Published in final edited form as:
Forensic Sci Int. 2008 January 30; 174(2-3): 173–177.

Excretion of Δ⁹-Tetrahydrocannabinol in Sweat

Marilyn A. Huestis[1,*], **Karl B. Scheidweiler**[1], **Takeshi Saito**[1,2], **Neil Fortner**[3], **Tsadik Abraham**[1], **Richard A. Gustafson**[4], and **Michael L. Smith**[5]

1 *Chemistry and Drug Metabolism, Intramural Research Program, National Institute on Drug Abuse, National Institutes of Health, Baltimore, MD, USA*

2 *Tokai University School of Medicine, Kanagawa, Japan*

3 *ChoicePoint, Inc., Alpharetta, GA*

4 *Lieutenant Commander, U S Navy, Navy Drug Screening Laboratory, Jacksonville, FL USA*

5 *Division of Forensic Toxicology, Office of the Armed Forces Medical Examiner, Armed Forces Institute of Pathology, Rockville, MD, USA*

Abstract

Sweat testing is a noninvasive technique for monitoring drug exposure over a 7-day period in treatment, criminal justice, and employment settings. We evaluated Δ^9-tetrahydrocannabinol (THC) excretion in 11 daily cannabis users after cessation of drug use. PharmChek® sweat patches worn for 7 days were analyzed for THC by gas chromatography-mass spectrometry (GC/MS). The limit of quantification (LOQ) for the method was 0.4 ng THC/patch. Sweat patches worn the first week of continuously monitored abstinence had THC above the United States Substance Abuse Mental Health Services Administration's proposed cutoff concentration for federal workplace testing of 1 ng THC/patch. Mean ± S.E.M. THC concentrations were 3.85 ± 0.86 ng THC/patch. Eight of 11 subjects had negative patches the second week and one produced THC positive patches for four weeks of monitored abstinence. We also tested daily and weekly sweat patches from 7 subjects who were administered oral doses of up to 14.8 mg THC/day for five consecutive days. In this oral THC administration study, no daily or weekly patches had THC above the LOQ; concurrent plasma THC concentrations were all less than 6.1 μg/L. In conclusion, using proposed federal cutoff concentrations, most daily cannabis users will have a positive sweat patch in the first week after ceasing drug use and a negative patch after subsequent weeks, although patches may remain positive for four weeks or more. Oral ingestion of up to 14.8 mg THC daily does not produce a THC positive sweat patch test.

Keywords

THC; sweat; excretion; GC/MS; cannabinoid; marijuana

*Address correspondence to this author at: Intramural Research Program, National Institute on Drug Abuse, National Institutes of Health, 5500 Nathan Shock Drive, Baltimore, MD 21224. Fax 410-550-2468; email mhuestis@intra.nida.nih.gov.

The opinions and assertions in this article are those of the authors and are not to be construed as representing those of the National Institute on Drug Abuse, National Institutes of Health, Department of Defense, Department of the Navy, or the American Registry of Pathology.

