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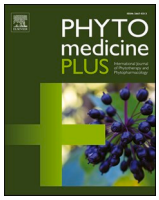

Cure-All cannabidiol? The cannabidiol content of commercial products

Michaela Mouton, Minja Gerber, Frank Van der Kooy *

Centre of Excellence for Pharmaceutical Sciences (Pharmacen™), North-West University, Private Bag X6001, Potchefstroom 2520, South Africa

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ABSTRACT

Background: The recent easing of regulations around the world regarding *Cannabis sativa* and its main active compounds, such as cannabidiol (CBD), led to an explosion in the number of over-the-counter consumer products. The number of product types is surpassed by the vast quantity of products of each type, but even this is exceeded by the associated health claims which range from the benign, such as 'fighting inflammation', to the completely asinine such as 'fighting the tyranny of the urgent' or 'shedding light on your inner darkness'. Any health claim should in the first instance be supported by the product containing the correct actives at the correct dosage.

Purpose: The purpose of this study was to test a diverse range of commercially available product types including soft drinks, honey, coffee, oils, gummy bears, chocolate, etc. that claim to contain CBD and compare the results to their label claims.

Study design: Forty commercially available products were extracted and quantitatively analyzed.

Methods: Extraction efficiency for all product types was conducted over a 1 h period using acetonitrile and ultrasonication. Samples were taken every five min and analyzed using a validated HPLC method. All products were then extracted in triplicate using the applicable extraction time and quantitatively analyzed.

Results: Fifteen min of sonication was found to be adequate for the oils and drinks samples. The honey, chocolate and gummies samples required initial dissolution in water followed by extraction with acetonitrile. The remaining products required sonication of 45 min. It was found that only three products (7.5 %) contained CBD levels within 90–110 % of their label claim. Two products had trace amounts of delta-9-tetrahydrocannabinol and some of the products were completely devoid of CBD.

Conclusion: Mislabeling is of serious concern and this study shows that the problem not only includes problems with the content of CBD, but also regarding the chemical properties such as containing "water-soluble CBD" while it is insoluble in water, and the diverse number of health claims that in some cases have no foundation in reality. This highlights not only the lax attitude of producers but also of the regulatory authorities in ensuring the consistent quality of these products.

Introduction

The use of cannabidiol (CBD) containing products has gained interest in recent years since it has been legalized in many countries. In 2019, the World Health Organization (WHO) also proposed several changes be made when cannabis preparations do not contain the psychoactive compound, Δ^9-tetrahydrocannabinol (Δ^9-THC) since CBD is not intoxicating and has little evidence that it is of a public health concern (McGregor et al., 2020).

Since legalization and the recommendations by the WHO were made, a vast array of CBD products has been produced and can be purchased in almost all health stores. Various product types are available including cosmetics, personal hygiene products, edibles, oils, vaporizer products, veterinary products, and a large number of health products making an equally large number of (low-level) health claims. There has been a marked increase in the popularity of these CBD products, devoid of the psychoactive compound Δ^9-THC, for its purported health benefits to such an extent that the market was valued at $3.67 billion in 2021 vs only $2.8 billion in 2020 and is expected to grow at a compounded annual rate of 47.5 % from 2022 to 2028 (Fortune Business Insights,

Abbreviations: ACN, acetonitrile; CBD, cannabidiol; CBDA, cannabidiolic acid; FDA, Food and Drug Administration; WHO, World Health Organization; Δ^9-THC, Δ^9-tetrahydrocannabinol; Δ^9-THCA, Δ^9-tetrahydrocannabinolic acid; U.A.E, United Arab Emirates,.

* Corresponding author at: Center of Excellence for Pharmaceutical Sciences, North-West University, Private Bag X6001, Potchefstroom, 2520, South Africa.
E-mail address: frank.vanderkooy@nwu.ac.za (F. Van der Kooy).

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2021).

