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Heavy metal and phthalate contamination and labeling integrity in a large sample of US commercially available cannabidiol (CBD) products

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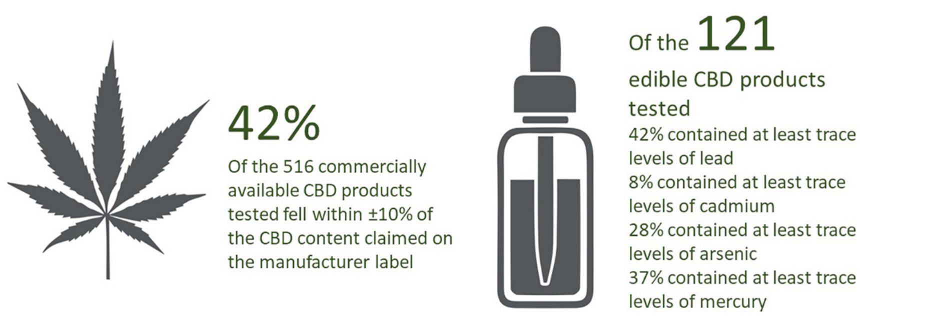
HIGHLIGHTS

- Heavy metal and phthalate contamination in CBD may counter-balance its proposed health benefits.
- Heavy metals (Pb, Cd, As, Hg), phthalates, and CBD label accuracy were quantified in CBD products.
- Only 42 % of products fell within ±10 % of the CBD claimed on the manufacturer label.
- Low-level heavy metal and phthalate contamination of edible CBD was pervasive.
- Tight regulations for CBD product label integrity are needed.

GRAPHICAL ABSTRACT



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ABSTRACT

Background: The demand and availability of commercially available cannabidiol (CBD) products has grown substantially, which is of particular interest among medically vulnerable people. Because the cannabis plant is recognized as a bioaccumulator, which is highly effective at absorbing and retaining contaminants (e.g., heavy metals) in soil, it is important to characterize the degree of contamination in CBD products and their label accuracy to better estimate potential health benefits and risks associated with consumption.

Methods: Levels of lead, cadmium, arsenic, mercury, four phthalates, and CBD labeling accuracy were quantified in a selection of commercially available CBD products in the US. Heavy metal concentrations were quantified by inductively coupled plasma-mass spectrometry. Phthalates were quantified by liquid chromatography-tandem mass spectrometry. CBD labeling accuracy was determined by extracting samples into a suitable organic solvent and analyzing using liquid chromatography with diode array detection.

Results: Lead was detected in 42 %, cadmium in 8 %, arsenic in 28 %, and mercury in 37 % of 121 edible CBD products. Four edible CBD products exceeded the California Proposition 65 threshold for daily lead consumption of 0.5μg in two servings. The percentage of edible products with detectable phthalate concentrations varied between 13 % and 80 % across the four phthalates, with DEHP being most prevalent. Among all products tested for CBD labeling accuracy (topicals, edibles, $N = 516$), 40 % contained <90 % of the CBD indicated on the product label, 18 % contained >110 %, and only 42 % of products fell within ±10 % of the CBD claimed on the manufacturer label. Concentrations of heavy metals and phthalates were not associated with CBD potency.

Conclusions: Low-level contamination of edible CBD products with heavy metals and phthalates is pervasive. There is substantial discrepancy between the product label claims for CBD potency and the amount measured in both edible and topical products, underscoring the need for tight regulations for CBD product label integrity to protect consumers.

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1. Introduction

Cannabis is a plant of the Cannabaceae family and contains more than eighty biologically active chemical compounds. The two most prevalent cannabis compounds are delta-9-tetrahydrocannabinol (D9-THC) and cannabidiol (CBD). THC is a psychotropic compound that produces the "high" associated with marijuana use. Cannabis, however, is not intoxicating and its non-psychotropic components have the potential to help regulate physiological and cognitive processes (Corroon and Felice, 2019; Golombek et al., 2020). Significant potential health benefits, including CBD's analgesic, anti-inflammatory, antioxidant, antipsychotic, neuroprotective, and cardioprotective effects have been observed in some recent studies, though more research is needed (Blessing et al., 2015; Elsaid et al., 2019; Kaul et al., 2021; Sarris et al., 2020). Therapeutic use of unregulated CBD among children and adults is growing rapidly for complementary care for cancer, mood disorders, pain, sleep disturbances, blood pressure, neurocognitive impairments, and many other health conditions (White, 2019), but the therapeutic benefits have not been established. Because CBD use is widespread and prevalent in medically vulnerable populations (Moltke and Hindocha, 2021; Silvestro et al., 2019), greater understanding about its safety is needed. Cannabis is considered a bioaccumulator and a phytoremediator because of its ability to absorb and retain contaminants from the soil in which it is grown, most notably heavy metals (Mead, 2017; Bengyella et al., 2021). Because cannabis can accumulate contaminants from contaminated soils, it is also considered a potential source of risk for human health (Atapattu and Johnson, 2020; Craven et al., 2019; Ma et al., 2018). To weigh the potential risks and benefits of cannabis use across the population, we first need to elucidate the contamination levels in commercially available CBD products.

