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Detection of Δ^9 -tetrahydrocannabinol (THC) in oral fluid using two point-of-collection testing devices following oral administration of a THC and cannabidiol containing oil

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Abstract

Point-of-collection testing (POCT) devices are widely used in roadside and workplace drug testing to identify recent cannabis use by measuring the presence of Δ^9 -tetrahydrocannabinol (THC) in oral fluid (OF). However, the performance of POCT devices with oral medicinal cannabis products remains poorly described. In a randomised, double-blinded, crossover trial, adults with insomnia disorder ($n = 20$) received a single (2 mL) oral dose of oil containing 10 mg THC + 200 mg cannabidiol, or placebo, prior to sleep. Participants were tested with the Securetec DrugWipe[®] 5S (10 ng/mL THC cut-off) and Dräger DrugTest[®] 5000 (25 ng/mL THC cut-off) POCT devices at baseline (pre-treatment) and then at 0.5, 10, and 18 h post-treatment. An OF sample, taken at each time point, was also analysed using liquid chromatography–tandem mass spectrometry. Large individual variability in OF THC concentrations was observed 0.5 h post-treatment (range: 0–425 ng/mL; mean (SD) 48.7 (107.5) ng/mL). Both the Securetec DrugWipe[®] 5S and DrugTest[®] 5000 demonstrated poor sensitivity to THC at 0.5 h post-treatment (25% and 50%, respectively). At 10 and 18 h post-treatment, all participant OF THC concentrations were below screening cut-offs, and all test results were negative. These findings highlight the relatively poor sensitivity of both devices in detecting recent use of an oral medicinal cannabis product. They also suggest a low probability of obtaining a positive THC result the morning after ('one-off') use. Further research is required to establish the probability of obtaining a positive THC result with regular medicinal cannabis use.

KEYWORDS

cannabis, drug testing, oral fluid, point-of-collection testing, THC

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1 | INTRODUCTION

The increasing legal use of medical and non-medical cannabis products across many jurisdictions raises significant questions around road and workplace safety. The main psychoactive component of cannabis, Δ^9 -tetrahydrocannabinol (THC), can cause intoxication that is characterised by a range of transient effects including sensory, perceptual, and hedonic changes and acute impairment in cognitive and psychomotor performance.^{1–3} This can compromise the performance of safety-sensitive tasks such as driving,² increasing the risk of error, accident, and injury. Accordingly, some jurisdictions and employers have enacted roadside and workplace screening programmes for the presence of THC in drivers and employees. In contrast to THC, the other major cannabinoid found in cannabis, cannabidiol (CBD), is non-intoxicating and does not cause cognitive, psychomotor, or driving impairment, even at very high doses (e.g., 1500 mg).^{2,4}

All jurisdictions in Australia currently prohibit driving with any THC present in blood and oral fluid (OF)—and attempt to identify THC-positive drivers through random *mobile drug testing* (MDT). Patients using legally prescribed THC-containing medicines have no defence against conviction should a positive MDT arise (except in the state of Tasmania).⁵ MDT is performed using fast and non-invasive screening devices often termed point-of-collection testing (POCT) devices. Such devices are also used to identify THC-impaired drivers in Canada⁶ and Europe^{7–10} and are also increasingly used for workplace drug testing. In Australia, MDT involves an initial test for OF THC using the Securetec DrugWipe® (DW) device. If a positive result is obtained, this is followed by a second test using the Dräger DrugTest® 5000 (DT5000). If both POCT tests produce positive results, confirmatory analysis of an OF sample using mass spectrometry techniques is then performed.

Prior studies administering THC via inhalation (e.g., smoking or vaporising cannabis) indicate that both the DW and DT5000 have high specificity (~80–90%; i.e., ability to correctly identify a genuinely negative test result) but relatively poor sensitivity (~25–55%; i.e., ability to correctly identify a genuinely positive test result),^{11,12} particularly as OF THC concentrations begin to decline.^{12–16} Indeed, in one study of inhaled cannabis, the sensitivity of both the DW and DT5000 was the highest at 10 min post-inhalation (68% and 88%, respectively) before dropping to 17% and 50%, respectively, at 1 h post-inhalation.¹² The THC that is present in OF is thought to originate exclusively from contamination of the oral mucosa upon inhalation or oral ingestion of cannabis products, with no transfer of THC from blood into OF.^{17,18} With inhalation, THC rapidly adheres to the oral mucosa resulting in elevated concentrations of THC in OF. The same occurs with oral consumption of edible products (e.g., a cannabis brownie); albeit however, OF THC concentrations tend to be lower compared with inhaled methods.¹⁹ Of note, oral consumption of encapsulated THC (dronabinol)—that does not contaminate the oral mucosa—does not deposit THC in OF.²⁰

