TECHNICAL NOTE

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An Indoor Air Quality-Pharmacokinetic Simulation of Passive Inhalation of Marijuana Smoke and the Resultant Buildup of 11-Nor-Delta-9-Tetrahydrocannabinol-9-Carboxylic Acid in Urine

REFERENCE: Giardino NJ. An indoor air quality—pharmacokinetic simulation of passive inhalation of marijuana smoke and the resultant buildup of 11-nor-delta-9-tetrahydrocannabinol-9-carboxylic acid in urine. J Forensic Sci 1997;42(2): 323–325.

ABSTRACT: In military courts of law, the good soldier defense is often used by the defendant to explain the presence of 11-nor-delta-9-tetrahydrocannabinol-9-carboxylic acid in urine (hereafter referred to as THCA) above the Department of Defense (DOD) established limit of 15 ng/mL. The defense will contend the defendant unwittingly breathed side-stream marijuana smoke, thus resulting in the presence of THCA in the defendant's urine.The purpose of this work was to link an indoor air quality model (IAQ) with a pharmacokinetic (PK) model to predict a passive marijuana smoker's resultant concentration of the major urinary metabolite THCA.

KEYWORDS: forensic science, forensic toxicology, modeling, passive inhalation, 11-nor-delta-9-tetrahydrocannabinol-9-carboxylic acid, urinalysis

There have been many human studies on the psychological and physiological effects for both active and passive marijuana smokers. Most studies follow the buildup in plasma and urine of THCA for all participants. These studies have been designed to reflect a gathering of people in mid- to small-size rooms, as well as persons traveling in automobiles (1). Still there is a dearth of pharmacokinetic data on marijuana absorption through breathing and resultant metabolism and excretion (2,3). Also, only crude measurements of IAQ parameters exist for these experiments.

No one set of human experiments on marijuana smoking can be used to address every scenario for exposure due to breathing side-stream smoke. This is why a computer simulation that links both an IAQ model with a PK model for passive inhalation exposure to marijuana smoke would be useful. Such a model allow the flexibility of exploring effects of changing parameters like air-exchange rates, room volumes, and activity patterns on air concentration, inhalation dose, and THCA concentration in urine.

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Received 10 May 1996; and in revised form 22 July 1996; accepted 7 Aug. 1996.

Methods and Results

The purpose of this microcomputer simulation is to determine whether or not a passive marijuana smoker, who is in the source room or the rest of the house, can receive enough of a total dose to have an amount equal to or greater than the DOD legal limit of 15 ng/mL of THCA in their urine. This microcomputer simulation of passive marijuana smoking for a typical residence uses assumed activity patterns and takes pharmacokinetic parameters from the literature.

A three-compartment design is used for the residence consisting of: The source room (30 m^3), the rest of the house (250 m^3), and the outdoors. The air-exchange rate between the source room and the rest of the house is 1.0 air-changes per hour (ACH), and between the rest of house and outdoors 0.5 ACH. These values are typical of a small residence (4). The source term is 0.24 mg/h of THC released to the air by the person smoking the marijuana. This is equivalent to a total of six 2.5% NIDA certified marijuana cigarettes smoked over the course of 1 h.

The PK model is built using real-world measurements taken from the literature for a standard 70-kg male. The PK model treats the body as a single compartment in which absorption takes place through inhalation of side-stream marijuana smoke. Assumptions for the PK model are listed below. Two percent absorption of THC from by passive inhalation (1). A respiration rate of 1.0 m^3/h is typical for resting adults (4). An average urination rate of 76 mL/h is assumed (5). Data was used from an experiment in which a 4-mg intravenous dosing of delta-9-THC was given followed by periodic collection of urine samples for 72 h. Urinalysis was done on the collected samples for determination of THCA. This data provided an integrated average cumulative dose (mg) by time (hours). This value is defined as the area under the curve (AUC). The AUC value has implicitly contained within it all the metabolic steps from inhaled THC to THCA excreted in urine (7).

Equations describing the residence and PK model are linked, first-order differential equations. These equations are solved simultaneously (using a 4th-order, Runge-Kutta numerical scheme) over specified time periods for air concentrations in the source room and the rest of the house, for dose, and for concentration of THCA in urine. These differential equations are:

$$Cg_1' = S/V_1 + (q_{21}/V_2)*Cg_2 - (q_{12}/V_1)*Cg_1 - (q_{13}/V_1)*Cg_1 \quad (1)$$

$$Cg_2' = (q_{12}/V_1)*Cg_1 - (q_{21}/V_2)*Cg_2 - (q_{23}/V_2)*Cg_2 \quad (2)$$

$$D_1' = Cg_1'*IR*F_a \quad (3)$$

$$Cu_1' = AUC*(D_1/F_u)*1 \times 10^{-6} \quad (4)$$

$$D_2' = Cg_2'*IR*F_a \quad (5)$$

$$Cu_2' = AUC*(D_2/F_u)*1 \times 10^{-6} \quad (6)$$

The output from this modeling exercise is summarized graphically, allowing easy visual tracking with time of changing air concentrations in the residence, inhalation dose, and concentration in urine of THCA (see Fig(s). 1, 2, and 3)

Figure 1 shows an initial linear buildup and then an exponential decay, after cessation of smoking at the one hour point, of air concentration of THC in the two main compartments of the residence. Figure 2 shows an initial buildup in bodily dose for both passive smokers up to 1 h and then a continued rise in dose due to the presence of drug in the air and total exposure time spent in the residence. Figure 3 shows the changing urinary concentrations of THCA with time for each of the passive smokers.

