Cannabinoid Characterization across Toxicological Biosamples in Adolescents and Young Adults by Frequent Cannabis Vaping or Smoking

Natasha E. Wade, Alexander L. Wallace, Rachel Baca, Gianna Andrade, Joe Happer, Kelly E. Courtney, Uwe Christians, Marilyn A. Huestis, & Joanna Jacobus

Cannabis use is common, with 24 states with legalized recreational cannabis laws in the United States. In addition, following the passing of the 2018 Farm Bill, hemp-based cannabidiol (CBD) products are legal in all 50 states. This rise in CBD production contributes to the rise in CBD-derived intoxicating cannabinoids with similar chemical structure to the primary intoxicating cannabinoid constituent, delta-9-tetrahydrocannbinol (THC), such as Δ8-THC (LoParco et al., 2023). Recent proliferation of cannabis products beyond typically smoked flower, such as vaping concentrate or use of tincture and oils, is further complicated by varying and increasing rates of potency of THC (ElSohly et al., 2021). Concerningly, adolescents and young adults may be particularly vulnerable to the impact of cannabis use due to ongoing neurodevelopment, yet 36% of 12th graders and 42.4% of young adults (ages 19-30) report past year use (Miech et al., 2024; Patrick et al., 2024). The variability in cannabis products contributes to difficulty in accurately assessing the impact of cannabis use in vulnerable populations such as adolescents and young adults.

Method of cannabis use (e.g., flower, vaping) and frequency of use influence the bioavailability and pharmacokinetic profile of THC (Sharma et al., 2012; Spindle et al., 2018, 2019), with greater fluctuations of measured cannabinoid concentration connected to occasional rather than regular use (Huestis & Smith, 2018). Cannabinoid concentration in biosamples are influenced by a number of factors, including frequency of cannabis use (Newmeyer et al., 2017), THC potency (Fabritius et al., 2013; Greene et al., 2018), and the genetic makeup of the individual (Hryhorowicz et al., 2018; Stout & Cimino, 2014). Yet toxicological measures offer one quantitative value despite each of these sources of variation. It may be, then, that toxicological biosamples are an effective means of accounting for individual differences.

Toxicological biomarkers previously showed fair correlation with self-report and sensitivity in predicting neurocognitive and psychiatric outcomes. Our group found evidence of self-report of cannabis use was linked with poorer initial learning and delayed recall while urine THCCOOH significantly predicted poorer total learning and long-delayed recall (Wade et al., 2021). For hair, one study used cannabinoid concentrations in hair in adults, finding samples with THC related to cognitive and psychiatric functioning, with the presence of CBD having a positive, moderating effect (Morgan et al., 2012). In a sample of pre-teens (10-12 years-old, n=246), we found hair cannabinoid content related to inhibitory control and verbal performance (Wade et al., 2024). For blood, meta-analytic analyses reveal THC and THCCOOH concentration in blood generally relate to greater impairment in cognitive tasks, particularly in occasional (<weekly) users (McCartney et al., 2022). Combining biosamples has added strengths, such as in pairing the longer windows of detection from hair samples (e.g., 3 months) with more acutely sensitive methods for quantification of a larger range of cannabinoids from blood. Others have compared blood serum to hair cannabinoids (Zinka et al., 2019), but without consideration of self-report or product type in individuals who frequently use cannabis. Together, then, toxicological results across biological matrices reveal important cannabis-behavior relationships which may or may not be detectable when relying on self-report alone, though this needs further investigated in a well-characterized sample of participants who use cannabis.

Here we aim to combine and describe self-reported cannabis use days with a range of toxicological matrices (oral fluid, urine, plasma, and hair) to assess concurrence and strengths across measures. We also consider whether cannabinoid concentration across toxicological matrices varies by popular product formulations (i.e., flower and vaped concentrate). Finally, as an initial investigation into the utility of a range of toxicological biomarkers, we assess which

cannabis metrics relate to depression symptoms, as depression is established as being linked to cannabis use (Feingold & Weinstein, 2021).

Methods

Data were drawn from a larger parent longitudinal study on cannabis and nicotine and tobacco product use in young adults in the San Diego region (Wallace et al., Under Review). Participants included 94 individuals (64%; ages 18-21) who did and did not use cannabis. Hair and blood sample collection began in July 2023, and all participants with scheduled appointments since then were asked to contribute these biosamples for toxicological testing. No participants had repeat data collection within this timeframe (July 2023-June 2024), and all analyses are cross-sectional. A total of 94 participants had urinalysis; in addition, hair and plasma (n=71), hair only (n=17), or plasma only (n=4).

Inclusion criteria included use of cannabis or nicotine products in the past six months, or controls who reported no cannabis or nicotine use in the past 6 months. Exclusion criteria included acute substance intoxication, current pregnancy, MRI contraindications, non-fluent in English, visual or hearing difficulties without corrective aids, developmental disorder, >10 lifetime episodes of illicit substances, current or past psychiatric disorder (other than cannabis or tobacco use disorder), major neurological disorder, history of severe head trauma, prenatal alcohol exposure or tobacco exposure or illicit drug exposure, premature birth (<24 week gestation or birth weight <5lbs, or greater than 100 episodes of alcohol use in their lifetime.