1. Introduction

Sweat testing is used to monitor drug use in treatment, criminal justice and employment programs [1,2]. Sweat patches cleared for clinical purposes are used to collect sweat over periods of time, usually weekly [2,3]. Patches are tested for drugs of abuse giving a cumulative record of the individual's drug use during the period of observation. Sweat patches are a less invasive means of collection than required for blood testing and circumvent the privacy issues of urine collection. A disadvantage is the possibility of time-dependent drug loss from the patch by drug degradation on the patch or skin, reabsorption into the skin and volatile losses through the covering membrane of the patch [4]. There also have been reports of possible contamination of patches by cocaine, heroin or methamphetamine not removed from the skin during cleansing, prior to applying the patch [5]. Despite these limitations, patches are useful if proper wash procedures are used prior to application and patch removal is properly timed. Investigators have reported results of clinical studies for opiates [1,6,7], cocaine [2,3,8–11], amphetamine [12], methamphetamine [13], and MDMA [14,15]. There are few studies of Δ^9-tetrahydrocannabinol (THC) excretion in sweat, the psychoactive compound in cannabis, although it is the most prevalent illicit drug of abuse. Several investigators have detected THC in sweat collected on wipes from drugged drivers [16,17]. The metabolites, 11-hydroxy-THC and 11-nor-9-carboxy-THC (THCCOOH), were not detected at the methods' LOQ [17,18]. One problem for wipes and continuous wear patches is that the amount of THC in sweat is low requiring sensitive analytical methods. The Substance Abuse Mental Health Services Administration (SAMHSA) in the United States has proposed a cutoff concentration of 1 ng THC/patch for federally mandated workplace testing programs [19]. Saito et al. reported a validated gas chromatography-mass spectrometry (GC/MS) method with a LOQ of 0.4 ng THC/patch and found concentrations of 0.9 to 3.1 ng THC/patch in several 24-hour sweat patches from one cannabis user [20]. The expected disposition of THC in sweat from chronic cannabis users has not been reported. There also have been no publications describing expected sweat patch results during and following controlled oral administration of THC, e.g. dronabinol, Sativex®, or hemp oil, or cannabis smoking. Goodwin et al. found that plasma concentrations of THC after oral ingestion of THC were lower than those following equivalent smoked doses [21]. Lower circulating amounts of THC may reduce the amount of parent drug found in sweat. Here we report results of two clinical studies. One determined the disposition of THC in sweat from a group of daily cannabis users who were admitted to a closed, secure research unit and abstained from drug use for two to four weeks. The other determined THC in daily and weekly sweat patches collected from subjects before, during and after administration of multiple oral doses of THC over a period of ten weeks.

2. Materials and methods

2.1. Subjects and study design

All subjects resided in the secure clinical research unit of the Intramural Research Program (IRP), National Institute on Drug Abuse (NIDA), National Institutes of Health, Baltimore, Maryland, USA, while participating in Institutional Review Board approved clinical studies. Participants provided informed consent and were financially compensated for their time and effort. Before admission, they underwent thorough medical (physical exam, electrocardiography and blood and urine chemistries) and psychological evaluations, including self-reported past and recent drug use history. Subjects were admitted to the study only if they provided a urine specimen with greater than 135 μg cannabinoids/L by fluorescence polarization immunoassay (TDx, Abbott© Laboratories, Abbott Park, IL, USA). Twenty-four hour medical surveillance while residing in the secure research unit prevented access to unauthorized licit or illicit drugs.

Group 1 consisted of eleven healthy individuals (7 males, 4 females, 9 African Americans, 1 American Indian, 1 Hispanic) with histories of daily cannabis use. Subjects had body mass indices ranging from 18.6 to 32.9 kg/m^2 and ages 21 to 32 years. PharmChek® sweat patches (PharmChem Inc., Ft Worth, TX, USA) were applied upon admission and collected weekly throughout the study for two to four weeks. Patches were applied to the chest or abdomen following manufacturer guidelines, which included thoroughly cleaning the skin with ethanol to remove residual THC prior to application [3]. Specimens were stored at −20°C and shipped on dry ice to PharmChem Inc., Fort Worth, TX, USA, for THC testing using the procedure described in the GC/MS methods section. Blind low, medium and high concentration quality control samples, prepared by spiking known amounts of THC onto drug-free patches, were stored and shipped with the specimens to independently evaluate testing performance.

Group 2, consisting of one female and six males ages 32 to 41 years, body mass indices 17.8 to 33.2 kg/m^2, all African American, each with a history of routine cannabis use, received multiple doses of THC while residing on the closed secure research unit for 10 to 11 weeks. A more detailed description of the subjects was published previously [21,22]. The protocol was a randomized, double blind, double-dummy and placebo-controlled study design. Participants did not receive the first drug administration until their urine cannabinoid concentrations were below 10 μg cannabinoids/L by fluorescence polarization immunoassay (Abbott Laboratories, Abbott Park, IL, USA). Upon admission, PharmChek® sweat patches were applied to the chest or abdomen. Patches were collected daily and weekly during the washout period, during dosing and for one week following the last dose. Each dosing condition entailed supervised administration of 15 mL hemp oil and two capsules three times per day with meals for five consecutive days with no more than one of the dosage forms containing THC. Subjects freely selected food choices, without restriction, from clinical research unit menus. Exact times of dosing were recorded, but target times each day were 0800, 1300 and 1730 h. After five consecutive dosing days, there was a 10-day washout period prior to the next dosing condition. Subjects had five dosing conditions involving placebo, low-dose liquid hemp oil (9 μg/g or a daily dose of 0.39 mg THC), low-dose hemp oil in capsules (92 μg/g or a daily dose of 0.47 mg THC), high-dose hemp oil (347 μg/g or a daily dose of 14.8 mg THC) and dronabinol (2.5 mg/capsule or a daily dose of 7.5 mg THC). Sweat patches were stored at −20°C until THC analysis.