With increased consumer use of cannabis-derived processed products, manufacturing contaminants must also be considered, including heavy metals and endocrine disrupters (e.g., phthalates). The four heavy metals of greatest concern include the potent neurotoxins lead and mercury (Bellinger, 2008; Myers and Davidson, 2000; Téllez-Rojo et al., 2006), arsenic (a known carcinogen) (Smith et al., 2018; Tokar et al., 2010), and cadmium, also a neurotoxin, carcinogen, and renal toxin (Noonan et al., 2002; Rigon et al., 2008). Although lead is well documented as a neuro- (Sanders et al., 2009) and reproductive (Apostoll, 1998; Kumar, 2018) toxin, until recent years, it has largely remained unregulated in US food safety regulatory policy (Food and Administration, 2004) with a few exceptions (Food and Administration, 2006). Similarly, cadmium, arsenic, and mercury have largely been excluded from food safety regulatory policy. Chronic exposure to cadmium (low level over an extended period of time) is linked to kidney (Prozialeck and Edwards, 2012), bone (Kazantzis, 2004) and lung (Lampe et al., 2008) disease. When it comes to arsenic, exposure is not limited to toxic waste sites and massive poisoning events. Chronic exposure continues to be a major public health problem worldwide, affecting hundreds of millions of people (Naujokas et al., 2013). The U.S. Environmental Protection Agency maximum contaminant level (MCL) in drinking water is 10 μg/L; however, concentrations of >3000 μg/L have been found in wells in the United States (Naujokas et al., 2013). In addition, exposure through diet is of growing concern. Knowledge of the scope of arsenic-associated health effects has broadened; arsenic leaves essentially no bodily system untouched. Arsenic is a known carcinogen associated with skin, lung, bladder, kidney, and liver cancer. Dermatological, developmental, neurological, respiratory, cardiovascular, immunological, and endocrine effects are also evident. Mercury exposure has long been largely associated with seafood consumption, dental amalgams, and artisanal and small-scale gold mining. Exposure to mercury, a potent neurotoxin that bioaccumulates in fish, is especially of concern to women of childbearing age and children in high fish consuming populations (Feingold et al., 2020). Elemental (metallic) mercury and all of its compounds can be absorbed through the lungs and skin and result in hypersensitivity reactions. Ingestion of inorganic mercury compounds can cause severe, potentially fatal damage to the kidneys, gastrointestinal tract and other organ systems and even very low levels of exposure can impair the immune system (Agency for Toxic Substances and Disease Registry, 2022).

Phthalates are a class of hormone disrupting chemicals with a wide spectrum of industrial uses including food applications. Human exposure is largely through ingestion, inhalation, or dermal exposure, as these compounds can be easily released from plastics to water, food, soil, and air, making them ubiquitous environmental contaminants. Some types of phthalates affect the reproductive system of laboratory animals. Phthalates have also been associated with disrupted thyroid hormone levels, increased levels of oxidative stress, and illnesses such as endometriosis and breast cancer (Gari et al., 2019; Gaspar et al., 2014; Moreno, 2014).

The CBD industry has experienced significant growth in the US with the passing of the Agriculture Improvement Act of 2018 (Conaway, 2018). However, the Food and Drug Administration (FDA) states that it is currently illegal to market CBD by adding it to a food or labeling it as a dietary supplement. Despite this, the US CBD marketplace was valued at 4.6 billion in 2020 and is projected to surpass $20 billion by 2025 (Still, 2021). Numerous consumer (Nichols, 2021; Steven D'Souza and Sadler, 2021; Yamka, 2021) and academic studies (Bonn-Miller et al., 2017; Dunn et al., 2021; Gurley et al., 2020; Hazekamp, 2018; Poklis et al., 2019; Wheeler et al., 2020) have highlighted quality control issues within CBD retail products including discrepancies in label accuracy. In the absence of clear federal regulation and enforcement, CBD products could have additional quality control issues with potential toxicological impacts. Utilizing a retail basket sampling approach, we examined the label accuracy and heavy metal and phthalate contamination of best-selling CBD gummies, capsules, tinctures, and topicals.

