Evaluating the Impact of Hemp Food Consumption on Workplace Drug Tests

Gero Leson* and **Petra Pless**
Leson Environmental Consulting, P.O. Box 10075, Berkeley, California 94709

Franjo Grotenhermen
Nova Institute, Goldenbergstraße 2, 50354 Hürth, Germany

Harold Kalant
ARF Division of Centre for Addiction and Mental Health and Department of Pharmacology, University of Toronto, Toronto, Ontario, M5S 1A8, Canada

Mahmoud A. ElSohly
ElSohly Laboratories, Inc., 5 Industrial Park Drive, Oxford, Mississippi 38655

Abstract

Foods containing seeds or oil of the hemp plant (*Cannabis sativa* L.) are increasingly found in retail stores in the U.S. The presence of Δ^9-tetrahydrocannabinol (THC) in these foods has raised concern over their impact on the results of workplace drug tests for marijuana. Previous studies have shown that eating hemp foods can cause screening and confirmed positive results in urine specimens. This study evaluated the impact of extended daily ingestion of THC via hemp oil on urine levels of its metabolite 11-nor-9-carboxy-Δ^9-tetrahydrocannabinol (THC-COOH) for four distinct daily THC doses. Doses were representative of THC levels now commonly found in hemp seed products and a range of conceivable daily consumption rates. Fifteen THC-naïve adults ingested, over four successive 10-day periods, single daily THC doses ranging from 0.09 to 0.6 mg. Subjects self-administered THC in 15-mL aliquots (20 mL for the 0.6-mg dose) of four different blends of hemp and canola oils. Urine specimens were collected prior to the first ingestion of oil, on days 9 and 10 of each of the four study periods, and 1 and 3 days after the last ingestion. All specimens were screened for cannabinoids by radioimmunoassay (Immunalysis Direct RIA Kit), confirmed for THC-COOH by gas chromatography–mass spectrometry (GC–MS), and analyzed for creatinine to identify dilute specimens. None of the subjects who ingested daily doses of 0.45 mg of THC screened positive at the 50-ng/mL cutoff. At a daily THC dose of 0.6 mg, one specimen screened positive. The highest THC-COOH level found by GC–MS in any of the specimens was 5.2 ng/mL, well below the 15-ng/mL confirmation cutoff used in federal drug testing programs. A THC intake of 0.6 mg/day is equivalent to the consumption of approximately 125 mL of hemp oil containing 5 µg/g of THC or 300 g of hulled seeds at 2 µg/g. These THC concentrations are now typical in Canadian hemp seed products. Based on our findings, these concentrations appear to be sufficiently low to prevent confirmed positives from the extended and extensive consumption of hemp foods.

* Author to whom correspondence should be addressed.

Introduction

Since the mid-1990s, the use of food products containing the seeds or oil of the hemp plant in the U.S. has increased considerably. These "hemp foods", which are often found in "natural foods" stores, include cold-pressed oil for cooking, salad dressings, and capsules as nutritional supplements. The seeds are usually hulled prior to their use in snack bars, tortilla chips, nut butters, and other spreads. Hulled seeds are also sold in bulk for cooking and baking. Whole, that is, unhulled, hemp seeds are a traditional ingredient in birdfeed blends, but human consumption is limited to only a few snack items.

Several factors contribute to the growing demand for hemp foods. Much of the initial interest may have been stimulated by the "mystique" of hemp, caused by its relationship to marijuana. Limited nutritional research on the fatty acid and protein composition of hemp seeds also indicates that hemp seeds may offer some nutritional benefits compared to other sources of vegetable fat and protein. These benefits include a desirable ratio of the two essential fatty acids, α-linolenic acid and linoleic acid, the presence of minor fatty acids such as gamma-linolenic acid (GLA), and a seed kernel, or meat, with a reasonably complete amino acid

Reproduction (photocopying) of editorial content of this journal is prohibited without publisher's permission.

spectrum. Chemical composition and quality, particularly the taste of the seed products, varies considerably with both hemp variety and processing of the seeds. If not handled properly, the triple-unsaturated fatty acids are easily oxidized, resulting in rancidity (1–4).

Hemp and marijuana, varieties of the same species, *Cannabis sativa* L., mainly differ in their cannabinoid content. Cannabinoids, some of which are psychoactive in humans, are primarily found in resins secreted by gland cells on leaves and bracts of the mature plant. The psychoactive potential of cannabis products is measured by the content of Δ^9-tetrahydrocannabinol (THC), the most pharmacologically active cannabinoid in marijuana[1]. Drug varieties contain typically 2–5% THC (per dry weight) in their female flowers, but THC levels of 15–20% have been reported (5–7). In comparison, "industrial" hemp varieties grown for fiber and seeds and licensed for farming in the European Union (EU) and Canada must legally be bred to maintain a THC content of less than 0.3% (8,9).

Federal law in the U.S. currently prohibits commercial farming of any variety of *Cannabis sativa* but allows for the importation and use of non-viable hemp seeds. Initially, hemp foods in the U.S. were produced from sterilized imported Chinese birdseeds. Since 1998, seeds and oil have been primarily imported from Canada and Western Europe.

THC in hemp seed products

Seeds and oil, even from low-THC varieties, generally contain measurable amounts of THC (10,11). For example, a 1997 survey of hemp oils in the U.S. found THC levels between 11 and 117 µg/g (parts per million or ppm) (12). These oils had been produced from imported Chinese seeds. A similar survey conducted in Germany found THC levels in hemp oil between 4 and 214 µg/mL (13). THC concentrations as high as 3568 µg/g were found in various Swiss hemp oils (10). The authors attributed these high levels to the origin of the seeds from high-THC varieties, which were legal to grow in Switzerland, and the lack of specific cleaning procedures. THC levels in hemp oil as high as 1500 µg/g were also reported by another Swiss group (14).

