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Cannabinoids in Blood and Urine after Passive Inhalation of *Cannabis* Smoke

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ABSTRACT: To test the possibility that cannabinoids are detectable following passive inhalation of *Cannabis* smoke the following study was performed. Five healthy volunteers who had previously never used *Cannabis*, passively inhaled *Cannabis* smoke for 30 min. *Cannabis* smoke was provided by other subjects smoking either marijuana or hashish cigarettes in a small closed car, containing approximately 1650 L of air. Δ^9-Tetrahydrocannabinol (THC) could be detected in the blood of all passive smokers immediately after exposure in concentrations ranging from 1.3 to 6.3 ng/mL. At the same time total blood cannabinoid levels (assayed by radioimmunoassay [RIA]) were higher than 13 ng/mL in four of the volunteers. Both THC and cannabinoid blood concentrations fell close to the cutoff limits of the respective assays during the following 2 h. Passive inhalation also resulted in the detection of cannabinoids in the urine by RIA and enzyme multiple immunoassay technique (EMIT®) assays (above 13 and 20 ng/mL, respectively). It is concluded that the demonstration of cannabinoids in blood or urine is no unequivocal proof of active *Cannabis* smoking.

KEYWORDS: toxicology, tetrahydrocannabinol, marijuana, passive inhalation

The possibility of absorption of *Cannabis* constituents after passive inhalation of *Cannabis* smoke could be of considerable health and legal importance. To demonstrate the phenomenon one would require the detection of cannabinoids[3] in blood and urine (or other biological fluids) after well-controlled exposure to *Cannabis* smoke. To our knowledge this has been subject to very limited investigation previously. In a study conducted on one person living with five active regular marijuana smokers, cannabinoids were probably detected in the urine on several occasions [*1*]. In another study two nonsmoking subjects were together with four marijuana smoking subjects under various experimental conditions [*2,3*]. In that study 78 of a total of 80 urine samples were considered negative for cannabinoids by the enzyme multiple immunoassay technique (EMIT®) [*2,3*]. In an experiment with one single passive smoker, detectable concentrations of Δ^9-tetrahydrocannabinol (THC) were demonstrated in plasma [*2,4*]. With this background we would like to report our study which was conducted to find out to what extent

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[3]Naturally occurring cannabinoids including tetrahydrocannabinol as well as their metabolites are referred to as "cannabinoids" in this article.

passive inhalation of *Cannabis* could take place under conditions aimed at passive absorption of *Cannabis* smoke.

Experimental Design

Subjects

Ten volunteers (three women, seven men) aged between thirty-five and fifty years served as test subjects. All gave their informed consent to participate in the study. None had previous experience with *Cannabis* smoking. All were healthy and of normal weight in relation to their height, age, and sex. Two studies with five subjects participating in each were carried out as follows.

Study 1 (Hashish Experiment)—Three subjects smoked two cigarettes each during 30 min using approximately 15 min on each cigarette. The cigarettes were made by mixing tobacco and hashish of known (determined) THC concentration. Each cigarette contained 15 mg of THC, final concentration 1.5% (w/w). The subjects were instructed to inhale the smoke as little as possible to increase the amount of side-stream smoke diffusing into the surrounding atmosphere and, hence, the amount of THC available for passive inhalation. The smoking took place in a small car with an available air volume of approximately 1650 L. Two subjects not smoking, but breathing normally, were also present in the car. All subjects left the car immediately after the 30-min smoking period. Blood and urine samples were taken before the *Cannabis* exposure. Blood samples were also taken immediately after the exposure and 2 h later and, in all cases, in another room than the smoking chamber. Urine samples were collected on several occasions after the experiment as described in the Results section. All samples were stored frozen (−20°C) until analysis.

Study 2 (Marijuana Experiment)—Two subjects smoked six marijuana cigarettes each during 30 min using approximately 5 min on each cigarette in the same car as used for Study 1. Each cigarette contained 7.5 mg of THC, final concentration 1.5% (w/w). The theoretical total amount of THC smoked during the 30-min period was thus 90 mg as in Study 1. The instruction to the smokers was the same. Exposure time and sampling were similar to Study 1. In this study there were three passive smokers.

