American Journal of Biomedical and Life Sciences
2023; 11(3): 41-46
http://www.sciencepublishinggroup.com/j/ajbls
doi: 10.11648/j.ajbls.20231103.12
ISSN: 2330-8818 (Print); ISSN: 2330-880X (Online)

Profiling Trace Metal Contaminants of Toxicological Interest in Commercially Available Cannabidiol (CBD) Tincture Oils

Amaya Foran[1], Lily Slater[1], Bert Woods[2], Robert Thomas[3], Tom Gluodenis[1, *]

[1]Department of Chemistry and Physics, Lincoln University of Pennsylvania, Oxford, PA, USA
[2]Agilent Technologies, Wilmington, DE, USA
[3]Scientific Solutions, Gaithersburg, MD, USA

Email address:

tgluodenis@lincoln.edu (Tom Gluodenis)
[*]Corresponding author

To cite this article:

Amaya Foran, Lily Slater, Bert Woods, Robert Thomas, Tom Gluodenis. Profiling Trace Metal Contaminants of Toxicological Interest in Commercially Available Cannabidiol (CBD) Tincture Oils. *American Journal of Biomedical and Life Sciences*. Vol. 11, No. 3, 2023, pp. 41-46. doi: 10.11648/j.ajbls.20231103.12

Received: May 6, 2023; **Accepted**: May 23, 2023; **Published**: June 6, 2023

Abstract: There is legitimate concern over the rise in chronic health issues related to metals contamination in hemp derived cannabidiol (CBD) infused products. Hemp is a hyperaccumulator plant increasingly used for environmental reclamation given its unique ability to tolerate heavy metal stress. Cannabidiol and other cannabinoids are extracted from hemp and infused into consumer products, hence the potential exists for the transfer of heavy metals. Current U.S. state-based testing regulations primarily target cadmium (Cd), mercury (Hg), arsenic (As), and lead (Pb). The objective of this study was to evaluate the effectiveness of the currently mandated testing requirements and assess the potential need for testing other metals of toxicological interest. Fifty-two commercially available full spectrum, CBD tincture oils were analyzed for Cd, Hg, As, and Pb as well as the additional 20 metals recommended by the International Council for Harmonization (ICH) Guideline for Elemental Impurities Q3D (R1) in medicinal products. Samples were prepared using microwave assisted acid digestion and analyzed by inductively coupled plasma mass spectrometry (ICP-MS). The fifty-two samples tested were in compliance with current regulations for Cd, As, and Hg. Lead results were more variable with four of the fifty-two samples analyzed (8%) exceeding 0.5 ppm which is the maximum contaminant level (MCL) for oral consumption in many states. Given that independent laboratory tests conducted by the manufacturer or their agents certified the products to be in compliance at the time of shipping, a question exists as to whether the Pb contamination originated from the hemp biomass or the product packaging. The results for the other 20 metals were all well within the Permitted Daily Exposure (PDE) levels recommended by the ICH indicating no evidence based upon this limited sample population for the need for expanded metals testing requirements.

Keywords: Cannabidiol, CBD, Metals, Lead, Tin, Hemp

1. Introduction

Cannabidiol (CBD) is the main non-psychoactive cannabinoid found in the hemp plant (cannabis sativa). Sales of CBD derived products to U.S. consumers are predicted to grow to $17 billion dollars by 2025 driven by demand for lotions, edibles, tinctures, and supplements. Globally, CBD infused products accounted for 4% of the vitamin and dietary supplements market and is expected to grow to over 20 percent by 2027. [1]

This growing popularity is raising legitimate concern over the rise in chronic health issues related to metals contamination in hemp derived, CBD infused products. Hemp, which has been classified as a hyperaccumulator plant, boasts the high biomass, long roots, short life cycle, and genetic structure ideally suited for absorbing and phytoaccumulating heavy metals such as lead (Pb), nickel (Ni), cadmium (Cd), zinc (Zn), and chromium (Cr) from the soil in which it was grown. Ahmad et. al. identified the two heavy metal responsive genes, glutathione-disulfide reductase (GSR) and phospholipase D-α (PLDα) in hemp and demonstrated their role in imparting heavy metal stress tolerance to the plant. [2] Subsequently, hemp has been used for soil remediation near the Chernobyl site in the Ukraine and in several remediation pilot projects both in the U.S. and around the world. [3]

