Analysis of Heavy Metals in Typical Cannabis-Based Products by Shimadzu Inductively Coupled Plasma – Mass Spectrometer 2030

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Introduction

While more and more states across U.S. continually adopt legal medical and/or recreational cannabis, new cannabis-based products like edibles as an emerging market are anticipated to bolster this growing industry in the coming years. Most of the states that have legalized the medical and/or recreational cannabis have enacted regulations for acceptable limits of toxic heavy metal including Cd, Pb, As, and Hg in cannabis. New regulations are likely to evolve to include more heavy metals for cannabis-based products to manage this emerging market to ensure product quality and safety. Analytical methods are needed to develop to meet this trend. In this work, we explore and discuss the applicability of the Shimadzu inductively coupled plasma – mass spectrometer 2030 (Shimadzu ICPMS-2030) to the qualification and quantification of 17 different heavy metals in cannabis-based products.

Experimental

Sample Preparation

- Method was developed for 17 target elements.

Cadmium (Cd)	Mercury (Hg)	Chromium (Cr)	Copper (Cu)	Arsenic (As)	Lead (Pb)	Nickel (Ni)
Antimony (Sb)	Selenium (Se)	Manganese (Mn)	Silver (Ag)	Barium (Ba)	Iron (Fe)	Zinc (Zn)
Palladium (Pd)	Vanadium (V)	Molybdenum (Mo)				

Elements listed in both state regulations and ASTM draft test method

Elements listed in state regulations but not in ASTM draft test method

Elements listed in ASTM draft test method but not in state regulations

- Seven matrices were selected as representative of cannabis-based products, including cookie, chocolate, gummy bear, olive oil, butter, hard candy, and hops.
- Approximately 500 mg of each sample was weighted into a sealed Teflon™ reaction vessel that contained 4 mL of 70% HNO_3 and 2 mL of ultrapure water. The sample was then digested with a Multiwave GO microwave digestion system (Anton Par Inc.) using Organic A method: ramp time of 20 min to 180 °C and hold time of 10 min before cooling down. A blank sample consisting only of the reagents was also prepared for quality control.
- Fortified samples were prepared by spiking 1 mL stock standard solution into the reaction vessels before digestion to confirm the quantitative recovery of the analytes. Because the matrices usually have high amounts of common mineral elements like Fe, Ba, Cu, Mn and Zn, and low amounts of other target elements, stock standard solution was prepared to contain elements at different levels of concentrations such that different elements can be calibrated and spiked at different ranges. The stock standard solution contains 50 ppm of Fe, 10 ppm of Ba, Cu, Mn and Zn as well as 500 ppb of Ag, As, Cd, Cr, Hg, Mo, Ni, Pb, Pd, Sb, Se, and V.
- Digested samples were diluted to contain 5% HNO_3 before measurements. Calibration standards also contained 5% HNO_3 for matrix match. When samples have element at a concentration out of the calibration range, samples were further diluted for measurement.

Instrumentation

- Digested diluted samples were analyzed with a Shimadzu inductively coupled plasma – mass spectrometer 2030 coupled with a AS-10 autosampler. The ICPMS system was configured with the standard sample introduction system consisting of a coaxial glass nebulizer, a double-pass cyclone spray chamber, and a mini-torch. The interface consists of a copper sampling cone and a copper skimmer cone. The ICPMS is equipped with a collision cell that is used helium (He) to discriminate polyatomic interferences based on kinetic energy. Data with selected elements were collected with He gas on to minimize the polyatomic interferences. While various isotopes were measured for one single element, the isotope with the least interference was chosen for quantification. Table 1 lists the operating conditions used for the ICPMS-2030. Analytical elements and their corresponding measurement parameters are listed in Table 2.
- The ICPMS-2030 was automatically tuned to adjust torch position, lens voltage and mass resolution to optimize the signal intensity. The Labsolutions ICPMS software also collects screening data across the entire mass range from 5-260 m/z, referred to as Total Mass Scan. The function of Total Mass Scan can provide mass spectra in the entire mass range to help identify possible interference when post-processing the measurement data.
- Scandium (Sc), indium (In) and bismuth (Bi) were selected as internal standard elements to cover the entire mass range. The internal standard solution was added to the calibration standards and samples using an internal standard automatic addition kit, which utilizes a T-shaped glass tube and a peristatic pump for mixing the analysis sample with the internal standard sample and introducing the mixture to the nebulizer.

