CBN standards were purchased from Farmalyse (Zaandam, the Netherlands).

Preparation of Cigarettes

The tobacco was mixed with the cannabis material before preparing the cigarettes. The cannabis and tobacco were mechanically mixed in order to obtain a homogenous sample. In total 5 ratios were prepared as to contain the following percentages of cannabis: batch 1, 100% cannabis ($n = 3$); batch 2, 90% cannabis ($n = 5$); batch 3, 75% cannabis ($n = 5$); batch 4, 50% cannabis ($n = 5$); and batch 5, 25% cannabis ($n = 5$). Commercial available cannabis cigarette paper (109.0 mm length, 6.0 mm radius at filter and 12.5 mm radius at the tip) was used (Mountain High, Rotterdam, The Netherlands). The cigarette paper did not contain a filter. The cigarettes were prepared individually by hand as to contain 700 mg of material each. The exact weight was determined for each cigarette.

Small-Scale Smoke Machine

The small-scale smoke machine used during these experiments is described by Van der Kooy et al. (2008). The cigarettes were lit by hand and the lighting puff was also included in the analysis. Only one cigarette was smoked at a time, and the cigarette was smoked until no material remained. After each cigarette was smoked the whole system was cleaned with ethanol and the settings were tested and adjusted if needed for the next sample. Figure 1 illustrates the experimental setup of the smoking machine.

HPLC Analysis

An Agilent 1200 HPLC with photodiode array (PDA) detection was used to analyze the smoke condensate samples. The HPLC method of Hazekamp et al. (2004) was used to quantify

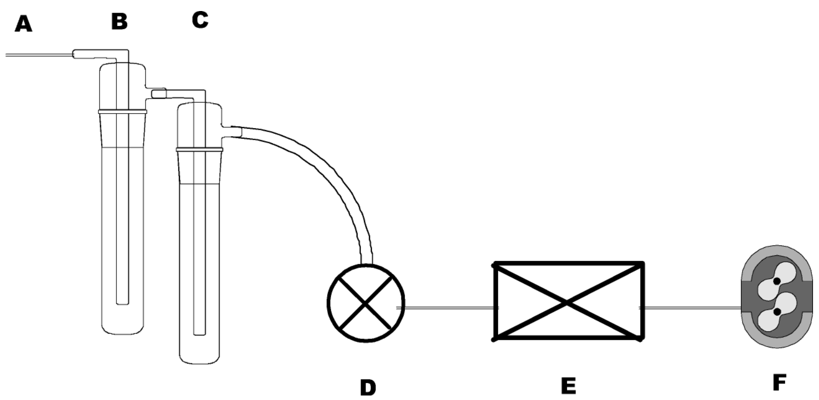

FIG. 1. Diagram of the small-scale smoke machine used during the experiments: A, cigarette; B, solvent trap one; C, solvent trap two; D, suction volume regulator; E, puff frequency and puff duration regulator; F, vacuum pump.

the amount of cannabinoids present in the smoke condensate by using a five-point standard curve of each cannabinoid standard. In short, the system consisted of a Phenomenex RP18 (2) 150 $\times$ 4.6 mm, 5-μm column. The mobile phase consisted of 0.1% formic acid (A) and methanol/0.1% formic acid (B). The gradient system employed was: 0 min 65% B, 28 min 100% B, 30 min 100% B, 31 min 65% B 33 min 65% B.

Moisture Content of Material and Recovery of THC

The moisture content of the material was determined by drying the material at 80°C for 1 wk. The moisture content of the material was determined to be 4.13 $\pm$ 0.06%. For the recovery experiments, known amounts of THC (at concentrations similar to those that were trapped during the smoking experiments) were added into the trap system and recovered as with the smoke samples. The recovery for THC was found to be 99.5 $\pm$ 5.2%. Due to the small amount of material for the other three standards, no recovery experiments were performed for the THCA, CBG, and CBN cannabinoids.

Smoking Experiment

The cigarettes were smoked using the conditions described by Van der Kooy et al. (2008). In short, the following conditions were used: a total puff volume of 35 ml, a puff length of 3 s, and a between-puff interval 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 trapped in a 1:1 mixture of ethanol and hexane (80 ml) at room temperature.

Sample Preparation and HPLC Analysis

The samples were dried on a rotary evaporator at 40°C. A 1-mg/ml solution of each sample were prepared in ethanol, after which 5 μl was injected into the HPLC system. From the standard curves the concentrations of cannabinoids in the smoke condensate were calculated.

RESULTS AND DISCUSSION

Table 1 gives the results of the total yields obtained from the trapped smoke, the actual concentration of THC in the smoke condensate per gram of cigarette, and the amount of THC released per gram of cannabis. The total yield refers to the part of smoke that was collected from the solvent traps, dried, and weighed, and excludes the sidestream smoke and the material remaining in the burned ash. There were a couple of unexpected results obtained during these experiments. The total yield remained stable, which was not expected. Research has shown that the total yield obtained from tobacco smoke is about 50% compared to cannabis smoke (Lee & Novotny, 1976; Novotny et al., 1982). It was therefore expected that the yields would gradually decrease with an increase of tobacco concentration in the cigarettes. A 1:1 mixture of tobacco and cannabis should theoretically give a total yield of about 75 mg/g, while the actual yields obtained were 109.24 $\pm$ 13.28 mg/g. It can be calculated that this is a 40% higher value than expected. This result can be partially explained by the increase of THC obtained in the resulting smoke condensate, which will lead to a increase in the total yield obtained.