Product Preference Grouping. Product groups were created based on participants self-reported past 90-day cannabis use and preferred method of cannabis use: smoked flower (n=32), vaped concentrate (n=30), or edibles (n=8). A control group (n=24) of individuals who denied

using cannabis within the past 90 days was included. Stated preferred method was also consistent with their TLFB most reported method of use in the past 90 days.

Procedures. After seeing an electronic or physical flyer for the study, participants were screened for eligibility to the longitudinal study. Trained staff confirmed eligibility on a brief phone screener. Participants were then scheduled for on-site sessions to complete mental health and substance use inventories, neurocognitive assessments, biosample collection, EEG, MEG, and MRI. Participants were asked not to use cannabis on the day of their appointment. All participants provided written informed consent in accordance with the University of California, San Diego Human Research Protections Program.

Measures

Self-reported sociodemographics and substance use. Participants reported sociodemographic characteristic, including age, race, ethnicity, sex assigned at birth, and highest level of education achieved. For self-reported substance use, the Timeline Followback (TLFB) was used to measure past-30- and past-90-day substance use days (Robinson et al., 2014; Sobell & Sobell, 1992). Staff queried participants regarding method of cannabis use (smoked flower, concentrate, edible, tincture, or other) on each day of reported use. Participants also were asked the typical THC potency (either from the label on dispensary products or participant-estimated potency) of the product they used and reported their preferred method of consumption (smoked flower, concentrate, edible, tincture, or other). Participants also completed the Cannabis Use Disorder Identification Test – Revised (CUDIT-R) as a screener for cannabis use disorder (Adamson et al., 2010).

BDI. The Beck Depression Inventory-II (BDI) is a 21-item measure regarding depression symptoms experienced over the past two weeks (Beck et al., 1996).

Oral fluid. Oral fluid samples were collected and examined on the examined Draeger DrugTest® 5000. The cutoff for THC was 5 ng/mL THC. The Draeger is highly sensitive and effective measure of past 12 hour substance use (including cannabis use) (Desrosiers et al., 2014; Wille SM et al., 2010)

Urinalysis. Quantified urinary THCCOOH concentrations and normalized THCCOOH to creatinine ratios were provided by Redwood Toxicology Laboratory (Santa Rosa, CA). THCCOOH was confirmed at 5ng/mL (Laboratory, 2020). Creatinine-normalized THCCOOH accounted for the individual's state of hydration and reduced variability (Huestis et al., 2019; Huestis & Cone, 1998), and was used in all analyses.

Plasma. Plasma samples anticoagulated with ethylenediaminetetraacetic acid (EDTA) were shipped to iC42 Clinical Research and Development (University of Colorado, Aurora, CO, USA) on dry ice, where 17 cannabinoids including THC and CBD and their major metabolites were quantified using an established and validated high-performance liquid chromatography-tandem mass spectrometry (LC-MS/MS) assay (Sempio et al., 2022; Sempio et al., 2024). Most importantly, among others, the lower limits of quantification of THC and CBD were 0.39 ng/mL, of 11-OH THC 1.56 ng/mL and of THC-COOH 0.78 ng/mL. Intra- and inter-batch trueness and imprecision were ±15% and ≤15%, respectively; there were no significant carry-over and matrix interferences (Sempio et al., 2022; Sempio et al., 2024).

Hair. Around 50-60 mg of 3.9 cm hair closest to the root was collected for analysis by trained research associates. Samples were then stored securely in sealed envelopes in locked filing cabinets until shipment to US Drug Testing Laboratory (USDTL; Des Plaines, IL). Once received, samples which were longer than 3.9 cm were trimmed to 3.9. Though it is often recommended to wash hair samples to remove potential external contamination (Cooper et al.,

2012), as participants were recruited to a cannabis study, there was no reason to suspect false positives. Further, pilot data within this sample (unpublished) revealed similar patterns in washed and unwashed samples. Samples then underwent enzymatic digestion prior to being quantified by LC-MS/MS. LOD and LOQ are displayed by cannabinoid in Table 1.

Table 1. Hair Cannabinoid Cut-offs.

Drug Analyte	**Routine Cutoff (pg/mg)**	**LOQ (pg/mg)**	**LOD (pg/mg)**
THCA (THCCOOH)	0.05	0.02	0.01
Delta 8 THC	40	16	8
Delta 9 THC	40	16	8
Delta 10 THC	40	16	8
CBD	40	16	8

Notes: LOQ = Level of quantitation; LOD = Level of detection

Statistical Analysis

Descriptive Rates of Toxicological Results. Sociodemographic differences by group status were assessed using chi-square analyses. Rates of positives and negatives by matrix are presented. Sensitivity, specificity, positive predictive value (PPV; a positive result accurately predicting use), and negative predictive value (NPV; a negative result accurately indicating no use) were calculated for this small study of emerging adults who use and do not use cannabis using comparisons of self-report with toxicological results. Pearson correlations were run across self-report and toxicological THCCOOH concentration across matrices.