In addition to the accumulation of metals from the soil, unhealthy levels of metals can be introduced into CBD infused products by fertilizers, nutrients, pesticides, water and from other environmental pathways. Elemental contaminants can likewise be introduced from the metallic equipment used during the preparation and processing of the various concentrates and oils. Once incorporated in the raw or partially processed plant material, varying amounts of heavy metals can be extracted depending upon the solvent and/or the temperature and pressure used in the extraction/distillation. Furthermore, the level of heavy metals can be elevated from the purification and concentration steps further down the processing line. Finally, the devices used to deliver these products such as inhalers and vaporizers, can act as additional sources of elemental impurities from internal metal components.

The vast number of CBD infused products are unregulated by the U.S. Federal Government. Rather, the quality and safety of these products is the responsibility of the state in which they were produced. The result is a highly fragmented regulatory environment with inconsistent product standards and testing protocols. Most states have set regulatory limits for only four heavy metals: Pb, As, Cd, and Hg. In some instances, the limits are based upon the metals concentration in the cannabis plant and/or flower, some are based upon daily consumption, others on body weight of the consumer, and still others on the delivery method i.e. oral, inhalation, or transdermal. Exacerbated by a lack of scientific peer-reviewed research on the efficacy, quality and toxicity of these CBD infused consumer products, public health and safety concerns have escalated. [4-9]

In contrast, pharmaceutical products undergo much more uniform and extensive protocols for trace metal profiling. The International Council for Harmonization (ICH) Guideline for Elemental Impurities Q3D (R1) evaluated toxicity data for potential elemental impurities, established a Permitted Daily Exposure (PDE) level for each element of toxicological concern, and applied a risk-based approach to controlling elemental impurities in drug products. [10] The Guideline specifies 24 elements to be considered in any risk assessment along with permitted daily exposure levels based upon current toxicological data. Similarly, the FDA and the U.S. Pharmacopeia (USP) Chapter 232 Elemental Impurities-Limits specifies limits for the concentrations of 24 elemental impurities in drug products. These two empirically determined lists of potential elemental contaminants and acceptable exposure limits derived from structured risk assessments and toxicological data are in stark contrast to the 4 elemental impurities that most U.S. states require manufacturers to certify prior to the sale of CBD infused products.

The growing list of product recalls and pending lawsuits involving elevated metals contamination coupled with the on-going investigation into the use of industrial hemp as a phytoremediation agent for environmental reclamation raise serious questions about the potential chronic toxicity of consumer-based CBD products. The goal of this study was to identify and quantify elemental contaminants of toxicological interest in a sampling of commercially available CBD tincture oils. The objectives were to assess the effectiveness of currently mandated heavy metals testing while assessing the adequacy of those requirements relative to a broader range of elements.

2. Materials and Methods

2.1. CBD Samples

In an effort to instill confidence in consumers, several industry organizations have been established to promote best practices and elevated product standards through certification programs for hemp growers and product manufacturers. The samples for this study, henceforth referred to as “certified” samples, were purchased from companies certified by one such organization with the expectation that the products would represent the highest quality available. Fifteen samples of CBD tincture oil were purchased, each from a different manufacturer. Two additional purchases for a total of three samples per manufacturer, were made at six month increments so that lot to lot variations could be assessed for each manufactured product. In an attempt to minimize experimental variables, each product purchased was a full spectrum tincture oil (containing all cannabinoid extracts including <0.3% tetrahydrocannabinol or THC), unflavored or natural flavored if possible, and contained as close to 50 mg/mL of CBD as possible. Some variations from this schema were present as not all manufacturers offered products of the same potency or flavors. The extraction method, the solvent in which the CBD was suspended and the source of the hemp for each product was noted to the extent that it was made available on the manufacturers website (Table 1). It should be noted that in the case of samples 8, 10, and 15 the product purchased was either discontinued or the manufacturer ceased operations during the course of the study preventing the purchase of three distinct sample lots.