2. Methods

2.1. Sample purchasing

A total of 516 CBD edible and topical products were purchased from open stream of commerce, including brand websites and digital marketplaces sources, representing a broad convenience ("retail basket") sample. Only finished consumer products were included, with no dried flower or biomass, and no inhaled products. Out of this total sample, 121 were intended for edible consumption and provided serving size instructions. Of these 121 edible products, heavy metal concentrations were measured in all 121 and phthalates in 84. The sample was chosen to represent the current consumer shopping experience in the United States across a range of price points. The packaging for each sample was retained and the list of ingredients and reported CBD content were recorded.

2.2. Measurement of heavy metals, phthalates, and CBD

The contaminants of interest included lead, cadmium, mercury, arsenic, and four phthalates (benzyl butyl phthalate, bis (2-ethylhexyl) phthalate, dibutyl phthalate, and dihexyl phthalate). All contaminants were examined as mcg per serving. CBD was measured in mg per serving. All testing was completed at an ISO 17025 accredited lab.

2.2.1. Heavy metal analysis by ICP-MS

The method for preparation and analysis of CBD samples for heavy metals was completed under the scope for the analysis of hemp-based CBD products using inductively coupled plasma - mass spectrometry (ICP-MS). This method was adapted from the EPA Method 6020A. Prior to analysis, CBD samples were homogenized until a uniform texture was achieved. Approximately 0.25 g of homogenized sample was digested using an acid solution of 4 mL nitric acid (HNO3) + 1 mL hydrochloric acid (HCl) in MarXpress TFM vessels using a microwave digester (MARS6 One Touch microwave, CEM). The digest protocol utilized a 20 min ramp to 200 °C followed by a 20 min hold at 200 °C and 50 min cool down to room temperature. Following digestion, the samples were transferred to 50 mL polypropylene tubes and diluted to 40 mL with acid diluent. The diluent was comprised of 10 % HNO_3 + 2 % HCl + 0.4 % gold (Au) + 3 % methanol (MeOH) + internal standards.

Heavy metals analysis was conducted using ICP-MS (NexION 350, PerkinElmer). Samples were analyzed using kinetic energy distribution (KED) mode, which uses energized helium to collide with polyatomic interferences to isolate target elements, improving the accuracy of results. All standards were prepared using the same diluent as was used for diluting samples above. ICP-MS data was processed using Syngistix Software (PerkinElmer).

The heavy metals were detected by the isotopic masses of 75 (arsenic (As)), 114 (cadmium (Cd)), 102 (mercury (Hg)), and 208 (lead (Pb)). The internal standards used were recommended by the reference EPA methos, 6020A, and Perk and Elmer. These included 74Ge, 89Y, 115In, 159 Tb, in a 10 ppm mix. If any internal standard intensity fell below a 70 % intensity limit the sample was deemed unacceptable and triggered a recalibration, verification of calibration, and reanalysis procedure. For quality control purposes, the minimum acceptable correlation coefficients (R^2) for the calibration curve for both metals for each run was 0.998; the maximum acceptable percent relative standard deviation (RSD%) for matrix spike duplicates was 15 %; the maximum acceptable variability for the low-level and mid-level calibration verification was 30 % and 20 %, respectively. The estimated measurement uncertainty for both analytes was found to be 2.4 %, determined by measuring the precision of spiked samples. The limits of quantification (LOQ) were determined to be 16 μg/kg for arsenic and 8 μg/kg for cadmium, mercury, and lead, respectively. The method detection limits (MDL) for this method were determined in method blank solutions and were not matrix-corrected. The measurement accuracy for each matrix was determined using matrix spike and matrix spike duplicates held to a 20 relative percent difference (RPD) for precision. Before reach sample sequence, an initial calibration verification (ICV) was run to verify the calibration curve.

2.2.2. Phthalates analysis by LC-MS/MS

The method for preparation and analysis of CBD samples for phthalates was completed by solvent extraction followed by liquid chromatography-tandem mass spectrometry (LC-MS/MS). The method utilized a 1260 Infinity II HPLC (Agilent Technologies) coupled to a 6420A mass spectrometer (Agilent Technologies). The separation was performed on a Poroshell 120 encapped C18 column (Agilent Technologies) using a gradient elution program with acidified water and acidified methanol mobile phases. All solvents and chemical reagents were high pressure liquid chromatography (HPLC) or liquid chromatography mass spectrometer (LCMS) grade including Acetonitrile (ACN), Methanol (MeOH), and Formic acid (FA) as well as deionized water (dH_2O), see Supplemental Table 1 for HPLC gradient and instrument parameters. Quantitation of target phthalates was performed using internal standard calibration, applying isotopically-labeled phthalate standards to correct for method recovery and ion suppression effects. Each sample was spiked with internal standards (Stock internal standard mix came from manufacture labeled as "Custom Phthalate Standard Mix", Restek catalog # 574365), then extracted using MeOH or ACN, depending on the sample type, then the samples were filtered prior to analysis by LC-MS/MS. For quality control, each batch was run with appropriate blanks, calibration verification samples, and matrix spike, and spike duplicate samples. A labeled internal standard representing each analyte ensured suppression and unforeseen matrix effect were accounted for during the extraction and data acquisition process. The proper generation of this curve was confirmed when the values for each phthalate in the low, mid and high ICV sample showed at concentration ± 20 % of 12 ppb, 40 ppb, 120 ppb respectively. To ensure report accuracy, phthalates had to possess and be integrated by a standard curve with an R^2 value greater than or equal to 0.995. If the curve had a value <0.995, reported values were considered an estimate. The Ion ratios for each analyte were ± 30 % to ensure specificity.