Group Differences and Predictive Utility in Toxicological Measures. In order to assess whether preferred cannabis product type (flower or vaped cannabis), ANOVAs were run to assess whether product groups differed in cannabis use patterns, withdrawal symptoms, or toxicological

concentration. In order to assess the potential predictive utility of biomarkers from toxicological testing, linear regression models were run assessing self-report and cannabinoid concentration by matrix in predicting a construct which is linked to cannabis use (here, depression symptoms), while controlling for biological sex.

Results

Sociodemographics. Participants were a majority female (64%) and 19 years on average (range = 18-21). Fifty-six participants met criteria for cannabis use disorder (CUD, 15 mild, 15 moderate, 25 severe). In individuals who use cannabis, there was no difference in prevalence of CUD by preferred product type (χ^2=3.55, p=.17). See Table 2 for full descriptive details.

Table 2. Sociodemographics and Substance Use Characteristics by Preferred Cannabis Product

Characteristic	**Smoked Flower** n = 32	**Vaped Concentrate** n = 30	**Other Cannabis Product** n = 8	**Controls** n = 24
Age	18.7 (±0.6) *[18 - 20]*	18.8 (±0.7) *[18 - 20]*	19.0 (±1.3) *[18 - 21]*	19.7 (±0.8) *[18 - 21]*
Highest Grade Completed				
11th Grade	0 (0%)	0 (0%)	0 (0%)	1 (4.2%)
12th Grade	15 (47%)	18 (60%)	4 (50%)	1 (4.2%)
13th Grade	13 (41%)	6 (20%)	3 (38%)	8 (33%)
14th Grade	4 (13%)	5 (17%)	1 (13%)	9 (38%)
15th Grade	0 (0%)	1 (3.3%)	0 (0%)	4 (17%)
16th Grade	0 (0%)	0 (0%)	0 (0%)	1 (4.2%)
% Female	21 (66%)	19 (63%)	6 (75%)	14 (58%)
% Hispanic	10 (31%)	16 (53%)	3 (38%)	9 (38%)
% White	17 (53%)	13 (43%)	6 (75%)	5 (21%)
Days since last cannabis use	4.5 (±8.7) *[1 - 47]*	9.0 (±16.6) *[0 - 80]*	8.1 (±11.8) *[1 - 36]*	482.3 (±524.3) *[100 - 1,635]*

Characteristic	Smoked Flower n = 32	Vaped Concentrate n = 30	Other Cannabis Product n = 8	Controls n = 24
Past 30 days cannabis use	15.8 (±10.7) *[0 - 30]*	14.6 (±11.3) *[0 - 30]*	7.0 (±6.1) *[0 - 15]*	--
Past 90 days cannabis use	47.9 (±32.0) *[1 - 90]*	41.1 (±32.8) *[1 - 90]*	19.5 (±15.3) *[1 - 42]*	--
Past Year CUD Diagnosis	26 (81%)	25 (83%)	4 (50%)	1 (4.2%)

Mean (±SD); *[Range]*; n (%)

Cannabis Product Characteristics. There were no unexpected cannabis positives (false positives) on toxicological assessment, as all participants with positive results reported using cannabis within the past 90 days. Twenty-four participants reported no cannabis use in the past 90 days (Controls), and 29 individuals in the cannabis groups denied cannabis use in the past 30 days. Thirty-four participants reported they primarily used smoked flower, 30 reported vaping concentrate, eight used edibles, and one used other concentrate as their primary method of use. The majority of participants (66%) reported smoking flower or vaping concentrate as their first and second preferred methods of use. Three reported using CBD-only products while two reported using delta-8-THC products in addition to other cannabis use. Participant's flower potency ranged from 0.3-91.0% THC, and concentrate ranged from 40.0-98.5% THC.

Descriptives of Positive Toxicological Results.

Overall positive and negative results, by matrix, are presented in **Table 3**. In **Table 4**, sample-specific sensitivity, specificity, PPV, and NPV are calculated, based on past 30-day cannabis use report (or past-90-day for hair). In **Table 5**, we provide the minimum self-reported cannabis use days for a positive toxicological result and the maximum number use days yet still resulting in a negative toxicological result.

Table 3. Rates of toxicological results by matrix.

Matrix		Control	Flower	Vape	Other
Oral Fluid	Pos	0%	6%	11%	0%
	Neg	100%	94%	89%	100%
Urine	Pos	0%	59%	56%	44%
	Neg	100%	41%	44%	56%
Plasma	Pos	0%	69%	64%	22%
	Neg	100%	31%	36%	78%
Hair	Pos	0%	74%	70%	63%
	Neg	100%	26%	30%	37%

Table 4. Sensitivity, Specificity, PPV, and NPV in a young adult cohort of individuals who use and do not use cannabis.

Matrix	Sensitivity	Specificity	PPV	NPV
Urine	60%	100%	100%	53%
Plasma	74%	100%	100%	68%
Hair	73%	100%	100%	60%

Table 5. Descriptives of days of cannabis use reported with positive and negative results.

Matrix	Minimum with Positive	Maximum with Negative
Urine	1 day	30 days
Plasma	2 days	11 days
Hair	6 days	41 days

Notes: Data within the table detail the minimum number of self-reported cannabis use days for a participant a positive result on a matrix and, conversely, the number of days of use but still have a negative result by matrix. Self-report windows were 30 days for urine and plasma and 90 days for hair.