A significant issue for patients who use cannabis medicinally by night (i.e., for conditions such as insomnia or chronic pain), and their prescribing physicians, is the possibility of a positive roadside or workplace drug test the following day, even though there is limited

evidence that ‘next day’ impairment occurs.^{21,22} However, there are very limited data available around the sensitivity of POCT devices following oral ingestion of THC-containing products. While several studies have examined the concentration of cannabinoids (and their metabolites) in OF following oral cannabis administration,^{19,23,24} few studies have evaluated POCT device performance following oral administration of THC,¹⁹ with none examining oil-based formulations.

The aim of the current study was to investigate the performance of two commonly used POCT devices in detecting THC in the OF of patients at various time intervals following the administration of a single oral dose of oil containing THC and CBD by night. The performance of the DW and DT5000 testing devices was evaluated against ‘gold standard’ liquid chromatography–tandem mass spectrometry (LC–MS/MS)-quantified OF THC. This was part of a larger study, published elsewhere, investigating the effects of THC/CBD on sleep quality and sleep architecture in insomnia disorder.

2 | METHODS

The protocol of the primary randomized, double-blinded, placebo-controlled, crossover trial has been published elsewhere²¹ and is registered on the Australian New Zealand Clinical Trials Registry (ACTRN12619000714189). The current article summarises the results of the substudy only. This investigation was approved by Bellberry Human Research Ethics Committee (2018-04-284). The study site and sponsor were the Woolcock Institute of Medical Research, a research institute and specialist sleep clinic in Sydney, Australia.

2.1 | Participants

Healthy adults (aged between 25 and 65 years) presenting with insomnia disorder, determined clinically as self-reported difficulty initiating and/or maintaining sleep on more than three nights per week and for >3 months and an Insomnia Severity Index score >15, were recruited. The main exclusion criteria were self-reported use of cannabis in the past 3 months (abstinence confirmed using a urinary drug screen); lifetime major psychiatric illness; history of clinically significant adverse reaction to cannabis; use of any central nervous system (CNS)-active medications including hypnotics in the past 3 months; and active hypertension or cardiovascular disease. Participants were recruited through referral from sleep specialists, online advertisement, and social media (e.g., Facebook and Twitter). All participants were informed about the nature and risk of experimental procedures by the study doctor and the trial coordinator before their written informed consent was obtained.

2.2 | Study procedures

This study included two 24 h overnight treatment sessions that were separated by a washout period ≥ 7 days. Participants were instructed

to abstain from caffeine and alcohol for 24 h prior to each treatment session, and to avoid using illicit drugs (including cannabis) and all CNS-active medications including hypnotics for 3 months prior to and during the trial.

Participants arrived at the research clinic at 16:00 on the afternoon of each treatment session and completed a urinary drug test (DrugCheck® NxStep Onsite Urine Drug Test) and pregnancy test (as applicable; Human Chorionic Gonadotrophin Cassette, Alere™). None of the participants tested positive for any drug (cannabis, amphetamine, methamphetamine, cocaine, and opiates) at the start of either treatment session.

2.3 | Investigational product

The investigational product was a plant-derived oral formulation containing a 1:20 ratio of THC to CBD, that is, 5 mg/mL THC and 100 mg/mL CBD suspended in medium-chain triglyceride oil ('THC/CBD'), manufactured at a Good Manufacturing Practice (GMP)-certified facility (Linnea SA, Lavertezzo, Switzerland). Participants were administered a single fixed dose of THC/CBD (2 mL containing 10 mg THC and 200 mg CBD) or matched placebo (2 mL containing no cannabinoids). Participants were instructed to ingest one peppermint lozenge (Fisherman's Friend Mint; Lofthouse of Fleetwood, England) to mask any possible differences in taste and/or smell. One hour prior to the participant's habitual bedtime, participants were directed to gently push down the plunger of a pre-prepared plastic syringe, administering a 2 mL dose of oil under the tongue before immediately swallowing and drinking a small glass of water. This was to ensure consistency in the administration of the oil as this could affect the distribution of cannabinoids in the oral cavity while minimizing the unpleasant gustatory experience of consuming oil.