Many users of these products consider it as a cure-all medication, which is mainly attributed to poor consumer education (Zenone et al., 2021). One of the problems that has come to light is the many misleading and false claims regarding the health benefits of CBD products. Even though CBD is considered safe, these misleading claims can potentially lead to some consumers, who suffer from serious ailments, not getting the correct medication or treatment that they need (FDA, 2019; FDA 2020a).

With this rapidly increasing interest in CBD-containing products, the need for proper regulations as well as quality control of these products has become essential. For example, in a recent study, 80 CBD products were tested, and it was shown that Δ^9-THC was detected above the legal limit in 52 of these products (Johnson et al., 2022a). In another study, 25 commercially available products were tested for Δ^9-THC and CBD and only three products were close to the label claim, 13 products contained less than 50 % of the label claim, three products had Δ^9-THC levels that exceeded 0.3 % and one product consisted of 45 % Δ^9-THC (Gurley et al., 2020). Most of the non-prescription products have a relatively low CBD daily dose, varying from 10 to 50 mg or 50–100 mg/ml in concentration. These doses were found to be therapeutically suboptimal in clinical trials (Miller et al., 2020). Currently, in the United States of America, CBD is regulated through intended use. Since CBD is a natural product biosynthesized by *Cannabis sativa* L. (Cannabaceae) it is regulated as either hemp or marijuana and is categorized as such based on the Δ^9-THC content. Products that are derived from hemp, which is defined in the Agricultural Marketing Act as a cannabis plant that contains less than 0.3 % Δ^9-THC, are legal to sell, however, products that are derived from marijuana are illegal to buy, sell or possess unless under a Schedule I license (Li et al., 2021). In 2018, the Food and Drug Administration (FDA) approved the drug Epidiolex for the treatment of seizures in Lennox-Gastaut syndrome and Dravet syndrome and it was also approved for treatment in tuberous sclerosis complex in 2020 (FDA, 2018, 2020b).

In South Africa, Δ^9-THC is still regarded as an illicit substance unless it is found in registered medications for therapeutic use, whereupon it is regarded as a schedule 6 substance that can be obtained with a valid prescription. Products that are processed from cannabis seeds may not contain more than 0.001 % of Δ^9-THC and are regarded as industrial hemp. CBD is listed as a Schedule 4 or Schedule 0 substance depending on whether it adheres to the following regulations: the maximum total amount of CBD per sales pack is 600 mg and the maximum daily dose of CBD is set out to be 20 mg with acceptable low-level health claims. For preparations that are derived from processed cannabis plant material

Table 1
Categories of CBD products, dosages and country of origin.

Product ID	Claimed CBD per dose (mg)	Dose (mL)	Δ^9-THC content claim	Lab tested	Country of origin
Oils					
1	8.30	1.00	No claim	Yes	USA
2	10.00	1.00	Δ^9-THC free	Yes	RSA
3	20.00	1.00	No claim	No	RSA
4	2.50	0.75	No claim	No	RSA
5	16.70	1.00	No claim	No	USA
6	10.00	1.00	Δ^9-THC free	No	USA
7	6.00	1.00	No claim	No	RSA
8	6.00	1.00	No claim	No	RSA
9	10.00	1.00	No claim	No	RSA
10	nas	nas	No claim	No	Spain
11	5.00	0.50	No claim	No	RSA
12	6.25	1.00	No claim	No	RSA
13	50.00*	1.00*	Δ^9-THC free	No	Spain
14	nas	nas	No claim	No	Spain
15	19.99	1.00	Δ^9-THC free	Yes	RSA
16	nas	nas	No claim	No	Spain
Topicals					
17	nas	nas	Δ^9-THC free	No	RSA
18	15.00	8.00	No claim	No	Netherlands
19	nas	nas	No claim	No	RSA
20	nas	nas	No claim	No	Dubai
21	nas	nas	No claim	No	RSA
Drinks					
22	5.00	50.00	Δ^9-THC free	No	RSA
23	5.00	50.00	No claim	No	RSA
24	5.00	15.00	Δ^9-THC free	No	RSA
25	5.00	7.00	No claim	No	RSA
26	10.00	300.00	No claim	No	RSA
27	5.00	500.00	No claim	No	RSA
28	6.00	300.00	No claim	No	RSA
29	6.00	300.00	No claim	No	RSA
30	20.00	100.00	Δ^9-THC free	No	RSA
31	20.00	100.00	Δ^9-THC free	No	RSA
32	20.00	100.00	Δ^9-THC free	No	RSA
33	5.00	1.00	No claim	No	RSA
Other					
34 Sachet	10.00	1.00 g	No claim	No	RSA
35 Honey	5.00	5.00 g	No claim	No	RSA
36 Coffee	20.00	5.00 g	No claim	No	RSA
37 Chocolate	20.00	50.00 g	Δ^9-THC free	No	Indonesia
38 Coffee	4.00	10.00 g	Δ^9-THC Free	No	RSA
39 Gummies	20.00	5.00 g	No claim	No	USA
40 Capsules	5.00	1 capsule	No claim	No	RSA

