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Analytical Characterization of Cannabis-Based Products Marketed in Portugal: Evidence of Labeling Inaccuracies and Regulatory Gaps

Oliver Grant[1], David Clark[1]*, Sophia Nguyen[2]

[1]Department of Clinical Research and Healthcare Innovation, University of Glasgow, Glasgow, United Kingdom.
[2]Department of Biomedical and Medical Sciences, National University of Singapore, Singapore.

Abstract

In the past few years, items derived from cannabis have sparked considerable interest due to their supposed therapeutic qualities (featuring cannabinoids such as THC and CBD) and their extensive presence on the market. That said, the accuracy of cannabinoid content on product labels is often questionable. Our investigation, conducted with goods available in Portugal, revealed substantial gaps between advertised claims and the actual cannabinoid profiles. A fully validated analytical technique was developed to profile various products collected from pharmacies and street vendors (infusions, plant matter, lipid extracts, and personal care items) using high-performance liquid chromatography interfaced with a diode-array detector. The dynamic range for linearity covered 0.4 to 100 µg/mL (0.04–10 µg/mg) (THC, 8-THC, CBD, CBG, CBDA, CBGA), 0.1–100 µg/mL (0.01–10 µg/mg) (CBN), 0.4–250 µg/mL (0.04–25 µg/mg) (THCA-A), and 0.8–100 µg/mL (0.08–10 µg/mg) (CBCA). In the beverage category, none of the samples contained measurable cannabinoid levels, even though the wrapping suggested their presence. Correspondingly, lipid extracts commonly deviated from the cannabinoid contents listed on their labels, with some specimens containing CBD concentrations far higher than declared. These mismatches generate profound alarm over consumer welfare and the ability to make knowledgeable choices. In addition, our results highlight the acute need for stringent regulatory oversight and standardized testing procedures to verify the accuracy and integrity of cannabis-based products.

Keywords: Cannabis, THC, Cannabidiol, Market products

Corresponding author: David Clark
E-mail: david.clark@gmail.com

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Introduction

The relationship between human populations and cannabis, along with its derivatives, stretches back to antiquity [1]. Cannabinoids belong to the terpene phenolic class, with Δ9-tetrahydrocannabinol (THC) serving as the chief psychoactive agent, accordingly listed among controlled substances [2-4]. Beyond THC, a Cannabis plant synthesizes more than a hundred further cannabinoids [5]. Notable among them is cannabidiol (CBD), a non-intoxicating cannabinoid that, rather like THC, demonstrates a spectrum of pharmacological activities possessing remedial worth for tackling diverse medical states, including epilepsy, persistent pain, Tourette syndrome, Huntington's and Parkinson's diseases, dyskinesias, and multiple sclerosis [2, 4, 6]. Seeing that CBD does not carry the same dependence-forming traits as THC, the US Food and Drug

Administration (FDA) gave the green light, as of June 2018, to a CBD oral formulation (Epidiolex®) for seizure management tied to childhood epilepsy [6, 7]. Aside from the substances already named, other primary cannabinoids meriting attention are cannabinol (CBN), cannabigerol (CBG), tetrahydrocannabivarin (THCV), cannabichromene (CBC), tetrahydrocannabinol acid (THCA-A), cannabidiol acid (CBDA), cannabigerol acid (CBGA), tetrahydrocannabivarin acid (THCVA), delta-8 tetrahydrocannabinol (8-THC), cannabidivarin (CBGV), and cannabinovarin (CBNV) [4, 6, 7]. Cannabis merchandise is continually evolving, with edible formats and vaping oils rising in demand. That said, the inhalation of combusted dried cannabis blossom persists as the foremost route of consumption and delivery of this drug [8]. Hemp and marijuana denote separate variants of the species Cannabis sativa L., set apart by the levels of psychoactive constituents they elaborate; vegetation yielding less than 0.3% THC is designated as hemp, whereas anything exceeding that threshold is classified as drug-type [1, 3, 9]. While hemp finds its main application in industrial outputs like fibers and structural supplies, marijuana is habitually tied to recreational and medicinal contexts thanks to its complement of THC and CBD [1, 4, 6]. Lately, the distinction between naturally occurring and laboratory-made cannabinoids has blurred, introducing new, user-targeted compounds developed and delivered to consumers [7]. Based on the 2023 European drug report [10], cannabis remains overwhelmingly the most commonly taken illicit substance across Europe, with the potency of cannabis goods climbing annually while prices hold at a fairly consistent level [11]. The move to legalize cannabis continues to fuel intense debate, as various jurisdictions enforce their own regulatory structures with respect to possession and intake. However, adoption and authorization for medicinal use are on the rise [7]. Across the United States, prevailing public sentiment molds cannabis policy, with a medical and wellness-oriented mindset expanding steadily among care providers and lay communities alike [12]. As in 2021, a total of 36 states had enacted statutes for lawful medical cannabis applications, and 18 of those had also endorsed its regulated recreational use [12]. Multiple other nations worldwide—among them Canada, Brazil, Italy, Israel, Germany, the United Kingdom, and the Netherlands—similarly operate legislation and initiatives that sanction cannabis for medicinal purposes [12]. Within the Portuguese legal framework (Law n.º 33/2018 and Decreto-Lei n.º 8/2019), pharmaceutical preparations and related cannabis-based substances (e.g., Sativex® oral sprays) are lawful provided they comply with the stipulations and conditions governing cultivation, processing, and commercial distribution [13, 14]. Spurred by this legislative backdrop and the straightforward procurement of emerging cannabis-derived goods (retail outlets, digital platforms, among others), these products have proliferated, turning up in drinks, herbal samples, oils, personal care products, and beyond.

Nevertheless, as documented in other countries [2, 8, 15-19], the extent to which all these items are subjected to stringent examination of cannabinoid identity and quantity remains unclear. This oversight gap could present a public health hazard, since cannabinoid strengths can differ across marketed products. Documented risks cover motor vehicle crashes linked to operating a vehicle under cannabis influence or concurrent consumption with other drugs, such as ethanol. Cannabis is also repeatedly implicated in episodes of on-the-job injury, child custody litigation, or substance-enabled crimes [5].

The goal of this study was to profile cannabis-based products retailed for both therapeutic and non-therapeutic applications and bought in Portugal.