2.4 | Randomisation

Each participant was randomly allocated to one of two treatment sequences: (1) THC/CBD–placebo or (2) placebo–THC/CBD using a prepopulated randomisation schedule. The schedule was randomly generated in a 1:1 ratio using a computerised random number generator by the unblinded trial investigator and held in a central location. Identical containers were labelled according to the randomisation schedule by the drug distributor. Neither the unblinded trial investigator nor the drug distributor had any contact with any prospective or enrolled participants. All participants, trial personnel (including study doctors), and the outcome assessors were blinded to the treatment allocation.

2.5 | OF cannabinoid concentrations

OF samples were collected at baseline (pre-treatment) and at 0.5, 10, and 18 h post-drug administration using Quantisal™ collection devices (Immunoassay, Pomona, California, USA). Devices were placed

under the tongue until indicators turned blue, or for a maximum of 10 min, before being placed into the stabilising buffer. Samples were kept at +4°C prior to analysis using LC–MS/MS. OF THC and CBD concentrations appear to be stable under these conditions for at least 90 days,²⁵ and most samples (94%) were analysed within this time frame (range: 5–120 days). Further analytical parameters, including limits of detection and lower limits of quantification, are provided in the Supporting Information and Table S1.

2.6 | DW5S and DT5000

The DrugWipe 5S (DW5S) (Securetec, Neubiberg, Germany) detects cannabis, opiates, cocaine, and (meth)amphetamines. The DW5S had a manufacturer-specified detection limit of 10 ng/mL THC. The DW5S device has two small sampling pads which collect OF (approximately 10–20 µL). Participants were instructed to run their tongue around the inside of their mouth in a circular motion three times before slowly gliding the sampling pads from the middle of their tongue to the tip. The sampling pad was then attached to the device, and the test was performed as per the manufacturer's instructions. A positive test was indicated by the appearance of a red line (even if the test line only underwent a slight or incomplete colour change).

The DT5000 (Drägerwerk AG & Co., Lübeck, Germany) detects cannabis, opiates, (meth)amphetamines, methadone, ketamine, and benzodiazepines. The DT5000 had a manufacturer-specified detection limit of 25 ng/mL THC. Although authorities in Australia have not revealed the screening cut-off used in current MDT, it is thought that a cut-off of 25 ng/mL THC may be in use, in line with recommendations from the Canadian Society of Forensic Sciences Drugs and Driving Committee.²⁶ A 25 ng/mL THC cut-off negates the possibility of individuals testing positive to THC as a result of passive exposure (which tends to be lower than the screening cut-off).^{27–29} The test consists of a test cassette (with a sampling pad) and an analytical instrument. Participants were instructed to wipe the sampling pad around the inside of their cheeks and across their gums until sufficient OF had been collected (indicated by the appearance of a blue line or after 4 min). The test cassette was then inserted into the analysing instrument with the results (nonnegative, negative, or invalid) printed on paper.

A researcher read and filed the test results for both devices at baseline (pre-treatment) only. To maintain the blind, a staff member independent of the study team who had no direct contact with the participants read and filed all remaining timepoints post-treatment. The results were only made available to the study team upon completion of the study. OF was sampled using the Quantisal collection device, DW5S, and DT5000 at the same time in quick succession.

2.6.1 | Data analysis

Results of the DW5S and DT5000 tests were classified as previously described³⁰: (a) a *true positive* (TP) was a positive test result that was

TABLE 1 Oral fluid (OF) Δ^9 -tetrahydrocannabinol (THC) concentrations and corresponding THC test result on the Securetec DrugWipe® 5S (DW5S; cut-off 10 ng/mL) and Dräger DrugTest® 5000 (DT5000; cut-off 25 ng/mL) devices.