nas = no amount stated.
* = total CBD mg/mL.

and only contain the number of cannabinoids that are naturally present in the source material, the final product may not exceed 0.001 % of Δ^9-THC and a total of 0.0075 % CBD (Viviers et al., 2021).

Since the change in legislation in 2018, the South African market has been flooded with different CBD-containing products. The aim of this study was to test a variety of commercially available products to determine if the CBD content correlates with the label claim and test for the presence\absence of Δ^9-THC. This study was conducted due to various other international studies that have shown discrepancies between the products' label claims and the actual CBD content (Gurley et al., 2020; Johnson et al., 2022a). This may lead to further evidence for the need for stricter legislation regarding the quality control of CBD-containing products.

Material and methods

Product selection and categorization

All CBD products were purchased at local retail stores in South Africa of which 29 were produced in South Africa and the remaining 11 in the USA (4), Spain (4), U.A.E. (1), the Netherlands (1) and Indonesia (1) (Table 1). Products were selected based on claims of CBD content which included products that were listed as containing "hemp", "*Cannabis sativa* seed" and "Cannabis Extract". No duplicate products were analyzed; however, products from the same manufacturer were included. Upon arrival, all products were inspected for packaging integrity to ensure all products received were in original packaging and not tampered with. All products were given a unique product ID. The purchased products were categorized based on product type namely, "Oils", "Drinks", "Topicals" and "Other". All products were stored as per labelled storage instructions and products that did not provide labeling instructions, were stored at room temperature away from direct light.

Sample preparation

Products were subjected to extraction testing over a 1-hour period. This was conducted after it was observed that the honey sample immediately solidified upon the addition of acetonitrile (ACN) risking encapsulating CBD which might lead to the inadequate extraction of the target analyte. ACN was added to all product types and sonicated for one hour with 2 ml samples taken every 5 min for analysis to determine the optimal time of extraction. Products such as honey (35), chocolate (37), and gummies (39) did not dissolve fully in ACN even after sonication for 100 min. These products were first dissolved in water (50 ml), sonicated for 15 min after which the same volume of ACN was added followed by sonication for another 15 min.

Products 1–16 (oils – 1 ml each) and 22–33 (drinks – 10 ml each) were extracted with ACN (100 ml), followed by 15 min of sonication. The samples were filtered with a 0.45 μm syringe filter into HPLC vials and diluted to a concentration range that falls within the calibration curve based on the product's label claim (Laanet et al., 2022). Products 17–21 (topicals – 0.5 g each) and products 34, 36, 38 and 40 (0.5 g each) were extracted with ACN but sonicated for 45 min. Products 34–40 were weighed before extraction and dilution to ensure the correct amount of product was diluted. All products were prepared in triplicate.