Presence of THC in hemp seed products is predominantly caused by external contact of the seed hull with cannabinoid-containing resins in bracts and leaves during maturation, harvesting, and processing. This is supported by several recent studies that showed that the majority of THC is located on the outside of the seed hulls (15–17). The seed kernel is not entirely THC-free but contains, depending on the hemp variety, less than 0.5 µg/g of THC. These studies also showed that the use of low-THC cultivars and thorough seed cleaning is effective in reducing THC levels in the main products currently made from the seed kernel for human consumption, that is, oil and hulled seeds.

Since 1998, more thorough seed drying and cleaning appears to have considerably reduced THC levels in seeds and oil available in the U.S. Results from the mandatory THC analysis of seeds and oil produced in Canada and a study evaluating the effectiveness of various dry and wet cleaning methods show typical THC levels of 5 and 2 µg/g, respectively, in oil and hulled seeds from Canada (18,19). However, oils containing 10–20 µg/g and hulled seeds containing 2–3 µg/g of THC are still found in commercial products in the U.S. (20).

The presence of THC residues in hemp foods and their increasing availability to consumers has raised concerns among health and drug officials in several Western countries. These concerns relate to both the known pharmacodynamic effects of THC when ingested and its established potential to cause positive test results under workplace drug-testing programs instituted by many public and private institutions. A positive drug test may cause loss or rejection of employment. Employees may also allege that a positive test actually caused by marijuana use was due to their consumption of hemp foods. Thus, it must be ascertained under what conditions hemp food ingestion produces positive urine tests for marijuana.

Impact on workplace drug tests

Several scientific studies have shown that ingestion of single or multiple doses of commercial hemp food products can cause confirmed positive test results (2,12,14,21–26). Urine specimens often exceeded the 50-ng/mL screening cutoff and the 15-ng/mL cutoff for gas chromatographic–mass spectrometric (GC–MS) confirmation. In one study, confirmation by GC–MS detected 11-nor-9-carboxy-Δ^9-tetrahydrocannabinol (THC-COOH), the major THC metabolite in urine, in several urine specimens at levels above 100 ng/mL (14).

Most drug-testing programs in the U.S. employ immunoassays with a 50-ng/mL (parts per billion or ppb) cutoff to screen for marijuana use. Positive specimens are routinely confirmed by GC–MS. Employers usually apply a 15-ng/mL cutoff, at or above which a test is considered confirmed positive. Some employers, law enforcement agencies, and drug-treatment programs apply a 20-ng/mL screening cutoff and a GC–MS confirmation cutoff of 10 ng/mL. Few employers rely exclusively on the use of a screening test (27,28).

Most of these studies were conducted in 1996–1997 when THC levels in hemp oil routinely exceeded 50 µg/g. Those studies that quantitated the THC dose usually administered single or multiple doses in excess of 1 mg. It is reasonable to assume that the reductions in THC levels since 1998 have also lowered THC intake from hemp food consumption and correspondingly reduced THC-COOH levels in the urine of consumers and the risk of a positive workplace drug test. The objectives of the present study were to establish a correlation between extended daily ingestion of known amounts of THC via commercially available hemp foods and THC-COOH levels in urine. The results were expected to identify a maximum daily THC ingestion rate, which did not produce confirmed positive tests for marijuana.

Materials and Methods

Study design

The study involved 15 adult volunteers (ages 29–84; 10 female; 5 male; average weight, 72.9 kg; average height, 169.4 cm), none of whom had, as confirmed by a baseline specimen, recent exposure to THC in hemp foods or medicinal or recreational drugs.

[1] In this paper, the term "THC" refers to total THC as determined by GC–MS. It includes both free (phenolic) Δ^9-tetrahydrocannabinol and THC acids A and B.

Subjects were not compensated for their participation. They were instructed in person on the study protocol and provided written informed consent. All volunteers ingested, under self-controlled conditions, four different THC doses, each for a 10-day period. Daily doses ranged from 0.09 to 0.6 mg and were increased stepwise after each period. These doses were selected to cover the conceivable range of THC intake from consumption of currently available hemp products. The study regimen for THC ingestion and urine collection is shown in Figure 1. Additional information on oil ingestion rates, THC concentrations and doses, and equivalent amounts of hemp oil and hulled seeds is provided in Table I.

Literature estimates of the plasma elimination half-life of THC in humans vary widely. A summary by Baselt and Cravey (29) gives a range of 20–57 h for infrequent users of marijuana. For long-term and heavy users, longer mean plasma half-lives of 4.1 and 4.3 days, respectively, have been reported in two studies. Maximum half-lives measured in individuals in these two studies were 5 and 12.6 days, respectively (30,31). Because the lower doses inhaled by infrequent users are more closely similar to the doses obtained by consumption of hemp foods, the authors assumed 48 h as a reasonable choice for the metabolic half-life of THC. Steady-state drug levels in plasma and tissues are typically reached within five half-lives. Thus, ingestion of each of the four THC-doses for 10 days was assumed sufficiently long for the achievement of steady-state conditions in most persons. This choice was supported by one study, which showed that peak THC-COOH concentrations from repeated ingestion of a specific daily THC dose reached their maximum after 4–6 days (12). Some individuals, however, may require longer periods to achieve metabolic steady state and peak urine levels of THC-COOH from extended hemp food consumption might possibly increase beyond the 10-day period.