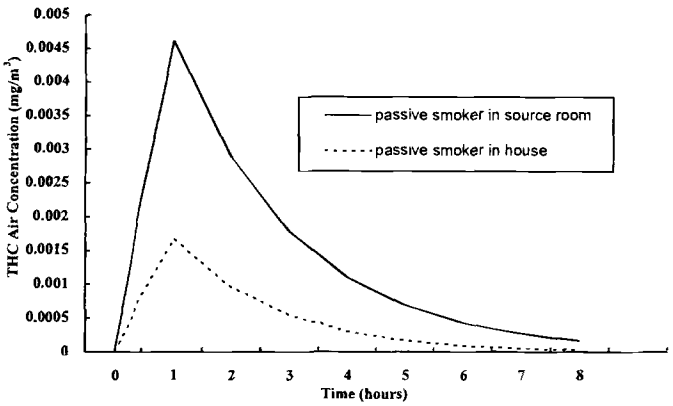

FIG. 1—*THC concentration in air with time.*

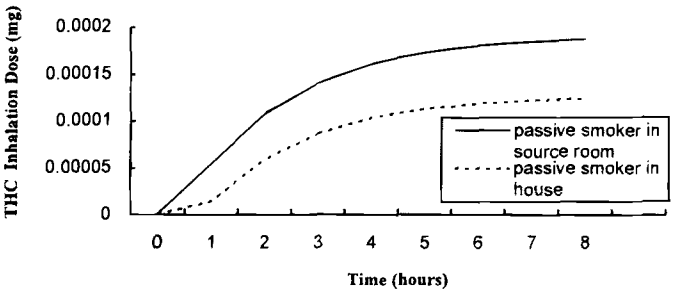

FIG. 2—*Dose of total drug via inhalation with time.*

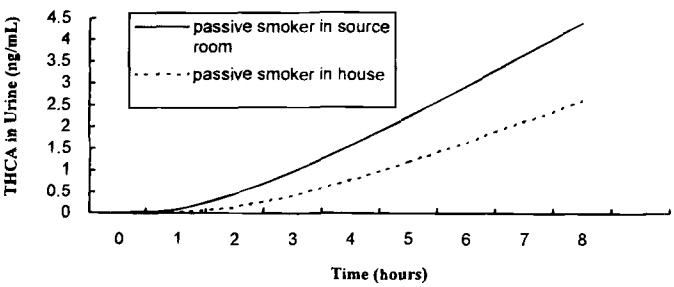

FIG. 3—*THCA concentration in urine with time.*

For initial results, simple activity patterns are established. It is assumed that both passive smokers stay in the house for 8 h. For the first hour, the source term is on, and then it is off for the remaining 7 h of exposure. The simulated smoking can be assumed to be a constant source of marijuana smoke. Initial results indicate that at the end of the 8-h exposure period, the passive smoker in the source room attains a level of 4.4 ng/mL THCA in urine, and the passive smoker in the rest of house 2.6 ng/mL. The majority of inhalation exposure in this simulation occurred during the 7-h period when the source term was off. This is a function of THC air concentration and activity patterns. These values are comparable to experimental results reported by others (6).

Conclusions

Computer simulations on how passive inhalation of marijuana smoke affects a person's urine concentration of THCA, would be exciting and timely information. Such simulations could have a significant impact upon the prosecution and defense of cases based upon positive urinalysis results for THCA. The results of this type of modeling are conservative in that the predicted urinary concentrations of THCA are reported the DOD cutoff, even under exposure scenarios expected to yield high predictions for THCA in urine. So the computer model is biased in favor of the Air Force (AF) member.

This type of modeling will directly address an issue that is often raised by the defense in cases in which an AF member has tested positive for THCA. There are some scientific articles that both trial and defense counsel use now when the issue is raised. However, there are few such studies, and those that do exist give very specific and inflexible circumstances under which the use occurred. Invariably, the accused never has a situation similar to the one in the articles. This makes it difficult to address the defense fully. Very often, the accused will claim he was in a room with another person who was smoking, but of course he did not partake. He then combines the passive inhalation defense with witnesses attesting to his good military character. Then the defense counsel argues the accused was positive due only to passive inhalation, as he is the type of person who would never use illegal drugs.

The more scientific evidence that can be used to address this defense, the better for courtroom practice and justice. Currently, the United States Air Force (USAF) has DOD cut-off levels established to remove any real possibility of a positive due to passive

TABLE 1—*Model parameters defined.*

Parameter	Value
Cg	mg/m^3
S	mg/h
V	m^3
q	m^3/h
D	mg
C_u	ng/mL
IR	m^3/h
F_a	fraction
F_u	m^3/h

NOTE—Numbers 1, 2, and 3 used in the equations designate the source room, adjacent room, and the outdoors. Paired numbers in conjunction with the symbol for air-rate, q, designate the originating compartment of the flow and the compartment into which the air flows. The conversion factor 1 by 10^{-6} is used to normalize all concentrations to ng/mL.

inhalation. Nonetheless, the defense is successfully used. If this, or any other study, would show that the DOD cut-off levels are either too high or too low as they relate to the passive inhalation issue, that study could influence a change to the cut-off levels.

The purpose of the USAF Urinalysis Drug Testing Program is to detect and deter drug abuse. The battle against the use of illicit drugs is about saving money, equipment, and lives. The USAF cannot have an effective fighting force with drug abuse occurring. The more that is understood about the use and conditions under which use occurs, the more effectively the program will operate. Computer simulations such as this have the potential to provide much better tools in the battle against drugs than what currently exists in the area of passive inhalation of marijuana smoke.

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