2.2. GC/MS analysis

Group 2 patches were tested using a previously published GC/MS method [20]. Briefly, THC and deuterated THC internal standard were added directly to sweat patches and allowed to air dry at room temperature. Patches were extracted with 3.0 ml methanol/sodium acetate buffer pH = 5, while mixed on a horizontal reciprocating shaker. Analytes were isolated from 2.0 mL of patch extract solution using solid phase extraction, derivatized with trifluoroacetic anhydride and identified and quantified by GC/MS in a negative ion chemical ionization mode of operation. Percent recovery from patches was 44–46%, LOQ was 0.4 ng THC/patch and coefficients of variation were < 10%. All weekly patches were tested. Some daily patches were not tested if no THC was found in the corresponding weekly patch.

Group 1 patches were analyzed at PharmChem Inc. with a procedure similar to that used for testing patches from Group 2 with the following exceptions: 1) 2.5 mL of buffer was used to extract THC from the patches instead of 3.0 mL, 2) 1.0 mL of extract was applied to the solid phase column instead of 2.0 mL and 3) the deuterated THC was added to the 1.0 mL extract prior to solid phase extraction instead of adding directly to the patch. LOQ and inter-assay coefficients of variation were the same as for the GC/MS assay used for analyzing patches from Group 2.

3. Results

Blind quality control patches were submitted along with specimens from the excretion study, Group 1, to determine if THC quantification was equivalent at both laboratories. Table 1 shows that accuracy and precision for this group were acceptable. Measured concentrations of THC/patch were within 20% of target across the range of the assay. Coefficients of variation were less than 12%.

Figure 1 depicts THC concentrations in weekly sweat patches from Group 1. Subjects were daily cannabis users who abstained from drug use during the study. All but one of eleven subjects had THC first-week patch concentrations above the LOQ with a mean ± S.E.M. of 3.85 ± 0.86 ng/patch. Concentrations decreased over time, with patches from two subjects worn the fourth week containing more than 0.4 ng THC (Table 2). Table 2 details the numbers of patches exceeding assay LOQ and SAMHSA proposed cutoff concentration of 1 ng THC/patch. Using the SAMHSA cutoff concentration, most subjects had negative sweat patches after the first week following cessation of drug use. One of five subjects was still positive using this cutoff concentration after four weeks.

Prior to receiving their first THC dose, frequent cannabis users (Group 2) produced their first negative urine specimen, i.e. less than 10 μg/L, within one to three weeks. During this washout phase, the first weekly sweat patch from two of seven subjects had THC above the assay LOQ. One weekly patch contained 0.93 ng THC/patch, with none of the seven daily sweat patches worn this week positive for THC. The other weekly sweat patch contained 0.82 ng THC/patch, with only the first daily patch positive for THC at 0.44 ng of THC/patch.

After oral THC administration, none of the weekly or daily patches contained measurable THC. Various oral doses were administered three times daily for five consecutive days during the study period and included doses up to 14.8 mg THC daily for the five-day regimens. For the same subjects, Goodwin et al. reported that all plasma THC concentrations were less than 6.1 μg/L [21]. Measured plasma THC concentrations during this oral administration study were much lower than THC concentrations observed during cannabis smoking [23].

4. Discussion

THC was first reported in sweat in 1990 [24]. Parent drug is the primary analyte found in sweat. Due to the fact that the concentration of THCCOOH in sweat is lower than the detection limit of most common confirmation methods, its presence in sweat has not been reported [18]. SAMHSA proposes a confirmation cutoff concentration of 1 ng THC/patch for federally mandated workplace drug testing programs, with the PharmChek® sweat patch used in our study the only patch currently cleared for clinical use by the Food and Drug Administration. The manufacturer recommends that the patches be worn for one week. In the present study, sweat patches worn by daily cannabis users the first week of monitored abstinence had THC concentrations averaging 3.85 ng/patch. There are no other published studies reporting sweat patch THC concentrations after cessation of use for comparison. Investigators have collected sweat wipes from drugged drivers and measured THC in those that screened positive for cannabinoids [16,17]. Kintz reported forehead sweat concentrations of 4 to 152 ng THC/pad. No 11-hydroxy-THC or THCCOOH were detected using a GC/MS operated in the electron impact mode. LOQ were not reported [17].