Analytical procedures

A Shimadzu iNexera LC-2040C system consisting of a quaternary pump, solvent degasser, autosampler, column oven, and photodiode array detector was used. A validated chromatographic analytical method was used with separation achieved with a Zorbax Eclipse Plus C_{18} column (2.1 × 50 mm, 1.8 μm), with 0.1 % formic acid (A) and ACN containing 0.1 % formic acid (B) used as the mobile phase. Gradient elution was used and started at 65 % B for 2 min, increased to 100 % B at 2.5 min, and was kept at 100 % until 4.5 min, the system then returned to 65 % until 7.5 min to allow for re-equilibration. The flow rate was set at 0.4 ml/min and the column oven at 40 °C, the autosampler at 6 °C, and the injection volume was 2 μL. The detection and quantification of the cannabinoids were conducted at 210 nm for CBD and Δ^9-THC and 221 nm for CBDA and THCA (Mouton et al., 2023).

Confirmation of the presence/absence of Δ^9-THC was conducted using the more sensitive Agilent Ultivo triple-quadrupole mass spectrometer consisting of a 1260 Infinity II autosampler, 1200 quaternary pump, column oven and the Ultivo TQ. A Multiple reaction monitoring method for Δ^9-THC was developed and the MRM transition of 315.2 to 77.1 *m/z* was used for quantification (MS settings; fragmentor voltage 96 V, collision energy 77 V, Gas temperature 325 °C, Gas flow 13 L/min, nebulizer pressure 45 psi and capillary voltage 5000 V). The chromatographic system was the same as described above.

Reference standards of 1,000 μg/ml in ACN were purchased from LCG standards (London, UK). The reference standards and their dilutions were stored in vials that were wrapped in Parafilm®, protected from light, and stored at −20 °C. Water was obtained from a Rephile direct Ultrapure & RO Lab water system (Boston, MA, US). HPLC grade methanol, ACN, and formic acid were purchased from Sigma-Aldrich (Johannesburg, RSA). The calibration standards were a mixture solution containing CBD, cannabidiolic acid (CBDA), Δ^9-THC, and Δ^9-tetrahydrocannabinolic acid (Δ^9-THCA). This was prepared with an initial concentration of 200 μg/ml in ACN, and serially diluted to obtain seven concentrations of: 50.00, 25.00, 12.50, 6.25, 3.13, 1.56 and 0.78 μg/ml. Calibration standards were prepared fresh before analysis.

Results and discussion

Extraction efficiency

All product types were tested for extraction efficiency over a 1 h period. Fig. 1 provides the CBD concentration curve at different times using 50 % ACN as the extraction solvent. It is clear that the sugary content of chocolate, honey and gummies played a significant role in reducing the extraction efficiency of ACN. For these product types, it seems essential to first dissolve the product in water after which ACN is added to extract the hydrophobic CBD. The oils and drinks were adequately extracted using ACN and sonication for 10–15 min whereas the topicals and products 34, 36, 38 and 40 required sonication of 45 min for adequate extraction (**Fig. S1** - Supplementary material).

Assessment of labeling accuracy

Products were assessed on their labeling accuracy, and this was determined by the United States Pharmacopeia products purity guidance, which sets the acceptable range for the labeling of products as ±10 %. Products were classified as over-labeled <90 %, under-labeled >110 % and correctly labeled, 90–110 % (Table 2) (Allen et al., 2014).

Oils

Of the 16 samples tested in this category, sample 13 had the highest claimed amount of CBD per ml (50 mg/ml). However, this was also the product with the biggest variation by having 98.43 % less CBD than claimed. Product 14 was produced by the same manufacturer and clearly states that it consists of "essential CBD oil blends". However, the amount of CBD is not stated, and no detectable levels of CBD could be measured. Products 7–9 were produced by the same company with product 7 claiming to be a CBD "Oil Isolate", product 8 a CBD oil "Broad Spectrum", and product 9 "Full Spectrum". A broad-spectrum CBD product is generally produced from hemp extracts with selective removal of Δ^9-THC, whilst the other minor cannabinoids are retained. While full-spectrum CBD products may still contain up to 0.3 % Δ^9-THC and other minor cannabinoids after processing, CBD isolates (product 7) are supposed to only contain CBD. Both broad and full spectrum