2.2.3. Cannabinoid labeling accuracy analysis by LC-DAD

The method for extraction and analysis of cannabinoid labeling accuracy in CBD samples was completed by extracting samples into a suitable organic solvent and analyzing using liquid chromatography with diode array detection (LC-DAD). The method utilized a 1260 Infinity II LC-DAD (Agilent Technologies) for separation and detection of target cannabinoids. The separation was performed using a Poroshell 120 endcapped C18 column (Agilent Technologies), using a gradient elution program with formate buffered water and acidified acetonitrile. ISO 17034 accredited reference standards were used for each cannabinoid (Neutral: CBDV, CBG, CBD, THCV, CBN, d9-THC, CBL, CBC; Acidic: CBDVa, CBDa, CBGa, THCVa, CBNa, THCa-A, CBCa). Chemical reagents and solvents included HPLC and LCMS grade deionized water, methanol, acetonitrile, formic acid, ammonium formate and a certified reference standard for each cannabinoid; see Supplemental Table 2 for HPLC gradient and instrument parameters. Quantitation was performed using external standard calibration, using separate calibration curves for neutral and acidic cannabinoids to provide maximum stability. The samples underwent analyte extraction, in most cases using MeOH, before being filtered and analyzed by LC-DAD. The measured cannabinoid concentrations were compared against the content claims on the original packaging to determine label accuracy. Quality control parameters were met to ensure correct extraction and quantitative accuracy for each analyte. For method validation by analyte, see Supplemental Table 3.

2.3. Statistical analysis

The distribution of lead, cadmium, mercury, arsenic, and the four phthalate compounds in edible CBD samples was examined. Then, the percentage of products that exceeded the California proposition 65 threshold for daily lead consumption (0.5 μg) was identified. We examined the unadjusted association between the measured CBD in each serving with the heavy metals and phthalates using Spearman correlation coefficients due to the non-normal distributions of the variables.

Next, we compared the CBD potency claim on the package label with the CBD potency measured in the product sample. We divided the mcg measured in the product sample by the mcg listed on the package label and identified all samples with measured potency >10 % higher or lower than the product claim. We examined the difference in the observed and labeled CBD content of all tested products, as well as in the subset of all edible products.

3. Results

Table 1 shows the distribution of lead, cadmium, arsenic, mercury, and the four phthalates across the sample of edible CBD products. No edible CBD samples exceeded 0.5 μg of lead per serving, but four edible products exceeded 0.5 μg in two servings. The measured amount of CBD in each product was not correlated with lead (Spearman CC = 0.04, p = 0.69), cadmium (Spearman CC = -0.12, p = 0.18), or arsenic (Spearman CC = 0.06, p = 0.53), but slightly negatively correlated with mercury (Spearman CC = -0.28, p = 0.002), and not associated with any of the phthalates (benzyl butyl Spearman CC = 0.12, p = 0.29, Bis2 Spearman CC = -0.06, p = 0.62, dibutyl Spearman CC = 0.11, p = 0.31, dihexyl CC = 0.14, p = 0.19).

Fig. 1 shows the comparison between the measured CBD in each product and that which is claimed on the label, including all edibles and topicals (N = 516). The differences (observed-claimed) varied substantially, from −996 mg (−99.6 % of the product label claim) to +491 mg (197 % of the product label claim), and as a percentage of the product label claim, the differences ranged from −100 % to 339 %. Among all products, 40 % contained <90 % of the CBD indicated on the product label, and 18 % contained >110 % of the CBD indicated on the product label, with 42 % of products falling within ±10 % of the CBD amount claimed on the product label.

This variability was similar in the analysis restricted to 121 edible products with serving size instructions, which ranged from −192 mg (−64 % of the product label claim) to +100 mg (16 % of the product label claim), and as a percentage of the product label claim, the differences ranged from −91 % to 68 %. Among the edible products (Fig. 2), 29 % of the samples contained <90 % of the CBD indicated on the product label, and 17 % of the samples contained >110 % of the CBD indicated on the

Table 1
The distribution of lead, cadmium, arsenic, mercury, and four phthalates across the edible CBD products.