Eight of eleven daily cannabis users had negative second-week patches using the SAMHSA cutoff concentration of 1 ng THC/patch. One subject was still positive four weeks after ceasing drug use. Clinicians operating treatment programs can expect most chronic cannabis users to have a one-week washout phase but will have some patients who require more than four weeks. The elimination period for THC in sweat appears to be similar to that of THCCOOH in urine

for some chronic cannabis users. Urine and sweat testing are employed for monitoring drug users in workplace, treatment and judicial programs. The advantage of sweat testing is that it is not subject to the periodic fluctuations in concentration found in sequential urine specimens that make identifying new drug use more difficult [25]. Also, a single sweat patch analysis provides a summary of drug use or drug washout for the previous week, instead of multiple urine collections and analyses required to cover the same period with urine testing.

This controlled administration study demonstrated that THC does not readily enter sweat following oral ingestion. None of the weekly or daily patches from the seven subjects had THC above the LOQ of 0.4 ng/patch following oral administration of up to 14.8 mg/day THC. Subjects ingested THC for five consecutive days with patches collected daily and at the end of each week. During one five-day regimen, subjects ingested 7.5 mg of dronabinol daily and during another, 14.8 mg THC. For comparison, doses of dronabinol administered to most patients are in the range of 2.5 to 30 mg daily with doses as high as 175 mg daily for some patients with severe cancer pain. An explanation for the negative sweat patches may be that there is less THC in blood available to distribute into sweat following oral ingestion compared to smoking, due to degradation in the stomach and first pass metabolism via the oral route. For subjects in the present study, Goodwin et al. reported plasma THC concentrations less than 6.1 μg/L [21]. Subjects smoking a cigarette containing 15.8 mg THC had mean maximum plasma THC concentrations of 84.3 μg/L [23]. One implication of our results is that claims of innocent oral ingestion of THC causing a positive sweat patch are unlikely to be true. Our study did not evaluate results following oral administration of cannabis or new formulations such as Sativex®, a 50:50 mixture of THC and cannabidiol (CBD) that is administered by the oromucosal route, but it is unlikely that post-administration sweat patches would be positive for THC due to the low plasma THC concentrations achieved. In a phase I study of sublingual delivery of a THC-CBD plant extract, there was no statistical difference in mean plasma Cmax, half-life, and area under the curve for THC and 11-OH-THC following 25 mg THC and 25 mg CBD compared to 25 mg THC alone [26]. A subsequent study with 10 mg THC and 10 mg CBD by sublingual, buccal and oro-pharyngeal and oral administration found similar plasma profiles [27]. These studies indicate that plasma THC concentrations are not altered significantly by the addition of CBD, and one might expect that migration of THC into sweat would not be altered. The studies did find that plasma THCCOOH concentrations were higher when CBD was co-ingested with THC, but this polar metabolite does not appear to enter sweat in amounts that are detectable with current techniques. CBD in sweat has not been studied, but one might expect lower concentrations than for THC since bioavailability and plasma concentrations following equivalent THC and CBD doses always had lower CBD concentrations than those for THC [26]. In addition, CBD is similar in size, but is more polar than THC; therefore, its incorporation into sweat should be lower.

5. Conclusions

Results of our clinical study indicate that daily cannabis users will excrete THC into sweat in concentrations above the SAMHSA cutoff of 1 ng/patch. During abstinence, negative patches are expected after one week, but some may have a longer washout period of four weeks or more. The sensitivity of sweat patches to detect new drug use following cannabis smoking is not known and requires an independent controlled smoked cannabis administration study. Our results indicate that patients who take THC orally up to 14.8 mg daily, either intentionally or unknowingly, will not produce a positive sweat patch using a cutoff concentration of 0.4 ng THC/patch.

Acknowledgements

This research was supported in part by the Intramural Research Program of the NIH, NIDA and the American Registry of Pathology. We thank PharmChem Inc., Fort Worth, TX, USA, for providing sweat patches used in this study.