Materials and Methods

Reagents and standards

Pure reference substances for the following compounds were purchased from Sigma-Aldrich S.A. (Lisboa, Portugal): Δ9-tetrahydrocannabinolic acid (THCA-A), Δ8-tetrahydrocannabinol (8-THC), cannabinol (CBN), cannabidiol (CBD), cannabidiolic acid (CBDA), cannabigerol (CBG), cannabigerolic acid (CBGA), cannabichromenic acid (CBCA), Δ9-tetrahydrocannabinol (THC), and ketoprofen, the latter designated to serve as internal standard (IS). Sovents and additives—namely trifluoracetic acid, ethanol, acetonitrile, and methanol, all meeting HPLC-grade specifications—were supplied by Enzymatic (Santo Antão do Tojal, Portugal).

Two stock working solutions for the full analyte panel, one at 1 mg/mL and another at 100 µg/mL, were constituted in methanol. These were kept refrigerated (4 °C) and shielded from ambient light pending subsequent use.

Chromatographic analysis

The instrumentation selected for this work consisted of an HPLC system fitted with a photodiode array detector (HPLC-DAD, model 1290 from Agilent Technologies, handled by Soquímica, Lisbon, Portugal). Analyte separation relied on a reverse-phase Cortes Shield RP18 column (4.6 × 150 mm, packed with 2.7-micron particles) supplied by Waters Portugal (Lisboa, Portugal). An isocratic elution regime was adopted, the mobile phase being a 41:59 (v/v) blend of 0.1% trifluoracetic acid in water and acetonitrile, delivered at a flow rate of 1 mL/min. Throughout the operation, the column enclosure was thermostatted to 35 °C, and the sample compartment was thermostatted to 4 °C. Each injection introduced 20 µL onto the column. The diode-array acquisition channel

was set to 228 nm [20]. The retention behavior of each analyte under these chromatographic conditions is collated in **Table 1**. For visual reference, **Figure 1** reproduces a chromatographic trace obtained from a mixed standard solution containing all target cannabinoids at 0.8 µg/mL.

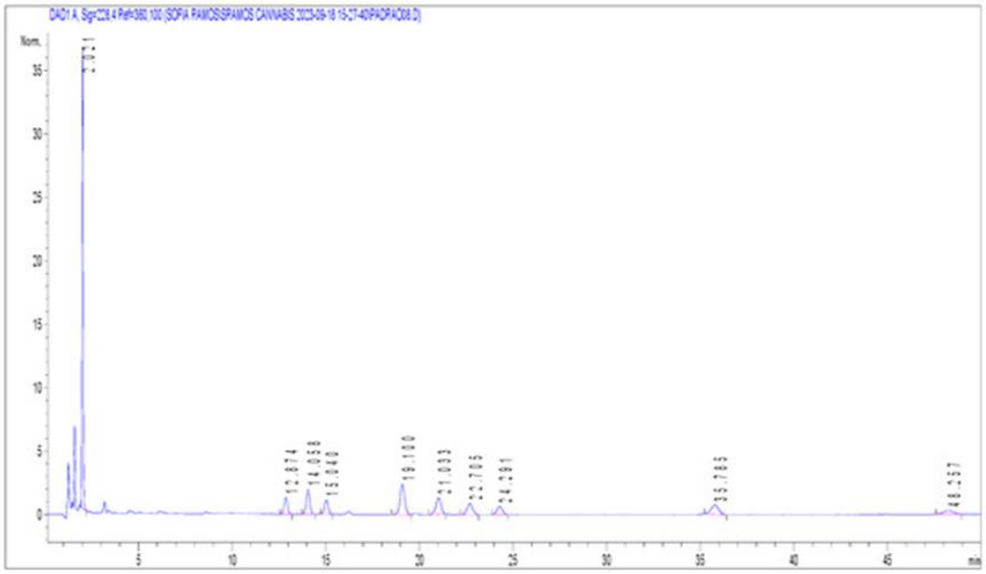

Figure 1. Chromatogram at 0.8 µg/mL of all cannabinoids. The y-axis reports absorbance, and the x-axis reports retention time in minutes. Ketoprofen (2.02 min); CBD (12.87 min); CBDA (14.06 min); CBG (15.04 min); CBN (19.10 min); CBGA (21.03 min); THC (22.71 min); 8-THC (24.29 min); THCA-A (35.79 min); CBCA (48.26 min).

Table 1. Retention times for the identification of the target analytes.

Analyte	Retention time (min)
KET *	2.02
CBD	12.87
CBDA	14.06
CBG	15.04
CBN	19.10
CBGA	21.03
THC	22.71
8-THC	24.29
THCA-A	35.79
CBCA	48.26

Internal Standard. Δ8-tetrahydrocannabinol (8-THC), Δ9-tetrahydrocannabinol (THC), Δ9-tetrahydrocannabinolic acid (THCA-A), cannabichromenic acid (CBCA), cannabidiol (CBD), cannabidiolic acid (CBDA), cannabigerol (CBG), cannabigerolic acid (CBGA), cannabinol (CBN), and ketoprofen (KET).

Sample preparation

Thirty-one distinct commercial articles falling under the umbrella of cannabis-based goods—herbal preparations (including teas intended for infusion), drinkable products, semi-solid creams, and lipid oils—were gathered from a mixture of physical retail channels (large-format supermarkets, smaller grocery outlets, dedicated hemp boutiques) as well as pharmacies, and were then processed for analysis.

Preparation of herbal samples commenced with size reduction to a finely divided, uniform powder, a step taken to guarantee representative subsampling. For both solid botanical materials and semi-solid cosmetic creams, the procedure entailed weighing 0.5 g of the specimen, then combining it with 20 mL of acetonitrile and agitating for 15 minutes. At this juncture, 200 µL of IS at 1 mg/mL was added. The resulting suspension was centrifuged (2579 g, 15 min, 4 °C). The supernatant fraction was carefully recovered, driven through a cellulose membrane filter with a 0.22 µm pore rating, and a 100 µL portion of the clarified filtrate was placed into an autosampler vial.

Handling oil-based products required a 1:1000 dilution. To this end, a 50 µL aliquot of each oil was dispensed into a 50 mL volumetric flask, which was then brought to volume with absolute ethanol. A volume of 70 µL drawn from this dilute solution was transferred to a vial, to which 20 µL of acetonitrile and 10 µL of IS were also added.

For beverages, approximately 3 mL was collected and immediately pressed through a cellulose membrane filter (0.22 µm pore size). An aliquot of 90 µL of the permeate was subsequently transferred to a vial, where it was mixed with 10 µL of IS.