	N	% Detected	Median	IQR	Range	Minimum Detected
Lead μg/serving	121	42 %	ND	ND-0.01	ND-0.38	0.002
Cadmium μg/serving	121	8 %	ND	ND-ND	ND-7.67	0.004
Arsenic μg/serving	121	28 %	ND	ND-0.01	ND-1.47	0.003
Mercury μg/serving	121	37 %	ND	ND-0.003	ND-0.08	0.002
Benzyl butyl μg/serving	84	47 %	ND	ND-0.06	ND-1.53	0.0003
Bis(2-ethylhexyl) μg/serving	80	80 %	0.30	0.10–1.77	ND-16.85	0.01
Dibutyl μg/serving	84	62 %	0.03	ND-0.19	ND-3.39	0.002
Dihexyl μg/serving	84	13 %	ND	ND-ND	ND-0.20	0.01
CBD mg	121	99 %	261	101–555	ND-3069	0.14

product label, with 54 % of products falling within ±10 % of the CBD amount on the product label.

4. Discussion

This study represents the first comprehensive analysis of toxic contaminants, including heavy metals and phthalates, in addition to CBD labeling accuracy in a large sample of commercially available CBD products in the US market. Results indicate that low level contamination of edible CBD products with lead, cadmium, arsenic, mercury, and phthalates is pervasive. In addition, our findings suggest substantial discrepancy between the product label claims for CBD content and the amount measured in the sample across all product types. The growing recognition of CBD's potential to treat a wide range of pediatric and adult health concerns, including pain, psychological, and neurological impairments, has resulted in a substantial increase of both demand and production of commercially available CBD products over the past decade. In order for physicians and consumers to feel confident recommending and using these products, evidence of both product purity and product labeling accuracy across the CBD market is important.

Lead is a known neurotoxin and there is no safe level of lead exposure (Balali-Mood et al., 2021). Lead contamination was detected in 42 % of the 121 edible CBD products tested, but typically at low concentrations, and four exceeded the California proposition 65 threshold for daily lead consumption of 0.5 μg in only two servings. This is noteworthy as CBD containing products are only one of many prevalent exposure sources of lead, which also include degrading paint, food, water, and household products including dishware. Cadmium is also a potent neurotoxin, and a renal and reproductive toxin that bioaccumulates in the body (Balali-Mood et al., 2021). Cadmium was less frequently detected in the edible CBD samples, and none exceeded any regulatory thresholds. Across all tested edible products, levels of heavy metal contaminants were not associated with increased CBD concentration. It is important to recognize that the appearance of heavy metals in retail products is not necessarily the result of its accumulation in the raw cannabis plant material. Carriers, excipients, flavorings, and other ingredients, as well as processing apparatuses and storage containers may all serve as sources of heavy metal contamination in the final products. The variability of heavy metal contamination levels across the products underscores the ability to substantially limit this contamination in CBD products and the value of repeated and frequent testing for contamination by product manufacturers.

The strong potential for heavy metal contamination in cannabis plants and products is established (Montoya et al., 2020). Heavy metals, including lead, cadmium, arsenic, and mercury, are easily absorbed by cannabis plants grown in contaminated soil, and are then incorporated into the tissues throughout the plant. The high levels of heavy metals in cannabis grown in contaminated soil is primarily unintentional and only identifiable through testing the soil and plants, but there have also been reports of