	Placebo				THC/CBD			
	OF concentration (ng/mL)		Securetec DW5S result	Dräger DT5000 result	OF concentration (ng/mL)		Securetec DW5S result	Dräger DT5000 result
	THC	CBD			THC	CBD		
Baseline								
1	<LOQ	<LOQ	NEG	NEG	<LOQ	<LOQ	NEG	NEG
2	<LOQ	<LOQ	NEG	NEG	<LOQ	<LOQ	NEG	–
3	<LOQ	<LOQ	NEG	NEG	<LOQ	<LOQ	NEG	–
4	<LOQ	<LOQ	NEG	NEG	<LOQ	<LOQ	NEG	NEG
5	<LOQ	<LOQ	NEG	NEG	<LOQ	<LOQ	NEG	NEG
6	<LOQ	<LOQ	NEG	NEG	<LOQ	<LOQ	NEG	NEG
7	<LOQ	<LOQ	NEG	NEG	<LOQ	<LOQ	NEG	NEG
8	<LOQ	<LOQ	NEG	NEG	<LOQ	<LOQ	NEG	NEG
9	<LOQ	<LOQ	NEG	NEG	<LOQ	<LOQ	NEG	NEG
10	–	–	–	–	–	–	–	–
11	–	–	–	–	–	–	–	–
12	–	–	–	–	–	–	–	–
13	<LOQ	<LOQ	NEG	NEG	–	–	–	–
14	<LOQ	<LOQ	NEG	NEG	<LOQ	<LOQ	NEG	NEG
15	<LOQ	<LOQ	POS	NEG	<LOQ	<LOQ	NEG	NEG
16	<LOQ	<LOQ	NEG	NEG	<LOQ	<LOQ	NEG	NEG
17	<LOQ	<LOQ	NEG	NEG	<LOQ	<LOQ	NEG	NEG
18	<LOQ	<LOQ	NEG	NEG	<LOQ	<LOQ	NEG	NEG
19	<LOQ	<LOQ	NEG	NEG	<LOQ	<LOQ	NEG	NEG
20	<LOQ	<LOQ	NEG	NEG	<LOQ	<LOQ	NEG	NEG
0.5 h post-treatment								
1	<LOQ	<LOQ	NEG	NEG	80.62	1228.3	NEG	POS
2	<LOQ	<LOQ	NEG	NEG	48.61	885.3	NEG	–
3	<LOQ	<LOQ	NEG	NEG	<LOQ	1019.8	NEG	–
4	<LOQ	<LOQ	NEG	NEG	5.01	152.9	NEG	NEG
5	<LOQ	<LOQ	NEG	NEG	425.17	2636.0	NEG	POS
6	<LOQ	<LOQ	NEG	NEG	5.00	140.2	NEG	NEG
7	<LOQ	<LOQ	NEG	NEG	<LOQ	9.1	NEG	NEG
8	<LOQ	<LOQ	NEG	NEG	3.49	74.4	NEG	NEG
9	<LOQ	<LOQ	NEG	NEG	21.37	533.2	NEG	POS
10	–	–	–	–	–	–	–	–
11	–	–	–	–	–	–	–	–
12	–	–	–	–	–	–	–	–
13	<LOQ	<LOQ	NEG	NEG	–	–	–	–
14	<LOQ	<LOQ	NEG	NEG	5.28	162.4	NEG	NEG
15	<LOQ	<LOQ	NEG	NEG	1.73	42.0	POS	NEG
16	<LOQ	<LOQ	NEG	NEG	11.50	293.6	POS	NEG
17	<LOQ	<LOQ	NEG	NEG	68.20	1965.0	NEG	–
18	<LOQ	<LOQ	NEG	NEG	44.50	975.6	NEG	NEG
19	<LOQ	<LOQ	NEG	NEG	29.10	785.7	POS	NEG
20	<LOQ	<LOQ	NEG	NEG	2.72	46.2	NEG	NEG
10 h post-treatment								
1	<LOQ	<LOQ	NEG	NEG	4.3	16.6	NEG	NEG

TABLE 1 (Continued)