In addition to the “certified samples”, a random sampling of 10 additional products purchased locally at gas stations, smoke shops, and other outlets were analyzed for comparison. These will henceforth be referred to as “non-certified” samples. As these were randomly purchased, there was more variability in product attributes (Table 2). It was determined that “non-certified” sample 23 was available for purchase on the manufacturer’s website so three different lots of that tincture oil were purchased to assess lot to lot variability.

2.2. Sample Preparation and Analysis

A 0.25g aliquot of each sample was transferred into a 15mL digestion vessel using the dropper integrated into the CBD oil product packaging. To the sample was added 2.5mLs of concentrated HNO_3 (PlasmaPURE Plus, SCP Science) and 0.5mLs of concentrated HCl (PlasmaPURE

Plus, SCP Science). The samples were capped and placed in a 15 position carousel along with a digestion blank and a quality control standard. The samples were then digested in a Milestone ultraWAVE microwave digestion system (Milestone, Inc., Shelton, CT), quantitatively transferred to a 50mL DigiTube (SCP Science) and diluted to a final volume of 25mLs with 18MΩ deionized water. Three replicate aliquots were digested for each tincture oil. The microwave program used for the digestion of the CBD oil samples is given in Figure 1.

Table 1. *Profile of "Certified" CBD Oils Analyzed.*

Sample Number	Solvent	CBD Potency	Oil Type	Extraction Process	Flavor	Hemp Source
1	MCT	25 mg/mL	Full Spectrum	Ethanol	Natural/Hemp	Undisclosed
2	Hemp seed oil	50 mg/mL	Full Spectrum	CO_2	Natural/Hemp	Colorado/Oregon
3	MCT	83 mg/mL	Full Spectrum	CO_2	Natural/Hemp	Undisclosed
4	Olive Oil	50 mg/mL	Full Spectrum	Ethanol	Natural/Hemp	Colorado
5	Olive Oil	27 mg/mL	Full Spectrum	Undisclosed	Natural/Hemp	Undisclosed
6	MCT	25 mg/mL	Full Spectrum	CO_2	Peppermint	Kentucky
7	MCT	25 mg/mL	Full Spectrum	CO_2	Natural/Hemp	North Carolina
8	Hemp seed oil	50 mg/mL	Full Spectrum	CO_2	Natural/Hemp	Undisclosed
9	MCT	50 mg/mL	Full Spectrum	Ethanol	Mint	Tennessee
10	MCT	50 mg/mL	Full Spectrum	Undisclosed	Natural/Hemp	Kentucky
11	Hemp seed oil	50 mg/mL	Full Spectrum	Undisclosed	Peppermint	Kentucky
12	Hemp seed oil	60 mg/mL	Full Spectrum	CO_2	Natural/Hemp	Colorado
13	MCT	50 mg/mL	Full Spectrum	Undisclosed	Natural/Hemp	Montana
14	Hemp seed oil	33 mg/mL	Full Spectrum	CO_2	Natural/Hemp	Colorado
15	MCT	25 mg/mL	Full Spectrum	CO_2	Natural/Hemp	Kentucky

Table 2. *Profile of "Non-Certified" CBD Oils Analyzed.*

Sample Number	Solvent	CBD Potency	Oil Type	Extraction Process	Flavor	Hemp Source
16	MCT	25 mg/mL	Full Spectrum	CO_2	Mango	Kentucky
17	MCT	8 mg/mL	Broad Spectrum	CO_2	Peppermint	Undisclosed
18	MCT	6 mg/mL	Full Spectrum	Undisclosed	Natural	Undisclosed
19	MCT	83 mg/mL	Broad Spectrum	CO_2	Natural	Undisclosed
20	MCT	8 mg/mL	Full Spectrum	Undisclosed	Natural	USA
21	MCT	33 mg/mL	Full Spectrum	Undisclosed	Coconut	Undisclosed
22	MCT	25 mg/mL	Full Spectrum	Undisclosed	Natural	Undisclosed
23	MCT	16 mg/mL	CBD Isolate	Undisclosed	Cotton Candy	Undisclosed
24	Hemp Oil	50 mg/mL	Undisclosed	Undisclosed	Sour Sweet	Undisclosed
25	Glycerin	10 mg/mL	Broad Spectrum	CO_2	Natural	USA
26	MCT	100 mg/mL	Broad Spectrum	CO_2	Natural	Undisclosed