TABLE 1
Total yield and amount of THC in the smoke condensate, produced in the cannabis samples mixed with different ratios of tobacco

Sample	Total yield (mg/g cigarette)	Total yield of THC (mg/g cigarette)	Yield of THC from cannabis (mg/g)
100% cannabis	100.78 $\pm$ 7.61	32.67 $\pm$ 2.29	32.67
90% cannabis	94.25 $\pm$ 10.39	29.89 $\pm$ 2.08	33.21
75% cannabis	105.90 $\pm$ 5.58	29.86 $\pm$ 2.64	39.81
50% cannabis	109.24 $\pm$ 13.28	26.85 $\pm$ 4.07	53.70
25% cannabis	99.44 $\pm$ 6.55	14.72 $\pm$ 2.30	58.88

Note. The theoretical amount of THC produced per gram of cannabis material is also included.

For the 100% cannabis cigarettes the THC yield per gram of cigarette in the smoke condensate is 32.67 $\pm$ 2.29, while a yield of 14.72 $\pm$ 2.30 for the 25% cannabis cigarettes was obtained. Decreases of THC amount in the smoke condensate per gram of cigarette of 8.51, 9.14, 17.80, and 54.94% for the 90, 75, 50, and 25% cannabis cigarettes were observed, respectively, if compared to the pure cannabis cigarette. Another unexpected result was the amount of THC released per gram of cannabis. The 90, 75, 50, and 25% cannabis cigarettes showed increases of 1.62, 17.93, 39.16, and 44.51% in the yield of THC per gram of cannabis, respectively, compared to the pure cannabis cigarettes. This effect might be explained by an improvement of the burning efficiency that the tobacco has on the cigarette. By improving the burning efficiency the average temperature of the cigarette will be higher and therefore will lead to an improved volatilization of the cannabinoids. Another effect that might also contribute to this result is that tobacco burns at a different temperature, which might lead to the observed increase of the cannabinoids in the trapped smoke condensate.

Table 2 gives the results of the three major cannabinoids in the smoke condensate. It also includes the ratio of the three cannabinoids. From Table 2 it can be seen that the amount of CBN decreases gradually compared to the amount of THC. A ratio of 10.00:1.24 was obtained for the 100% cannabis cigarette and a 10.00:0.54 for the 25% cannabis cigarette. This is indicates a decrease of 56.45% of the concentration of CBN compared to THC. The ratio of THC:CBG remained relatively constant, with 10.00:0.77 for the 100% cannabis cigarette and 10.00:0.68 for the 25% cannabis cigarette. Taking into account the standard deviations, this is not a significant difference. This would indicate

TABLE 2
Yields of the major cannabinoids in the smoke condensate produced under the different conditions and the ratios between them

Sample	THC	CBN	CBG	Ratio THC:CBN:CBG
Cannabis 100%	32.67 ± 2.29	4.04 ± 0.49	2.50 ± 0.24	10.00:1.24:0.77
Cannabis 90%	29.89 ± 2.08	3.40 ± 0.48	2.19 ± 0.20	10.00:1.14:0.73
Cannabis 75%	29.86 ± 2.64	3.21 ± 0.37	2.14 ± 0.09	10.00:1.08:0.72
Cannabis 50%	26.85 ± 4.07	1.96 ± 0.17	1.71 ± 0.25	10.00:0.73:0.64
Cannabis 25%	14.72 ± 2.30	0.80 ± 0.05	1.00 ± 0.10	10.00:0.54:0.68

that CBG and THC behaved similarly under the conditions tested while CBN behaved significantly differently.

CONCLUSIONS

These results have shown that when smoking cannabis mixed with tobacco no significant reduction in the total amount of yield occurs. From a medical point of view this should be enough to persuade medicinal cannabis users not to employ this method of smoking cannabis, as the amounts of by-products are significantly higher than when smoking pure cannabis. A pure cannabis cigarette contains on average 32.42% THC, while a 25% cannabis cigarette contains only 14.80% THC. The results have shown that mixing tobacco with cannabis does, however, lead to a more efficient release of THC per gram of cannabis, which might be explained by the more efficient burning of the cigarette when mixed with tobacco and the difference in combustion temperature between the cannabis and tobacco material. Another explanation for the results is that the vapor pressure of THC under the different conditions tested will have a different equilibrium when mixed with different ratios of tobacco. This might also contribute to the observed increase of THC in the trapped smoke condensate. Taking into account the standard variation in the results, it can be concluded that mixing cannabis with up to 50% of tobacco might lead to the user inhaling a similar amount of THC compared to a 100% cannabis cigarette. These results suggest that further work should be conducted on the different ways of smoking cannabis for either medicinal or recreational use.

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