References

1. Huestis MA, Cone EJ, Wong CJ, Umbricht A, Preston KL. Monitoring opiate use in substance abuse treatment patients with sweat and urine drug testing. J Anal Toxicol 2000;24:509–521. [PubMed: 11043653]
2. Liberty HJ, Johnson BD, Fortner N. Detecting cocaine use through sweat testing: multilevel modeling of sweat patch length-of-wear data. J Anal Toxicol 2004;28:667–673. [PubMed: 15538962]
3. Liberty HJ, Johnson BD, Fortner N, Randolph D. Detecting crack and other cocaine use with fastpatches. Addict Biol 2003;8:191–200. [PubMed: 12850778]
4. Uemura N, Nath RP, Harkey MR, Henderson GL, Mendelson J, Jones RT. Cocaine levels in sweat collection patches vary by location of patch placement and decline over time. J Anal Toxicol 2004;28:253–259. [PubMed: 15189676]
5. Kidwell DA, Smith FP. Susceptibility of PharmChek drugs of abuse patch to environmental contamination. Forensic Sci Int 2001;116:89–106. [PubMed: 11182260]
6. Fogerson R, Schoendorfer D, Fay J, Spiehler V. Qualitative detection of opiates in sweat by EIA and GC-MS. J Anal Toxicol 1997;21:451–458. [PubMed: 9323525]
7. Schwilke EW, Barnes AJ, Kacinko SL, Cone EJ, Moolchan ET, Huestis MA. Opioid disposition in human sweat after controlled oral codeine administration. Clin Chem 2006;52:1539–1545. [PubMed: 16740647]
8. Huestis MA, Oyler JM, Cone EJ, Wstadik AT, Schoendorfer D, Joseph RE Jr. Sweat testing for cocaine, codeine and metabolites by gas chromatography-mass spectrometry. J Chromatogr B Biomed Sci Appl 1999;733:247–264. [PubMed: 10572984]
9. Winhusen TM, Somoza EC, Singal B, Kim S, Horn PS, Rotrosen J. Measuring outcome in cocaine clinical trials: a comparison of sweat patches with urine toxicology and participant self-report. Addiction 2003;98:317–324. [PubMed: 12603231]
10. Kidwell DA, Kidwell JD, Shinohara F, Harper C, Roarty K, Bernadt K, McCaulley RA, Smith FP. Comparison of daily urine, sweat, and skin swabs among cocaine users. Forensic Sci Int 2003;133:63–78. [PubMed: 12742691]
11. Kacinko SL, Barnes AJ, Schwilke EW, Cone EJ, Moolchan ET, Huestis MA. Disposition of cocaine and its metabolites in human sweat after controlled cocaine administration. Clin Chem 2005;51:2085–2094. [PubMed: 16166169]
12. de la Torre R, Farre M, Navarro M, Pacifici R, Zuccaro P, Pichini S. Clinical pharmacokinetics of amfetamine and related substances: monitoring in conventional and non-conventional matrices. Clin Pharmacokinet 2004;43:157–185. [PubMed: 14871155]
13. Fay J, Fogerson R, Schoendorfer D, Niedbala RS, Spiehler V. Detection of methamphetamine in sweat by EIA and GC-MS. J Anal Toxicol 1996;20:398–403. [PubMed: 8889675]
14. Pichini S, Navarro M, Pacifici R, Zuccaro P, Ortuno J, Farre M, Roset PN, Segura J, de la Torre R. Usefulness of sweat testing for the detection of MDMA after a single-dose administration. J Anal Toxicol 2003;27:294–303. [PubMed: 12908943]
15. Samyn N, De Boeck G, Wood M, Lamers CT, De Waard D, Brookhuis KA, Verstraete AG, Riedel WJ. Plasma, oral fluid and sweat wipe ecstasy concentrations in controlled and real life conditions. Forensic Sci Int 2002;128:90–97. [PubMed: 12208028]
16. Samyn N, De Boeck G, Verstraete AG. The use of oral fluid and sweat wipes for the detection of drugs of abuse in drivers. J Forensic Sci 2002;47:1380–1387. [PubMed: 12455668]
17. Kintz P, Cirimele V, Ludes B. Detection of cannabis in oral fluid (saliva) and forehead wipes (sweat) from impaired drivers. J Anal Toxicol 2000;24:557–561. [PubMed: 11043659]
18. Staub C. Chromatographic procedures for determination of cannabinoids in biological samples, with special attention to blood and alternative matrices like hair, saliva, sweat and meconium. J Chromatogr B Biomed Sci Appl 1999;733:119–126. [PubMed: 10572977]
19. D.o.H.a.H. Services, Proposed revisions to mandatory guidelines for federal workplace drug testing programs, 2004.
20. Saito T, Wtsadik A, Scheidweiler KB, Fortner N, Takeichi S, Huestis MA. Validated gas chromatographic-negative ion chemical ionization mass spectrometric method for delta(9)-tetrahydrocannabinol in sweat patches. Clin Chem 2004;50:2083–2090. [PubMed: 15271860]