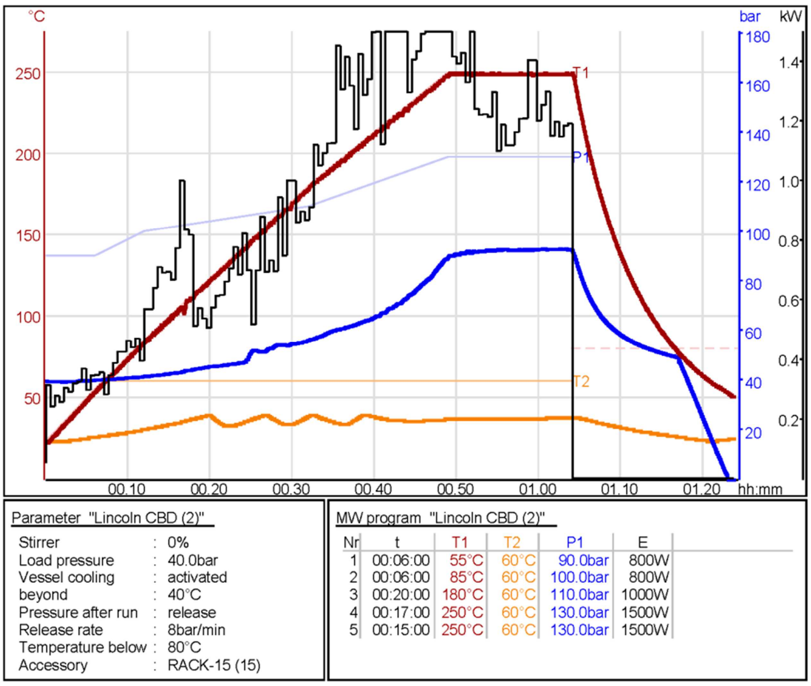

Figure 1. *Microwave Program For the Digestion of CBD Tincture Oils. Nr = step number in the microwave program; t = time for each step in the program; T1 = maximum temperature; P1 = maximum pressure; E = microwave power.*

The digested samples were analyzed with an Agilent 7850 Inductively Coupled Plasma Mass Spectrometer (ICP-MS) using the Association of Official Agricultural Chemists (AOAC) method 2021.03-2021 Heavy Metals in a Variety of Cannabis and Cannabis Derived Products. The accuracy and precision of the ICP-MS-based method had been previously demonstrated to meet the AOAC Standard Method Performance Requirements [11] as published by Nelson et al. [12] Instrument operating conditions are given in Table 3.

The ICP-MS was calibrated using multi-element standards (Agilent Technologies, Santa Clara, CA) at concentrations of 0, 0.1, 0.5, 1.0, 10, 50, and 100 ppb in a 2% HNO_3/0.5% HCl matrix. Mercury calibration standards were at concentrations of 0, 0.01, 0.05, 0.1, 1.0, 5.0 and 10ppb in a 2% HNO_3/0.5% HCl matrix. The internal standards used were tellurium (125ppb), germanium (50ppb), bismuth (50ppb), indium (50ppb), lutetium (50ppb), and scandium (100ppb). The calibrations were verified through analysis of NIST Standard Reference Material 1643F Trace Elements in Water. Recoveries of 91% to 107% were achieved for all certified elements. Samples were analyzed in batch with a 50ppb multielement/5ppb mercury continuing calibration verification (CCV) standard analyzed after every 10 samples. Recoveries of the CCV standard ranged from 92% – 103% with <4% RSD.