Table 1. Operating conditions of Shimadzu ICPMS-2030

Parameter	Setting	Parameter	Setting
Radio Freq. Power	1.20 kW	**Mix Gas**	0.00 L/min
Sampling Depth	5.0 mm	**Cell Gas**	6.0 mL/min
Plasma Gas	8.0 L/min	**Cell Voltage**	-21 V
Auxiliary Gas	1.10 L/min	**Energy Filter**	7.0 V
Carrier Gas	0.70 L/min	**Chamber Temp.**	5 °C

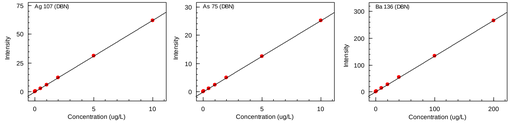
Table 2. Analytical elements and their corresponding measurement parameters

Element	Mass	Internal Standard	Cell Gas	Calibration Range (ppb)	Calibration R	Detection Limit (ppb)	Integration Time (sec)	No. of Scan	Repeat No.	Spiked Concen. (ppb)[a]
Ag	107	In (115)	Off	0.05 - 10	0.99998	3.15E-4	2.0	10	3	6.25
As	75	Sc (45)	Off	0.05 - 10	0.99998	9.02E-4	2.0	10	3	6.25
Ba	136	In (115)	Off	1 - 200	0.99979	0.0121	2.0	10	3	125
Cd	114	In (115)	Off	0.05 - 10	0.99997	4.33E-4	2.0	10	3	6.25
Cr	53	Sc (45)	Off	0.05 - 10	0.99970	0.0134	2.0	10	3	6.25
Cu	63	Sc (45)	Off	1 - 200	0.99982	0.0850	2.0	10	3	125
Fe	54	Sc (45)	Off	5 - 1000	0.99994	2.95	2.0	10	3	625
Hg	198	Bi (209)	On	0.05 - 10	0.99996	0.0132	2.0	10	3	6.25
Mn	55	Sc (45)	Off	1 - 200	0.99998	1.14E-3	2.0	10	3	125
Mo	98	In (115)	Off	0.05 - 10	0.99991	3.43E-3	2.0	10	3	6.25
Ni	60	Sc (45)	On	0.05 - 10	0.99986	0.0784	2.0	10	3	6.25
Pb	208	Bi (209)	Off	0.05 - 10	0.99999	4.41E-4	2.0	10	3	6.25
Pd	108	In (115)	Off	0.05 - 10	0.99995	6.80E-5	2.0	10	3	6.25
Sb	121	In (115)	On	0.05 - 10	0.99997	1.24E-3	2.0	10	3	6.25
Se	77	In (115)	Off	0.05 - 10	0.99992	0.0305	2.0	10	3	6.25
V	51	Sc (45)	On	0.05 - 10	0.99992	6.64E-4	2.0	10	3	6.25
Zn	66	Sc (45)	Off	1 - 200	0.99997	0.311	2.0	10	3	125

a. Spiked concentration is the spiked concentrations of different elements in the final measurement solutions after dilution.

Calibration

- Calibration curves for the target elements are shown in Figure 1. All of the calibration curves show excellent linearity across the respective calibration range.



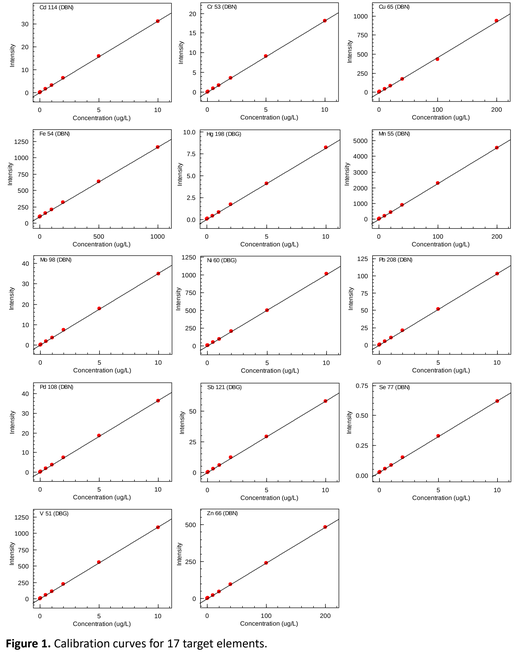


Figure 1. Calibration curves for 17 target elements.

Results and Discussion

- All of the seven different matrices were completely decomposed, leaving clear solutions after digestion, except hops, which showed small white flaky precipitates. Those are silicone components that are difficult to decompose in HNO_3. The precipitates were removed from the hop solution by filtration through a 0.45 µm polytetrafluoreethylene (PTFE) membrane filter before analysis. Control sample collected by passing 5% HNO_3 blank sample through a PTFE membrane filter was analyzed, and no significant contamination by filtration was observed.
- Table 3 shows the concentrations of elements in ppb in digested solutions of original and fortified samples for seven different matrices as well as blank sample. All of the target elements are below the detection limit for the blank sample, except Ni and Zn, which present less than 1 ppb in blank sample, possibly due to contamination brought in during sample preparation.
- Most of relative standard deviations (RSD) are below 5, except those highlighted in red in Table 3, indicating the high precision of the Shimadzu ICPMS-2030. All spiked recoveries except Ag in the hop sample were within ±10% of the added amounts, further validating the methodology and the accuracy of the Shimadzu ICPMS-2030.