Results and Discussion

Validation procedure

A series of performance characteristics was systematically assessed in alignment with internationally recognized validation standards.

Selectivity

The term selectivity refers to a method's capacity to pick out and resolve the compounds of interest against a backdrop of other species that may coexist in the specimen, including metabolic byproducts, exogenous substances, co-formulated drugs, breakdown derivatives, or endogenous matrix constituents. In the context of this investigation, both a reagent blank (composed of methanol plus mobile phase) and analyte-free matrices representing each sample category—beverages, *Urtica dioica*, oils, and cosmetic formulations—all spiked with internal standard **(Figure 2)**, were contrasted against a supplemented sample prepared at the lowest limit of quantification (LLOQ) (n = 10). The methodology proved to be satisfactorily selective for the set of cannabinoids under examination, as the reagent blank and the various blank matrices generated no discernible interference at the retention times characteristic of the target analytes. Signals from the reagent blank and blank samples were below 15% compared with those from the analytes. They remained below 5% when measured relative to the response attributable to the internal standard (200 µL at 1 mg/mL for cosmetic items and herbal extracts, and 10 µL at 100 µg/mL for beverages and oils). The peaks corresponding to the individual analytes were fully baseline-resolved, with no co-eluting interferences.

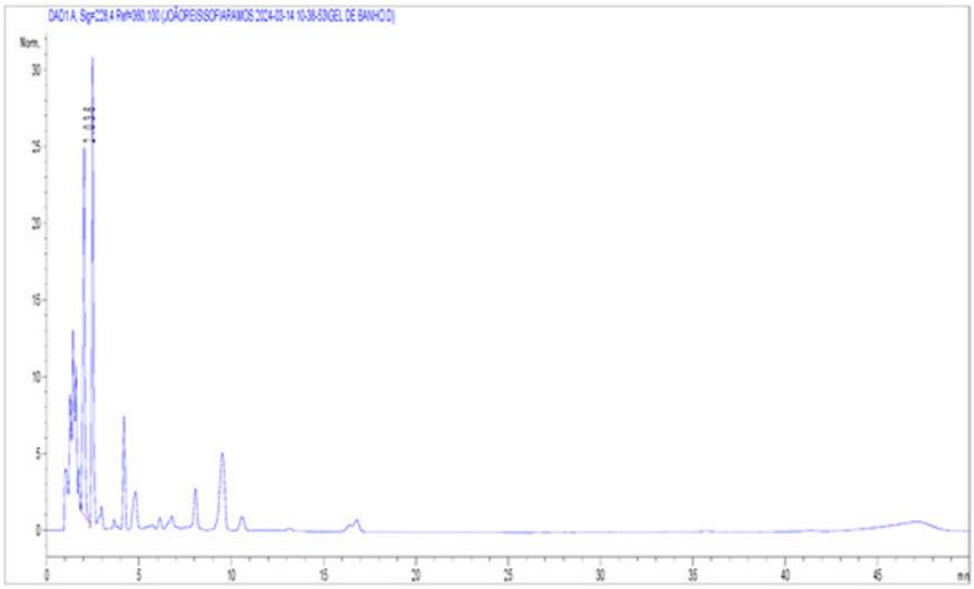

Figure 2. Chromatogram of a blank sample (cosmetic product) with IS. The y-axis corresponds to absorbance readings, while the x-axis indicates retention time expressed in minutes.

Calibration curves and limits

The linearity investigation (n = 5) was conducted by subjecting the system to a series of solutions containing progressively higher levels of each cannabinoid of interest. The adopted criteria for method acceptability stipulated that the back-calculated concentrations must exhibit a mean relative error (RE) contained within a band of ± 15% relative to the nominal spiked value, with the sole exception being the LLOQ, at which an extended tolerance of ± 20% is permitted. Across the panel of analytes, the calibration standards were distributed at uniform intervals over a concentration window extending from 0.4 to 100 µg/mL (0.04–10 µg/mg) for the majority of the included substances, with the following differentiated ranges: CBN from 0.1 to 100 µg/mL (0.01–10 µg/mg), THCA-A from 0.4 to 250 µg/mL (0.04–25 µg/mg), and CBCA from 0.8 to 100 µg/mL (0.08–10 µg/mg). The LLOQ was designated as the lowest concentration level at which each cannabinoid could be reliably measured while satisfying dual criteria—namely, a precision expressed through the coefficient of variation (CV%) remaining ≤ 20%, and an accuracy reflected by the RE staying within ±20% of the target concentration. The LLOQs thereby established were 0.1 µg/mL (0.01 µg/mg) for CBN, 0.8 µg/mL (0.08 µg/mg) for CBCA, and 0.4 µg/mL (0.04 µg/mg) for all remaining cannabinoids. A formal limit of detection (LOD) was not subjected to dedicated experimental determination and was therefore treated, for practical purposes, as coinciding with the LLOQ. **Table 2** consolidates the collected linearity and limit data.

Table 2. Linearity data (n = 5).