3. Results and Discussion

Results for the commonly regulated metals (As, Hg, Cd, Pb) for each lot of the 15 "certified" CBD oils are given in Table 4. Although acceptable concentrations for these elements vary by state, they are generally regulated at the following maximum contaminant levels for orally consumed products: Pb 0.5ppm, As 1.5ppm, Cd 0.5ppm and Hg 3.0ppm. It can be observed from Table 4 that the concentrations for each of the "certified" samples tested are well below these regulated levels with the exception of sample 9 in which the first lot contained 0.69ppm Pb and the third lot contained 3.7ppm Pb. Table 5 displays the results of the "non-certified" samples for the same four elements. Once again the concentrations for each of the samples tested are well below the regulated levels with the exception of sample 23 in which the first lot tested was determined to contain 1.3ppm Pb and the third lot 0.59ppm Pb.

***Table 3.** ICP-MS Instrument Operating Parameters.*

Tune Mode:	He
Plasma Conditions	
Plasma Mode	HMI
Aerosol Dilution	Low
RF Power	1600 W
RF Matching	1.35 V
Sampling Depth	10.0 mm
Nebulizer Gas	0.83 L/min
Option Gas	0.0%
Nebulizer Pump	0.1 rps
Spray Chamber Temp	2°C
Gas Switch	Dilution Gas
Make Up/Dilution Gas	0.15 L/min
Collision Cell	
Use Gas	Yes
He Flow	On
He Flow Rate	4.5 mL/min
H_2 Flow	Off
H_2 Flow Rate	0.0 mL/min
Octupole RF	200 V
Energy Discrimination	5.0 V

Twenty-two additional elements which are not often state regulated but are of toxicological interest per the International Council for Harmonization (ICH) Guideline for Elemental Impurities Q3D (R1) were also quantified. The majority of the elements in both the "certified" and "non-certified" samples were in the low parts-per-billion range well within the established permitted daily exposure (PDE) levels as published by the ICH. [10]

***Table 4.** Concentrations of the Commonly Regulated Metals (As, Hg, Cd, Pb) in Each Lot of the "Certified" CBD Oils Tested.*

Sample_Lot	[As] ppb	[Cd] ppb	[Hg] ppb	[Pb] ppb
CBD Oil 1_1	1.2	ND	1.8	45
CBD Oil 1_2	1.4	ND	6.6	7.0
CBD Oil 1_3	1.7	ND	4.9	82
CBD Oil 2_1	1.1	2.3	8.7	5.9
CBD Oil 2_2	0.4	ND	1.4	8.2
CBD Oil 2_3	1.5	ND	2.4	12
CBD Oil 3_1	6.4	ND	2.6	17
CBD Oil 3_2	1.6	0.2	29	4.3
CBD Oil 3_3	2.6	ND	2.4	49
CBD Oil 4_1	0.7	ND	2.9	29
CBD Oil 4_2	1.4	ND	1.5	20
CBD Oil 4_3	1.7	ND	2.8	21
CBD Oil 5_1	10	ND	0.6	8.4
CBD Oil 5_2	28	0.5	1.5	6.4
CBD Oil 5_3	19	ND	2.8	6.3
CBD Oil 6_1[a]	0.5	ND	6.0	110
CBD Oil 7_1	1.2	ND	3.3	42
CBD Oil 7_2	0.3	0.2	9.1	1.8
CBD Oil 7_3	3.8	ND	9.7	12
CBD Oil 8_1[a]	1.4	ND	2.9	6.5
CBD Oil 8_2[a]	0.4	0.9	2.9	7.7
CBD Oil 9_1	1.3	1.5	6.4	690[b]
CBD Oil 9_2	2.2	3.1	14	38
CBD Oil 9_3	1.4	ND	1.8	3700[b]
CBD Oil 10_1[a]	0.9	ND	3.2	43
CBD Oil 10_2[a]	0.2	ND	2.1	9.6
CBD Oil 11_1	1.7	ND	3.3	14
CBD Oil 11_2	2.0	ND	2.3	11
CBD Oil 11_3	0.7	1.7	5.1	17
CBD Oil 12_1	0.9	ND	2.3	5.4
CBD Oil 12_2	0.5	ND	1.9	7.3
CBD Oil 12_3	1.9	1.3	4.9	12
CBD Oil 13_1	6.5	ND	3.0	46
CBD Oil 13_2	ND	ND	6.9	1.9
CBD Oil 13_3	1.6	1.0	6.1	2.2
CBD Oil 14_1	0.6	1.2	5.1	6.1
CBD Oil 14_2	0.9	ND	1.1	7.6
CBD Oil 14_3	1.0	1.5	3.9	8.0
CBD Oil 15_1[a]	0.9	ND	2.8	49

[a] The CBD oil tested was either no longer available for sale and/or the producer was no longer in business precluding the ability to analyze three lots of this particular product.