	Placebo				THC/CBD			
	OF concentration (ng/mL)		Securetec DW55 result	Drager DT5000 result	OF concentration (ng/mL)		Securetec DW55 result	Drager DT5000 result
	THC	CBD			THC	CBD		
2	<LOQ	<LOQ	NEG	NEG	<LOQ	117.7	NEG	—
3	<LOQ	<LOQ	NEG	NEG	<LOQ	9.8	NEG	—
4	<LOQ	<LOQ	NEG	NEG	<LOQ	40.7	NEG	NEG
5	<LOQ	<LOQ	NEG	NEG	9.4	221.0	NEG	NEG
6	<LOQ	<LOQ	NEG	NEG	5.29	79.1	NEG	NEG
7	<LOQ	<LOQ	NEG	NEG	<LOQ	13.8	NEG	NEG
8	<LOQ	<LOQ	NEG	NEG	0.4	11.3	NEG	NEG
9	<LOQ	<LOQ	NEG	NEG	2.2	47.4	NEG	NEG
10	—	—	—	—	—	—	—	—
11	—	—	—	—	—	—	—	—
12	—	—	—	—	—	—	—	—
13	<LOQ	<LOQ	NEG	NEG	—	—	—	—
14	<LOQ	<LOQ	NEG	NEG	3.4	31.8	NEG	NEG
15	<LOQ	<LOQ	NEG	NEG	<LOQ	12.2	NEG	NEG
16	<LOQ	<LOQ	NEG	NEG	1.1	12.3	NEG	NEG
17	<LOQ	<LOQ	NEG	NEG	2.9	7.3	NEG	NEG
18	<LOQ	<LOQ	NEG	NEG	2.6	92.4	NEG	NEG
19	<LOQ	<LOQ	NEG	NEG	3.4	57.6	NEG	NEG
20	<LOQ	<LOQ	NEG	NEG	<LOQ	7.3	NEG	NEG
18 h post-treatment								
1	<LOQ	<LOQ	NEG	NEG	<LOQ	7.1	NEG	NEG
2	<LOQ	<LOQ	NEG	NEG	<LOQ	<LOQ	NEG	—
3	<LOQ	<LOQ	NEG	NEG	<LOQ	<LOQ	NEG	—
4	<LOQ	<LOQ	NEG	NEG	<LOQ	<LOQ	NEG	NEG
5	<LOQ	<LOQ	NEG	NEG	<LOQ	31.8	NEG	NEG
6	<LOQ	<LOQ	NEG	NEG	<LOQ	4.30	NEG	NEG
7	<LOQ	<LOQ	NEG	NEG	<LOQ	<LOQ	NEG	NEG
8	<LOQ	<LOQ	NEG	NEG	<LOQ	<LOQ	NEG	NEG
9	<LOQ	<LOQ	NEG	NEG	<LOQ	1.7	NEG	NEG
10	—	—	—	—	—	—	—	—
11	—	—	—	—	—	—	—	—
12	—	—	—	—	—	—	—	—
13	<LOQ	<LOQ	NEG	NEG	—	—	—	—
14	<LOQ	<LOQ	NEG	NEG	<LOQ	<LOQ	NEG	NEG
15	<LOQ	<LOQ	NEG	NEG	<LOQ	<LOQ	NEG	NEG
16	<LOQ	<LOQ	NEG	NEG	<LOQ	1.1	NEG	NEG
17	<LOQ	<LOQ	NEG	NEG	<LOQ	1.3	NEG	NEG
18	<LOQ	<LOQ	NEG	NEG	<LOQ	2.5	NEG	NEG
19	<LOQ	<LOQ	NEG	NEG	<LOQ	2.1	NEG	NEG
20	<LOQ	<LOQ	NEG	NEG	<LOQ	<LOQ	NEG	NEG

Note: Bolded text indicates a positive THC test result. Shaded grey area with a dash ‘—’ indicates missing value, that is, either a missing liquid chromatography–tandem mass spectrometry–quantified THC value or point-of-collection testing device test result (nine DT5000 tests could not be completed: eight due to temporary malfunction of the DT5000 analytical instrument and one produced an invalid result and could not be repeated due to time constraints), all omitted from the evaluation of point-of-collection testing device performance.

Abbreviations: CBD, cannabidiol; LOQ, limit of quantification; NEG, negative, OF, oral fluid; POS, positive.

subsequently confirmed by LC-MS/MS (i.e., confirmed value on LC-MS/MS \geq confirmatory cut-off AND positive result obtained); (b) a *true negative* (TN) was a negative test result which was confirmed by LC-MS/MS (i.e., confirmed value $<$ confirmatory cut-off AND negative result obtained); (c) a *false positive* (FP) was a positive test result which was not confirmed by LC-MS/MS (i.e., confirmed value $<$ confirmatory cut-off AND positive result obtained); and (d) a *false negative* (FN) was a negative test result that was not confirmed by LC-MS/MS (i.e., confirmed value \geq confirmatory cut-off AND negative result obtained).

The confirmatory cut-off of 10 ng/mL THC was used for the DW5S and 25 ng/mL for the DT5000 (equivalent to the respective screening cut-offs for each device). Sensitivity $[\text{TP} / (\text{TP} + \text{FN})] * 100$, specificity $[\text{TN} / (\text{TN} + \text{FP})] * 100$, and accuracy $[(\text{TP} + \text{TN}) / (\text{TP} + \text{TN} + \text{FP} + \text{FN})] * 100$ were also calculated. Given that the cut-offs used for confirmatory analysis by police in MDT procedures are typically much lower than the screening cut-offs, these parameters were also calculated relative to THC cut-offs of 2 ng/mL (THC limit of quantification [LOQ]) and 1 ng/mL (THC lower limit of detection).