Analyte	Sample type	Weighting	LLOQ (µg/mL or µg/mg)	R^2	Intercept	Slope	Calibration range (µg/mL or µg/mg)
CBD	Beverage/oil	1/x	0.4	0.9990 ± 0.0004	−0.0058 ± 0.0065	0.1206 ± 0.0283	0.4–100
	Herbal matrix	1/x	0.04	0.9953 ± 0.0017	0.0011 ± 0.00137	0.0161 ± 0.0008	0.04–10
	Cosmetic formulation	1/x	0.04	0.9943 ± 0.0038	0.0009 ± 0.00168	0.0223 ± 0.0070	0.04–10
CBDA	Beverage/oil	1/x	0.4	0.9986 ± 0.0004	−0.0110 ± 0.0115	0.1952 ± 0.0364	0.4–100
	Herbal matrix	1/x	0.04	0.9974 ± 0.0016	−0.0001 ± 0.0029	0.0256 ± 0.0008	0.04–10
	Cosmetic formulation	1/x	0.04	0.9959 ± 0.0025	0.0030 ± 0.0049	0.0366 ± 0.0012	0.04–10
CBG	Beverage/oil	1/x	0.4	0.9979 ± 0.0020	−0.0076 ± 0.0073	0.1198 ± 0.0315	0.4–100
	Herbal matrix	1/x	0.04	0.9953 ± 0.0040	0.0101 ± 0.0182	0.0165 ± 0.0022	0.04–10
	Cosmetic formulation	1/x	0.04	0.9941 ± 0.0032	−0.0025 ± 0.0063	0.0244 ± 0.0037	0.04–10
CBN	Beverage/oil	1/x	0.1	0.9984 ± 0.0007	−0.0059 ± 0.0099	0.2778 ± 0.0738	0.1–100
	Herbal matrix	1/x	0.01	0.9937 ± 0.0026	−0.0296 ± 0.0535	0.0353 ± 0.0049	0.01–10
	Cosmetic formulation	1/x	0.01	0.9928 ± 0.0013	−0.0291 ± 0.0527	0.0438 ± 0.0042	0.01–10
CBGA	Beverage/oil	1/x	0.4	0.9987 ± 0.0003	−0.0142 ± 0.0134	0.1986 ± 0.0355	0.4–100
	Herbal matrix	1/x	0.04	0.9945 ± 0.0037	0.0009 ± 0.0022	0.0265 ± 0.0040	0.04–10
	Cosmetic formulation	1/x	0.04	0.0035 ± 0.0033	−0.0280 ± 0.0573	0.0374 ± 0.0011	0.04–10
THC	Beverage/oil	1/x	0.4	0.9988 ± 0.0004	−0.0059 ± 0.0104	0.1119 ± 0.0294	0.4–100
	Herbal matrix	1/x	0.04	0.9975 ± 0.0005	−0.0310 ± 0.0556	0.0171 ± 0.0019	0.04–10
	Cosmetic formulation	1/x	0.04	0.9961 ± 0.0019	−0.0023 ± 0.0054	0.0241 ± 0.0031	0.04–10
Δ8-THC	Beverage/oil	1/x	0.4	0.9989 ± 0.0004	−0.0060 ± 0.0052	0.0975 ± 0.0244	0.4–100
	Herbal matrix	1/x	0.04	0.9963 ± 0.0021	−0.0309 ± 0.0561	0.0151 ± 0.0019	0.04–10
	Cosmetic formulation	1/x	0.04	0.9960 ± 0.0017	−0.0053 ± 0.0117	0.0178 ± 0.0020	0.04–10
THCA-A	Beverage/oil	1/x	0.4	0.9967 ± 0.0021	0.0036 ± 0.0358	0.1738 ± 0.0267	0.4–250
	Herbal matrix	1/x	0.04	0.9930 ± 0.0200	−0.0315 ± 0.0556	0.0195 ± 0.0034	0.04–25
	Cosmetic formulation	1/x	0.04	0.9939 ± 0.0044	0.0029 ± 0.0060	0.0326 ± 0.0030	0.04–25
CBCA	Beverage/oil	1/x	0.8	0.9987 ± 0.0005	−0.0092 ± 0.0089	0.0684 ± 0.0143	0.8–100
	Herbal matrix	1/x	0.08	0.9953 ± 0.038	−0.0307 ± 0.0562	0.0102 ± 0.0014	0.08–10
	Cosmetic formulation	1/x	0.08	0.9940 ± 0.0044	−0.0316 ± 0.0582	0.0141 ± 0.0016	0.08–10

Mean values ± standard deviation. Δ8-tetrahydrocannabinol (8-THC), Δ9-tetrahydrocannabinol (THC), Δ9-tetrahydrocannabinolic acid (THCA-A), cannabichromenic acid (CBCA), cannabidiol (CBD), cannabidiolic acid (CBDA), cannabigerol (CBG), cannabigerolic acid (CBGA), and cannabinol (CBN).

The LLOQs achieved through this work compare favorably with those reported by other research groups using comparable extraction solvent systems and HPLC-UV instrumentation for the chromatographic resolution and detection of cannabinoids. The analytical approach detailed here achieved LLOQs below those documented by Aubin *et al*. [20], who proposed a methodology for quantifying 16 cannabinoids across flower and extract matrices with established values of 4 µg/mL. In a parallel fashion, Mudge and Brown [21] introduced an alternative analytical strategy directed at nine cannabinoids present in Cannabis sativa dried inflorescences and oil preparations, reporting LLOQ figures of 0.5 µg/mL for CBN, 1 µg/mL for both THC and CBD, and 5 µg/mL for THCA-A alongside CBDA. Viewed as a whole, the LLOQs published by these investigators exceed those obtained in the present study, suggesting that the methodology described here provides superior sensitivity for the selected panel of cannabinoids. Even so, and despite HPLC-UV being the dominant instrumental platform referenced in the literature for this class of analytes, certain authors have advanced protocols based on gas chromatography interfaced with mass spectrometry (GC-MS). Fernández *et al*. [2] put forward a GC-MS-based procedure tailored to the measurement of THC, CBN, and CBD within commercially distributed preparations available in Argentina. The disclosed LLOQs from that study are 0.1 µg/mL for THC and CBD, and 0.04 µg/mL for CBN, which are below the thresholds we reported. This advantage may well stem from the inherent sensitivity of MS detection combined with the use of diethyl ether during sample purification. It is pertinent to note that, while those authors report sample preparation recoveries ranging from 95 to 103%, the recoveries achieved in our protocol range from 61 to 99%.

Furthermore, it can be argued that the method presented herein has greater ambition, as it expands coverage to nine cannabinoids rather than a narrower subset. Another

instance of a GC-MS-reliant technique incorporating diethyl ether in the sample preparation sequence was contributed by Franzin *et al*. [22], who set out to determine seven cannabinoids within therapeutic preparations originating from a specific Italian region; their uniformly reported LLOQ came to 0.2 µg/mL across all included compounds. The sole instance in which the present method is outmatched concerns CBN, where we attained an LLOQ of 0.1 µg/mL (0.01 µg/mg). Here again, the pairing of GC-MS detection with diethyl ether-based sample work-up may have enhanced the sensitivity documented by those authors.