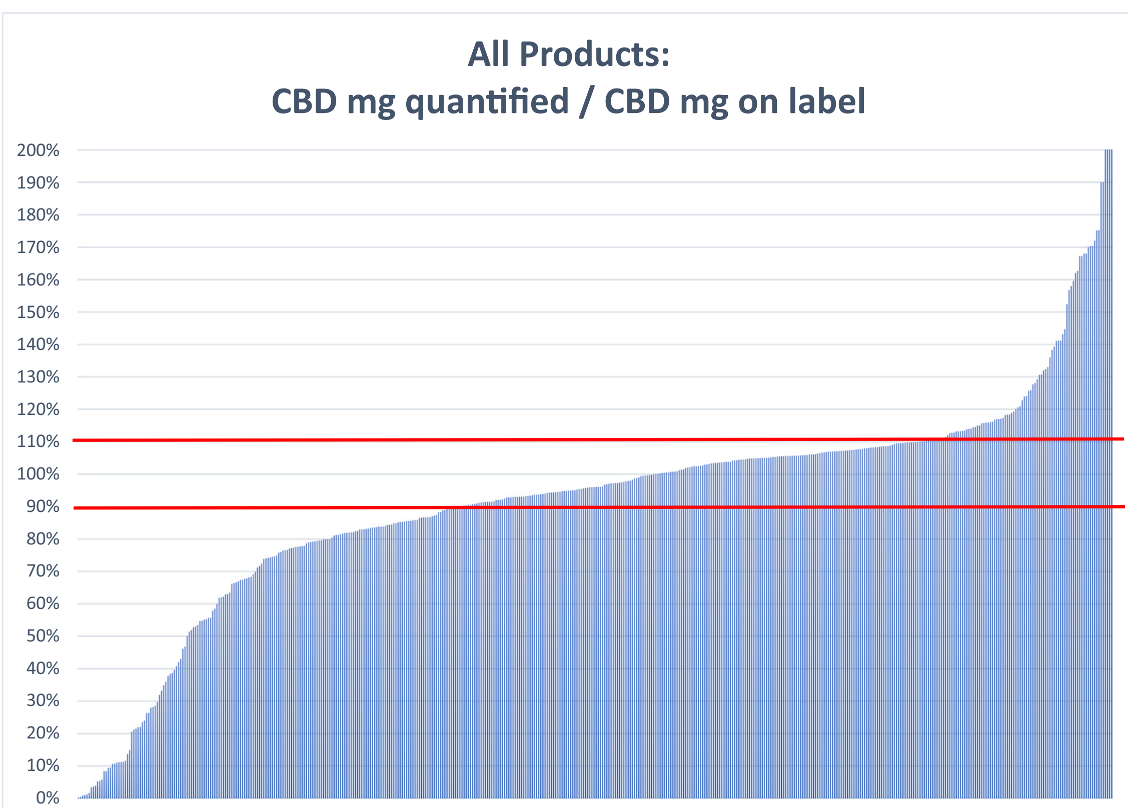

Fig. 1. Comparison between the measured CBD in each product in the full sample (topicals and edibles, N = 516) and that claimed on the label.

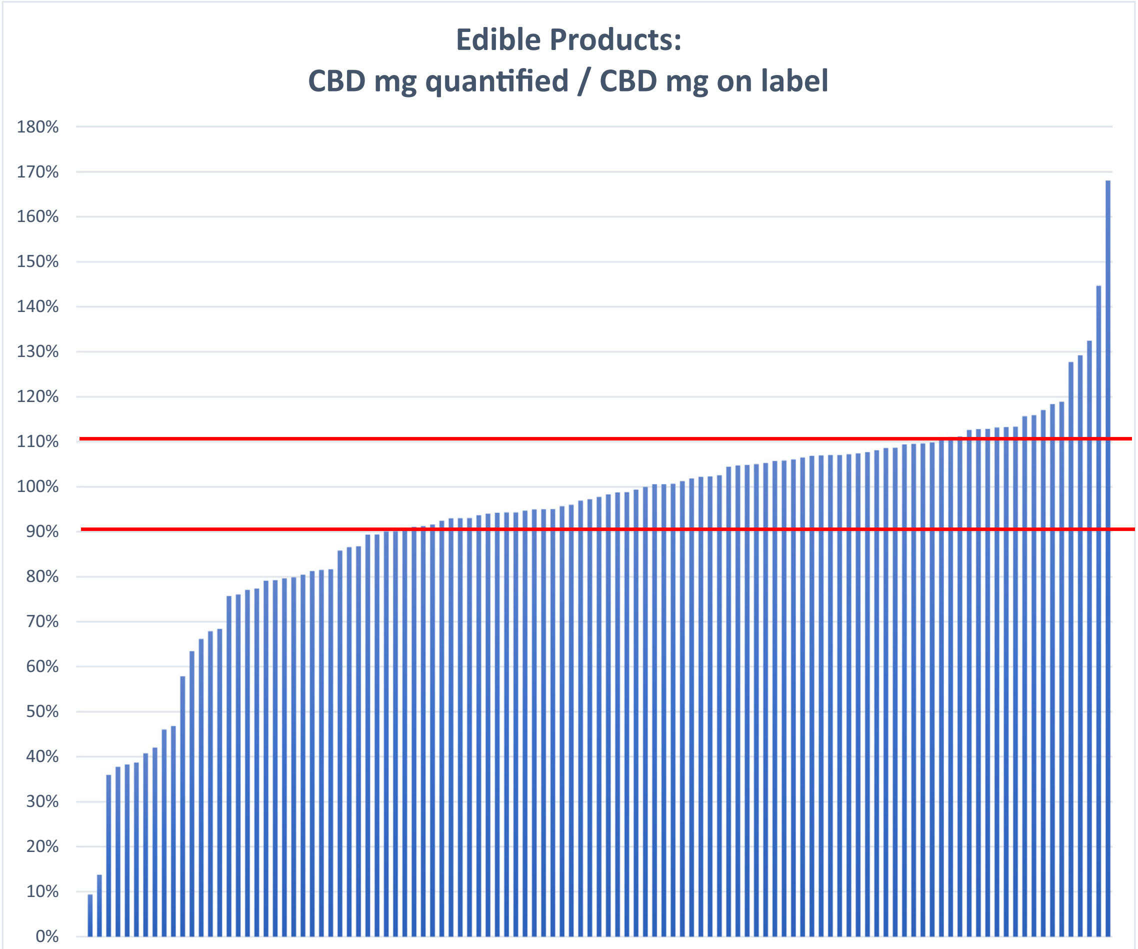

Fig. 2. Comparison between the measured CBD in the edible products ($N = 121$) and that claimed on the label.