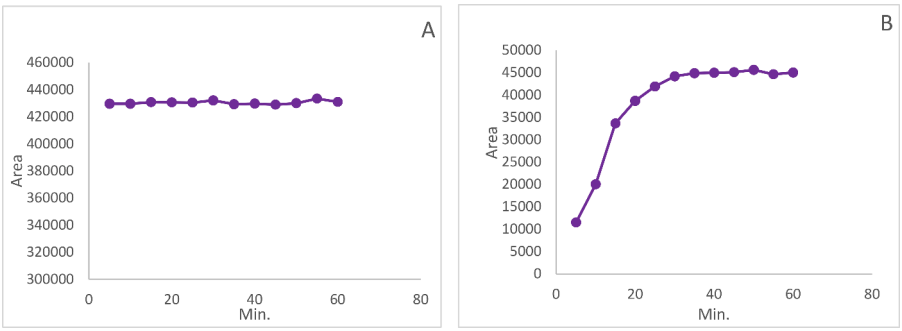

Fig. 1. Extraction efficiency of dissolving Honey (A) and chocolate (B) in water followed by extraction with ACN.

Table 2
CBD product test results.

Sample ID	Claimed concentration (μg/mL)	Measured concentration (μg/mL ± SD)	Product concentration variation (μg/mL)	% Deviation from label claim	% Recovery
Oils					
1	41.29	45.05 ± 1.55	3.76	+9.09	109.01
2	39.84	33.42 ± 0.61	6.42	−16.11	83.71
3	41.58	39.44 ± 0.80	3.11	−5.15	94.65
4	33.00	49.31 ± 0.67	16.31	+49.42	149.18
5	41.57	43.86 ± 1.80	2.29	+5.51	105.35
6	39.84	50.79 ± 1.10	10.95	+27.48	126.71
7	20.00	11.42 ± 0.08	8.57	−42.83	57.09
8	20.00	16.11 ± 0.08	3.81	−19.06	80.74
9	33.33	17.03 ± 0.07	16.31	−48.92	50.93
10	nas	<LOD	na	na	na
11	33.33	18.37 ± 0.08	14.96	−44.88	55.18
12	31.25	5.23 ± 0.02	26.02	−83.26	16.73
13	41.67	0.66 ± 0.02	41.01	−98.43	1.57
14	nas	<LOD	na	na	na
15	33.33	24.08 ± 0.07	0.04	−27.74	72.14
16	nas	<LOD	na	na	na
Topicals					
17	nas	1.57 ± 0.03	1.57	na	na
18	50.68	0.78 ± 0.01	49.89	−98.29	1.54
19	50.15	24.15 ± 0.08	26.00	−51.84	48.15
20	2609.73	<LOD	na	na	na
21	44.63	<LOD	na	na	na
Drinks					
22	20.00	11.02 ± 0.11	8.98	−44.89	55.01
23	20.00	2.77 ± 0.05	17.23	−86.13	13.87
24	16.67	14.56 ± 0.05	2.10	−12.61	87.15
25	1.85	1.55 ± 0.01	0.30	−16.24	5.28
26	11.11	2.04 ± 0.05	9.07	−81.63	18.21
27	2.50	0.09 ± 0.02	2.41	−96.55	62.25
28	5.00	1.69 ± 0.04	3.31	−66.21	33.25
29	5.00	1.54 ± 0.05	3.46	−69.10	30.39
30	10.00	0.43 ± 0.03	9.57	−95.73	4.22
31	10.00	5.19 ± 0.05	4.81	−48.07	51.75
32	10.00	5.18 ± 0.04	4.82	−42.83	51.50
33	16.67	1.32 ± 0.01	15.35	−92.09	7.91
Other					
34 Sachet	50.00	15.70 ± 0.05	34.3	−68.58	31.41
35 Honey	38.46	18.75 ± 0.06	19.7	−51.19	48.77
36 Coffee	50.77	<LOD	na	−100.00	na
37 Chocolate	16.53	3.67 ± 0.01	12.85	−77.78	22.21
38 Coffee	20.05	7.19 ± 0.08	12.86	−64.12	35.88
39 Gummies	50.77	<LOD	na	−100.00	na
40 Capsules	50.00	42.11 ± 0.09	7.89	−15.77	84.22

nas = no amount stated.
na = not applicable.
LOD = limit of detection.