Oral Fluid & THC. Five participants (5%) tested positive for THC on oral fluid testing, having reported last using 1-2 days before their session. However, one participant who used cannabis the same day as their session and another 35 participants who last used 1-2 days before their session tested negative for THC on oral fluid.

Plasma & Cannabinoids. Forty-five percent (n=25/53) of participants reporting cannabis use were positive for THCCOOH on plasma testing, while 32% (n=17/53) were positive for THC. Two participants were positive for CBD-COOH, with no participants positive for CBD. All participants positive on plasma THCCOOH reported using cannabis within the past 12 days, and the vast majority (68% of plasma positives) reported using within the past 24 hours preceding their visit. Reported use days for those testing positive on plasma testing ranged from (2-30) in the past 30 days. Participants negative on plasma THCCOOH ranged in reported use days from 0-11 in the past 30 days.

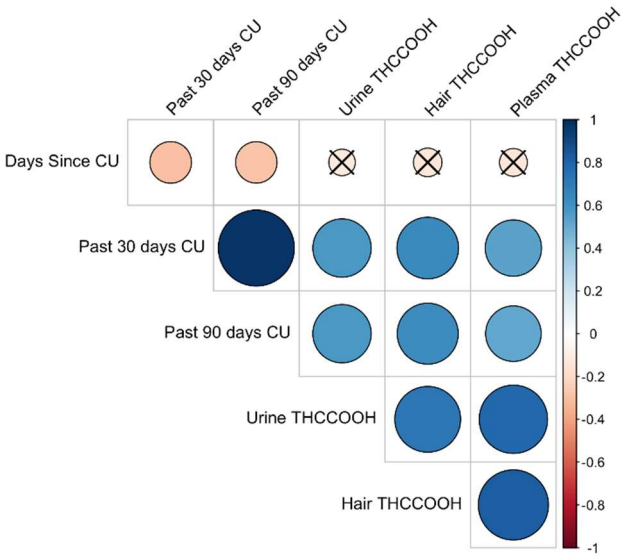
Urine & THCCOOH. Forty-two percent (n=39/93) of participants were positive on urine testing. Self-reported use days ranged from 2 to 30 in the past 30 days. All participants positive on urine THCOOH reported using cannabis within the past 21 days, and the vast majority (79% of urine positives) reported using within the past 24 hours preceding their visit.

Hair & THCCOOH. Fifty-two percent (n=44/84) of participants were positive on hair testing. Seven participants (10% of those reporting past 90-day cannabis use) had hair positive for Delta-8, with no participants who reported using Delta-8 positive for Delta-8 in hair. No samples were positive for Delta-10. Three participants were positive for CBD; no participants who reported CBD-only products were positive for CBD.

Correlations by Cannabinoid Metric. As seen in Figure 1, nearly all measures of cannabis exposure were significantly correlated, with the exception of self-reported days since last use and all three toxicological measures of THCCOOH.

Figure 1. Matrix of Correlations between Cannabis Metrics.

	Past 30 Days CU	Days Since CU	Urine THCCOOH	Plasma THCCOOH	Hair THCCOOH



Past 90 Days CU	r=.97, **p<.001**	r=-.029, **p=.01**	r=.57, **p<.001**	r=.51, **p<.001**	r=.63, **p<.001**
Past 30 Days CU	--	r=-0.29, **p=.009**	r=.57, **p<.001**	r=.52, **p<.001**	r=.64, **p<.001**
Days Since CU		--	r=-.12, p=.32	r=-.12, p=45	r=-.14, p=.26
Urine THCCOOH			--	r=.87, **p<.001**	r=.81, **p<.001**
Plasma THCCOOH				--	r=.83, **p<.001**

Group differences by flower or vaped cannabis. Two preferred product groups were assessed: flower and vaping cannabis.

Groups did not differ by past 30- or 90-day cannabis use days (p=.66; p=.41, respectively), nor by reported using to avoid withdrawal symptoms (p=.16). Similarly, they did not differ quantitatively on any toxicological measure (hair: p=.3; blood: p=.78; urine: p=.57).

Predictive Utility of Biomarkers on Depression Symptoms. Plasma THCCOOH concentration predicted increased total depression symptoms as measured on the BDI (beta=2.73, t=2.21, p=.03). Self-reported past-month cannabis use days were not associated with BDI symptoms (beta=0.15, t=1.66, p=.10). Similarly, hair THCCOOH concentration (beta=0.35, t=0.35, p=.73) and urinary THCCOOH-creatinine ratios (beta=0.90, t=.85, p=.40) were not associated with BDI symptoms. Finally, sex was not associated with BDI in any models.

Discussion

The present study suggests general concurrence between biomatrices of cannabinoid concentration and self-reported cannabis use days in a sample of adolescents and young adults (ages 18-21), the majority of whom regularly use cannabis. Quantitated THCCOOH

concentration across matrices did not differ significantly regardless of typical and preferred product formulation (smoked flower or vaped concentrate). Finally, when assessing which cannabis metrics relate to self-reported depression symptoms, only plasma THCCOOH significantly predicted increased depression.

