

Likelihood of Positive Urine Screens of THC-COOH After Daily Use of Full-Spectrum Hemp Extracts Varies as a Function of Screening Criterion Used

To the Editor:

Recent studies have shown that even low amounts of $\Delta 9$ -tetrahydrocannabinol (THC) within a cannabidiol (CBD) product can result in positive 11-nor-9-carboxy- $\Delta 9$ -tetrahydrocannabinol (THC-COOH; a metabolite of THC) urine drug screens.^{1,2} One study reported positive drug screening in 2/6 participants after acute administration of vaporized CBD-dominant cannabis flower (10.5% CBD; 0.39% THC) using liquid chromatography tandem mass spectrometry (LC-MS/MS; which distinguishes between THC-COOH and other cannabinoids/metabolites) at a criterion of ≥ 15 ng/mL THC-COOH.¹ Another study found that 7/14 patients who used a hemp-derived CBD extract (0.02% THC) for 4 weeks yielded positive 50 ng/mL drug screens, 6 of which were ≥ 15 ng/mL as confirmed by GC/MS.² However, neither of these 2 studies evaluated commercially available products. Therefore, in this study, urine toxicology testing of daily users of retail oral hemp-derived CBD products ($\leq 0.3\%$ THC) was conducted using 2 different screening criteria and confirmatory testing techniques.

MATERIALS AND METHODS

The study was approved by the New England Institutional Review Board. Participants were recruited via the Realm of Caring e-mail lists, social media, and word of mouth. Participants included Colorado residents who had been using oral hemp-derived CBD extracts daily for at least 30 days and who did not report to using nonhemp cannabis products ($\geq 0.3\%$ THC) or other illicit drugs in the previous 2 months. Respondents were not informed of eligibility criteria. Participants provided consent, completed hemp-use questionnaires (Table 1), provided an unobserved urine sample, and were compensated \$25. Urine samples were aliquoted into 2 samples—1 was subjected to immunoassay (IA) testing and the other frozen (-20°C) and shipped overnight to a third-party laboratory for confirmation testing. Federal workplace guidelines recommend a two-stage analysis approach for urine drug testing.³ Herein, the first stage included screening with 4 commercial IA “dipstick” tests—2 with a 20 ng/mL detection criterion, and 2 with a 50 ng/mL detection criterion (Table 1).⁴ All samples were sent for confirmation testing, independent of screening test outcomes. The Dominion Diagnostics (North Kingstown, RI; CLIA Certified, FDA GLP) LC-MS/MS analysis (ABSciex API4000/API4500 or equivalent/Shimadzu Nexera/Prominence UPLC) protocol⁵ was applied, with the federally recommended criterion for detection of illicit cannabis use (≥ 15 ng/mL THC-COOH)³ as the test limit. The LC-MS/MS analysis method used had a limit of detection of 0.5 ng/mL and a limit of quantification of 5 ng/mL.⁵

RESULTS

All participants ($N = 19$, 37% female; 74% Caucasian; $M_{\text{age}} = 48.95$, $SD_{\text{age}} = 15.58$) disclosed to using full-spectrum hemp-derived CBD and all tested positive using a 20 ng/mL IA criterion, with 3/19 (16%) testing positive at a 50 ng/mL IA criterion. At the 15 ng/mL detection criterion using LC-MS/MS testing, 8/19 (42%) patients had positive confirmation drug test results. Fifty-eight percent (58%) of the participants (11/19) who screened positive at the 20 ng/mL IA criterion had results below the 15 ng/mL detection criterion after confirmatory LC-MS/MS testing. Two of the 3 participants who screened positive using the 50 ng/mL IA criterion also showed positive results above 50 ng/mL using LC-MS/MS testing. Three additional participants who screened negative at the 50 ng/mL IA criterion showed positive results of above 50 ng/mL after LC-MS/MS analysis (Table 1).

DISCUSSION

To the best of our knowledge, this study is the largest and most commercially generalizable examination of urine drug screens among full-spectrum CBD users. Our findings showed that the daily use of oral hemp-derived CBD extracts consistently resulted in positive urine IA screening results for THC-COOH at the 20 ng/mL detection criterion; however, positive results at the 50 ng/mL criterion were rare. Confirmation testing of each sample using LC-MS/MS analysis showed a positivity rate of 42% (range 37–178 ng/mL) at the ≥ 15 ng/mL criterion, which was intermediate to the 2 IA screening tests, suggesting that the IA 20 ng/mL and 50 ng/mL tests

Supported by a grant from the Institute for Research on Cannabinoids (IROC), a 501(c)(3) nonprofit organization supported by individual donations.

