



## RESEARCH ARTICLE

# Orally administered cannabidiol does not produce false-positive tests for $\Delta^9$ -tetrahydrocannabinol on the Securetec DrugWipe<sup>®</sup> 5S or Dräger DrugTest<sup>®</sup> 5000

Danielle McCartney<sup>1,2,3,4</sup>  | Richard C. Kevin<sup>1,2,3</sup>  | Anastasia S. Suraev<sup>1,2,3,4</sup> | Christopher Irwin<sup>5</sup> | Ronald R. Grunstein<sup>4,6,7</sup> | Camilla M. Hoyos<sup>2,3,4</sup> | Iain S. McGregor<sup>1,2,3</sup>

<sup>1</sup>Lambert Initiative for Cannabinoid Therapeutics, University of Sydney, Sydney, New South Wales, Australia

<sup>2</sup>Brain and Mind Centre, University of Sydney, Sydney, New South Wales, Australia

<sup>3</sup>Faculty of Science, School of Psychology, University of Sydney, Sydney, New South Wales, Australia

<sup>4</sup>Centre for Sleep and Chronobiology, Woolcock Institute of Medical Research, University of Sydney, Sydney, New South Wales, Australia

<sup>5</sup>Menzies Health Institute Queensland, School of Health Sciences and Social Work, Griffith University, Gold Coast, Queensland, Australia

<sup>6</sup>Royal Prince Alfred Hospital, Sydney, New South Wales, Australia

<sup>7</sup>Faculty of Medicine and Health, Central Clinical School, University of Sydney, Sydney, New South Wales, Australia

## Correspondence

Danielle McCartney, Lambert Initiative for Cannabinoid Therapeutics, University of Sydney, Camperdown, Sydney, NSW, Australia 2050.

Email: danielle.mccartney@sydney.edu.au

## Abstract

Many jurisdictions use point-of-collection (POC) oral fluid testing devices to identify driving under the influence of cannabis, indexed by the presence of  $\Delta^9$ -tetrahydrocannabinol (THC), an intoxicating cannabinoid, in oral fluid. Although the use of the non-intoxicating cannabinoid, cannabidiol (CBD), is not prohibited among drivers, it is unclear whether these devices can reliably distinguish between CBD and THC, which have similar chemical structures. This study determined whether orally administered CBD produces false-positive tests for THC on standard, POC oral fluid testing devices. In a randomised, double-blind, crossover design, healthy participants ( $n = 17$ ) completed four treatment sessions involving the administration of either placebo or 15-, 300- or 1500-mg pure CBD in a high-fat dietary supplement. Oral fluid was sampled, and the DrugWipe<sup>®</sup>-5S (DW-5S; 10 ng·ml<sup>-1</sup> THC cut-off) and Drug Test<sup>®</sup> 5000 (DT5000; 10 ng·ml<sup>-1</sup> THC cut-off) devices administered, at baseline (pretreatment) and ~20-, ~145- and ~185-min posttreatment. Oral fluid cannabinoid concentrations were measured using ultra-high performance liquid chromatography–tandem mass spectrometry. Median (interquartile range [IQR]) oral fluid CBD concentrations were highest at ~20 min, quantified as 0.4 (6.0), 15.8 (41.6) and 167 (233) ng·ml<sup>-1</sup> on the 15-, 300- and 1500-mg CBD treatments, respectively. THC, cannabinol and cannabigerol were not detected in any samples. A total of 259 DW-5S and 256 DT5000 tests were successfully completed, and no THC-positive tests were observed. Orally administered CBD does not appear to produce false-positive (or true-positive) tests for THC on the DW-5S and DT5000. The likelihood of an individual who is using a CBD (only) oral formulation being falsely accused of DUI therefore appears low.