[b] Concentration exceeds the maximum contaminant level set in most state.

ND = not detected

Table 5. *Concentrations of the Commonly Regulated Metals (As, Hg, Cd, Pb) in Each of the "Non-certified" CBD Oils Tested.*

Sample _ Lot	[As] ppb	[Cd] ppb	[Hg] ppb	[Pb] ppb
CBD Oil 16	0.3	ND	4.5	9.7
CBD Oil 17	0.1	ND	7.7	8.2
CBD Oil 18	1.1	ND	6.1	52
CBD Oil 19	0.3	ND	1.8	8.4
CBD Oil 20	0.2	ND	3.7	10
CBD Oil 21	0.2	ND	3.9	8.0
CBD Oil 22	0.2	ND	7.8	8.5
CBD Oil 23_1[a]	0.9	ND	2.0	1300[b]
CBD Oil 23_2[a]	1.4	ND	6.2	6.6
CBD Oil 23_3[a]	1.0	0.8	9.7	590[b]
CBD Oil 24	1.0	1.2	6.0	1.2
CBD Oil 26	0.4	ND	1.7	8.5

[a] This product was available for purchase through the manufacturers website so it was possible to procure three different lots of the material for testing.
[b] Concentration exceeds the maximum contaminant level set in most states
ND = not detected

The samples analyzed were in compliance with currently accepted maximum contaminant levels (MCLs) for Cd, Hg and As with good lot to lot reproducibility. Lead concentrations were more variable both within sample lots as well as between samples with four (8%) of the analyzed products exceeding regulated levels; namely samples 9_1, 9_3, 23_1, and 23_3. The websites of the respective manufacturers both indicated that the products had been tested by an independent laboratory with Pb concentrations determined to be within acceptable levels.

Assuming reports from the independent testing laboratories were correct, this suggests that the Pb contamination was introduced at some point post-manufacturing. Pickett and Giovinazzi had reported on the preliminary results of a study suggesting that in some cases Pb could be leached from the packaging material into the product over time, specifically from the dropper and ink used to denote dosage. [13] Attempts to explore this hypothesis by reanalyzing the samples in question over a period of time were inconclusive as there were no detectable changes in concentration. Contribution of Pb from the packaging remains a possible explanation as it is conceivable that the product had reached an equilibrium state with the packaging in the time it took to bottle, store, ship, and analyze the sample in the author's laboratory. It is interesting to note that the elevated Pb levels were present in different lots of the same two samples – one from a "certified" producer and one from a "non-certified" producer. It is difficult to draw conclusions based on the limited sampling but the possibility exists that there is a systematic root cause underlying these observations.

In addition to Cd, Pb, Hg, and As, twenty-two additional elements were quantified and found to be well within the Permitted Daily Exposure (PDE) levels recommended by the ICH (Table 6). It is worth noting, however, that the ICH PDE safety assessment focused only on inorganic Sn whereas Sn toxicity is heavily dependent upon the form (inorganic vs organic) in which it is present in the product. Some organotin compounds have been shown to result in neurotoxicity, hepatotoxicity, renal toxicity or dermal toxicity. This is largely due to the lipophilic nature of organotin compounds allowing them to be readily absorbed from the gastrointestinal tract where they can then distribute to other parts of the body such as the central nervous system [14]. According to the Center for Disease Control (CDC) Agency for Toxic Substances and Disease Registry (ATSDR), the minimum contaminant level (the highest level of the contaminant that is allowed without deleterious effects) for inorganic tin is 0.3mg/kg/day - 60x higher than that of dibutyl tin for intermediate duration oral exposure (0.005 mg/kg/day) and 100x higher than tributyl tin (0.0003mg/kg/day) which is significantly more toxic. [15] Two of the CBD oil samples tested contained >100ppm Sn which exceeds the 0.0003mg/kg/day guideline set for tributyl tin (assuming a 70kg male and a 1ml dose taken three times daily as recommended by most CBD oil manufacturers). The form of the tin present in the CBD oils is currently unknown and there have been no known speciation studies conducted to date.