Analytical Procedure

Blood samples were analyzed specifically for THC by gas chromatography-mass spectrometry (GC/MS) according to Rosenthal et al [*5*] (cutoff limit 0.5 ng/mL). Cannabinoids in blood and urine were analyzed by a radioimmunoassay (RIA) technique with tritiated THC [*6*] (cutoff limit 13 ng/mL, when calibrated versus pure THC standards and expressed equivalent to nanograms of THC). The antiserum was purchased from Guildhay Antisera, Guildford, Surrey, U.K. The relative cross-reactivities of THC, its OH and COOH metabolites were 1:1:1. Pure THC (Makor Chem., Jerusalem, Israel) was used to prepare standards for quantitation in both types of assay. Urine was also analyzed for cannabinoids by an EMIT technique, using a kit (Syva, Palo Alto, CA, USA) with calibrators prepared by the manufacturer (cutoff limit 20 ng/mL).

Results

Blood Analysis

Cannabinoids in blood measured by RIA increased from levels lower than the cutoff limit before the experiment to clearly detectable levels after 30-min exposure to *Cannabis* smoke in four of the five passive smokers (Fig. 1*a*). Two hours later measurable values were still found in

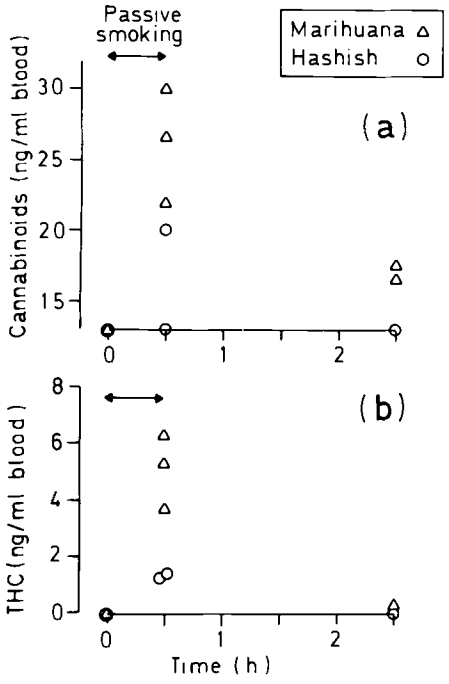

FIG. 1—*Individual blood concentrations of cannabinoids* (a) *and THC* (b) *in five passive smokers. Cannabinoid concentrations were determined against standards of pure THC and are expressed equivalent to nanograms of THC.*

two of these subjects. It should be noted that the corresponding blood levels of the active smokers were of the same order of magnitude, ranging from 16 to 30 ng/mL at 30 min, and from below the cutoff limit to 23 ng/mL at 2 h 30 min. Note, however, that these levels resulted from smoking which cannot be compared to "real-life" *Cannabis* smoking (see Experimental Design section).

THC (measured by GC/MS) was present in the blood of all five passive smokers after 30 min (Fig. 1*b*). Two hours later the levels were in all cases close to the cutoff limit. Similar results were observed in the active smokers, who had peak values that also ranged from 1.3 to 6.3 ng/mL and final values ranging from 0 to 1.3 ng/mL.

The ratio between blood cannabinoid levels and THC levels was much lower than observed in our usual forensic science samples. This was probably a consequence of the immediate sampling after exposure which only permitted short time periods for the formation of THC metabolites in our test subjects.

Urine Analysis

Urine samples were first tested for cannabinoids by an EMIT technique. The results for the passive smokers are shown in Table 1. Neither of the two subjects participating in the hashish experiment demonstrated positive values on the day of the experiment or on the subsequent four days. Of the three persons exposed to marijuana smoke, one had positive values on the experimental day and on the two following days (P3 in Table 1). Another had two positive samples on the experimental day (P5, Table 1). Among the three active smokers participating in the hashish experiment, one single positive sample was recorded on Day 2. One of the two ac-

TABLE 1—*Cannabinoids (EMIT) in urine of five subjects after passive inhalation.*[a]

Subject	Day 1 (Experimental)			Day 2 Morning	Day 3 Morning	Day 4 Morning	Day 5 Morning
	Before	0 to 4 h	4 to 24 h				
P1		−		−	−	−	−
P2	−	−		−	−	−	−
P3	−	+		+	+	−	−
P4	−	−	− − −	−	−	−	−
P5	−	−	+ +	−	−	−	−

[a]Each sample analyzed is marked with: + (above 20 ng/mL of urine), − (below 20 ng/mL of urine). Subjects P1 and P2 participated in the hashish experiment, P3 to P5 in the marijuana experiment.

tive marijuana smokers voided samples that were positive for the first three days, urine from the other was positive for the experimental day only.