intentional lead added to cannabis (Montoya et al., 2020). Despite the known potential for heavy metal contamination in cannabis products, the data on heavy metals in CBD edible products is very limited. This paucity represents a public health concern due to the growing popularity of these products, including in medically vulnerable populations. A recent study of 29 CBD oil products in the United Kingdom reported small concentrations of lead (0.01–0.24 ppm) in an unspecified number of products tested, with no products having detectable levels of cadmium (Liebling et al., 2022). The authors noted that in their study the daily doses of heavy metals did not exceed the levels permissible in pharmaceutical products according to the International Council for Harmonisation guidelines, but did exceed the food limit safety levels. In another study of 29 commercially available veterinary hemp supplements, heavy metals were detected in four of the products, with lead being most apparent and detected in three of those products, with 2296 μg/mL being the highest detected lead concentration (Wakshlag et al., 2020).

We are not aware of any other studies that have examined phthalate contamination in CBD products. The current study specifically looked at four distinct phthalate compounds as potential contaminants in CBD products. Phthalates were detected in between 13 % to 80 % of the CBD samples depending on the specific phthalate compound. Phthalates represent a broad class of endocrine disrupting chemicals that are present as plasticizers in plastics, particularly polyvinyl chloride (PVC), and as a component of fragrance used in scented products. Benzyl butyl phthalate, which was detected in nearly half of the samples is commonly used to soften PVC and is often found in food conveyor belts, vinyl gloves, and adhesives (Herrero et al., 2015). Because it is not tightly bound to the plastic, it migrates out easily and is therefore able to contaminate the environments in which it is used. It is included on the Substance Priority List (SPL) by the Agency for Toxic Substances and Disease Registry. Bis(2-ethylhexyl) phthalate (DEHP) was detected in 80 % of samples and represents the most common class of phthalates in the environment. It is also used in the manufacture of flexible PVC products, including hoses, tubing, and tablecloths, and in many other common household products (e.g., furniture, flooring, clothing, toys, shower curtains). Though DEHP is prevalent in homes the current study provides evidence of another relevant ingestion exposure source. Under California's Proposition 65, DEHP is classified as a "chemical known to the State of California to cause cancer and birth defects or other reproductive harm" (Gov, 2017). Dibutyl phthalate (DBP) is also a highly prevalent plasticizer used in PVC and was detected in 62 % of samples. Its use has been restricted in children's toys; it has been listed as a teratogen in California's Proposition 65 list, and is included on the EPA's Priority Pollutant List (Gao and Wen, 2016). Lastly, dihexyl phthalate is a phthalic acid ester and is common in food and beverage products, including food packaging materials and bottled water. In the current study dihexyl was detected in 13 % of CBD samples.

Though data are lacking on phthalates as contaminants in edible CBD products, there has been significant recent attention paid to the presence of phthalates as contaminants in the food supply (Giuliani et al., 2020). Despite regulations to limit the use of phthalates in many commercial products, including toys and products intended for use by children, exposure to phthalates continues to remain prevalent in the home environment. Phthalate exposure has been associated with a wide range of adverse health effects including impaired reproductive and neurodevelopmental health, childhood asthma, hormone related cancers, birth outcomes, thyroid function, developmental disabilities, cardiotoxicity, diabetes, and obesity (Eales et al., 2022). The results of the current study show that phthalate contamination is highly prevalent in CBD products. Since phthalates are not covalently bound polymers, their exposure to heat has the potential to transfer-migrate into food and consumer products (De Toni et al., 2017; Skinner, 2016; Thomas et al., 1984). During the process of manufacturing CBD edibles and topicals, the manufacturing facility must carefully control temperatures and be mindful of the potential for phthalate contamination from extraction and distillation contact surfaces. Ingredients other than CBD used in multi-ingredient products can also be a source of phthalate contamination. By utilizing manufacturer provided certificates of analysis or random testing of incoming raw materials for phthalate contamination, finished CBD product manufacturers can minimize phthalate contamination in finished products. The phthalate test results add to the already present concerns related to the multiple pathways of human exposure and the ubiquitous presence of these pollutants in consumer products and their long-term effect on human health. To limit this toxic exposure among consumers, the manufacturers should be conducting periodic testing of both their finished products and raw ingredients and identifying potential sources of phthalate contamination in their manufacturing process, equipment, storage and packaging materials.

