



Introduction

Cannabis-based products are available in a wide variety of formulations ranging from dry plant material, plant concentrates including waxes and distillates, and infused products such as foods and candies. Given the variety of sample matrices, existing sample preparation procedures developed for inductively coupled plasma-based techniques can be applied to cannabis products. For example, trace element analysis of plant and nutritional supplement materials is a well-established application

(1). Following acidic digestion to break down the primary components of the plant-based samples, inductively coupled plasma–mass spectrometry (ICP-MS) or ICP-optical emission spectrometry (OES) is often used for quantitative analysis because of the multielement capability, speed, and robustness of each technique. ICP-OES is suited to the analysis of mineral and micronutrients such as K, Ca, Mg, Cu, Fe, Mn, Zn, Cu, Mo, and Ni—vital elements required for plant growth. When the required analytes also include trace elements such as As, Se, Cd, Pb, and Hg, which may require lower detection limits, ICP-MS offers greater sensitivity, delivering detection limits and accurate analysis down to nanogram-per-liter (part-per-trillion) levels.

Most of the states that have legalized the use of marijuana for either medicinal or recreational use have enacted regulations for acceptable limits of toxic elements (Cd, Pb, As, and Hg) in cannabis and cannabinoid products (2). As shown in Table I (3), the limits can vary among states, and regulations governing the safety and quality of cannabis-based products are likely to evolve to include more elements.

	California (Action level)			Colorado	Connecticut	Nevada	New Mexico
	Medical Edible Cannabis Products, Sublingual Products, and Other Manufactured Products	Inhaled Medical Cannabis Goods	Topical and Transdermal Medical Cannabis Goods	Acceptable Limits per Gram (Flower, Water, Food, and Solvent-Based Medical Marijuana Concentrates; Medical Marijuana-Infused Product)			Natural Health Products Acceptable Limits
	µg/g (ppm)			µg/g (ppm)	µg/kg BW/day (ppb BW/day)		
Cd	0.5	0.2	5	<0.4			<0.09
Pb	0.5	0.5	10	<1.0			<0.29
As	1.5	0.2	3	<0.4			<0.14
Hg	3	0.1	1	<0.2			<0.29

Experimental

Preparation of Cannabis Samples Two cannabis plant samples were analyzed in this study. Approximately 0.15 g of buds from each cannabis plant was weighed into a quartz vessel. Then 4 mL of nitric acid (HNO₃) and 1 mL of hydrochloric acid (HCl) were added and the samples were microwave digested using a onestep program: ramp time of 20 min to a temp of 240 °C and hold time of 15 min. Hydrochloric acid was included to ensure the stability of Ag and Hg in solution.

The digested samples were diluted using a mix of 1% HNO₃ and 0.5% HCl. National Institute of Standards and Technology (NIST) 1547 Peach Leaves and NIST 1573a Tomato Leaves standard reference materials (SRMs) were prepared using the same method to verify that the digestion was complete and confirm the quantitative recovery of the analytes.

ICP-MS Parameter	Setting	ICP-OES Parameter	Setting
RF power (W)*	1600	RF power (kW)	1.3
Sampling depth (mm)*	10	Auxiliary gas flow (L/min)	1.00
Carrier gas flow (L/min)*	0.80	Plasma gas flow (L/min)	12.0
Dilution (HMI) gas flow (L/min)*	0.15	Nebulizer gas flow (L/min)	0.70
Helium cell gas flow (mL/min)	4.3	Viewing mode	Axial
Energy discrimination (V)	3.0	Viewing height (mm)	8

Instrumentation The ICP-MS system used for the analysis was a standard 7800 (Agilent), which includes the High Matrix Introduction (HMI) system. The ICP-OES system used was a standard 5110 SVDV (Agilent) fitted with an Advanced Valve System (AVS) six-port valve. Both instruments were used with an SPS 4 autosampler (Agilent). The ICP-MS system was configured with the standard sample introduction system consisting of a Micromist glass concentric nebulizer, a quartz spray chamber, and a quartz torch with a 2.5-mm i.d. injector. The interface consisted of a nickel-plated copper sampling cone and a nickel skimmer cone. The ICP-OES sample introduction system consisted of a SeaSpray nebulizer, a double-pass cyclonic spray chamber, and a 1.8-mm i.d. injector torch. Both instruments can perform a rapid screening measurement together with the quantitative analysis. Using a standard feature of the respective software, semiquantitative results can be reported for elements not included in the calibration standards.