Daily dosage was controlled by blending the base hemp oil, containing approximately 32 µg/g of total THC, with food-grade canola (rape seed) oil to produce four batches of different THC concentrations, ranging from 6.2 to 31.7 µg/g, and by prescribing a daily oil intake rate. The respective THC concentrations and daily doses are shown in Table I. A prolonged daily oral intake of 15 mL of oil blend in a single dose was determined to be the maximum palatable to most volunteers. During study period 4, 3 of the 15 subjects ingested 0.6 mg of THC per day instead of 0.45 mg/day by increasing daily oil intake to 20 mL. The oil mixtures used in this study contained higher THC concentrations than most hemp oils and other foods now commercially available (18,19). Because of the laxative effect of vegetable oils, it was assumed that this high concentration/low volume administration of a given THC dose would result in more efficient THC absorption from the intestine and cause higher THC-COOH levels in urine compared with ingestion of larger quantities of more dilute oil offering the same daily THC dose.

Subjects were asked to collect urine 4–8 h after oil ingestion. Previous studies had shown that peak concentrations of THC-COOH in urine from the ingestion of THC typically occur during that period (12,32). Individual differences in food uptake conditions, metabolism, and excretion may result in THC-COOH peaks outside of this time window. Subjects were instructed not to collect the first void. It generally represents the most concentrated urine specimen and thus the most conservative correlation between THC dose and THC-COOH level. However, because collection of the first void is impractical in programs that obtain specimens in a workplace setting, first void analysis was deemed not to yield urinary THC-COOH levels representative of test conditions under such programs.

Radioimmunoassay (RIA) was selected as the screening method because it appears to be generally more effective in identifying true positives and to achieve better precision and sensitivity than more commonly used immunoassay methods (33). To minimize the impact of the choice of immunoassay, THC-COOH levels in all specimens were confirmed by GC–MS.

The final design of this study incorporated extensive recommendations by the members of an independent scientific advisory board.

Table I. THC Concentration in Oil, daily Doses, and Equivalent Oil and Seed Consumption

Study period	Oil dose (mL/day)	THC concentration in oil (µg/g)	Daily THC dose (mg/day)	Equivalent to daily consumption of hulled hemp seeds (g/day) at 2 µg/g THC	Equivalent to daily consumption of hemp seed oil (mL/day) at 5 µg/g THC
1	5	6.2 ± 0.5	0.09	45	19
2	15	13.3 ± 0.8	0.19	95	40
3	15	20.7 ± 1.2	0.29	150	63
4	15	31.7 ± 1.4	0.45	225	95
4	20	31.7 ± 1.4	0.60	300	126

Preparation and analysis of oil samples

Hemp oil was expeller ("cold") pressed and filtered by a Canadian processor of hemp seeds. Seeds were intentionally cleaned less thoroughly than usual, in order to achieve THC levels of 30–50 µg/g in the oil, thus allowing for administration of the highest targeted THC-dose with 15 mL of oil.

Websar Laboratories, Inc. (Ste. Anne, MB, Canada) quantitated the concentration of total THC in the oil in triplicate by the method used to meet regulatory requirements in Canada (34). The

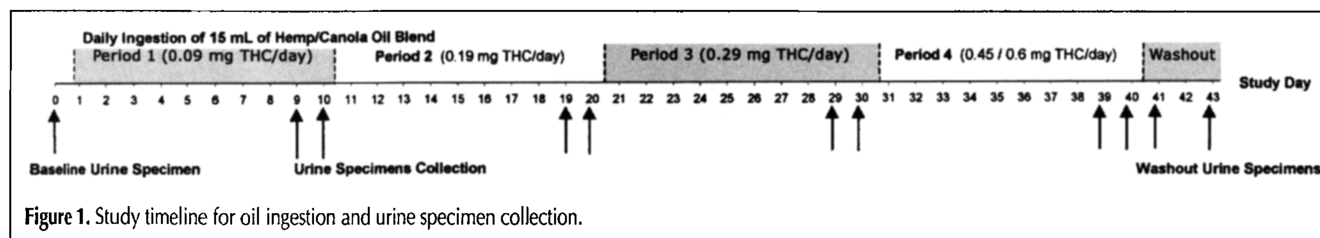

Figure 1. Study timeline for oil ingestion and urine specimen collection.

procedure is modified from the method of Giroud and Rivier (35) using GC–MS with deuterated THC as internal standard (limit of detection 0.2 µg/g; limit of quantitation 1.0 µg/g). The method yields a linear response from 1 to 62 µg/g.

The raw oil was found to contain 32.8 ± 1.5 µg/g of total THC, including both its free and acid forms. Four batches of hemp seed oil were diluted by Websar Laboratories with food-grade canola oil purchased in Winnipeg (MB, Canada) to obtain target concentrations of 7, 14, 21, and 32.8 µg/g, which would allow target doses of 0.1, 0.2, 0.3, and 0.47 mg THC to be ingested in 15-mL aliquots. Following blending, the batches were analyzed in triplicate to confirm the actual concentrations of THC. Results were 6.2 ± 0.5, 13.3 ± 0.8, 20.7 ± 1.2, and 31.7 ± 1.4 µg/g; the corresponding actual doses per 15-mL aliquots, using a specific density of 0.95 for all four oil blends, were 0.09, 0.19, 0.29, and 0.45 mg THC (see Table I). Batches of these oil blends were express-shipped in sealed containers to the U.S. and bottled in 240-mL narrow-mouth glass bottles prior to distribution to the subjects. Except during transport from Canada, oil blends were kept refrigerated until consumed. All ingestion of oil by the subjects occurred within four months from the date of initial analysis by Websar Laboratories.

Identification of THC species

The relative abundance in the oil of free (phenolic) THC and the THC acids A and B was determined in a sample of the undiluted oil (Batch #4) by ElSohly Laboratories (Oxford, MS), after it had been kept refrigerated for approximately four months. Analysis of the sample for total THC by GC–MS showed a concentration of 33.04 µg/g, which is in good agreement with the concentrations measured by Websar Laboratories. Analysis of the trimethylsilyl (TMS) derivatized extract, which separates free THC from THC acid A or B, showed a concentration of 27.12 µg/g of free THC. Thus, free THC represented by far the majority, approximately 82%, of total THC in the oil sample.