Intermediate, intra-, and inter-day precision and accuracy

Inter-day precision and accuracy underwent evaluation over a five-day window, with the assay encompassing nine concentration levels (0.4, 0.8, 1.6, 3.1, 6.3, 12.5, 25, 50, and 100 µg/mL; corresponding to 0.04, 0.08, 0.16, 0.31, 0.63, 1.25, 2.5, 5, and 10 µg/mg) for nearly every cannabinoid targeted. Given the extended lower range attainable for CBN, the calibration series was expanded to include 11 levels total, with the addition of 0.1 and 0.2 µg/mL (0.01 and 0.02 µg/mg). For THCA-A, the upper boundary of the working range was extended by including a 250 µg/mL (25 µg/mg) calibrator. The CBCA curve, by contrast, was constructed using eight calibrators distributed from 0.8 (LLOQ) to 100 µg/mL (0.08–10 µg/mg). Across this dataset, the CVs for all analytes and calibrators remained below 13.16%; the only exception was THCA-A, for which the LLOQ calibrator (0.4 µg/mL; 0.04 µg/mg) had a CV of 17.02%. Regarding inaccuracy, the greatest RE observed among all cannabinoids and levels tested did not exceed ± 13.33%.

To probe intra-day precision and accuracy, replicate measurements (n = 6) were conducted on specimens spiked at four distinct levels (LLOQ, 1, 50, and 100 µg/mL; LLOQ, 0.1, 5, and 10 µg/mg), with all analyses performed within a single working day. In the specific cases of CBN and THCA-A, the intra-day assessment additionally covered concentrations of 0.4 and 250 µg/mL (0.04 and 25 µg/mg), respectively. The findings from the intra-day study showed CVs usually remaining below 12.22%, and the worst inaccuracy observed for any target analyte was within ± 14.50%.

The method's intermediate precision and accuracy were also characterized. This entailed analyzing four quality control (QC) specimens over five non-consecutive days. The QC levels selected were set at the LLOQ, 1, 10, and 100 µg/mL (LLOQ, 0.1, 1, and 10 µg/mg), with each assayed in triplicate per daily run for most cannabinoids. In keeping with the approach described above, intermediate precision and accuracy for CBN and THCA-A were further checked at 0.4 and 250 µg/mL (0.04 and 25 µg/mg), respectively. The intermediate-precision results showed CV values that peaked at 14.70% for all analytes, except THCA-A, whose CV reached 15.51%, as observed at the LLOQ calibrator. Regarding trueness, the RE remained within ± 14.60% across the entire analyte set. Taken together, these validation outcomes affirm that the described analytical methodology delivers both precision and accuracy fit for the quantitative determination of the chosen cannabinoids.

Recovery

The concept of recovery captures the percentage correspondence between the signal generated by the detector for a measured quantity of analyte introduced into and subsequently isolated from the sample matrix, relative to the signal that would correspond to the identical quantity of analyte were it natively present in that matrix. In the protocol detailed here, an extraction stage was implemented specifically for herbal and cosmetic sample types. To gauge recovery for the cannabinoids of interest within these matrices, a comparison was drawn between the peak areas arising from two parallel sample series: one series subjected to fortification before extraction (using cannabinoid-free *U. dioica* flowers and a blank cosmetic product), and a second series that first underwent extraction undisturbed and only then received the analytes into the resulting extract. In both series, the internal standard was spiked after the extraction was completed. Following the precedent set by Mudge and Brown [21], *U. dioica* flowers served as the surrogate matrix for this assessment due to their morphological similarity to cannabis flowers and herbal preparations (such as teas), and the practical advantage of a confirmed absence of cannabinoids in their composition. For both beverage and oil matrices, linearity was demonstrated through straightforward dilution of the neat compound standards; accordingly, recovery was not computed for these sample categories.

Table 3 presents the recovery percentages for each cannabinoid. Three fortification levels were employed to evaluate this parameter (LLOQ, 50, and 100 µg/mL; LLOQ, 5, and 10 µg/mL), covering most target analytes. In the case of CBN and THCA-A, recovery was additionally examined at 0.4 and 250 µg/mL (0.04 and 25 µg/mg), respectively. Triplicate analyses were run at each of these levels. Broadly, the recovery results proved to be quite acceptable, falling within the following intervals: 69%–99% for CBD, 73%–93% for CBDA, 76%–99% for CBG, 61%–97% for CBN, 64%–95% for CBGA, 74%–91% for THC, 63%–90% for 8-THC, 77%–89% for THCA-A, and 67%–87% for CBCA.

Table 3. Study of the recovery (%) at three concentration levels (n = 3).

Product type	Analyte	25 µg/mg	10 µg/mg	5 µg/mg	0.08 µg/mg	0.04 µg/mg	0.01 µg/mg
U. dioica	CBD		91.29 ± 0.84	77.87 ± 1.08		69.10 ± 0.70	
	CBDA		92.68 ± 0.65	72.74 ± 0.59		73.46 ± 8.26	
	CBG		99.47 ± 3.90	75.50 ± 1.50		82.97 ± 10.48	
	CBN		87.35 ± 0.82	76.46 ± 0.84		61.37 ± 2.52	76.98 ± 0.96
	CBGA		87.82 ± 1.88	74.82 ± 1.53		64.39 ± 1.36	
	THC		90.90 ± 2.32	87.02 ± 2.49		74.15 ± 6.67	
	Δ8-THC		83.64 ± 2.27	75.72 ± 2.75		62.54 ± 2.17	
	THCA-A	80.58 ± 1.20	86.48 ± 0.78	86.10 ± 3.76		84.43 ± 3.50	
	CBCA		83.08 ± 0.30	75.01 ± 1.49	67.10 ± 3.45		
Cosmetic products	CBD		98.82 ± 9.17	93.93 ± 4.22		91.76 ± 4.71	
	CBDA		92.80 ± 3.54	91.05 ± 0.35		87.37 ± 2.89	
	CBG		91.95 ± 3.61	81.40 ± 2.69		77.93 ± 0.61	
	CBN		96.76 ± 0.53	96.76 ± 2.23		75.74 ± 5.04	72.28 ± 4.89
	CBGA		95.35 ± 1.63	82.50 ± 2.55		78.55 ± 4.17	
	THC		87.40 ± 3.96	83.65 ± 0.92		80.35 ± 4.03	
	Δ8-THC		87.75 ± 4.88	89.85 ± 2.05		83.55 ± 8.41	
	THCA-A	88.75 ± 0.92	86.14 ± 4.12	84.55 ± 7.14		76.85 ± 0.64	
	CBCA		86.35 ± 2.90	77.25 ± 3.40	77.50 ± 5.80		

Mean values ± standard deviation. Δ8-tetrahydrocannabinol (8-THC), Δ9-tetrahydrocannabinol (THC), Δ9-tetrahydrocannabinolic acid (THCA-A), cannabichromenic acid (CBCA), cannabidiol (CBD), cannabidiolic acid (CBDA), cannabigerol (CBG), cannabigerolic acid (CBGA), and cannabinol (CBN).