Experimental

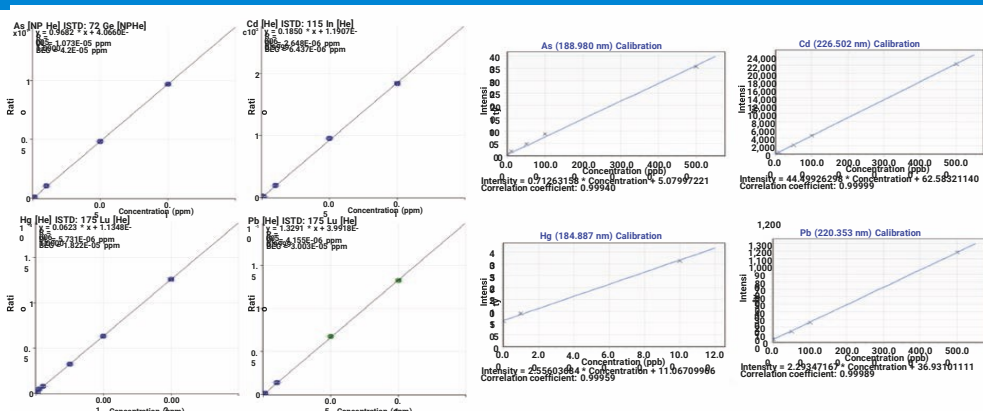


Figure 1: (a) ICP-MS and (b) ICP-OES calibration curves for As, Cd, Pb, and Hg.

Calibration Representative ICP-MS and ICP-OES calibration curves for the critical trace elements As, Cd, Pb, and Hg are shown in Figure 1.

All curves show excellent linearity across the respective calibration ranges.



Results and Discussion

To verify the digestion procedure used for the cannabis samples, two plant material SRMs were analyzed by ICPMS and ICP-OES. Some plant samples may contain high levels of rare earth elements (REEs), which can be problematic for the analysis of low concentrations of As and Se by ICP-MS. REEs have low second ionization potentials, so they readily form doubly-charged ions (REE⁺⁺). As the quadrupole mass spectrometer separates ions based on their mass-to-charge ratio (*m/z*), these doubly charged ions appear at half their true mass. Doubly charged ions of the REEs 150Nd, 150Sm, 156Gd, 156Dy, 160Gd, and ¹⁶⁰Dy therefore appear at *m/z* 75, 78, and 80, potentially causing overlaps that can bias the results for As and Se in samples that contain high levels of the REEs. The ICP-MS system corrects for these interferences using the “half mass correction” setting in the ICP-MS MassHunter software. The mean results shown in Table III were in good agreement with the certified concentrations, where provided, including for As in NIST 1547 and Se in both NIST 1547 and 1573a.