The urine samples collected after the marijuana experiment were further subjected to semiquantitative analysis by RIA. The results after passive inhalation are presented in Table 2. The levels peaked either on Day 1 or 2. The results were not in accordance with those presented in Table 1. This indicates that RIA and EMIT were either measuring different cannabinoids, or that some cannabinoid(s) was measured with different efficacy in the two types of assay or both. Cannabinoids assayed by RIA were detectable in urine of one active marijuana smoker only on the experimental day, 25 ng/mL. The next morning the urines of the two active smokers contained 16 and 38 ng/mL, respectively. The values then declined gradually to not detectable levels in both on Day 5.

No subject experienced any feeling of euphoria during the experiment. The discomfort caused by the heavy *Cannabis* smoke during the exposure period was universal among active and passive smokers.

Discussion

The present study shows that passive inhalation of *Cannabis* smoke may occur as demonstrated by the presence of THC in blood and cannabinoids in blood and urine of passive smokers. Some interindividual variation was found, but we would like to draw special attention to the fact that specific determination of THC (by GC/MS) was possible in blood samples of all five passive smokers. Our results thus confirm and extend the results obtained with one single person [2]. We measured THC blood levels after passive smoking that would correspond to plasma levels of at least 13 ng/mL [7]. The highest THC concentration measured in the present study was thus approximately six times higher than the highest concentration measured in

TABLE 2—*Cannabinoids (RIA) in urine in nanograms per millilitres of three subjects after passive inhalation of marijuana.*[a]

Subject	Day 1 (Experimental)		Day 2 Morning	Day 3 Morning	Day 4 Morning	Day 5 Morning
	Before	After				
P3	n.d.	20	22	14	n.d.	n.d.
P4	n.d.	26	30	23	21	n.d.
P5	n.d.	17	14	16	n.d.	n.d.

[a]n.d. = below cutoff limit (13 ng/mL). The figures represent nanograms per millilitres of urine as calibrated against THC standards.

the only subject demonstrating passive transfer of THC to blood reported so far [2]. This indicates more optimal conditions for the passive transfer of *Cannabis* smoke in the present study. This was probably a result of a smaller volume of air in our smoking chamber (approximately one half of that in the other study), since the amount of THC smoked and the exposure time were similar in the two studies.

A similar difference between the other study [2] and ours was also reflected by the results of urine EMIT analysis. We were able to find positive values for three days after passive inhalation, in contrast to previous studies [2,3] using the same analytical technique. We feel that the concentration of *Cannabis* smoke in the atmosphere of our experiment must have been close to the limit of what might be tolerated from a discomfort level. We do not know, however, whether the passive transfer of the principal psychoactive substance, THC, could have been increased by longer time of exposure, forced breathing by the passive smokers, or higher concentrations of THC in the smoking material.

The difference between the results of the hashish and the marijuana experiment, the latter resulting in higher blood and urine levels of cannabinoids, was probably because of difficulties in obtaining a successful combustion of the hashish tobacco mixture. We could not conclude that smoking of hashish includes a lower risk with regard to *Cannabis* exposure and passive smoking.

The highest concentration of plasma THC reached by passive inhalation in our study (13 ng/mL) is similar to the concentration measured in plasma approximately 30 min after active smoking of 15 mg of THC [8]. Such inhalation of THC and similar THC plasma levels are accompanied by mental [8–10], psychomotor [11], and physiological alterations [11,12] and failure to pass a roadside sobriety test [7]. The THC level measured in our study, shortly after passive inhalation, probably represented close to the highest THC concentrations obtained, while those concentrations reported 30 min after real smoking were preceded by much higher blood concentrations during and after smoking. This might explain the lack of mental effects in our study, but it should be noted that these type of effects were not particularly looked for. Further experiments aimed at psycho-physiological changes would clarify whether such could occur after passive inhalation of *Cannabis* smoke.

Conclusion

The main conclusion is presently that the demonstration of cannabinoids in blood or urine is not unequivocal proof of active *Cannabis* smoking. Therefore, the results of laboratory tests in this field, which might have both legal and other important consequences, should be interpreted with great caution.

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