An important consideration here is that, based on the recommendations of both the FDA and the EMA [23, 24], recovery percentages need not reach 100% to gain acceptance; a demonstration of reproducibility, consistency, and precision across replicates suffices.

Even so, when the extraction efficiencies of the present method are compared with those reported by other groups pursuing similar analytical aims, they can reasonably be viewed as somewhat lower. The study by Mudge and Brown [21] documents recoveries of 98%–108% for CBDA and 98%–104% for THC; recoveries for the remaining compounds were not investigated, a decision attributed to the expense of reference materials. Within the current work, the corresponding ranges were 73%–93% for CBDA and 74%–91% for THC. A modest decline in extraction efficiency was evident for the remainder of the panel. However, any comparative assessment remains impossible since Mudge and Brown [21] restricted their recovery experiments to those two species. The reliance of those authors on 80% methanol as the extraction medium could plausibly explain the discrepancies observed. Elevated recovery figures were likewise reported by Fernández *et al*. [2]. Those investigators report extraction efficiencies of 103% for CBD, 100% for THC, and 95% for CBN; by contrast, the values achieved with our method range from 69%–99% for CBD, 74%–91% for THC, and 61%–97% for CBN. No additional cannabinoids were included in the Fernández *et al*. [2] procedure, and here too the divergence may be traced, at least in part, to their adoption of a different sample work-up approach—specifically, the use of diethyl ether as the solvent of choice. It is worth noting that neither Aubin *et al*. [20] nor Franzin *et al*. [22], whose studies share thematic parallels with our own, presented any recovery-related data.

A final point that merits emphasis concerns the practical suitability of the developed method: the procedure is uncomplicated, operationally straightforward, and entirely appropriate for the routine quantitative determination of these compounds, particularly given that established pharmacopoeial standards—as illustrated by the German Pharmacopoeia (Official Part, 24.4.2018 B5, released 24 April 2018)—identify HPLC-DAD as the technique of choice.

Characterization of cannabis-based products

Samples were procured from both pharmacy outlets and street-level vendors, yielding a collection comprising 6 beverages (3 beers, 2 iced teas, and 1 carbonated drink), 10 oils, 6 herbal specimens, and 9 semi-solid formulations (cosmetic items) **(Table 4)**.

Table 4. Concentrations found in commercial products.

Oils			
Sample	**Analyte**	**Measured concentration**	**Labelled composition**
#1	CBD	7.50%	CBG 5% and CBN 5%

	CBG	5.80%	
	CBN	0.06%	
#2	n.d.	n.d.	No information provided
#3	CBD	1.82%	CBD 10% and < 0.2% THC
#4	CBD	16.13%	CBD 20%; CBN, CBC, CBDA, CBG, CBGA, and CBCA
#5	CBN	0.08%	No information provided
#6	CBD	5.00%	No information provided
	CBG	0.08%	
	THCA-A	0.05%	
#7	n.d.	n.d.	No information provided
#8	n.d.	n.d.	< 0.2% THC
#9	CBD	0.29%	No quantitative value (only CBD declared)
	THCA-A	0.07%	
#10	CBD	5.02%	CBD 10%
Herbal Products			
Sample	**Analyte**	**Measured concentration**	**Labelled composition**
#1	CBD	0.01%	No quantitative value (only < 0.2% THC stated)
	CBDA	0.01%	
#2	CBD	0.23%	No quantitative value (only < 0.2% THC stated)
	CBDA	0.23%	
	CBG	0.02%	
	CBN	3 × 10−3%	
	CBGA	0.01%	
	THC	0.01%	
	CBCA	0.01%	
#3	CBD	0.26%	No quantitative value (only < 0.2% THC stated)
	CBDA	0.31%	
	CBG	0.02%	
	CBN	3 × 10−3%	
	CBGA	0.01%	
	THC	0.01%	
	CBCA	0.01%	
#4	CBD	0.10%	No quantitative value (only < 0.2% THC stated)
	CBDA	0.10%	
	CBG	0.01%	
	CBGA	3 × 10−3%	
	THC	3 × 10−3%	
#5	CBD	0.07%	No quantitative value (only < 0.2% THC stated)
	CBDA	0.07%	
	CBG	4 × 10−3%	
	CBGA	3 × 10−3%	
	THC	1 × 10−3%	
#6	CBD	0.03%	No quantitative value (only < 0.2% THC stated)
	CBDA	0.03%	
	CBG	3 × 10−3%	
Cosmetic products			
Product	**Analyte**	**Measured concentration**	**Labelled composition**
Cream #1	CBD	0.24%	No quantitative value (only CBD stated)
	CBG	3 × 10−3%	
Cream #2	CBD	0.01%	No quantitative value (only CBD stated)
	CBG	3 × 10−3%	
Cream #3	CBD	0.01%	No quantitative value (CBD < 1%)
	THC	0.05%	
Shower gel #4	n.d.	n.d.	Cannabis sativa seed oil
Shampoo #5	CBD	4 × 10−3%	Cannabis sativa seed oil, Cannabis sativa seed extract
Balm #6	CBD	0.09%	No quantitative value (only CBD stated)
Cream #7	n.d.	n.d.	Cannabis sativa (Hemp) seed oil
Cream #8	CBD	0.01%	No quantitative value (only CBD stated)
Cream #9	n.d.	n.d.	Cannabis sativa seed oil

n.d. Not detected. Δ9-tetrahydrocannabinol (THC), Δ9-tetrahydrocannabinolic acid (THCA-A), cannabichromenic acid (CBCA), cannabidiol (CBD), cannabidiolic acid (CBDA), cannabigerol (CBG), cannabigerolic acid (CBGA), and cannabinol (CBN).

What emerged from the compositional and cannabinoid content determinations was a clear pattern: the bulk of the analyzed items carried labeling that did not align with their actual contents. Not a single one of the six beverages (three beers, two iced teas, and one carbonated beverage) tested positive for any cannabinoid. A close reading of the provided labels revealed that the producer made no explicit reference to the incorporation of Cannabis sativa extract. The packaging itself, nonetheless, deployed highly suggestive visual cues—the word "cannabis" was reiterated multiple times across the surface, and the imagery employed was plainly allusive, conveying to the prospective purchaser the distinct impression of a beverage derived from cannabis.