products can still contain some of the distinctive terpenes (Berthold et al., 2023). However, when looking at the chromatogram of these 3 products there is not much of an observable difference between the Oil Isolate and the Broad Spectrum with similar peaks arising on both chromatograms (Fig. 2). Only three products out of 16 in this category were within the range of 90–110 %, two of which are produced in USA and one in South Africa. Eight products were over-labeled and one product under-labeled. Three products did not state the amount of CBD and did not have any detectable amount of CBD.

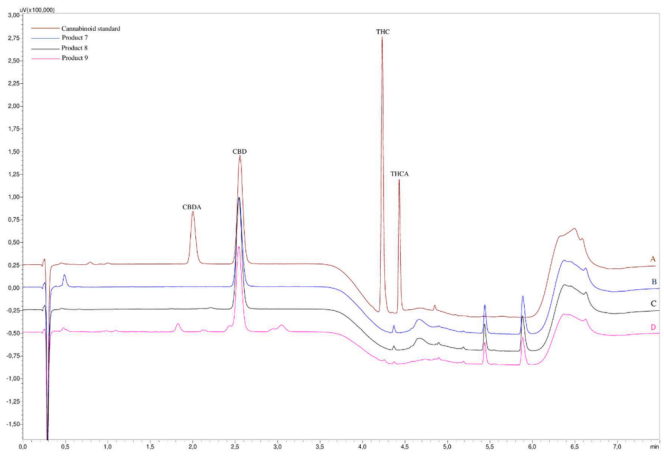

Fig. 2. Overlayed chromatograms from top to bottom; Cannabinoids reference standards, product 7–9.

Topicals

This category had a total of five products. Product 18 is sold as a face-mask, and states that it was clinically proven as an "anti-aging ingredient". This product had 98.29 % less CBD than stated on the packaging. Product 20 is of interest because the label claim states that it contains 10 000 mg CBD hemp oil. The ingredient list claims that this product consists of "*Cannabis sativa* leaf extract", however, no CBD could be detected. The very distinctive odor of *C. sativa* could also not be sensed by five colleagues and hence, this product is unlikely to contain any *C. sativa* extract. Product 21 is marketed as a CBD lip balm but contains no labeling nor any indication regarding a CBD concentration and no CBD was detected.

Drinks

Twelve products were tested in this category. None of the products fell within the 90–110 % range stated by the USP; however, this was the only group where all products were over-labeled. Product 27 showed a deviation of 96.55 % compared to the label claim. These products all had relatively low concentrations, which implies that they would probably not have therapeutic benefits when the CBD daily dose is taken into consideration (Millar et al., 2019).

Products 22–25 (10–50 ml volumes) are all marketed as CBD shots that the consumer is supposed to consume in entirety. Product 22 claims to contain 5 mg CBD in one serving size but only contains approximately 2.76 mg. Product 23 claims to help with "energy and focus" and also contains 5 mg CBD per 50 ml but contains 86.13 % less than claimed. Product 24 states that CBD has "15 x more bioavailability" and also that this product is a calming shot. This product was found to have the least variation in this group with the product containing only 12.61 % less CBD than claimed. All the products in this category are water-based and due to the low aqueous solubility of CBD, it might explain the far lower concentrations detected in all the products.