Data here include novel comparisons on cannabinoid concentration across biological matrices in young adults who regularly use cannabis. Prior work compared two matrices (hair and blood serum), but did not incorporate self-report or urinalysis (Zinka et al., 2019). Given expanding research into cannabinoid concentration predicting clinical outcomes (McCartney et al., 2022; Morgan et al., 2012; Wade et al., 2024), direct side-by-side comparisons across matrices are helpful. Here, THCCOOH concentration was significantly and strongly correlated between the three assessed matrices (hair, urine, plasma), and each moderately correlated with self-report cannabis use days. Specificity was excellent and sensitivity adequate across matrices. Unlike other studies which recruit large populations for general health assessment and use biosamples to identify underreporting of substance use (Steinhoff et al., 2023; Wade et al., 2023), our study with targeted recruited of individuals who use substances had no instances of underreporting (i.e., no unexpected positives). Studies aiming to incorporate toxicological measures are likely able to use any matrix that matches their needed window of detection and collection and storage capabilities.

The variety of cannabis products typically consumed introduce uncertainty in how to accurately measure cannabis use in retrospective studies. Acute toxicological profiles of vaped and smoked THC are documented in adults with occasional use (Spindle et al., 2019), finding vaporized cannabis resulted in greater concentration of THCCOOH in whole blood up to 8 hours after use in participants who had not used cannabis within a month of study enrollment.

Subjective high also varies by mode of use (Cloutier et al., 2022; Spindle et al., 2021). Here, however, we found no difference in THCCOOH concentration across matrices between participants who reported preferring to use smoked relative to vaped cannabis products. While plasma and blood cannabinoid concentration typically offer a short window of detection for cannabis use of 1-3 days, cannabinoids can be detected in blood samples even a month after cessation of use in participants who frequently use cannabis (Karschner et al., 2016). Studies using cannabinoid quantitation of those who use occasionally are likely wholly qualitatively different than those who use frequently (e.g., (Huestis et al., 2020; Sholler et al., 2022; Spindle et al., 2019)). The information garnered from toxicological samples across matrices likely varies by how frequently and how much an individual uses cannabis, though method of use is less likely to be impactful on measured cannabinoid concentration with regular cannabis use.

When considering potential downstream behavioral correlates of cannabinoid concentration, plasma THCCOOH concentration alone predicted increased depression symptoms. Smoked cannabis products quickly convert from THC to 11-OH-THC, an active metabolite, and then into THCCOOH, an inactive metabolite. THCCOOH is excreted over time as THC in deep tissue is released and converted into its metabolites, resulting in THCCOOH persisting much longer than THC or 11-OH-THC in plasma (Karschner et al., 2009). Plasma THCCOOH concentration after up to 33 days of monitored abstinence was previously associated with cognitive decrements (Karschner et al., 2016). In contrast to plasma, hair cannabinoid concentration is a cumulative measure over a relatively long period of time (3 months). Urinary cannabinoid excretion profiles are more variable than plasma, as repeat testing of urine samples demonstrates multiple THCCOOH peaks after cannabis use (Huestis et al., 2020). Thus, plasma

may offer a unique sensitivity window into brain-behavior relationships in individuals who regularly use cannabis.

Ten percent of individuals were positive for Δ8-THC in their hair, despite only two participants reporting Δ8-THC use. Δ8-THC is derived from hemp-based products through chemical processes to create Δ8-THC as an isomer of Δ9-THC. In the manufacturing process, there are known concerns for adulterants such as heavy metals and solvents being present in the product (Geci et al., 2023), potentially resulting in more negative outcomes due to the adulterants present. Though over 11% of 12th graders report Δ8-THC use in the past year (Harlow AF et al., 2024), individuals may not realize they are being exposed to delta-8-THC (Geci et al., 2023) and analyzed Δ8-THC product content is only weakly correlated with the advertised content in commercial products (Kaczor et al., 2024). Testing of drug samples or toxicological samples to identify use of delta-8 will be important for identifying use and assessing impact.

Limitations are noted. Participants retrospectively reported their cannabis use, and therefore were not limited to only one product type or method of consumption. Accordingly, while findings are more generalizable to real-world young adult cannabis use patterns, they may not fully reflect differences in cannabinoid concentration by mode of use in young adults use regularly use cannabis. For self-report we used a broadly defined cannabis use days count, while other groups suggest more nuanced integration of use information (e.g., iCannToolkit; CannaCount) (Lambros et al., 2023; Lorenzetti et al., 2022). Not all participants were able to equally contribute each biosample, which may impact results, particularly regarding depression symptoms. Though hair and plasma samples measure other minor cannabinoids, here we focused on THCCOOH. Comparisons between matrices and minor cannabinoids may be important to consider in the future.

In summary, data presented herein indicate largely concurrent cannabinoid concentration findings across toxicological matrices (urine, plasma, and hair, and to a more limited extent, oral fluid) and with self-reported cannabis use days in young adults who regularly use cannabis. THCCOOH concentration did not vary by preferred and most commonly used method of cannabis consumption (flower or vaped), and plasma THCCOOH concentration uniquely predicted self-reported depression symptoms. Findings support the use of toxicological samples across matrices in measuring cannabinoid concentration with high specificity and adequate sensitivity. Given the complexity of measuring cannabis use due to the plethora of available products and rise of new popular cannabinoids, use of toxicological results may offer new insights into brain-behavior relationships in those who frequently use cannabis.