Subject protocol

On study day 0, each subject collected a baseline urine specimen. Starting with the lowest THC concentration in oil and increasing concentration stepwise after each period (see Figure 1), subjects then ingested 15-mL aliquots of hemp/canola oil blend per day, each concentration for a 10-day period. Subjects were instructed to ingest, if possible, the entire dose prior to meals or, if considered impossible, with meals. To avoid losses, the oil was not to be blended with food prior to ingestion.

During the fourth 10-day study period, three subjects ingested 20 mL, instead of 15 mL, of oil from batch #4, that is, undiluted hemp oil (corresponding dose 0.6 mg THC/day). No dietary restrictions, other than refraining from the consumption of other cannabis products, were imposed. On days 9 and 10 of each 10-day period (study days 9, 10, 19, 20, 29, 30, 39, 40), urine specimens were collected in glass sampling jars with polytetrafluoroethylene (PTFE)-lined caps, with a target delay of 4–8 h after oil ingestion. To observe THC washout, urine specimens were also collected 1 and 3 days after the last ingestion (study days 41 and 43).

The urine specimens were sealed and frozen immediately after collection and kept frozen prior to analysis. A total of 160 urine specimens were collected by all volunteers and subsequently analyzed. One volunteer collected specimens on days 27 and 28, instead of days 29 and 30, and terminated participation for travel reasons after completion of study period 3. Another volunteer collected the second washout specimen on day 42, instead of day 43. The respective data points are identified in Figure 2 as "single values". One subject failed to collect one of the scheduled specimens.

Analysis of urine specimens

Cannabinoid analyses of the 160 urine specimens were performed by Chemical Toxicology Institute (Foster City, CA). All specimens were screened by radioimmunoassay (RIA), using the Immunalysis Direct RIA Kit (San Dimas, CA). The manufacturer's

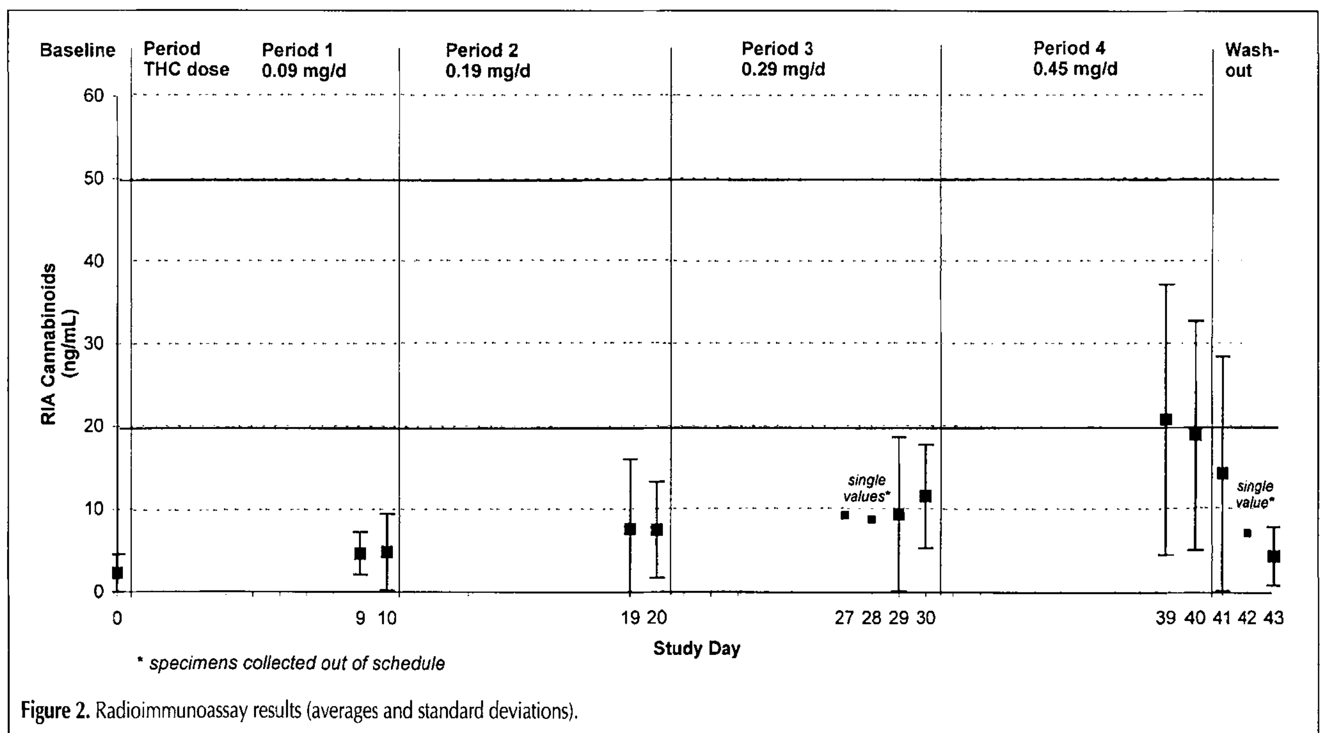

Figure 2. Radioimmunoassay results (averages and standard deviations).

recommended protocol was followed with the exception of the calibration curve, which was expanded to include urine calibrators containing 0, 10, 20, 50, and 100 ng/mL THC-COOH. All specimens were quantitated for THC-COOH, using a previously published GC–MS method (36), with a limit of quantitation of 2.5 ng/mL and calibrated at 2.5, 5, 10, and 50 ng/mL. To identify incidents of dilute urine, the creatinine concentration was determined for each specimen by a picric acid colorimetric method (Sigma Diagnostics catalog no. 555-A, St. Louis, MO) employing a Beckman model 25 visible spectrophotometer.