Finally, it is worth noting that during the course of this study both "certified" and "non-certified" products were examined. The primary difference between the two being that "certified" samples were manufactured by producers who belonged to industry organizations striving to increase consumer confidence in hemp derived products through added quality measures, sharing of best practices and self-regulation. The results of this study suggests that for the limited sample population tested both sets of products were largely equivalent relative to the metals content.

Table 6. *Permitted Daily Exposure (PDE) Levels for Oral Administration of Elemental Impurities as Established by the ICH.*

Element	Oral PDE, µg/day	Element	Oral PDE, µg/day
Cadmium (Cd)	5	Rhodium (Rh)	100
Lead (Pb)	5	Ruthenium (Ru)	100
Arsenic (As)	15	Selenium (Se)	150
Mercury (Hg)	30	Silver (Ag)	150
Cobalt (Co)	50	Platinum (Pt)	100
Vanadium (V)	100	Lithium (Li)	550
Nickle (Ni)	200	Antimony (Sb)	1200
Thallium (Tl)	8	Barium (Ba)	1400
Gold (Au)	300	Molybdenum (Mo)	3000
Palladium (Pd)	100	Copper (Cu)	3000
Iridium (Ir)	100	Tin (Sn)	6000
Osmium (Os)	100	Chromium (Cr)	11000

4. Conclusion

The objective of this study was to evaluate the effectiveness of the currently mandated testing requirements for commercially available CBD tincture oils and assess the potential need for testing other metals of toxicological interest. It was determined that the 52 samples tested were in conformance with currently accepted maximum contaminant levels (MCLs) for Cd, Hg and As with good lot to lot reproducibility. Lead was more variable with four of the fifty-two samples tested (8%) exceeding the MCL. It is worth noting that all four samples were produced by the same two manufacturers. The question exists as to whether the elevated

Pb concentrations originated from the hemp biomass or were introduced from the product packaging. Defining the origin of the contamination will require additional investigation.

Regarding the non-regulated elements which were quantified, the elevated tin concentrations might be of concern depending upon the chemical form in which it is present in the product. Speciation studies to address that question are the subject of a future investigation. Otherwise, being mindful that the majority of the samples were chosen as representative of the best of the industry i.e. “certified”, there was no evidence based upon this limited sample population for the need for an expanded elemental testing requirement.

Looking forward, it is recommended that this investigation be expanded to a broader sample population particularly relative to “non-certified” samples. Experimental design should include a time dependent sampling model as a means of identifying product contamination resulting from the packaging. There is also a need to better understand the effect, if any, of various product attributes such as potency, extraction process, flavor, and hemp source given the narrow constraints of this initial study. As noted previously, speciation studies are required to understand the nature of the metals present in the product and the subsequent impact on potential toxicity. Finally, CBD oils are one small segment of the overall market. Other matrices including vape oils, beverages, edibles, and other widely used consumer products should also be evaluated to ensure public health and safety.

Acknowledgements

This work was funded in part through the 2021-2022 Douglas M. Lucas Grant from the Forensic Science Foundation of the American Academy of Forensic Sciences. Support was also provided by the Lincoln University Office for Undergraduate Research through Title III Part A.

References

[1] Jan Conway, (2022). CBD Retail in the United States – Statistics and Facts. *Statista Market Report,* Aug 19, 2022 https://www.statista.com/topics/6262/cbd-retail-in-the-united-states/#topicOverview

[2] Rafiq Ahmad, Zara Tehsin, Samina Tanvir Malik, Saeed Ahmad Asad, Muhammad Shahzad, Muhammad Bilal, Mohammad Maroof Shah, Sabaz & Ali Khan. (2016). Phytoremediation Potential of Hemp (Cannabis sativa L.): Identification and Characterization of Heavy Metals Responsive Genes. *Clean Soil Air Water.* 44: 195-201 doi: 10.1002/clen.201500117.