Adamson, S. J., Kay-Lambkin, F. J., Baker, A. L., Lewin, T. J., Thornton, L., Kelly, B. J., & Sellman, J. D. (2010, Jul 1). An improved brief measure of cannabis misuse: the Cannabis Use Disorders Identification Test-Revised (CUDIT-R). *Drug Alcohol Depend, 110*(1-2), 137-143. https://doi.org/10.1016/j.drugalcdep.2010.02.017

Beck, A. T., Steer, R. A., & Brown, G. K. (1996). *Manual for the Beck Depression Inventory-II*. Psychological Corporation.

Cloutier, R. M., Calhoun, B. H., & Linden-Carmichael, A. N. (2022, Feb). Associations of mode of administration on cannabis consumption and subjective intoxication in daily life. *Psychol Addict Behav, 36*(1), 67-77. https://doi.org/10.1037/adb0000726

Cooper, G. A., Kronstrand, R., Kintz, P., & Society of Hair, T. (2012, May 10). Society of Hair Testing guidelines for drug testing in hair. *Forensic Sci Int, 218*(1-3), 20-24. https://doi.org/10.1016/j.forsciint.2011.10.024

Desrosiers, N. A., Milman, G., Mendu, D. R., Lee, D., Barnes, A. J., Gorelick, D. A., & Huestis, M. A. (2014, Jul). Cannabinoids in oral fluid by on-site immunoassay and by GC-MS using two different oral fluid collection devices. *Anal Bioanal Chem, 406*(17), 4117-4128. https://doi.org/10.1007/s00216-014-7813-9

ElSohly, M. A., Chandra, S., Radwan, M., Majumdar, C. G., & Church, J. C. (2021, Jun). A Comprehensive Review of Cannabis Potency in the United States in the Last Decade. *Biol Psychiatry Cogn Neurosci Neuroimaging, 6*(6), 603-606. https://doi.org/10.1016/j.bpsc.2020.12.016

Fabritius, M., Chtioui, H., Battistella, G., Annoni, J. M., Dao, K., Favrat, B., Fornari, E., Lauer, E., Maeder, P., & Giroud, C. (2013). Comparison of cannabinoid concentrations in oral fluid and whole blood between occasional and regular cannabis smokers prior to and after smoking a cannabis joint. *Anal Bioannal Chem, 405*, 9791-9803.

Feingold, D., & Weinstein, A. (2021). Cannabis and Depression. *Adv Exp Med Biol, 1264*, 67-80.

Geci, M., Scialdone, M., & Tishler, J. (2023, Apr). The Dark Side of Cannabidiol: The Unanticipated Social and Clinical Implications of Synthetic Delta(8)-THC. *Cannabis Cannabinoid Res, 8*(2), 270-282. https://doi.org/10.1089/can.2022.0126

Greene, N. Z., Wiley, J. L., Yu, Z., Clowers, B. H., & Craft, R. M. (2018, Nov). Cannabidiol modulation of antinociceptive tolerance to Delta(9)-tetrahydrocannabinol. *Psychopharmacology (Berl), 235*(11), 3289-3302. https://doi.org/10.1007/s00213-018-5036-z

Harlow AF, Miech RA, & AM, L. (2024). Adolescent Δ8-THC and Marijuana Use in the US. *JAMA, 331*, 861-865.

Hryhorowicz, S., Walczak, M., Zakerska-Banaszak, O., Slomski, R., & Skrzypczak-Zielinska, M. (2018, Feb). Pharmacogenetics of Cannabinoids. *Eur J Drug Metab Pharmacokinet, 43*(1), 1-12. https://doi.org/10.1007/s13318-017-0416-z

Huestis, M. A., Blount, B. C., Milan, D. F., Newmeyer, M. N., Schroeder, J., & Smith, M. L. (2019, Jul). Correlation of creatinine- and specific gravity-normalized free and glucuronidated urine cannabinoid concentrations following smoked, vaporized, and oral cannabis in frequent and occasional cannabis users. *Drug Test Anal, 11*(7), 968-975. https://doi.org/10.1002/dta.2576

Huestis, M. A., & Cone, E. J. (1998). Differentiating new marijuana use from residual drug excretion in occasional marijuana users. *J Anal Toxicol, 22*, 445-454.