21. Goodwin RS, Gustafson RA, Barnes A, Nebro W, Moolchan ET, Huestis MA. Delta(9)-tetrahydrocannabinol, 11-hydroxy-delta(9)-tetrahydrocannabinol and 11-nor-9-carboxy-delta(9)-tetrahydrocannabinol in human plasma after controlled oral administration of cannabinoids. Ther Drug Monit 2006;28:545–551. [PubMed: 16885723]
22. Gustafson RA, Levine B, Stout PR, Klette KL, George MP, Moolchan ET, Huestis MA. Urinary cannabinoid detection times after controlled oral administration of delta9-tetrahydrocannabinol to humans. Clin Chem 2003;49:1114–1124. [PubMed: 12816908]
23. Huestis MA, Henningfield JE, Cone EJ. Blood cannabinoids. I. Absorption of THC and formation of 11-OH-THC and THCCOOH during and after smoking marijuana. J Anal Toxicol 1992;16:276–282. [PubMed: 1338215]
24. Balabanova S, Schneider E. [Detection of drugs in sweat]. Beitr Gerichtl Med 1990;48:45–49. [PubMed: 2241828]
25. Huestis MA, Cone EJ. Differentiating new marijuana use from residual drug excretion in occasional marijuana users. J Anal Toxicol 1998;22:445–454. [PubMed: 9788519]
26. Guy GW, Robson PJ. A phase I, double-blind, three-way crossover study to assess the pharmacokinetic profile of cannabis based medicine extract (CBME) administered sublingually in variant cannabinoid ratios in normal healthy male volunteers (GWPK0215). Journal of Cannabis Therapeutics 2004;3:121–152.
27. Guy GW, Robson PJ. A phase I, open label, four-way crossover study to compare the pharmacokinetic profiles of a single dose of 20 mg of a cannabis based medicine extract (CBME) administered in 3 different areas of the buccal mucosa and to investigate the pharmacokinetics of CBME per oral in healthy male and female volunteers (GWPK0112). Journal of Cannabis Therapeutics 2004;3:79–120.