The authors have completed and submitted the ICMJE form for disclosure of potential conflicts of interest: M.L. Ferretti reports personal fees from the Canopy Corporation outside of the submitted work. R. Vandrey reports personal fees from Canopy Growth Corporation, personal fees from MyMD Pharmaceuticals, personal fees from Miral Therapeutics, personal fees from Radicle Science Inc, and personal fees from Syqe Medical Ltd, outside the submitted work. J.G. Irons reports a grant and non-financial support from the Canopy Growth Corporation outside the submitted work. M.J. Loflin reports personal fees and nonfinancial support from Jazz Pharmaceuticals. M.O. Bonn-Miller reports personal fees and non-financial support from Canopy Growth Corporation, personal fees and nonfinancial support from AusCann Group Ltd., personal fees and nonfinancial support from the Realm of Caring Foundation, and personal fees and non-financial support from The Lambert Center for the Study of Medicinal Cannabis and Hemp, outside the submitted work. M.O. Bonn-Miller had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of its presentation. Study concept and design: M.O. Bonn-Miller, R. Vandrey, M.J. Loflin; Acquisition, analysis, or interpretation of data: All authors; Drafting of the manuscript: All authors; Critical revision of the manuscript for important intellectual content: All authors; Administrative, technical, or material support: All authors; Study supervision: M.O. Bonn-Miller.

Neither the Institute for Research on Cannabinoids (IROC) nor the Canopy Growth Corporation played any role in the design or conduct of the study; collection, management, analysis, or interpretation of the data; preparation or approval of the manuscript; or the decision to submit the manuscript for publication. Copyright © 2022 Wolters Kluwer Health, Inc. All rights reserved.

TABLE 1. CBD Frequency, Dose Statistics, and Qualitative and Quantitative Results of THC Metabolites (THC-COOH) in Urine

Participant	Months of CBD Use	Amount per Occasion (mg)	# Of Times per Day	Qualitative EIP				Quantitative LC-MS/MS	
				20 ng/mL	20 ng/mL	50 ng/mL	50 ng/mL	>15 ng/mL	ng/mL
1	6	25	1	P	P	N	N	N	9
2	14	25	1	P	P	N	N	N	*
3	8	37.5	3	P	P	N	N	P	38
4	17	—	1	P	P	N	N	P	37
5	9	5	1	P	P	N	N	P	86
6	12	60	1	P	P	N	N	N	7
7	6	60	2	P	P	P	N	P	60
8	1	60	3	P	P	P	P	N	9
9	2	—	2	P	P	P	P	P	111
10	2	2	1	P	P	N	N	N	*
11	2	50	1	P	P	N	N	P	55
12	24	50	2	P	P	N	N	P	178
13	1	50	1	P	P	N	N	P	44
14	3	30	2	P	P	N	N	N	5.3
15	2	5	1–3	P	P	N	N	N	*
16	3.5	5	2–3	P	P	N	N	N	*
17	4	—	2	P	P	N	N	N	*
18	1	—	1	P	P	N	N	N	*
19	10	—	1	P	P	N	N	N	8.5

Unknown. Some participants did not provide dose information because of poorly labelled products.

*Not detected. LC-MS/MS testing: range = 5.3–178; median = 38. Using a 20 ng/mL detection criterion, there was 100% agreement between the 2 IA tests. Using a 50 ng/mL detection criterion, there was a 95% agreement between the 2 IA tests.

P, positive; N, negative.

used are subject to high rates of false-positive and false-negative results, respectively.^{1,2} This study extended on previously reported methodologies by including individuals who were using retail hemp-derived CBD products and subjecting each urine specimen to 5 tests (4 commercial IA tests and confirmatory LC-MS/MS testing). Many retail hemp product labels do not disclose that the products contain THC, and consumers may be unaware of positive urine drug screening risks. The tests used in this study reflect those commonly used in the workplace and criminal justice settings.

CONCLUSIONS

Efforts should be made to increase public awareness regarding the risk of positive drug test results after oral hemp-derived CBD product use. As CBD isolates generally do not lead to positive THC-COOH drug screens,¹ future research should investigate the threshold of hemp-derived THC, below which a negative drug test at varying criteria is highly probable. Regulators should reconsider

the use of a 20 ng/mL criterion for screening drug tests, as it appears to result in many false-positive screens among hemp-derived CBD users.

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ACKNOWLEDGMENTS

The authors thank the Realm of Caring Foundation for their facility and staff support for the execution of this project.

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