Results

Results of urine cannabinoid analyses, except for GC–MS readings below the 2.5 ng/mL quantitation limit, are shown in Figure 3 and summarized in Table II. Figure 2 shows averages and standard deviations for RIA analyses. For the same daily dose, both RIA and GC–MS results varied considerably between individuals. None of the volunteers ingesting between 0.09 and 0.45 mg/day of THC produced a positive RIA screening test at the 50-ng/mL cutoff. One of the three volunteers who had been ingesting 0.6 mg/day during study period 4 screened positive at the 50-ng/mL cutoff on day 41. However, confirmation of this urine specimen by GC–MS showed a THC-COOH level of only 3.0 ng/mL.

A total of 17 specimens out of 88 (19%) screened positive at the 20-ng/mL cutoff during study periods 2, 3, and 4. At this cutoff, 3% (1 in 30) screened positive during study period 2, 13% (4 in 30) during study period 3, and 43% (12 in 28) during study period 4.

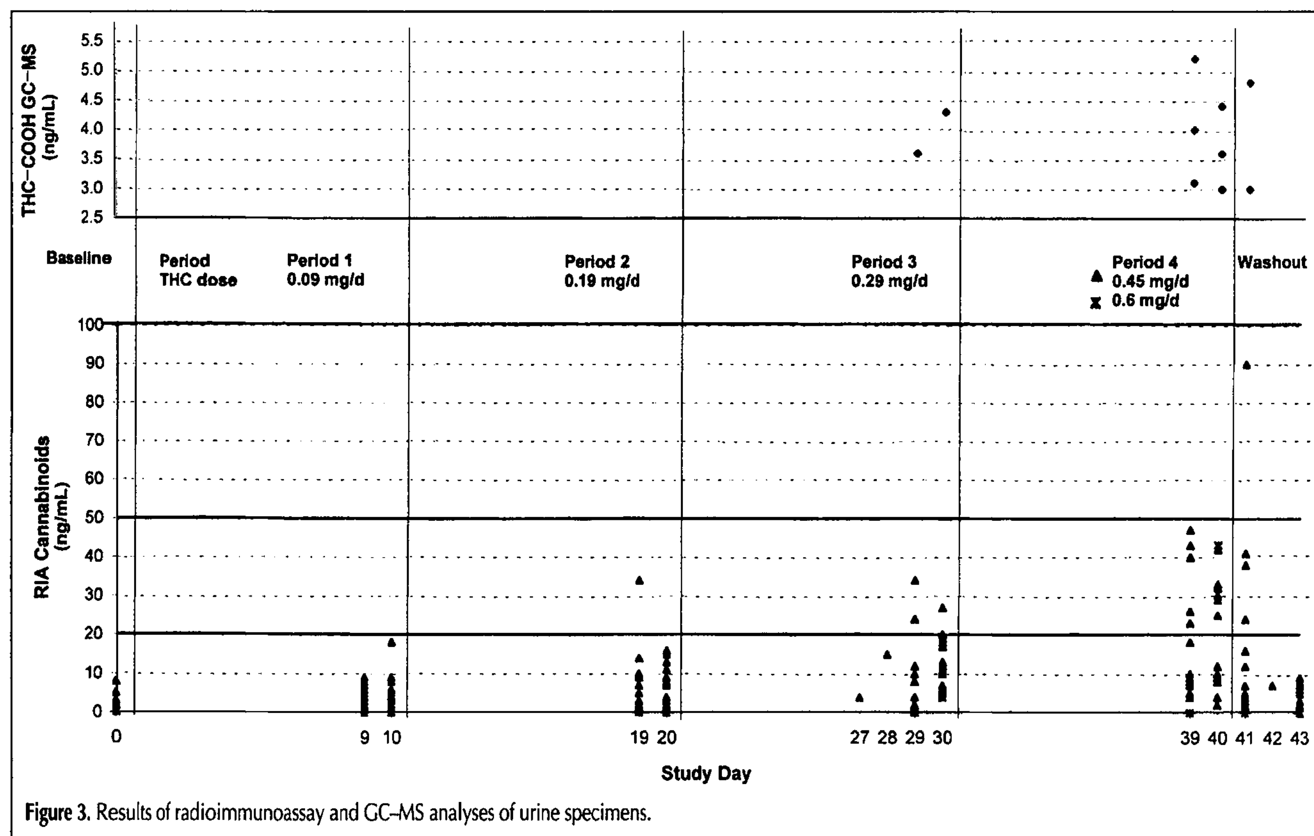

Figure 3. Results of radioimmunoassay and GC–MS analyses of urine specimens.

Table II. Summary of Urine Analyses by Radioimmunoassay and GC–MS

THC dose (mg/day)	# of Specimens n	GC–MS ≤ 2.5 ng/mL	GC–MS > 2.5 ng/mL*	RIA < 10 ng/mL	RIA < 20 ng/mL	RIA < 50 ng/mL	RIA < 100 ng/mL	RIA % Specimens ≥ 20 ng/mL
Baseline	15	15	0	15	0	0	0	0
0.09	29	29	0	28	1	0	0	0
0.19	30	30	0	21	8	1	0	3
0.29	30	28	2	17	9	4	0	13
0.45 (0.6)†	22 (6)	16 (6)	6 (0)	8 (3)	4 (1)	10 (2)	0 (0)	43
Washout day 1†	11 (3)	10 (2)	1 (1)	6 (2)	2 (0)	3 (0)	0 (1)	29
Washout day 3†	10 (3)	10 (3)	0 (0)	10 (3)	0 (0)	0 (0)	0 (0)	0
Total number of specimens including baseline	159	149	10	113	25	20	1	13
Total number of specimens excluding baseline	144	134	10	98	25	20	1	15

* Maximum GC–MS value measured 5.2 ng/mL.
† Values in parentheses refer to 0.6 mg/day dose in Period 4.