Huestis, M. A., Sempio, C., Newmeyer, M. N., Andersson, M., Barnes, A. J., Abulseoud, O. A., Blount, B. C., Schroeder, J., & Smith, M. L. (2020, Oct 12). Free and Glucuronide Urine Cannabinoids after Controlled Smoked, Vaporized and Oral Cannabis Administration in Frequent and Occasional Cannabis Users. *J Anal Toxicol, 44*(7), 651-660. https://doi.org/10.1093/jat/bkaa046

Huestis, M. A., & Smith, M. L. (2018, Feb). Cannabinoid Markers in Biological Fluids and Tissues: Revealing Intake. *Trends Mol Med, 24*(2), 156-172. https://doi.org/10.1016/j.molmed.2017.12.006

Kaczor, E. E., Greene, K., Babu, K. M., Berthold, E. C., Sharma, A., & Carreiro, S. P. (2024, Jan). Commercial Delta-8 THC Products: an Analysis of Content and Labeling. *J Med Toxicol, 20*(1), 31-38. https://doi.org/10.1007/s13181-023-00974-y

Karschner, E. L., Schwilke, E. W., Lowe, R. H., Darwin, W. D., Herning, R. I., Cadet, J. L., & Huestis, M. A. (2009). Implications of plasma Delta9-tetrahydrocannabinol, 11-

hydroxy-THC, and 11-nor-9-carboxy-THC concentrations in chronic cannabis smokers. *J Anal Toxicol, 33*, 469-477.

Karschner, E. L., Swortwood, M. J., Hirvonen, J., Goodwin, R. S., Bosker, W. M., Ramaekers, J. G., & Huestis, M. A. (2016, Jul). Extended plasma cannabinoid excretion in chronic frequent cannabis smokers during sustained abstinence and correlation with psychomotor performance. *Drug Test Anal, 8*(7), 682-689. https://doi.org/10.1002/dta.1825

Laboratory, R. T. (2020). *Laboratory testing cutoffs & methods*. Retrieved July 31 from

Lambros, A. M., Sagar, K. A., Dahlgren, M. K., Kosereisoglu, D., El-Abboud, C., Smith, R. T., & Gruber, S. A. (2023, Apr 11). CannaCount: an improved metric for quantifying estimates of maximum possible cannabinoid exposure. *Sci Rep, 13*(1), 5869. https://doi.org/10.1038/s41598-023-32671-9

LoParco, C. R., Rossheim, M. E., Walters, S. T., Zhou, Z., Olsson, S., & Sussman, S. Y. (2023, Jun). Delta-8 tetrahydrocannabinol: a scoping review and commentary. *Addiction, 118*(6), 1011-1028. https://doi.org/10.1111/add.16142

Lorenzetti, V., Hindocha, C., Petrilli, K., Griffiths, P., Brown, J., Castillo-Carniglia, A., Caulkins, J. P., Englund, A., ElSohly, M. A., Gage, S. H., Groshkova, T., Gual, A., Hammond, D., Lawn, W., Lopez-Pelayo, H., Manthey, J., Mokrysz, C., Pacula, R. L., van Laar, M., Vandrey, R., Wadsworth, E., Winstock, A., Hall, W., Curran, H. V., & Freeman, T. P. (2022, Jun). The International Cannabis Toolkit (iCannToolkit): a multidisciplinary expert consensus on minimum standards for measuring cannabis use. *Addiction, 117*(6), 1510-1517. https://doi.org/10.1111/add.15702

McCartney, D., Arkell, T. R., Irwin, C., Kevin, R. C., & McGregor, I. S. (2022, Mar). Are blood and oral fluid Delta(9)-tetrahydrocannabinol (THC) and metabolite concentrations related to impairment? A meta-regression analysis. *Neurosci Biobehav Rev, 134*, 104433. https://doi.org/10.1016/j.neubiorev.2021.11.004

[Record #1640 is using a reference type undefined in this output style.]

Morgan, C. J., Gardener, C., Schafer, G., Swan, S., Demarchi, C., Freeman, T. P., Warrington, P., Rupasinghe, I., Ramoutar, A., Tan, N., Wingham, G., Lewis, S., & Curran, H. V. (2012, Feb). Sub-chronic impact of cannabinoids in street cannabis on cognition,

psychotic-like symptoms and psychological well-being. *Psychol Med, 42*(2), 391-400. https://doi.org/10.1017/S0033291711001322

Newmeyer, M. N., Swortwood, M. J., Taylor, M. E., Abulseoud, O. A., Woodward, T. H., & Huestis, M. A. (2017, Aug). Evaluation of divided attention psychophysical task performance and effects on pupil sizes following smoked, vaporized and oral cannabis administration. *J Appl Toxicol, 37*(8), 922-932. https://doi.org/10.1002/jat.3440

Patrick, M. E., Miech, R. A., Johnston, L. D., & O'Malley, P. M. (2024). *Monitoring the Future Panel Study annual report: National data on substance use among adults ages 19 to 65, 1976-2023* (Monitoring the Future Monograph Series, Issue.

Robinson, S. M., Sobell, L. C., Sobell, M. B., & Leo, G. I. (2014, Mar). Reliability of the Timeline Followback for cocaine, cannabis, and cigarette use. *Psychol Addict Behav, 28*(1), 154-162. https://doi.org/10.1037/a0030992

Sempio, C., Almaraz-Quinones, N., Jackson, M., Zhao, W., Wang, G. S., Liu, Y., Leehey, M., Knupp, K., Klawitter, J., Christians, U., & Klawitter, J. (2022, Apr 21). Simultaneous Quantification of 17 Cannabinoids by LC-MS-MS in Human Plasma. *J Anal Toxicol, 46*(4), 383-392. https://doi.org/10.1093/jat/bkab030

Sempio, C., Campos-Palomino, J., Klawitter. J, Harrison, A., Peters, E. N., MacNair, L., Haghdoost, M., Bonn-Miller, M., Babalonis, S., Huestis, M. A., Christians, U., & Klawitter, J. (2024). LC-MS-MS quantification of Δ8-THC, Δ9-THC, THCV isomers and their main metabolites in human plasma. *J Anal Toxicol., 48*(7), 499-506.