[3] Dante F. Placido & Charles C. Lee. (2022). Potential of Industrial Hemp for Phytoremediation of Heavy Metals. *Plants (Basel), 11 (5): 595.* (2). doi: 10.3390/plants11050595.

[4] WTVD-TV News I-Team, (June 18 2018). Army Bans CBD Oil after rash of ER visits at Fort Bragg. https://abc11.com/fort-bragg-army-i-team-hemp-products/3617435/.

[5] Melissa Schiller.(October 5, 2020) Ohio Recalls Medical Cannabis Edibles Due to Heavy Metals, *Cannabis Business Times*, https://www.cannabisbusinesstimes.com/news/ohio-recalls-medical-cannabis-edibles-due-to-heavy-metals/

[6] Michigan Cannabis Regulatory Agency. (August 30, 2019). MRA Recalls Four Medical Marijuana Products Across the State. Press Release. https://www.michigan.gov/cra/spotlight/mra-recalls-four-medical-marijuana-products-across-the-state.

[7] HempIndustry Daily. (May 5, 2020). CBD Retailer Falsely Claimed Oils Were Heavy-Metal-Free, Lawsuit Says. https://hempindustrydaily.com/cbd-retailer-falsely-claimed-oils-were-heavy-metal-free-lawsuit-says/.

[8] Leo Bear-McGuinness. (Jun 9, 2020). Hawaiian Cannabis Vape Cartridges Are Contaminated with Ethanol and Lead, Tests Find, *Analytical Cannabis*. https://www.analyticalcannabis.com/news/hawaiian-cannabis-vape-cartridges-are-contaminated-with-ethanol-and-lead-tests-find-312447.

[9] Hemp Industry Daily, (May 18, 2020). Florida CBD company issues voluntary product recall for heavy lead content”, https://hempindustrydaily.com/florida-cbd-company-issues-voluntary-product-recall-for-heavy-lead-content/.

[10] International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) Q3D on elemental impurities – Step 5 – Revision 2, First published 03/05/2022, Legal effective date 24/09/2022, EMA/CHMP/ICH/353369/2013 https://www.ema.europa.eu/en/documents/scientific-guideline/international-conference-harmonisation-technical-requirements-registration-pharmaceuticals-human-use_en-16.pdf.

[11] SMPR 2020.001, Standard Method Performance Requirements for Determination of Heavy Metals in a Variety of Cannabis and Cannabis-Derived Products, https://www.aoac.org/wp-content/uploads/2020/07/SMPR-2020_001.pdf].

[12] Jenny Nelson, Craig Jones, Sam Heckle, & Leanne Anderson. (2021). Determination of Heavy Metals in a Variety of Cannabis and Cannabis-Derived Products, First Action 2021.03. *Journal of AOAC INTERNATIONAL*, 105, (6) 1640–1651, doi: 10.1093/jaoacint/qsab173.

[13] Diane Pickett & Serena Giovinazzi. (2021) Heavy Metals in Hemp Extract Products In the Florida Department of Agriculture and Consumer Services Food Safety Lab. *ASTM Workshop on Measurement of Elemental Contaminants in Cannabis and Hemp*, June 28-30, 2021, sponsored by ASTM Committees D37 on Cannabis.

[14] Elena A. Ostrakhovitch. (2022). Chapter 33 – Tin. *Handbook on the Toxicology of Metals (Fifth Edition).* Science Direct. https://www.sciencedirect.com/science/article/abs/pii/B9780128229460000295.doi: 10.1016/B978-0-12-822946-0.00029-5.

[15] U.S. Department of Health and Human Services, Public Health Service, Agency for Toxic Substances and Disease Registry, (2005) Toxicological Profile for Tin. https://www.atsdr.cdc.gov/toxprofiles/tp55.pdf.