Twenty-nine percent of the specimens collected on washout day 1 screened positive at the 20-ng/mL cutoff and none on washout day 3 (see Table II). Confirmation testing by GC–MS showed that 10 specimens showed THC-COOH levels > 2.5 ng/mL. Only 1 of the 160 specimens was confirmed above 5 ng/mL (5.2 ng/mL).

RIA and GC–MS readings decreased rapidly after termination of hemp oil ingestion. Within three days following ingestion of the last dose, RIA readings had returned to those levels measured for the baseline specimens, that is, below 10 ng/mL. None of the specimens collected on day 43 was confirmed by GC–MS at the 2.5-ng/mL level. The rapidity with which the urinary THC-COOH levels fell after day 40 is consistent with the assumed half-life of 48 h for THC.

Urine creatinine levels ranged from 39 ± 31 mg/dL (mean ± SD) to 196 ± 27 mg/dL. Mean and standard deviation refer to the set of specimens produced by each subject. Four specimens (2.5% of the total) were found to be dilute (creatinine concentration < 20 mg/dL) according to guidelines by the U.S. Department of Health and Human Services (37), with three of these produced by one individual. The remainder of that subject's specimens all had creatinine levels above 35 mg/dL. This renders the analyses by RIA and GC–MS relevant. Screening levels in the dilute specimens were within the range found in the valid specimens collected during the same period. The results for dilute samples were included in Figures 2 and 3 and Table II.

Discussion

This study found that daily ingestion of up to 0.45 mg THC in an oil matrix by 15 subjects on the same dosage regimen did not cause a positive screening test by RIA at the 50-ng/mL cutoff. At a daily THC intake of 0.6 mg, one sample screened positive. Several samples screened positive at the 20-ng/mL cutoff at doses as low as 0.19 mg/day.

The RIA method used in this study is now rarely employed by laboratories that analyze large numbers of specimens from workplace drug-testing programs. Thus, these RIA results may not always be representative of the predominantly used enzyme immunoassays (EIA) or other more common methods. Comparisons of various screening test methods with each other and with GC–MS have shown that, for cannabinoid assays, RIA can be more effective in identifying true positives than other assays (33). RIA also appears to achieve better precision and sensitivity than EIA. However, the performance of a specific immunoassay varied between manufacturers and even for a specific product, as a function of the reagent. Because of this variability in test method performance and the limited number of subjects in our study, it cannot be ruled out that daily THC intake of 0.45 mg/day might produce positive screening tests at the 50-ng/mL cutoff.

The GC–MS confirmation of all urine specimens provided more conclusive results. At daily THC intake rates of up to 0.6 mg, the highest measured THC-COOH concentration in urine of 5.2 ng/mL is well below the 15-ng/mL confirmation cutoff used by federal and many private employers. Thus, the common practice of confirming any screen positive results by GC–MS appears to minimize the risk that the consumption of as much as 0.6 mg/day of THC could produce confirmed positives. Programs, which rely exclusively on immunoassay screening tests and use a lower screening cutoff, can still encounter occasional positives, which are caused by the ingestion of hemp foods, rather than by consumption of marijuana.

The daily single-dose THC ingestion rate of 0.6 mg, for which no confirmed positives were observed in this study, provides a guideline for the development of regulatory limits for THC in food items. Such limits would be intended to reduce the risk of producing confirmed positive results in tests for marijuana. An oral THC dose of 0.6 mg corresponds to consumption of 125 mL of hemp oil containing 5 µg/g of THC or 300 g of hulled seeds at 2 µg/g, that is, THC levels now commonly achieved by Canadian hemp seed processors. Daily consumption of these quantities is difficult, if not impossible, to attain, even by avid consumers of hemp seed products. Thus, restricting THC levels to 5 µg/g for hemp oil and to 2 µg/g for hulled seeds would limit daily THC intake to 0.6 mg/day, a level found in this study to produce no confirmed positives.

Relative abundance of THC species

A significant fraction of the total THC in hemp food samples may be present in the form of THC acids A or B. The metabolic pathway of the two THC species appears to be analogous to that of free THC (38). THC acids A and B are thus metabolized to 11-nor-9-carboxy-Δ^9-tetrahydrocannabinol-2-carboxylic acid and 11-nor-9-carboxy-Δ^9-tetrahydrocannabinol-4-carboxylic acid, respectively. These species are not quantitated during GC–MS analysis of urine specimens for THC-COOH. Thus, hemp oil in which THC acids account for much of the total THC will produce a lower THC-COOH response per total THC ingested compared to products containing only free THC. Analytical methods used in Canada and the U.S. to measure THC in cannabis products effectively quantitate total THC because injection of underivatized extract into the GC results in total decarboxylation of any acid precursor (39).

Analysis of the undiluted oil used during this study indicated that about 82% of total THC was present as free THC. This is in good agreement with a previous study where THC acid A, the predominant acid species, typically accounted for less than 10% of the total THC content in hemp oils (14). The high proportion of free THC in oil used during this study thus represented a conservative condition with respect to the relative abundance of THC species.