Other

This category had a total of seven products, which included CBD-containing coffee, honey, capsules, gummy bears as well as sachets. Six of the seven products were over-labeled, and 1 product was under-labeled. Product 34 is sold as "water-soluble CBD sachets". However, when this product was prepared in water, sonicated, and filtered no CBD could be detected. By extracting with ACN, CBD could be quantified, and the amount deviated 68.58 % from the label claim. Product 35 was a CBD honey, which is said to help with "general well-being and immunity". This product was over-labeled and had 51.19 % less CBD than stated on the label claim. Two products contained no CBD, product 36 (CBD coffee) and product 39 (Gummies).

Product 36 very boldly proclaims "CBD Coffee" "CBD infused instant coffee" and "20 mg CBD per serving" and yet no CBD could be detected. Product 39 is of interest due to its somewhat outlandish claims such as "Our extra strength CBD gummies are perfect for shedding light on your inner darkness". Analyzing this product for its CBD content, however, revealed that it contains none.

Δ^9-THC content and laboratory testing

Twelve products claim to be Δ^9-THC-free (Table 1). No Δ^9-THC could be detected in any one of these products using LC-PDA and LC-MS and hence, seems to be correctly labeled in this regard. Two products, 5 and 34 contained trace amounts of Δ^9-THC. Product 5 is sold as a full spectrum product and hence, may contain low concentrations of Δ^9-THC. Product 34, however, only claims to contain CBD and yet trace amounts of Δ^9-THC was detected.

Three products (1, 2 and 15) claim to be laboratory tested. Claims such as this are designed to instill consumer confidence in the quality of the product and to distinguish them from competitors. The certificate of analysis for all three products was requested but only the US-based producer of product 1 responded, who, coincidentally, was also found to be the only product to be correctly labeled. Products 2 and 15, produced in SA, were over-labeled by 16.1 and 27.7 %, respectively.

Conclusions

The results demonstrate as others have also shown, the negligent mislabeling of CBD products (Johnson et al., 2022b; Liebling et al., 2022). This mislabeling is not limited to only the actual CBD content, but also regarding the chemical properties of CBD such as being water-soluble (product 34). With a logP value of >6, CBD is simply not soluble in water as was shown by preparing some of these products as prescribed which led to undetectable levels of CBD upon analysis.

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CRediT authorship contribution statement

Michaela Mouton: Investigation, Methodology, Conceptualization, Validation, Writing – original draft, Data curation. **Minja Gerber:** Writing – review & editing, Supervision. **Frank Van der Kooy:** Project administration, Supervision, Funding acquisition, Visualization, Writing – review & editing, Resources, Validation, Methodology.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.phyplu.2023.100520.

References

Allen, L.V., Bassani, G.S., Elder, E.J., Parr, A.F., 2014. Strength and stability testing for compounded preparations. USP Compound. Expert Committee 1–7.

Berthold, E.C., Kamble, S.H., Kanumuri, S.R.R., Kuntz, M.A., Senetra, A.S., Chiang, Y.H., McMahon, L.R., McCurdy, C.R., Sharma, A., 2023. Comparative pharmacokinetics of commercially available cannabidiol isolate, broad-Spectrum, and full-Spectrum products. Eur. J Drug Metab. Pharmacokinet 48, 427–435. https://doi.org/10.1007/s13318-023-00839-3.

Food and Drug Administration (2018). FDA approves first drug comprised of an active ingredient derived from Marijuana to treat rare, severe forms of epilepsy. https://www.fda.gov/news-events/press-announcements/fda-approves-first-drug-comprised-active-ingredient-derived-marijuana-treat-rare-severe-forms (Accessed 29 May 2023).

Food and Drug Administration (2019). *FDA is committed to sound, science-based policy on CBD*. https://www.fda.gov/news-events/fda-voices/fda-committed-sound-science-based-policy-cbd (Accessed 27 May 2023).

Food and Drug Administration (2020a). FDA concludes that existing regulatory frameworks for foods and supplements are not appropriate for cannabidiol, will work with congress on a new way forward. https://www.fda.gov/news-events/press-announcements/fda-concludes-existing-regulatory-frameworks-foods-and-supplements-are-not-appropriate-cannabidiol (Accessed 8 November 2023).