Element (Mass and Wavelength)	Certified Conc.	NIST 1547 Peach Leaves						NIST 1573a Tomato Leaves					
		ICP-MS			ICP-OES			ICP-MS			ICP-OES		
		Mean Measured Conc.*	Recovery [†]	QC Criteria (80–120%) [‡]	Mean Measured conc.*	Recovery [†]	QC Criteria (80–120%) [‡]	Mean Measure Conc.*	Recovery [†]	QC Criteria (80–120%) [‡]	Mean Measure Conc.*	Recovery [†]	QC Criteria (80–120%) [‡]
²³ Na	23.8	27.86	117	Pass	NA		136	119.2	88	Pass	<MDL		
²⁴ Mg (279.078 nm)	4320	4264.2	99	Pass	4232.0	98	Pass	12000 [§]	10213.1	85	Pass	10711.3	89
²⁷ Al (396.152 nm)	248.9	251.7	101	Pass	225.1	90	Pass	598	513.3	86	Pass	505.4	85
³⁹ K (769.897 nm)	24330	24434.9	100	Pass	20513.3	84	Pass	27000	25728.4	95	Pass	24886.7	92
⁴⁴ Ca (315.887 nm)	15590	17371.6	111	Pass	15773.3	101	Pass	50500	53983.3	107	Pass	48836.7	97
⁵¹ V	0.367	0.349	95	Pass	<MDL		0.835	0.698	84	Pass	<MDL		
⁵² Cr (205.560 nm)	1 [¶]	1.118	112		0.992	99	Pass	1.99	1.988	100	Pass	2.007	101
⁵⁵ Mn (257.610 nm)	97.8	99.6	102	Pass	97.9	100	Pass	246	238.7	97	Pass	237.8	97
⁵⁶ Fe (239.563 nm)	219.8	222.8	101	Pass	179.1	81	Pass	368	331.1	90	Pass	315.3	86
⁵⁹ Co	0.07 [§]	0.069	99		<MDL		0.57	0.510	89	Pass	<MDL		
⁶⁰ Ni (216.555 nm)	0.689	0.788	114	Pass	0.726	105	Pass	1.59	1.442	91	Pass	0.157	10
⁶³ Cu (324.754 nm)	3.75	3.649	97	Pass	3.932	105	Pass	4.7	4.330	92	Pass	4.826	103
⁶⁶ Zn (213.857 nm)	17.97	17.378	97	Pass	17.636	98	Pass	30.9	25.953	84	Pass	29.250	95
⁷⁵ As (188.980 nm)	0.06 [¶]	0.059	98	Pass	0.055	92	Pass	0.112	0.109	97	Pass	0.096	85
⁷⁸ Se (196.026 nm)	0.12 [¶]	0.108	90	Pass	0.105	88	Pass	0.054	0.064	119	Pass	0.044	81
⁹⁵ Mo	0.0603	0.054	90	Pass	<MDL		0.46 [§]	0.445	97	Pass	<MDL		
¹⁰⁷ Ag	#						0.017 [§]	0.019	112	Pass	<MDL		
¹¹¹ Cd (226.502 nm)	0.0261	0.028	107	Pass	<MDL		1.52	1.330	88	Pass	1.440	95	Pass
¹³⁷ Ba (455.403 nm)	123.7	124.9	101	Pass	121.6	98	Pass	63 [§]	56.500	90	Pass	59.660	95
²⁰¹ Hg	0.0317	0.028	88	Pass	<MDL		0.034	0.033	97	Pass	<MDL		
²⁰⁸ Pb	0.869	0.846	97	Pass	<MDL		#						
²³² Th	0.05 [§]	0.050	100	Pass	<MDL		0.12 [§]	0.091	76	Pass	<MDL		
²³⁸ U	0.015 [§]	0.014	93	Pass	<MDL		0.035 [§]	0.028	80	Pass	<MDL		

Results and Discussion

Spike Recoveries Quantitative results for the two cannabis samples showed that the concentrations of As (160.0 ppb), Cd (11.33 ppb), Pb (24.00 ppb), and Co (162.1 ppb) were relatively high in cannabis sample 1. Pb and Co were also high in cannabis sample 2, at 55.40 and 143.4 ppb, respectively. These concentrations were well below existing regulatory or guideline levels for As, Hg, Pb, and Cd, so a spike recovery test was carried out to check the accuracy of the ICP-MS and ICP-OES methods at the higher concentrations that may be encountered in actual sample analysis. The two cannabis sample digests were spiked with a premixed standard (Environmental Mix Spike, Agilent) containing multiple elements at 200 ppb, Na, Mg, K, Ca, and Fe at 2000 ppb, and Hg at 4 ppb. Using the ICP-MS and ICP-OES systems’ direct analysis methods, excellent spike recoveries were achieved for most elements in the spiked samples. All recoveries were within ±20% for Cd, Pb, As, and Hg, as shown in Table 3.