3 | RESULTS

3.1 | Participants

Twenty adults (16 female; median [SD] age, 46.1 [8.6] years) with insomnia disorder completed all treatment sessions between August 2019 and October 2021. The majority (75%) had either never tried cannabis or had less than 10 lifetime exposures to cannabis. All participants had not used cannabis in the last 3 months. All participants provided negative urinary drug screens (50 ng/mL THC-COOH screening cut-off) on the start of each treatment session.

3.2 | OF cannabinoid concentrations

Table 1 presents the OF THC and CBD concentrations for each participant alongside the corresponding test result on the DW5S and DT5000. Table 2 presents the average OF THC and CBD concentrations after

placebo and THC/CBD treatment. OF THC concentrations were determined for 132 samples; the remaining 28 samples (obtained from four participants) were unable to be analysed due to LC-MS/MS instrument failure with insufficient viable sample remaining for reanalysis.

3.3 | POCT device performance

Table 3 presents the overall performance (sensitivity, specificity, and accuracy) of both devices. The device performance characteristics when a 2 and 1 ng/mL confirmatory cut-off was applied are described in Table S2.

All OF samples collected prior to oral administration of a 10 mg THC + 200 mg CBD oil, or placebo, were negative for THC ($<$ LOQ) (Table 1). However, the DW5S device (cut-off 10 ng/mL) produced one FP result.

At 0.5 h post-treatment, 8 out of 16 OF samples contained THC concentrations above the DW5S device cut-off of 10 ng/mL; however, only two OF samples produced a TP test result (25% sensitivity). Notably, six OF samples containing the highest concentrations of THC (range, 44–425 ng/mL) were FNs. At 0.5 h post-treatment, the DW5S test device produced one confirmed FP (1.7 ng/mL THC). With the DT5000 device, 4 out of 13 OF samples contained THC above the DT5000 device cut-off of 25 ng/mL, and two of these (80 and 425 ng/mL THC) produced a TP test result (50% sensitivity). Another (false) positive test result showed a THC concentration of 21 ng/mL, close to the cut-off. The two FN test results on the DT5000 contained 29 and 44 ng/mL THC.

At 10 and 18 h post-treatment, all participant OF THC concentrations were below screening cut-offs on both devices, and all corresponding POCT test results were negative. With a 10 ng/mL confirmatory cut-off applied, the overall sensitivity, specificity, and accuracy of the DW5S were calculated as 25%, 98%, and 94%, respectively. Increasing the confirmatory cut-off to 2 and 1 ng/mL had a negligible effect on the number of FPs but substantially increased the number of FNs (Table S2). With a 25 ng/mL confirmatory cut-off, the overall sensitivity, specificity, and accuracy of the DT5000 device were calculated as 50%, 100%, and 98%, respectively. Fewer FPs and more FNs were observed with confirmatory cut-offs of 2 and 1 ng/mL (Table S2).

	OF THC concentration (ng/mL)		OF CBD concentration (ng/mL)	
	Placebo	THC/CBD	Placebo	THC/CBD
BL	<LOQ	<LOQ	<LOQ	<LOQ
+0.5 h	<LOQ	48.7 (107.5) [<LOQ–425.2]	<LOQ	694.4 (785.7) [<LOQ–2636]
+10 h	<LOQ	2.2 (2.7) [<LOQ–9.4]	<LOQ	48.6 (59.1) [<LOQ–221]
+18 h	<LOQ	<LOQ	<LOQ	3.3 (8.1) [<LOQ–31.8]

TABLE 2 Mean (SD) oral fluid (OF) concentrations at baseline and 0.5, 10, and 18 h after placebo and Δ^9 -tetrahydrocannabinol/cannabidiol (THC/CBD) treatment.

Abbreviations: BL, baseline (pre-treatment); LOQ, limit of quantification.

TABLE 3 Performance characteristics of the Securetec DrugWipe® 5S (DW5S; 10 ng/mL confirmatory cut-off) and Dräger DrugTest® 5000 (DT5000; 25 ng/mL confirmatory cut-off) point-of-collection testing devices when verified against liquid chromatography–tandem mass spectrometry quantified oral fluid Δ^9 -tetrahydrocannabinol concentrations.