Food and Drug Administration, 2020b. FDA *Approves New Indication for Drug Containing an Active Ingredient Derived from Cannabis to Treat Seizures in Rare Genetic Disease*. https://www.fda.gov/news-events/press-announcements/fda-approves-new-indication-drug-containing-active-ingredient-derived-cannabis-treat-seizures-rare (Accessed 27 May 2023).

Fortune Business Insights, 2021. Global cannabidiol market size, share, industry analysis. https://www.fortunebusinessinsights.com/cannabidiol-cbd-market-103215 (Accessed 30 November 2023).

Gurley, B.J., Murphy, T.P., Gul, W., Walker, L.A., Elsohly, M., 2020. Content versus label claims in cannabidiol (CBD)-containing products obtained from commercial outlets in the State of Mississippi. J. Diet. Suppl. 17, 599–607.

Johnson, E., Kilgore, M., Babalonis, S., 2022a. Cannabidiol (CBD) product contamination: quantitative analysis of Δ9-tetrahydrocannabinol (Δ9-THC) concentrations found in commercially available CBD products. Drug. Alcohol. Depend. 237, 109522 https://doi.org/10.1016/j.drugalcdep.2022.109522.

Johnson, E., Kilgore, M., Babalonis, S., 2022b. Label accuracy of unregulated cannabidiol (CBD) products: measured concentration vs. label claim. J. Cannabis Res. 4, 28. https://doi.org/10.1186/s42238-022-00140-1.

Laanet, P.R., Vaher, M., Saar-Reismaa, P., 2022. Micellar electrokinetic chromatography method for the analysis of synthetic and phytocannabinoids. J. Chromatogr. A 1673, 463080.

Liebling, J.P., Clarkson, N.J., Gibbs, B.W., Yates, A.S., O'Sullivan, O.S., 2022. An analysis of over-the-counter Cannabidiol products in the United Kingdom. Cannabis Cannabinoid Res. 7, 207–213. https://doi.org/10.1089/can.2019.0078.

Li, J., Carvajal, R., Bruner, L., Kaminski, N.E., 2021. The current understanding of the benefits, safety, and regulation of cannabidiol in consumer products. Food Chem. Toxicol. 157, 112600 https://doi.org/10.1016/j.fct.2021.112600.

McGregor, I.S., Cairns, E.A., Abelev, S., Cohen, R., Henderson, M., Couch, D., Arnold, J. C., Gauld, N., 2020. Access to cannabidiol without a prescription: a cross-country comparison and analysis. Int. J. Drug Policy 85, 102935. https://doi.org/10.1016/j.drugpo.2020.102935.

Millar, S.A., Stone, N.L., Bellman, Z.D., Yates, A.S., England, T.J., O'Sullivan, S.E., 2019. A systematic review of cannabidiol dosing in clinical populations. Br. J. Clin. Pharmacol. 85, 1888–1900. https://doi.org/10.1111/bcp.14038.

Miller, O.S., Elder, E.J., Jones, K.J., Gidal, B.E., 2020. Analysis of cannabidiol (CBD) and THC in nonprescription consumer products: implications for patients and practitioners. Epileps. Behav. 127, 108514 https://doi.org/10.1016/j.yebeh.2021.108514.

Mouton, M., Gerber, M., Van der Kooy, F., 2023. Validation of a fast LC-PDA method for the quantification of Cannabinoids in commercial tea samples. Rev. Bras. Farmacogn. https://doi.org/10.1007/s43450-023-00461-z.

Viviers, H.J., Petzer, A., Gordon, R., 2021. An assessment of the potency related to Cannabis-based products in the South African market. Forensic. Sci. Int. 322, 110754 https://doi.org/10.1016/j.forsciint.2021.110754.

Zenone, M.A., Snyder, J., Crooks, V., 2021. Selling cannabidiol products in Canada: a framing analysis of advertising claims by online retailers. BMC Public Health 21, 1285. https://doi.org/10.1186/s12889-021-11282-x.