## KEYWORDS

cannabidiol, cannabis, drug driving, oral fluid, point-of-collection testing

## 1 | INTRODUCTION

Cannabidiol (CBD) is a non-intoxicating cannabinoid found in the *Cannabis sativa* plant.<sup>1</sup> CBD has demonstrated considerable therapeutic potential at oral doses of ~300–1500 mg<sup>2</sup> and is increasingly being prescribed for the treatment of anxiety, epilepsy, pain and other conditions.<sup>3</sup> The use of non-prescription CBD has also become common in Europe and North America where low-dose 'nutraceuticals' (e.g., oils, capsules, topicals and edibles, often containing ~10–20 mg·ml<sup>-1</sup>) can be purchased over the counter.<sup>4</sup> Unlike the other major plant-derived cannabinoid,  $\Delta^9$ -tetrahydrocannabinol (THC),<sup>5,6</sup> CBD does not appear to impair cognitive function or induce intoxication.<sup>6,7</sup> Thus, although most jurisdictions worldwide have enacted legislation restricting THC use in conjunction with driving (i.e., *driving under the influence of cannabis* [DUIC]),<sup>8</sup> CBD use is not typically prohibited among drivers.

Although they are distinct chemical entities with differing pharmacological profiles, CBD is structurally related to THC with the latter being a transannular cyclisation product of the former.<sup>9</sup> THC, however, has a relatively flat and rigid fused tricyclic structure whereas CBD has a bicyclic core with an 'out-of-plane' geometry for the two rings.<sup>9</sup> Nevertheless, their chemical similarity is such that there may be some risk of CBD being mistakenly identified as- (i.e., cross-reactive with-) THC on rapid drug tests that use less-specific structure-dependent analytical methods (e.g., lateral flow immunoassays). This includes the point-of-collection (POC) oral fluid testing devices used by authorities to identify DUIC.<sup>10,11</sup>

POC oral fluid testing devices are currently used to identify DUIC in a number of countries including Norway, Germany, Belgium and Australia.<sup>12</sup> In Australia, this process is known as *mobile drug testing* and typically involves an initial test for THC in oral fluid using the Securetec DrugWipe<sup>®</sup> (DW). If positive, a second test may be performed using the Dräger DrugTest<sup>®</sup> 5000 (DT5000). If both devices yield positive results, confirmatory analyses are later completed on a stored oral fluid sample using more sophisticated mass spectrometry techniques. Recent studies have shown that although the DW-5S has high specificity (i.e., can distinguish between THC and placebo) ( $\geq 92\%$ ), its sensitivity (45%–51%) and accuracy (68%–79%) are poor.<sup>12,13</sup> Some, although not all, studies have also found the sensitivity (40%–100%<sup>12–14</sup>), specificity (71%–100%<sup>13–16</sup>) and accuracy (56%–90%<sup>12,13</sup>) of the DT5000 to be poor (ranges include data obtained at a screening cut-off  $\leq 10$  ng·ml<sup>-1</sup> and confirmatory cut-off  $\geq 1$  ng·ml<sup>-1</sup>, only<sup>12–19</sup>). Whether these devices, which use lateral flow immunoassay technology,<sup>10,11</sup> can effectively distinguish between different cannabinoids with similar molecular structures is, however, unclear.

The aim of the current study was to determine whether acute, oral CBD treatment at doses of 15, 300 and 1500 mg produces false-positive tests for THC on two standard, POC oral fluid testing devices: the DW-5S and DT5000. The study was conducted within another randomised controlled trial (RCT) investigating the effects of CBD on driving performance.<sup>20</sup>

## 2 | METHODS

The protocol of the parent RCT has been published elsewhere<sup>20</sup> and registered on the Australia and New Zealand Clinical Trials Registry (ACTRN12619001552178). The current article summarises the sub-study only. This investigation was approved by the University of Sydney's Human Research Ethics Committee (2019/474).

### 2.1 | Participant population

Participants were healthy males and females aged between 18 and 65 years who had not used cannabis in the last 3 months. Individuals were informed of the study requirements and risks before providing written informed consent. The full eligibility criteria and details of the recruitment and screening processes are published elsewhere.<sup>20</sup>

### 2.2 | Study design

Participants completed four treatment sessions involving the oral administration of either placebo, or 15-, 300- or 1500-mg CBD. Treatment order was randomised as described elsewhere<sup>20</sup> and double-blind. Sessions were separated by a washout period  $\geq 7$  days. Individuals were instructed to avoid using illicit drugs (including cannabis) throughout their involvement and to adhere to strict standardisation procedures (e.g., restricting alcohol and caffeine consumption) prior to each treatment session (see McCartney et al.<sup>20</sup> for further details).