The results of this study show substantial differences between the amount of CBD claimed on product packaging compared to the amount measured in product testing, including products with 0 % CBD detected and others with up to 339 % more CBD than the labeled value. The inaccuracies of the CBD labels were vast, with measured amounts both significantly lower and higher than the label claims. Specifically, the measured values of CBD were more likely to be less than the CBD labeling claimed on the label. Our finding of widespread inaccuracy in CBD label claims is consistent with the results of several other studies: Among 14 CBD oils commercially available in Europe, the CBD concentrations in nine samples (64 % of samples) varied by >10 % when compared to label claims (Pavlovic et al., 2018). Out of 29 CBD products for sale in the United Kingdom, only 11 (38 %) had concentrations that fell within 10 % of manufacturer claims, and 10 (34 %) of the samples had <50 % of the labeled CBD content, with one sample having no measured CBD content (Liebling et al., 2022). In a study of 20 commercially available CBD E-liquids in Switzerland, only seven samples (35 %) contained the correct CBD content as indicated by the manufacturer (in the range of the labeled CBD content ± 10 %) (Grafinger et al., 2020). The authors argued that the discrepancies were likely due to poor formulation, degradation of cannabinoids, bioconversion, or inappropriate laboratory analysis (Liebling et al., 2022; Wakshlag et al., 2020). The percentage of samples with quantified CBD content that was >10 % outside the manufacturer claims in the current study (58 % of products) is similar to those reported in the aforementioned previous work demonstrating consistency in international CBD mislabeling.

These results highlight the need for tight regulations over CBD product label integrity to protect consumers. Swift actions and reform by regulatory agencies (e.g., the FDA) have the potential to ensure label accuracy and alleviate concerns of vulnerable consumers who rely on these products for health promotion and lifestyle support. Regular consumption of unknown quantities of CBD has the potential for serious health consequences. It is incumbent upon manufacturers to recognize the prevalence of misleading claims on labels, identify the sources of the discrepancies between label claims and measured CBD content, and improve label accuracy through a commitment to frequent and thorough independent testing procedures.

This study represents the first large examination of edible CBD products in the United States in relation to heavy metal and phthalate contamination as well as product label accuracy for CBD content. An important strength of the current methodology is the low quantification limits (high sensitivity) for the tested heavy metals and phthalates which has allowed us to identify even low-level contamination of potent environmental toxins. However, some limitations are important to note. First, only one sample was tested per product instead of a composite of multiple product purchases. Therefore, we could not determine variability within or between batches. Additionally, these products were identified based on availability and popularity in local and online retail stores and do not represent a random representative sample of the market. Most importantly, for this study total arsenic and mercury content were measured, and the samples were not speciated into organic and inorganic varieties. Inorganic arsenic is regarded as being a more dangerous public health threat than organic arsenic. As a result, the true risk of arsenic exposure in these data is difficult to estimate. Future studies should speciate these metals in CBD products.

In the absence of regulatory guidance and enforcement, best practices within edible product safety and quality compliance are being overlooked. Given that the consumer demographic purchasing CBD products includes those afflicted with pain, insomnia, anxiety, and other health conditions, these findings could give consumers and medical practitioners hesitation about the benefits and potential harm of CBD use. If left unaddressed, these findings could lead to decline in consumer trust and public health concerns. CBD mistrust could lead to consumers and retailers abandoning this category of potentially efficacious medical therapies. More research is necessary to determine the root cause of the variability in CBD labeling accuracy and the sources of industrial and environmental contamination. Strict regulatory enforcement and surveillance is necessary to maintain category compliance, integrity, and public health protection.

CRediT authorship contribution statement

Hannah Gardener: Formal analysis, Investigation, Methodology, Visualization, Writing – original draft, Writing – review & editing. **Chela Wallin:** Data curation, Investigation, Methodology, Writing – original draft, Writing – review & editing. **Jaclyn Bowen:** Conceptualization, Data curation, Funding acquisition, Investigation, Methodology, Project administration, Supervision, Visualization, Writing – original draft, Writing – review & editing.

Data availability

The data that has been used is confidential.

Declaration of competing interest

This study was funded by an independent educational grant from Greenwich Biosciences LLC (a Jazz Pharmaceuticals Company).

Hannah Gardener has provided paid consulting regarding phthalate and heavy metal exposure avoidance to individuals. Hannah Gardener has provided legal expert witness testimony regarding heavy metals. Hannah Gardener received compensation by the Clean Label Project for this study.

Jaclyn Bowel and Chela Wallin declare no competing financial interests.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.scitotenv.2022.158110.

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