Sharma, P., Murthy, P., & Bharath, M. M. S. (2012). Chemistry, metabolism, and toxicology of cannabis: Clinical implications. *Iran J Psychiatry, 7*(4), 149-156.

Sholler, D. J., Spindle, T. R., Cone, E. J., Goffi, E., Kuntz, D., Mitchell, J. M., Winecker, R. E., Bigelow, G. E., Flegel, R. R., & Vandrey, R. (2022, May 20). Urinary Pharmacokinetic Profile of Cannabidiol (CBD), Delta9-Tetrahydrocannabinol (THC) and Their Metabolites following Oral and Vaporized CBD and Vaporized CBD-Dominant Cannabis Administration. *J Anal Toxicol, 46*(5), 494-503. https://doi.org/10.1093/jat/bkab059

Sobell, L. C., & Sobell, M. B. (1992). *Timeline Follow-Back*. Humana Press.

Spindle, T. R., Cone, E. J., Schlienz, N. J., Mitchell, J. M., Bigelow, G. E., Flegel, R., Hayes, E., & Vandrey, R. (2018, Nov 2). Acute Effects of Smoked and Vaporized Cannabis in Healthy Adults Who Infrequently Use Cannabis: A Crossover Trial. *JAMA Netw Open, 1*(7), e184841. https://doi.org/10.1001/jamanetworkopen.2018.4841

Spindle, T. R., Cone, E. J., Schlienz, N. J., Mitchell, J. M., Bigelow, G. E., Flegel, R., Hayes, E., & Vandrey, R. (2019, May 1). Acute Pharmacokinetic Profile of Smoked and Vaporized Cannabis in Human Blood and Oral Fluid. *J Anal Toxicol, 43*(4), 233-258. https://doi.org/10.1093/jat/bky104

Spindle, T. R., Martin, E. L., Grabenauer, M., Woodward, T., Milburn, M. A., & Vandrey, R. (2021, Jul). Assessment of cognitive and psychomotor impairment, subjective effects, and blood THC concentrations following acute administration of oral and vaporized cannabis. *J Psychopharmacol, 35*(7), 786-803. https://doi.org/10.1177/02698811211021583

Steinhoff, A., Shanahan, L., Bechtiger, L., Zimmermann, J., Ribeaud, D., Eisner, M. P., Baumgartner, M. R., & Quednow, B. B. (2023, Jul). When Substance Use Is Underreported: Comparing Self-Reports and Hair Toxicology in an Urban Cohort of Young Adults. *J Am Acad Child Adolesc Psychiatry, 62*(7), 791-804. https://doi.org/10.1016/j.jaac.2022.11.011

Stout, S. M., & Cimino, N. M. (2014, Feb). Exogenous cannabinoids as substrates, inhibitors, and inducers of human drug metabolizing enzymes: a systematic review. *Drug Metab Rev, 46*(1), 86-95. https://doi.org/10.3109/03602532.2013.849268

Wade, N. E., Baca, R., Courtney, K. E., McCabe, C. J., Infante, M. A., Huestis, M. A., & Jacobus, J. (2021, Jul). Preliminary Evidence for Cannabis and Nicotine Urinary Metabolites as Predictors of Verbal Memory Performance and Learning Among Young Adults. *J Int Neuropsychol Soc, 27*(6), 546-558. https://doi.org/10.1017/S1355617721000205

Wade, N. E., Sullivan, R. M., Tapert, S. F., Pelham, W. E., 3rd, Huestis, M. A., Lisdahl, K. M., & Haist, F. (2023, Jan 2). Concordance between substance use self-report and hair analysis in community-based adolescents. *Am J Drug Alcohol Abuse, 49*(1), 76-84. https://doi.org/10.1080/00952990.2023.2164931

Wade, N. E., Wallace, A. L., Huestis, M. A., Lisdahl, K. M., Sullivan, R. M., & Tapert, S. F. (2024, Mar). Cannabis use and neurocognitive performance at 13-14 Years-Old: Optimizing assessment with hair toxicology in the Adolescent brain cognitive

development (ABCD) study. *Addict Behav, 150*, 107930. https://doi.org/10.1016/j.addbeh.2023.107930

Wille SM, Samyn N, Ramírez-Fernández Mdel M, & G., D. B. (2010). Evaluation of on-site oral fluid screening using Drugwipe-5(+), RapidSTAT and Drug Test 5000 for the detection of drugs of abuse in drivers. *Forensic Sci Int., 198*, 2-6.

Zinka, B., Epple, S., Schick, S., Skopp, G., Graw, M., & Musshoff, F. (2019, Feb). Can a threshold for 11-nor-9-carboxy-Delta(9) -tetrahydrocannabinol in hair be derived when its respective concentration in blood serum indicates regular use? *Drug Test Anal, 11*(2), 325-330. https://doi.org/10.1002/dta.2496