Device	Time relative to drug administration (h)	N of tests	True positives	True negatives	False positives	False negatives	Sensitivity (%)	Specificity (%)	Accuracy (%)
DW5S	BL	33	0	32	1	0	-*	97	97
	+0.5 h	33	2	24	1	6	25	96	79
	+10 h	33	0	33	0	0	-*	100	100
	+18 h	33	0	33	0	0	-*	100	100
	Total	132	2	122	2	6	25	98	94
DT5000	BL	31	0	31	0	0	-*	100	100
	+0.5 h	30	2	25	1	2	50	96	90
	+10 h	31	0	31	0	0	-*	100	100
	+18 h	31	0	31	0	0	-*	100	100
	Total	123	2	118	1	2	50	100	98

Note: '-*' Sensitivity could not be ascertained as there were no true positives. Abbreviation: BL, baseline (pre-treatment).

4 | DISCUSSION

The present study evaluated the performance of two commonly used POCT devices in detecting THC in the OF of patients at various time intervals following oral administration of a THC and CBD-containing oil by night. Both POCT devices performed relatively poorly soon after drug administration (0.5 h post-treatment), yielding an array of FP and FN results. The next day, however, when OF THC concentrations were greatly reduced, both devices performed more accurately, with no FP or FN tests observed ≥ 10 h post-treatment. Overall, these findings show the relatively poor sensitivity of these two devices at short time intervals following oral consumption of a cannabis oil and indicate a low probability of obtaining a positive MDT result the morning after (≥ 10 h) a single evening dose of cannabis oil in individuals who infrequently use cannabis.

A striking observation, particularly with the DW5S given the stated manufacturer cut-off of 10 ng/mL, was the fact that these devices largely failed to detect recent use of an oral THC/CBD-containing product despite mean (SD) OF THC concentrations of 48.7 (107.5) ng/mL. The limited sensitivity at short time intervals (i.e., 0.5 h post-treatment) is problematic and may result in inaccurate detection of recent cannabis use. Of note, a recent study has shown that CBD (isolate) does not appear to cross-react with THC on POCT testing devices and does therefore not pose a risk for consumers using CBD-only products.³⁰

We observed major interindividual variability in OF THC concentrations, consistent with previous studies involving both inhaled and oral routes of administration. For example, Arkell et al.¹² reported OF THC concentrations ranging from 19 to 1318 ng/mL 10 min after vaporising cannabis containing ~ 13.75 mg THC in infrequent cannabis users. In another study, Spindle et al.³¹ reported OF THC concentrations ranging from ~ 11 to 414 ng/mL 12 min after oral administration of a 'brownie' containing 10 mg THC to non-current cannabis users. In the present study, OF THC concentrations ranged from <LOQ to

425.2 ng/mL at 0.5 h following oral administration of 10 mg THC (in combination with 200 mg CBD) in infrequent cannabis users. These highly variable results likely reflect the interindividual differences in the contact and distribution of cannabinoids in the oral cavity with both inhaled and oral routes of administration.^{13,16} Another relevant factor in previous studies is varying frequency of cannabis use (occasional vs. regular use) across participants which can lead to different baseline THC concentrations in OF prior to any drug administration.¹³ Other potential variables relating to OF collection include dry mouth (common side effect of cannabis/THC), OF collection volume, and individual differences in OF composition. It is important to bear in mind that interindividual variability in OF THC concentrations could be further magnified under 'real world' conditions where treatment administration is not standardised.

OF THC concentrations after consumption of orally ingested cannabis products tend to be lower than following inhaled routes.¹³ For instance, lower mean OF THC concentrations were observed after oral consumption of a cannabis brownie (202 [65–380] ng/mL) compared with smoked (837 [81–5914] ng/mL) or vaporised (545 [7.6–3278] ng/mL) cannabis, all doses ~ 50.6 mg THC.¹³ There may be lower overall exposure with oral intake due to swallowing causing less contamination of the oral cavity than inhaled methods, preservation of THC inside the edible or oil matrix (less dispersal of THC in the oral cavity), and lack of decarboxylation of tetrahydrocannabinolic acid to THC. Interestingly, the 'window of detection' with POCT devices appears to be even shorter following oral administration than with inhaled methods, with concentrations quickly falling below confirmatory cut-offs. This appears problematic from a safety perspective given that cognitive and psychomotor impairment typically peaks several hours following use of orally ingested cannabis products.³

On the day following drug administration (>10 h post-treatment), all OF samples had THC concentrations lower than the screening cut-off on the POCT devices, and all corresponding POCT test results were

negative. Clearly, OF THC concentrations were not high enough to elicit a positive test result ≥ 10 h after a single oral dose of a THC/CBD-containing oil in individuals who infrequently use cannabis. Research into the cognitive and psychomotor effects of THC likewise suggests that oral THC-induced impairment typically subsides within ~ 8 h (after ≤ 20 mg THC).^{3,22} As such, individuals who consume cannabis at night are unlikely to be impaired the next day (> 8 h post-treatment) and so a negative POCT THC result is generally an appropriate outcome.