### 2.3 | Experimental procedures

Participants arrived at the laboratory between 07:00 AM and 09:00 AM on the morning of each session and verbally acknowledged compliance to the standardisation procedures; they also completed a urine drug screen (DrugCheck<sup>®</sup> NxStep Onsite Urine Test Cup) to verify abstinence from illicit drugs.

The DW-5S and DT5000 POC oral fluid testing devices were administered at baseline (pretreatment) and on three occasions thereafter: ~20-, 145- and 185-min posttreatment. Separate oral fluid samples were also collected at these time points (as described below). The order of sample collection was (1) DW-5S; (2) DT5000; and (3) oral fluid. To maintain the blind, neither the participant nor researchers with whom they had direct contact were informed of the test results or of the measured oral fluid cannabinoid concentrations until the study had concluded.

### 2.4 | Study treatments

The investigational product (GD Cann<sup>®</sup>-C; GD Pharma Pty Ltd, Norwood, Australia) was an oral formulation of synthetic CBD (100 mg·ml<sup>-1</sup>) dissolved in medium chain triglyceride (MCT) oil. It was

administered in different volumes providing either 15, 300 or 1500 mg of CBD. Each dose was made up to a total equivalent volume of 15.0 ml via the addition of placebo (MCT) oil and administered (orally) in a high-fat supplement (100 ml; 50 g fat) (Calogen<sup>®</sup>, Nutricia, Macquarie Park, Australia) alongside a standardised breakfast. Neither treatment contained any other minor cannabinoids or terpenes/terpenoids. The intent of the high-fat supplement was to increase CBD's bioavailability in the parent RCT.<sup>21,22</sup>

## 2.5 | Data collection

### 2.5.1 | Oral fluid cannabinoid concentrations

Oral fluid (~1 ml) was collected using the Quantisal<sup>®</sup> Collection Device (Immunalysis Corporation, Pomona, CA, USA). Participants placed the cellulose collection pad under their tongues for between ~2 and 10 min until the indicator turned completely blue (all turned blue within 10 min); the pad was then transferred into the plastic tube containing the preservative buffer and stored at +4°C until analysis. Oral fluid THC and CBD concentrations appear to be 'stable' (i.e., remain within 20% of baseline levels) under these conditions for at least 90 days,<sup>23</sup> and most samples (81%) were analysed within this timeframe (range: 3–120 days).

Oral fluid CBD, THC, cannabinol (CBN) and cannabigerol (CBG) concentrations were measured using ultra-high performance liquid chromatography–tandem mass spectrometry (UHPLC–MS/MS). Briefly, cannabinoids were extracted from 400- $\mu$ l Quantisal-buffered oral fluid in triplicate via supported liquid extraction (Biotage Isolute 400- $\mu$ l capacity 96 well plates), using 700- $\mu$ l dichloromethane and 900- $\mu$ l methyl *tert*-butyl ether sequentially as extraction solvents. Extracted samples were dried under a gentle stream of nitrogen and reconstituted in a 1:1 mixture of 0.1% formic acid in water and acetonitrile for UHPLC–MS/MS analysis.

Cannabinoids were identified and quantified on a Shimadzu Nexera UHPLC equipped with an Agilent Zorbax XDB-C18 analytical column (2.1  $\times$  50 mm, 3.5- $\mu$ m particle size), coupled with a Shimadzu 8040 triple-quadrupole mass spectrometer operated in positive electrospray ionisation mode with multiple reaction monitoring. Gradient elution was performed using a mixture of (A) 0.1% formic acid in water and (B) acetonitrile, at a total flow rate of 0.6 ml/min and a column oven temperature of 50°C. Mobile phase composition was initially set 50% B where it was held for 1.5 min, before increasing to 75% B at 2.75 min and held until 4.75 min, followed by a final increase to 95% B at 5.25 min before re-equilibration at 50% B for a total run-time of 6 min. Accuracy, precision, linearity and sensitivity were assessed using Food and Drug Administration (FDA) guidelines for bioanalytical method validation.<sup>24</sup> Each analyte was quantified against a 7-point standard curve with deuterated internal standards ( $d_3$ -THC and  $d_3$ -CBD) used to account for matrix effects. Low, medium, and high-concentration quality control (QC) samples were added to each plate to ensure sufficient accuracy (100  $\pm$  15%) and precision (relative standard deviation <15%). Positive analyte