Element (Mass and Wavelength)	Cannabis Sample 1	Cannabis Sample 2	ICP-MS		ICP-OES	
			Measured Concentration, n = 3, ppb	Mean Recovery* ± 1σ	QC Criteria (80–120%) [†]	Mean Recovery* ± 1σ
²³ Na (589.592 nm)	7.372 ppm	50.02 ppm	110 ± 4%	Pass	115 ± 5%	Pass
²⁴ Mg (279.078 nm)	5426 ppm	5807 ppm	113 ± 10%	Pass	107 ± 9%	Pass
²⁷ Al (396.152 nm)	5.024 ppm	4.586 ppm	112 ± 12%	Pass	101 ± 5%	Pass
³⁹ K (769.897 nm)	41156 ppm	34101 ppm	NA	NA	NA	NA
⁴⁴ Ca (315.887 nm)	11394 ppm	9681 ppm	NA	NA	NA	NA
⁵¹ V (292.401 nm)	37.04	25.09	116 ± 8%	Pass	103 ± 2%	Pass
⁵² Cr (205.560 nm)	81.39	272.5	114 ± 5%	Pass	100 ± 1%	Pass
⁵⁵ Mn (257.610 nm)	114103	229650	NA	NA	NA	NA
⁵⁶ Fe (239.563 nm)	252188	219811	114 ± 6%	Pass	105 ± 0%	Pass
⁵⁹ Co (228.615 nm)	162.1	143.4	114 ± 5%	Pass	102 ± 1%	Pass
⁶⁰ Ni (216.555 nm)	108.2	185.7	113 ± 3%	Pass	101 ± 3%	Pass
⁶³ Cu (324.754 nm)	10865	13467	108 ± 1%	Pass	104 ± 1%	Pass
⁶⁶ Zn (213.857 nm)	72504	126816	96 ± 9%	Pass	100 ± 9%	Pass
⁷⁵ As (188.980 nm)	160.0	25.94	103 ± 6%	Pass	98 ± 2%	Pass
⁷⁸ Se (196.026 nm)	45.78	72.68	94 ± 13%	Pass	96 ± 0%	Pass
⁹⁵ Mo (202.032 nm)	3280	1589	118 ± 4%	Pass	100 ± 2%	Pass
¹⁰⁷ Ag (328.068 nm)	8.612	10.78	100 ± 10%	Pass	97 ± 2%	Pass
¹¹¹ Cd (226.502 nm)	11.33	7.471	110 ± 5%	Pass	100 ± 2%	Pass
¹³⁷ Ba (455.403 nm)	345.6	888.7	111 ± 12%	Pass	104 ± 1%	Pass
²⁰¹ Hg (184.887 nm)	29.19	27.06	107 ± 4%	Pass	99 ± 9%	Pass
²⁰⁸ Pb (220.353 nm)	24.00	55.40	112 ± 4%	Pass	104 ± 0%	Pass

*n = 3, replicate sample digestion, each in triplicate, two separate cannabis samples. [†]QC criteria FDA EAM 4.7 (80–120%) for NIST certified values. NA indicates that spike levels were too low (<5%) relative to the unspiked concentration.

Both techniques are suitable for trace metal screening of medicinal and recreational cannabis, as well as related products. ICP-OES has a lower capital cost and is somewhat easier to use, while ICPMS offers greater sensitivity and is more suitable for the ultratrace level analytes. To ensure that each method was simple enough to be applied to routine quality control (QC) and safety testing, the ICP-MS was operated in a single mode (helium collision mode) for all measurements. The ICP-OES was used with a 6-port valve system, suitable for high throughput applications. Based on the findings of the spike recovery test of two cannabis plant samples, both methods were found to be accurate for multiple elements over a wide concentration range. Suitability of the microwave-assisted sample preparation method was demonstrated by the good recovery results obtained for two plant-based SRMs.

References

- A. Filipiak-Szok, M. Kurzawa, M. Cichosz, and E. Szylyk, *Anal. Lett.* 48(16), 2627–2628, 2637 (2015)
- National Conference of State Legislatures, NCSL, State Medical Marijuana Laws, <http://www.ncsl.org/research/health/statemedical-marijuana-laws.aspx>.
- L. Rough, “Leafly’s State-by-State Guide to Cannabis Testing Regulations,” <https://www.leafly.com/news/industry/leaflys-state-by-state-guide-to-cannabis-testing-regulations>.
- P. J. Gray, W. R. Mindak, and J. Cheng, “Elemental Analysis Manual for Food and Related Products, ICP-MS Determination of Arsenic, Cadmium, Chromium, Lead, Mercury, and Other Elements in Food Using Microwave Assisted Digestion,” U.S. Food and Drug Administration publication (2015).