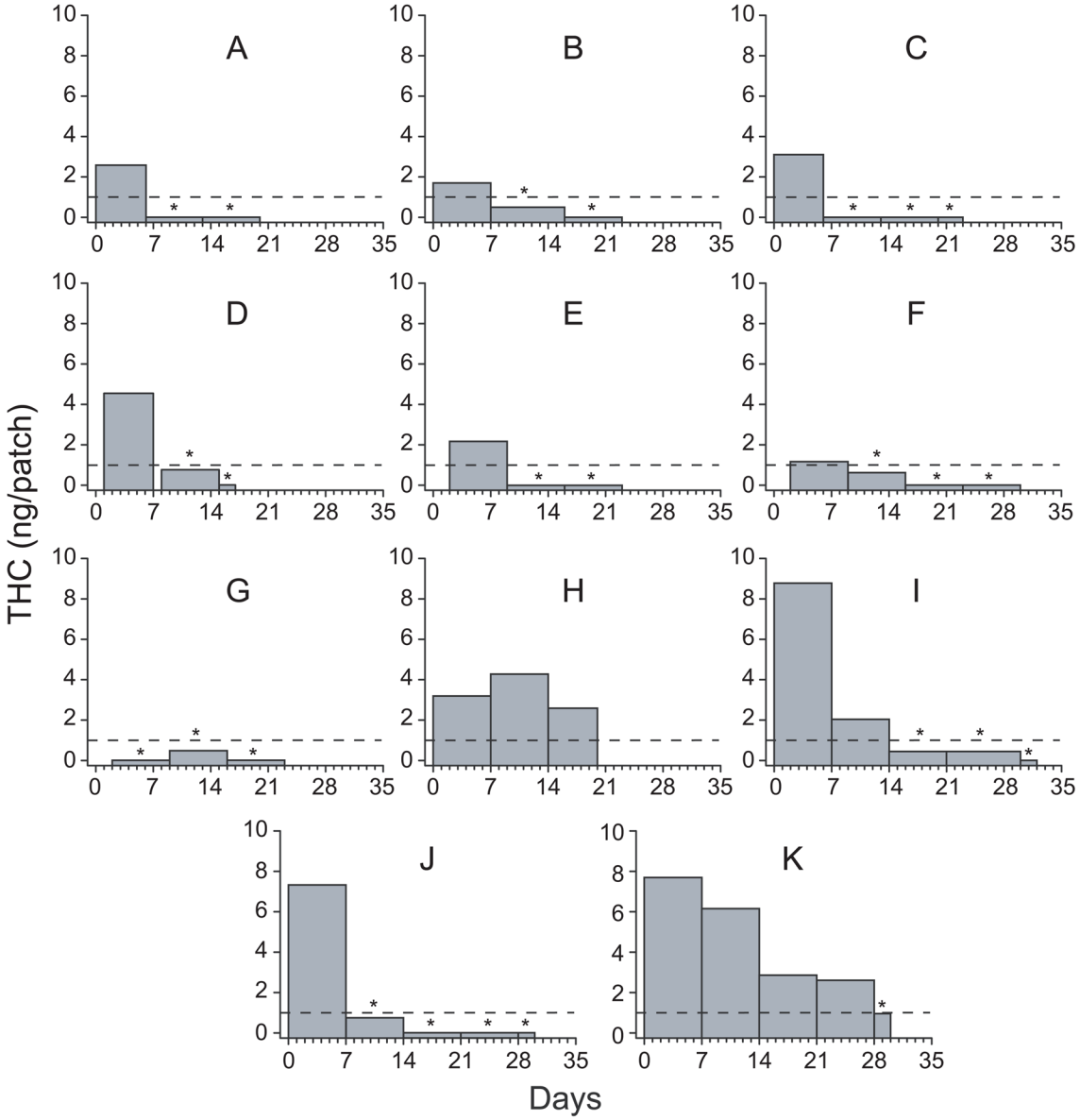

Figure 1.

Δ9-tetrahydrocannabinol (THC) excreted in sweat. Dashed line indicates 1.0 ng/patch cutoff concentration proposed by the Substance Abuse Mental Health Services Administration. * indicates amount of THC less than the assay limit of quantification (0.4 ng/patch)

Table 1

Accuracy and precision of analysis of Δ9-tetrahydrocannabinol-containing blind quality control (QC) sweat patches[a]

	Concentration (ng/patch)		
	Expected	Mean measured	CV%[b]
Low QC	0.6	0.59	10.0
Medium QC	4.0	4.63	11.7
High QC	8.0	8.36	7.88

[a] Δ9-Tetrahydrocannabinol quality control solution was fortified onto blank sweat patches prior to shipment on dry ice to PharmChem Inc. Patches were stored at −20°C upon arrival until analysis (n = 3 at each concentration).

[b] Coefficient of variation expressed as percentage

Table 2

Δ9-Tetrahydrocannabinol (THC) excreted in sweat from daily cannabis users during monitored cannabis abstinence.

Week	Mean THC (ng/patch ± s.e.m.)	n	SAMHSA[a] cutoff		Assay LOQ[b]	
			> 1 ng/patch	% Positive	> 0.4 ng/patch	% Positive
1	3.85 ± 0.86	11	10/11	90.9	10/11	90.9
2	1.47 ± 0.59	11	3/11	27.3	8/11	72.7
3	0.73 ± 0.33	10	2/10	20.0	3/10	30.0
4	0.73 ± 0.47	5	1/5	20.0	2/5	40.0

[a] Substance Abuse Mental Health Services Administration

[b] Limits of quantification