identification required a retention time match to analytical reference material together with correct ion transitions (one quantifier and one qualifier transition per analyte). Further analytical parameters, including limits of detection and lower limits of quantification are provided in Table S1.

### 2.5.2 | Securetec DrugWipe<sup>®</sup> 5S (DW-5S) and Dräger DrugTest<sup>®</sup> 5000 (DT5000)

The Securetec DrugWipe<sup>®</sup> 5S (DW-5S) detects cannabis (THC at concentrations >10 ng·ml<sup>-1</sup>), opiates, cocaine and (meth)amphetamines. Participants were instructed to circle the inside of their mouths with their tongue three times before gently wiping the collection pad from the centre-middle of their tongue to the tip. The pad was then attached to the device and the test performed as per the manufacturer's instructions.

The Dräger DrugTest<sup>®</sup> 5000 (DT5000) detects cannabis, opiates, (meth)amphetamines, methadone, ketamine and benzodiazepines. The limit of detection can be set to 5, 10 or 25 ng·ml<sup>-1</sup> THC; this study used a mid-range limit (10 ng·ml<sup>-1</sup>) comparable with that of the DW-5S as the authorities have not published the cut-offs used during mobile drug testing in Australia. Participants were instructed to move the collection pad around the inside of their mouths for between for ~1–4 min until the indicator turned blue. The pad was then inserted into the device and the test performed as per the manufacturer's instructions. Both of these devices generated qualitative results (i.e., positive, negative and invalid).

## 2.6 | Data analysis

The results of the DW-5S and DT5000 drug tests were classified as *true positive* (a positive drug test confirmed by a UHLC–MS/MS THC concentration less than or equal to the limit of quantification [LOQ]), *true negative* (a negative drug test confirmed by a UHLC–MS/MS THC concentration <LOQ), *false positive* (a positive drug test accompanied by a UHLC–MS/MS THC concentration <LOQ) or *false negative* (a negative drug test accompanied by a UHLC–MS/MS THC concentration  $\geq$ LOQ) based on the UHLC–MS/MS quantified oral fluid THC concentrations and a LOQ of 0.25 ng·ml<sup>-1</sup> THC. Data are presented as median (interquartile range [IQR]) unless otherwise stated.

## 3 | RESULTS

### 3.1 | Participants

Nineteen participants were initially randomised in this study. However, one was unable to complete all four treatment sessions within the 60-day (drug expiration) period due a suspension on face-to-face research during the SARS-CoV-2 pandemic and another had

detectable levels of 11-COOH-THC in plasma at baseline indicating that she had not abstained from cannabis as instructed (data reported elsewhere<sup>25</sup>). Both individuals were removed from the final sample. The characteristics of the 17 remaining participants are summarised in Table 1.

### 3.2 | Oral fluid cannabinoid concentrations

Oral fluid cannabinoid concentrations were determined for 240 samples (60 treatment sessions); the remaining 32 samples (obtained over eight treatment sessions: two each on the 1500- and 300-mg CBD treatments, three on the 15-mg CBD treatment and one on the placebo) were excluded because QC samples in those (two) batches failed to meet accuracy requirements; that is, the measured CBD concentration of the QC differed from the normative value by >15% (and there was insufficient sample remaining for reanalysis).

Oral fluid CBD concentrations are presented in Table 2 and Figure 1; CBD was not detected in oral fluid on the placebo trial or at baseline (pretreatment). THC, CBN and CBG were not detected in any samples, including those that did not meet accuracy requirements.