Shifting focus to the oil category, the manufacturer of oil sample #4 had communicated an anticipated composition featuring 20% CBD, coupled with a stated presence of several other cannabinoids (CBN, CBC, CBDA, CBG, CBGA, and CBCA). Against this backdrop, the actual measurements told a different story: CBD came in at 16.13%, and none of the additional claimed cannabinoids were observed. For oil sample #1 **(Figure 3)**, the analysis identified three species—CBD, CBG, and CBN—quantified at 7.50%, 5.80%, and 0.06%, respectively. The product's own label had projected concentrations of 5% CBG and 5% CBN, the latter of which was absent from the analytical record. Relative to the label declaration, the CBD result was substantially inflated, and the CBN information was demonstrably incorrect. As for CBG, the experimentally derived figure fell short of the stated value when evaluated against a 10% variability criterion borrowed from the US Pharmacopeia [25]. A comparable discrepancy surfaced in oil #10, where CBD registered at 5.02% compared to the labeled claim of 10%. For oil sample #3, the label led consumers to expect 10% CBD, while the measured amount was only 1.82%. The packaging of oil samples #2, #5, #6, and #7 offered scant compositional or concentration particulars. That said, all of these bore some mention of CBD on their exterior—oil #5 being the exception, as it invoked only the term "hemp." Given their positioning in the marketplace as cannabinoid oils, a meaningful CBD presence was reasonably expected. Yet, oils #2, #7, and #8 contained no detectable cannabinoids. Analysis of oil #5 returned only CBN at 0.08%. In oil #6, the quantified amounts were 5.00% CBD, 0.08% CBG, and 0.05% THCA-A. Rounding out the set, oil #9 tested positive for both CBD (0.29%) and THCA-A (0.07%), even though its label restricted mention to CBD alone.

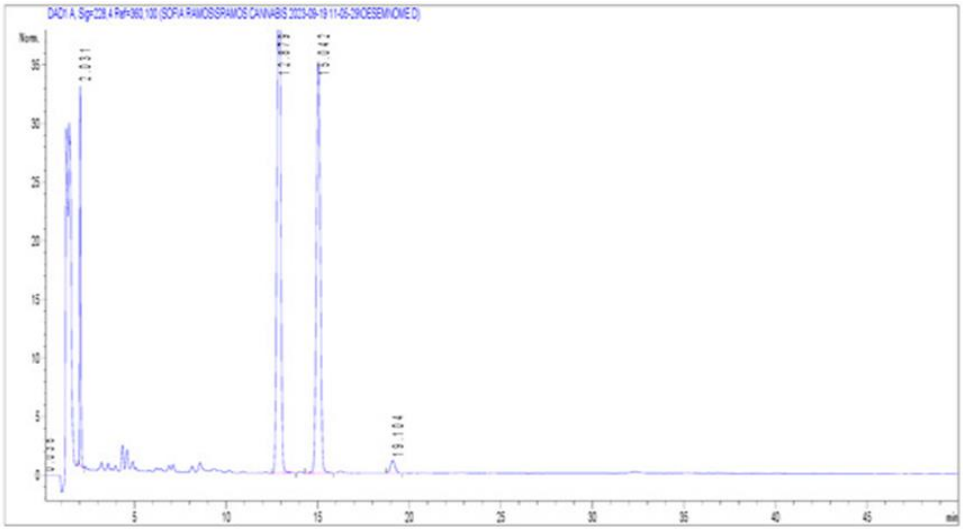

Figure 3. Chromatogram obtained after the HPLC-DAD analysis of oil #1. The y-axis shows absorbance, and the x-axis shows retention time in minutes. Ketoprofen (2.03 min); CBD (12.88 min); CBG (15.04 min); CBN (19.10 min).

Turning attention to the herbal samples, the only compositional claim advanced on their labels pertained to a THC concentration kept below 0.2%, in line with applicable regulatory thresholds. Across the board, this assertion was substantiated by the analytical data. A range of cannabinoids was indeed picked up, though uniformly at very low levels. Among the cosmetic items, only cream 3 provided any compositional disclosure regarding the cannabinoids targeted in this study. In that case, the CBD concentration determined by analysis conformed to the manufacturer's stated specification (CBD < 1%).

When viewed in their entirety, these articles—whose labels fall short of furnishing comprehensive compositional detail—provoke substantial unease. The deficiency lies in the way it strips consumers of the ability to exercise fully informed judgment regarding the nature of the product they elect to consume and the effects, whether therapeutic or otherwise, they aim to achieve through its use.

A body of published work addressing this same subject has emerged from researchers situated in other nations. 40 commercial offerings were subjected to quantitative scrutiny by Mouton *et al*. [15], whose investigation encompassed an eclectic assortment of products—soft drinks, honey, coffee, oils, gummy bears, chocolate, and other goods that claimed to contain CBD. The central question motivating their study was whether the CBD quantities actually borne by these items matched the figures displayed on their packaging. Drawing samples from South Africa, the United States, Spain, the Netherlands, and Indonesia, the authors assembled a collection representative of diverse international supply chains. What the data laid bare were labeling deviations of considerable magnitude: numerous articles carried declarations that either exaggerated or minimized the true CBD load, a subset made no quantitative disclosure whatsoever, and still others yielded CBD readings indistinguishable from zero. Within the subset of 16 oils, correct labeling—defined as alignment with the advertised range—was observed for only 3 products; 8 products claimed more than they delivered, and 1 claimed less than they delivered. Three additional oils, for which no CBD specification appeared on the label, likewise returned non-detectable results. A particularly dramatic instance emerged from the five topical preparations examined: product 18 registered a CBD content 98.29% shy of the figure printed on its container. Product 20, touted as containing 10 g of CBD hemp oil, similarly gave a null result. Within the beverages and miscellaneous product categories, over-labeling was the rule rather than the exception; the lone outlier was product 34, sold under the descriptor "water-soluble CBD sachets." This case illuminates how the mislabelling phenomenon reaches past mere dosage inaccuracy, bleeding into mischaracterizations of CBD's very physicochemical behavior—selling sachets on the premise of water solubility when CBD, by its nature, resists aqueous dissolution.