Comparison with other studies

The results of this study are in general agreement with those of a study by Bosy and Cole (12). When administering daily THC doses similar to those in the present study, these researchers found somewhat higher screening (FPIA and KIMS immunoassay) and GC–MS results. During their study, they exposed, over a period of 7 days, 6 males to single daily THC doses in hemp oil, ranging from 0.1 to 1.77 mg/day. They found that daily ingestion of 0.54 mg of total THC produces positive screening results at the 50-ng/mL cutoff and confirmed positives at the 15-ng/mL cutoff by GC–MS. Two individuals consuming 0.1 and 0.175 mg/day of THC, respectively, screened at > 20 ng/mL

and were confirmed by GC–MS at ~5 ng/mL, yet did not exceed the 50-ng/mL cutoff of the immunoassay and 15-ng/mL cutoff by GC–MS during the entire period. The small number of volunteers per dose tested by Bosy and Cole (12) (1 or 2) and the generally higher THC/oil ratio compared to this study may have contributed to the differences in findings between the two studies.

Conclusions

In the present study, daily ingestion of up to 0.6 mg of THC by 15 subjects did not produce confirmed positive urine THC results at the 10- or 15-ng/mL GC–MS cutoffs. Currently practiced seed cleaning methods appear to be successful in limiting THC concentrations in hemp oil and hulled seeds to 5 µg/g and 2 µg/g, respectively. At these THC residue levels, ingestion of 0.6 mg/day via hemp foods requires ingestion of unrealistically high amounts of such products. Thus, adopting THC limits for hemp oil and seeds at the above levels and practicing routine GC–MS confirmation of urine specimens screening positive appear to minimize the risk of producing confirmed positive urine tests from hemp food consumption. Use of a single immunoassay in this study limits its conclusiveness relative to screening tests, but because all specimens were confirmed by GC–MS, conclusions regarding the production of confirmed positive results remain valid.

Acknowledgments

The authors wish to thank Rudolf Brenneisen, University of Bern, Switzerland and Paul Mahlberg, University of Indiana, Bloomington, IN, who provided valuable input into the design and interpretation of this study.

We also wish to thank the following entities for their financial support of this study: Agricultural Research and Development Initiative (ARDI), Morris, MB, Canada; North American Industrial Hemp Council (NAIHC), Madison, WI; Atlas Corp., Los Angeles, CA; Canadian Hemp Corp., Vancouver, BC, Canada; Dr. Bronner's Magic Soaps, Escondido, CA; Fresh Hemp Foods, Winnipeg, MB, Canada; Galaxy Global Eatery, New York, NY; Hempola, Mississauga, ON, Canada; Hempwell, Long Island City, NY; Hempworld, Santa Barbara, CA; Kenex Ltd., Pain Court, ON, Canada; Nutiva, Sebastopol, CA; Spectrum Essentials, Petaluma, CA.

Valuable input to the experimental design of the study with respect to the preparation and use of the oil was provided by G.R. Barry Webster, Websar Laboratories, Inc., Ste. Anne, MB, Canada. We are also grateful to Randall C. Baselt, Chemical Toxicology Institute, Foster City, CA for his extensive input to the design of the overall study, and particularly design and quality control of urine analyses.

Finally, the authors wish to express their particular gratitude to the volunteers, whose reliable observation and documentation of the prescribed regimen were essential to the data quality of this study.

References

1. J.-L. Deferne and D. Pate. Hemp seed oil: a source of valuable essential fatty acids. *J. Int. Hemp Assoc.* **3:** 1, 4–7 (1996).
2. N. Fortner, R. Fogerson, D. Lindman, T. Iversen, and D. Armbruster. Marijuana-positive urine test results from consumption of hemp seeds in food products. *J. Anal. Toxicol.* **21:** 476–481 (1997).
3. R. Przybylski, J. Moes, and A. Sturko. Effect of growing conditions on composition of hemp oils. In *Proceedings Bioresource Hemp*, 2nd Symposium, Frankfurt, Germany, February 27–March 2, 1997, pp 505–514.
4. G. Scheifele, Kemptville College/University of Guelph, Thunder Bay, ON, Canada. 1999 comparison of industrial hemp grain composition for oil, protein, fibre, amino acids and fatty acids from across Northern Ontario. Report for CanAdapt, Kemptville College/University of Guelph, and the Thunder Bay Hemp Growers' Association, 2000.
5. U. Avico, R. Pacifici, and P. Zuccaro. Variations of tetrahydrocannabinol content in cannabis plants to distinguish the fibre-type from drug-type plants. *Bull. Narc.* **37:** 61–65 (1985).
6. F. Grotenhermen and R. Huppertz. *Hanf als Medizin: die Wiederentdeckung einer Heilpflanze.* Karl F. Haug Verlag, Heidelberg, Germany, 1997, pp 54–55.
7. M.A. ElSohly, S. Ross, Z. Mehmedic, R. Arafat, Y. Bao, and B. Bananhan. Potency trends of delta-9-THC and other cannabinoids in confiscated marijuana from 1980–1997. *J. Forensic Sci.* **45:** 24–30 (2000).
8. I. Bócsa and M. Karus. *The Cultivation of Hemp: Botany, Varieties, Cultivation and Harvesting.* Hemptech, Sebastopol, CA, 1998, pp 59–61.
9. Health Canada. Schedule 1089: Industrial Hemp Regulations (SOR/98-156), Amendment to Schedule II of the Controlled Drugs and Substances Act (SOR/98-157), Amendment to the Schedule to the Narcotic Control Regulations (SOR/98-158), Ottawa, ON, Canada, http://www.hc-sc.gc.ca/hpb-dgps/therapeut/, April, 1998.
10. V. Mediavilla, R. Derungs, A. Känzig, and A. Mägert. Qualität von Hanfsamenöl aus der Schweiz. *Agrarforschung* **4:** 449–451 (1997).
11. Mölleken and H. Husmann. Cannabinoids in seed extracts of *Cannabis sativa* cultivars. *J. Int. Hemp Assoc.* **4:** 1, 76–79 (1997).
12. T.Z. Bosy and K.A. Cole. Consumption and quantitation of Δ^9-tetrahydrocannabinol in commercially available hemp seed oils and products. *J. Anal. Toxicol.* **24:** 562–566 (2000).
13. A. Alt. Institut für Rechtsmedizin, Universitätsklinikum Ulm, Ulm, Germany, personal communication, 1999.
14. T. Lehmann, F. Sager, and R. Brenneisen. Excretion of cannabinoids in urine after ingestion of cannabis seed oil. *J. Anal. Toxicol.* **21:** 373–375 (1997).
15. S. Crew. HempOil Canada Inc., Ste. Agathe, MB, Canada. Laboratory analysis of THC content in industrial hemp seed. Report prepared for the Manitoba Rural Adaptation Council Inc. (MRAC), Winnipeg, MB, Canada, 2000.
16. S.A. Ross, Z. Mehmedic, T.P. Murphy, and M.A. ElSohly. GC-MS analysis of the total delta-9-THC content of both drug- and fiber-type cannabis seeds. *J. Anal. Toxicol.* **24:** 715–717 (2000).
17. G. Scheifele. Kemptville College/University of Guelph, Thunder Bay, ON, Canada. Delta 9 THC levels in hemp grain and oil from Northwestern Ontario in 1999, 2000.
18. S. Crew. HempOil Canada Inc., Ste. Agathe, MB, Canada. Development of hemp food products and processes. Report prepared for the Agricultural Research and Development Initiative (ARDI), Winnipeg, MB, Canada, 2000.
19. G.R.B. Webster. Websar Laboratories Inc., Ste. Anne, MB, Canada, personal communication, 2001.
20. K. Cole. Division of Forensic Toxicology, Armed Forces Institute of Pathology, Rockville, MD, personal communication, 2000.
21. A. Alt and G. Reinhardt. Speiseöle auf Hanfbasis und ihr Einfluß auf die Ergebnisse von Urin- und Blutanalysen. *Blutalkohol* 33: 347–356 (1996).