**TABLE 1** Participant characteristics

Characteristic	Participants (n = 17)
Sex (M/F) (n)	10/7
Age (years)	27.9 (7.0)
Weight (kg)	67.4 (23.0)
Body mass index (kg·m <sup>-2</sup> )	22.0 (4.3)
Lifetime cannabis exposures (n)	
≤10 uses	6
>10 uses	10
No use	1
Time since last cannabis use (n)	
3–6 months	3
6–12 months	5
1–2 years	3
2–4 years	2
>4 years	3
Lifetime CBD exposures (n)	
≤10 uses	1
>10 uses	2
No use	14
Time since last CBD use (n)	
3–6 months	0
6–12 months	2
1–2 years	1
2–4 years	0
>4 years	0

Note: Values are n, Median (IQR) and frequency (n) as appropriate. Abbreviations: CBD, cannabidiol; F, females; M, males.

Median (IQR) oral fluid CBD concentrations were highest ~20-min posttreatment, quantified as <LOQ, 0.4 (6.0), 15.8 (41.6) and 167 (233) ng·ml<sup>-1</sup> on the placebo and the 15-, 300- and 1500-mg CBD treatments, respectively.

### 3.3 | Securetec DrugWipe® 5S (DW-5S)

There were 259 DW-5S tests successfully completed (Table 3): 61 at baseline, 51 post-placebo, 48 post-15-mg CBD, 48 post-300-mg CBD and 51 post-1500-mg CBD. The remaining 13 tests could not be completed as there were insufficient DW-5S devices (awaiting shipment). No positive tests for THC (or any other substances) were observed (100% true negative).

### 3.4 | Dräger DrugTest® 5000 (DT5000)

There were 256 DT5000 tests successfully completed (Table 3): 65 at baseline, 45 postplacebo, 48 post-15-mg CBD, 50 post-300-mg CBD and 48 post-1500-mg CBD. Fifteen tests could not be completed due to technical difficulties (broken down DT5000 device); the remaining test produced an invalid result. No positive tests for THC (or any other substances) were observed (100% true negative).

## 4 | DISCUSSION

CBD did not produce any false-positive (or true-positive) tests for THC on the DW-5S or DT5000 when administered orally at doses of 15, 300 and 1500 mg in the current investigation. This suggests that the POC oral fluid testing devices used by authorities to identify DUI are able to distinguish between THC and CBD, despite their structural similarities.

Mobile drug testing is a major concern for medicinal cannabis patients in Australia: individuals using legal medicinal cannabis products are not exempt from roadside testing and will be charged if THC is detected in their oral fluid.<sup>26</sup> Around one-quarter of medicinal cannabis patients in Australia currently use CBD-dominant products<sup>3</sup> and may be anxious about the prospect of returning a THC-positive test, despite being on a low-THC or THC-free product. The current results therefore provide some reassurance that THC-positive roadside tests are unlikely to occur when CBD-only products are used.