Wiley *et al*. [16] undertook a wide-ranging examination of the scientific, promotional, and jurisprudential contours of CBD, yielding remarkable insights into claims advanced in the commercial sphere. CBD is positioned in the marketplace under multiple guises—as a dietary supplement, a food additive, an ingredient in cosmetics, or a drug—with each categorization triggering an entirely separate FDA regulatory apparatus. Pharmaceutical licensing entails exhaustive demonstration of safety and effectiveness, whereas dietary supplements, cosmetics, and food/beverage items face comparatively modest post-market safety obligations. The conspicuous absence of a coherent regulatory scaffold around CBD's commercial distribution and legal standing has catalyzed a proliferation of CBD-containing goods, granting marketers latitude to exploit gaps in oversight while tapping into broad-based consumer fascination with CBD's purported therapeutic virtues. The authors flagged a recurrent logical slippage: research findings about THC or whole cannabis preparations—which pair THC with CBD and numerous other cannabinoids—are routinely, and erroneously, marshaled as evidence for the isolated effects of CBD. Beyond the realm of spurious health claims, labeling inaccuracy remains an entrenched problem, corroborated by investigations that bring to light profound gulfs between declared CBD levels and those measured through independent analysis. Though certain firms advertise laboratory-verified CBD content, meaningful validation stays stubbornly out of reach, not least because CBD has yet to secure entry into the United States Pharmacopeia. Further compounding matters, even those products whose CBD content can be authenticated may still fall short of delivering doses sufficient to trigger the intended pharmacological response, a limitation particularly acute when the oral route is involved.

A parallel inquiry to that conducted by Mouton *et al*. [15] was mounted by Bonn-Miller *et al*. [17], who deliberately turned to internet-based vendors as their procurement channel, a choice motivated by the desire to maximize sample heterogeneity and capture the breadth of merchandise circulating in the marketplace. Their analysis spanned approximately 84 distinct products. The tally of labeling fidelity was disheartening, though hardly unforeseen: 42.85% of the samples were under-labeled for CBD, 26.19% were over-labeled, and only 30.95% were accurately labeled. When the analytical lens widened to encompass other cannabinoids, the detected levels were, by and large, minimal and of questionable practical import; notwithstanding this general pattern, the intoxicating compound THC made its presence known in virtually 22% of the tested specimens.

An evaluation of quality standards across 14 CBD oils retailed within European borders, an exercise that included chemical mapping of cannabinoids, terpenes, and oxidative degradation products, was spearheaded by Pavlovic *et al*. [18]. In view of the regulatory deficiencies already cataloged, the outcome was thoroughly foreseeable: CBD levels for 9 of the 14 oils diverged sharply from the declared values. At the same time, the remaining 5 remained within acceptable bounds. Oils 8 and 10 yielded CBD levels that exceeded the manufacturers' claims; conversely, oils 3 and 14 fell well below their stated specifications. The investigation also accomplished the quantification of six cannabinoids judged to carry the greatest significance: THC, THCA-A, CBDA, CBN, CBG, and CBGA [18]. It is noteworthy that across 12 of the 14 samples, THC was detected, and although the concentration range was wide, low-level presence (0.2%) was the most prevalent finding. Oil 6

constituted the sole instance in which THC registered at a noteworthy level (0.35%), a result rendered all the more concerning by the producer's explicit representation that the formula was devoid of THC. CBN was quantifiable in nearly all oils tested, except oil 14.

Edible cannabis items, which likewise occupy a space of minimal regulatory constraint, continue to trail behind the benchmark labeling accuracy expected of medicinal products. Vandrey *et al*. [19] provided empirical support for this critique by analyzing 75 edible products collected across three major US urban hubs. Of these, barely 17% met the standard of accurate labeling, 23% were under-labeled, and a full 60% carried claims exceeding their actual THC payload. The situation regarding CBD was no more reassuring: 44 of the products assayed contained detectable levels of CBD, yet appropriate CBD labeling could be confirmed for only 13. For upwards of half the articles tested, the cannabinoid loads measured were markedly inferior to those declared, some harboring THC amounts approaching negligibility. By contrast, a portion of the products bore THC burdens well in excess of their label claims, thereby exposing consumers to the prospect of unintended adverse reactions.

The deployment of a GC-MS methodology for cannabinoid quantification in Argentine cannabis oils was reported by Fernández *et al*. [2]. The team elaborated, validated, and implemented an assay targeting the primary cannabinoids THC, CBD, and CBN, complemented by a full-scan exploratory screen that detects THC, CBD, CBN, CBC, CBG, THCA-A, and CBDA. Among the 10 oils subjected to measurement, oils 1 and 2—representing controlled or regulated production—returned CBD values consonant with their labels, along with low THC readings, consistent with the expected profile of hemp-derived material. The picture shifted dramatically when the focus moved to oils originating from uncontrolled or unregulated production chains, where CBD, THC, and CBN concentrations told a very different story. High THC coupled with low or undetectable CBD was the pattern observed for oils 3 and 7; oils 6, 8, and 9 displayed undetectable CBD alongside THC concentrations ranging from 1.3 to 4.3 mg/mL. Such observations dovetail neatly with earlier published accounts, reinforcing the impression of a recurring motif in cannabinoid concentration data that cuts across independent investigations.

Seen in their entirety, the constellation of findings assembled by these prior studies, together with the experimental evidence advanced in the present paper, casts into stark relief an urgent and unavoidable imperative: the institution of rigorous analytical testing and robust quality control architecture across the landscape of cannabis-based products.

Conclusion

This manuscript outlines the validation record for an analytical strategy enabling the simultaneous measurement of nine cannabinoids by liquid chromatography coupled to diode-array detection. The entire methodology underwent exhaustive validation against criteria laid down in globally recognized guidance, and the resulting figures for precision and accuracy were entirely satisfactory. In the frame of the present study, 31 over-the-counter cannabis-based formulations purchased on the Portuguese market were submitted to testing. The data clearly show the widespread occurrence of serious discrepancies between label declarations and actual contents across a wide variety of product formats. For the vast majority of specimens assayed, the measured cannabinoid concentrations were lower than the levels claimed on their respective labels. An additional concern is that many of these articles furnished no data at all on the identity or quantity of the cannabinoids they contained, even though their external presentation—through repeated printed allusions to cannabis—fostered the strong expectation that cannabinoids were present. There is a pressing need to introduce uniform regulatory provisions backed by reliable quality assurance systems. Extending well beyond correcting labeling errors, the embedding of quality control measures serves the dual purpose of protecting end users' health and ensuring that products fulfill their stated purpose in a rapidly expanding cannabis sector.

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