22. A. Alt and G. Reinhardt. Nahrungsmittel auf Hanfbasis und deren forensische Bedeutung. *Blutalkohol* **34:** 286–293 (1997).
23. A. Alt and G. Reinhardt. Positive cannabis results in urine and blood samples after ingestion of hemp food products. *J. Anal. Toxicol.* **22:** 80–81 (1998).
24. J.C. Callaway, R.A. Weeks, L.P. Raymon, H.C. Walls, and W.L. Hearn. A positive THC urinalysis from hemp (cannabis) seed oil. *J. Anal. Toxicol.* **21:** 319–320 (1997).
25. A. Costantino, R.H. Schwartz, and P. Kaplan. Hemp oil ingestion causes positive urine tests for Δ^9-tetrahydrocannabinol carboxylic acid. *J. Anal. Toxicol.* **21:** 482–485 (1997).
26. R.E. Struempler, G. Nelson, and F.M. Urry. A positive cannabinoids workplace drug test following the ingestion of commercially available hemp seed oil. *J. Anal. Toxicol.* **21:** 283–285 (1997).
27. R.C. Baselt. Chemical Toxicology Institute, Foster City, CA, personal communication, 2000.
28. J. Meeker. PharmChem Laboratories Inc., Menlo Park, CA, personal communication, 2000.
29. R.C. Baselt and R.H. Cravey. *Disposition of Toxic Drugs and Chemicals in Man*, 4th ed. Chemical Toxicology Institute, Foster City, CA, 1995, pp 713–714.
30. E. Johansson, S. Agurell, L.E. Hollister, and M.M. Halldin. Prolonged apparent half-life of delta 1-tetrahydrocannabinol in plasma of chronic marijuana users. *J. Pharm. Pharmacol.* **40:** 374–375 (1988).
31. E. Johansson, M.M. Halldin, S. Agurell, L.E. Hollister, and H.K. Gillespie. Terminal elimination plasma half-life of delta 1-tetrahydrocannabinol (delta 1-THC) in heavy users of marijuana. *Eur. J. Clin. Pharmacol.* **37:** 273–277 (1989).
32. M.E. Wall, B.M. Sadler, D. Brine, H. Taylor, and M. Perez-Reyes. Metabolism, disposition, and kinetics of delta-9-tetrahydrocannabinol in men and women. *Clin. Pharmacol. Ther.* **34:** 3532–3563 (1983).
33. Evaluation of common immunoassay kits for effective workplace drug testing. In *Handbook of Workplace Drug Testing*, R.H. Liu and B.A. Goldberger, Eds. AACC Press, Washington, D.C., 1995, pp 67–124.
34. Health Canada, Therapeutic Products Programme, Bureau of Drug Research, Health Protection Branch, Health Canada. Industrial hemp technical manual: TPP-BDS-004 – Basic method for determination of THC in hempseed oil, 1992.
35. C. Giroud and L. Rivier. Forensic trouble arised from the trading of hemp seed oil in Switzerland. *Toxicorama* **7:** 15–23 (1995).
36. R.C. Baselt. *Analytical Procedures for Therapeutic Drug Monitoring and Emergency Toxicology*, 2nd ed. PSG Publishing, Littleton, MA, 1987, pp 67–69.
37. U.S. Department of Health and Human Services, Division of Workplace Programs. Notice to certified and applicant laboratories: Guidance for reporting specimen validity test results. Program Document 035, Rockville, MD, September 28, 1998.
38. R. Brenneisen, Institute of Pharmacy, University of Bern, Switzerland, personal communication, 2000.
39. M.A. ElSohly and A.B. Jones. Drug testing in the workplace: could a positive test for one of the mandated drugs be for reasons other than illicit use of the drug? *J. Anal. Toxicol.* **19:** 450–458 (1995).

Manuscript received August 16, 2000;
revision received June 22, 2001.