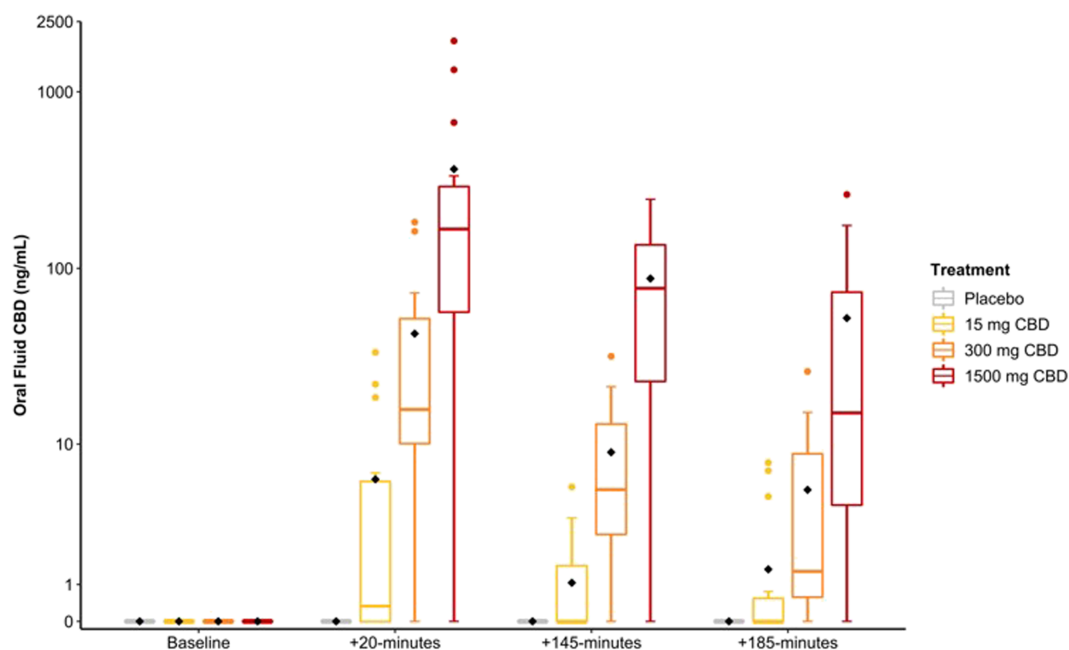
Although no previous studies appear to have determined whether POC oral fluid testing devices can distinguish between different cannabinoids, some relevant, albeit non-peer reviewed, data should be noted. First, Dräger states that the DT5000 is sensitive to CBD—but only at high (likely unattainable) concentrations (i.e., ≥90 000 ng·ml<sup>-1</sup>).<sup>10</sup> A second report states that the DW-5S is not sensitive to CBD at concentrations ≤10 000 ng·ml<sup>-1</sup>.<sup>27</sup> These reports should be interpreted with caution as the methods used to evaluate the DT5000 are not described, and the study of the DW-5S did not involve human participants (i.e., oral fluid samples were

**TABLE 2** Oral fluid CBD concentrations at baseline and ~20-, ~145- and ~185-min posttreatment on the placebo and the 15-, 300- and 1500-mg CBD treatments

	Oral fluid CBD concentrations (ng·ml <sup>-1</sup> )			
	Placebo	15-mg CBD	300-mg CBD	1500-mg CBD
Baseline	<LOQ	<LOQ	<LOQ	<LOQ
+20 min	<LOQ	0.4 (6.0)	15.8 (41.6)	167 (233)
+145 min	<LOQ	<LOQ (1.6)	5.4 (10.2)	77.0 (112)
+185 min	<LOQ	<LOQ (0.6)	1.4 (8.1)	15.1 (68.7)

Note: All values are median (IQR).

Abbreviations: CBD, cannabidiol; LOQ, limit of quantification.

**FIGURE 1** Oral fluid cannabidiol (CBD) concentrations at baseline and ~20-, ~145- and ~185-min posttreatment. Grey: placebo; yellow: 15-mg CBD; orange: 300-mg CBD; and red: 1500-mg CBD. The black diamond represents the mean value [Colour figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]**TABLE 3** Total number of Securetec DrugWipe® 5S (DW-5S) and Dräger DrugTest® 5000 (DT5000) drug tests performed under each treatment at each time point

	Placebo	15-mg CBD	300-mg CBD	1500-mg CBD
DW-5S				
Baseline	16	16	15	14
+20 min	17	16	16	17
+145 min	17	16	16	17
+185 min	17	16	16	17
DT5000				
Baseline	16	16	17	16
+20 min	15	16	17	16
+145 min	15	16	16	16
+185 min	15	16	17	16

Note: All values are *n*. The DW-5S and DT5000 were administered at baseline (pretreatment) and on three occasions thereafter, ~20-, ~145- and ~185-min posttreatment.

Abbreviation: CBD, cannabidiol.

collected, 'spiked' with varying amounts of CBD and then applied to the device). However, the current results appear to substantiate their claims indicating that CBD does not produce false-positive tests for THC at physiologically relevant concentrations.