The major strengths of the current study include use of a randomised, double-blinded, placebo-controlled study design with a pharmaceutical-grade cannabis product conducted in participants who were closely monitored over 24 h in a secure facility. A limitation of our study was that participants were only administered a single dose. Moreover, most of the participants infrequently used cannabis, and none had used cannabis in the past 3 months. In reality, medicinal cannabis patients are likely to use cannabis products on a regular (i.e., nightly) basis, and it is possible that this could produce different OF THC concentrations to those observed here. Indeed, one study observed longer persistence of THC in OF in frequent cannabis smokers compared with occasional cannabis smokers after a ≥ 96 h abstinence period (i.e., THC was detected in 55.6% frequent smokers' and in no occasional smokers' OF).¹⁹ Overall, caution is advisable in generalising these results to individuals who regularly use cannabis including those who administer their cannabis-based medication in small doses, several times a day. Future studies could usefully explore OF THC concentrations with repeated dosing of oral cannabis/THC products and determine whether composition of the oral product (e.g., edibles and oil- or ethanol-based liquid) influence the degree of THC contamination in the oral cavity.

5 | CONCLUSIONS

We evaluated the performance of two commonly used POCT devices, DW5S and DT5000, against LC-MS/MS-quantified OF THC concentrations following controlled oral administration of 10 mg THC (in combination with 200 mg CBD) oil and placebo. The DT5000 device performed somewhat better than the DW5S device; however, there was overall high risk for FP and FN results at short intervals after oral administration (0.5 h post-treatment) in the face of high variability in OF THC concentrations across participants. The next day (10 and 18 h post-treatment), both devices accurately produced negative results reflecting the fact that all samples had THC concentrations lower than the screening cut-offs on the POCT devices at these time points. Overall, these findings indicate a low probability of obtaining a positive THC result the next day after evening consumption of an oral cannabis oil containing 10 mg THC (in combination with 200 mg CBD) in individuals who infrequently use cannabis. However, these results cannot necessarily be generalised to those who regularly use THC or cannabis, including medicinal cannabis patients. Regular users may accumulate residual THC in OF, leading to higher baseline readings and an increased risk of obtaining a positive THC result with commonly used POCT devices.

CONFLICT OF INTEREST STATEMENT

I. S. M. is the Academic Director of the Lambert Initiative for Cannabinoid Therapeutics, a philanthropically funded research programme at the University of Sydney. He has served as an expert witness in various medicolegal cases involving cannabis and has received consulting fees from Medical Cannabis Industry Australia (MCIA) and Janssen. He currently acts as an advisor/consultant to Kinosis Therapeutics, Psylo, and Emyria. He reports research grants and salary support from the Australian National Health and Medical Research Council (NHMRC) and from Lambert Initiative for Cannabinoid Therapeutics. He is an inventor on patents WO2018107216A1 and WO2017004674A1, licensed to Kinosis Therapeutics involving use of novel small molecules (noncannabinoid) to treat addictions and social deficits. I. S. M. also has patents WO2020102857A1 and WO2021042178A1 related to use of small molecules (noncannabinoid) for treating weight gain and opioid withdrawal, as well as patents WO2019227167 and WO2019071302 issued, which relate to cannabinoid therapeutics. A. S. was supported by the Australian Government Research Training Program (RTP) and the Vice-Chancellor's Research Scholarship (VCRS) at the University of Sydney. A. S. has received consulting fees from the Medical Cannabis Industry Australia (MCIA). C. M. H. (APP1104003) was supported by R. R. G. and is funded by a NHMRC Investigator Grant, and C. M. H. is funded by a National Heart Foundation Future Leader Fellowship. R. R. G. was supported by an NHMRC Senior Principal Research Fellowship (APP1106974). All other authors have no competing financial or non-financial interests to declare. The investigational product was purchased from BOD Australia who were not involved in the conception or design of this study, data analysis (with no access to the data), or the decision to publish. All other commercially available equipment was purchased.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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