There are several caveats to this research. First, it is important to recognise that the current investigational product comprised of CBD in MCT oil, only. Some 'full spectrum' prescription medications and over-the-counter nutraceutical products also contain small amounts of THC (e.g., ~2.0 mg per 100 mg of CBD) and therefore have the potential to elicit true-positive tests on POC oral fluid testing devices. The only study that appears to have measured oral fluid THC concentrations after a 'low', oral dose of THC (i.e., <10 mg) found these rarely exceeded 10 ng·ml<sup>-1</sup> at a dose of 5 mg ( $C_{\max} = 6.0 [0.8-12.7]$  ng·ml<sup>-1</sup>; mean [range]).<sup>28</sup> Oral CBD formulations containing small amounts of THC therefore appear unlikely to elicit (true-)positive tests on POC oral fluid testing devices. That said, the same investigation<sup>28</sup> also observed low oral fluid THC concentrations at a dose of 15 mg ( $C_{\max} = 1.6 [0.7-20.5]$  ng·ml<sup>-1</sup>)—much lower than those reported with 10 mg of THC (oral) in other studies (i.e.,  $C_{\max} > 100$  ng·ml<sup>-1</sup>).<sup>29,30</sup> Further research is therefore required to confirm the likelihood of these formulations eliciting true-positive tests for THC on POC oral fluid testing devices.

Second, it is important to recognise that the current route of administration (i.e., oral ingestion) may produce lower oral fluid CBD concentrations than other methods; namely, inhalation. Indeed, a  $C_{\max}$  of 506 [15-2935] ng·ml<sup>-1</sup>; ~3-fold higher than the highest concentration observed in the current study (20-min post-1500-mg CBD: 167 [0-1942] ng·ml<sup>-1</sup>), has previously been observed following vapourisation of CBD (13.75 mg).<sup>12</sup> Some research also suggests that smoking and vapourisation produce higher oral fluid THC concentrations than oral ingestion.<sup>31</sup> Individuals inhaling relatively low doses of CBD (e.g., one 'light cannabis' cigarette may contain ~60-mg CBD<sup>32</sup>) could therefore achieve higher oral fluid CBD concentrations than observed in the current study—and it is unclear whether these have greater potential to elicit false-positive tests for THC on POC oral fluid testing devices.

Third, it is possible that the high-fat supplement (in which the CBD was administered; see Section 2.4 'Study treatments') reduced the amount of contact between CBD and the oral mucosa in the current study. Oral fluid CBD concentrations might therefore have been lower than otherwise observed if CBD had been administered in a small volume of MCT oil, only. Indeed, CBD's presence in oral fluid is believed to result from contamination of the oral cavity during administration (rather than the transfer from blood).<sup>33</sup> That said, it is difficult to predict whether the supplement affected oral fluid CBD concentrations as few studies appear to have measured these after oral CBD administration (i.e., providing reference data).

One final observation to note is that no oral fluid samples collected in the current study contained detectable levels of THC, CBN or CBG. Indeed, although a small amount of *in vitro* research suggests that CBD can undergo conversion to THC with prolonged exposure to simulated gastric fluid (e.g., 3-20 h),<sup>34,35</sup> several *in vivo* studies have failed to detect THC in human plasma,<sup>36,37</sup> the blood of rodents and

minipigs<sup>38,39</sup> and the small intestine and stomach of minipigs<sup>38</sup> following CBD treatment (sometimes at high doses, e.g., 700 mg·day<sup>-1</sup> for 30 days<sup>36</sup>). The current data add to this body of evidence providing further confirmation that CBD is unlikely to convert to THC, CBN or CBG in oral fluid.

## 5 | CONCLUSION

This study suggests that orally administered CBD is unlikely to elicit false-positive (or true-positive) tests for THC on the DW-5S or DT5000 POC oral fluid testing devices. The likelihood of an individual who is using a CBD (only) oral formulation being falsely accused of DUIC therefore appears low. However, further research is required to determine whether inhaled CBD and CBD formulations containing small amounts of THC have the potential to elicit positive tests.

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## DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

## ORCID

Danielle McCartney  <https://orcid.org/0000-0002-7783-5220>

Richard C. Kevin  <https://orcid.org/0000-0002-4912-4499>

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## SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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