Table 3. Concentrations of elements in ppb in digested solutions of original and fortified samples as well as recovery yields in percent

		^{107}Ag	^{75}As	^{136}Ba	^{114}Cd	^{53}Cr	^{65}Cu	^{54}Fe	^{198}Hg	^{55}Mn	^{98}Mo	^{60}Ni	^{208}Pb	^{108}Pd	^{121}Sb	^{77}Se	^{51}V	^{66}Zn
Blank	Mean value	n.d.	n.d.	n.d.	n.d.	n.d.	2.29	n.d.	n.d.	n.d.	n.d.	0.146	n.d.	n.d.	n.d.	n.d.	n.d.	0.563
	RSD (n = 3)	---	---	---	---	---	0.61	---	---	---	---	15.01	---	---	---	---	---	0.76
Fortified blank	Mean value	6.25	6.04	124	6.21	6.27	115	635	5.89	125	6.33	6.18	6.29	5.85	6.02	6.32	6.26	122
	RSD (n = 3)	0.29	0.73	1.75	0.84	0.27	0.83	0.42	0.57	0.29	1.38	0.87	0.31	0.87	3.14	2.27	0.35	0.18
Recovery (%)		100	97	99	99	100	90	102	94	100	101	97	101	94	96	101	100	97
Cookie	Mean value	n.d.	0.0902	5.60	0.0557	0.941	15.0	71.9	0.118	24.9	0.561	1.48	0.0815	n.d.	n.d.	0.341	0.175	41.7
	RSD (n = 3)	---	1.03	1.41	1.67	1.26	1.14	2.56	12.39	2.09	1.78	2.47	1.48	---	---	9.05	1.13	1.08
Fortified cookie	Mean value	6.02	6.50	126	6.49	6.55	131	645	6.67	144	7.21	7.25	6.44	6.44	6.22	7.00	6.58	177
	RSD (n = 3)	3.99	0.58	0.65	1.07	0.09	1.28	0.67	1.81	0.26	1.23	**6.65**	0.34	1.18	1.90	2.35	0.51	1.20
Recovery (%)		96	103	96	103	90	93	92	105	95	106	92	102	103	100	107	102	108
Chocolate	Mean value	n.d.	0.0599	41.2	1.53	5.89	72.7	333	0.0534	70.5	1.36	31.9	0.0777	0.0440	n.d.	0.378	0.279	161
	RSD (n = 3)	---	1.88	0.19	0.39	2.65	2.59	**6.80**	**13.32**	2.46	1.19	3.05	0.79	0.21	---	2.32	2.32	3.24
Fortified chocolate	Mean value	6.15	6.55	156	8.06	11.5	187	914	6.56	186	7.54	38.0	6.27	5.65	6.00	6.76	5.97	297
	RSD (n = 3)	1.16	0.96	0.76	2.22	1.33	1.17	1.64	3.09	2.45	1.16	1.32	2.15	1.24	2.27	1.74	0.97	0.80
Recovery (%)		98	104	92	104	90	91	93	104	92	99	98	99	90	96	102	91	109
Gummy bear	Mean value	n.d.	0.174	0.805	n.d.	0.111	11.4	16.1	0.0289	0.787	n.d.	0.272	0.0186	0.204	0.0140	0.114	0.175	7.3
	RSD (n = 3)	---	3.13	1.25	---	2.18	2.87	3.55	**13.99**	0.81	---	**13.20**	3.20	0.05	**8.74**	**10.85**	4.13	0.25
Fortified gummy bear	Mean value	6.28	6.70	121	6.47	6.30	124	606	6.24	123	6.29	6.80	6.12	6.46	6.30	6.32	6.37	129
	RSD (n = 3)	2.55	1.15	1.03	0.78	4.02	0.71	4.44	3.17	1.76	1.05	**5.96**	0.51	0.67	2.15	2.19	3.96	1.19
Recovery (%)		100	104	96	104	99	90	94	99	98	101	104	98	100	101	99	99	97
Olive oil	Mean value	n.d.	n.d.	0.629	n.d.	n.d.	n.d.	n.d.	0.0450	0.170	0.00760	0.153	0.0177	n.d.	0.00730	n.d.	n.d.	2.08
	RSD (n = 3)	---	---	1.52	---	---	---	---	**20.31**	2.30	2.92	**19.30**	2.89	---	**5.04**	---	---	3.56
Fortified olive oil	Mean value	6.09	6.77	124	6.65	6.20	125	607	6.56	112	6.26	6.07	6.13	6.62	6.55	6.90	6.26	114
	RSD (n = 3)	**6.24**	1.73	0.42	0.13	1.83	2.15	1.42	2.39	1.87	1.67	4.13	0.31	0.63	1.82	1.59	0.99	1.89
Recovery (%)		97	108	99	106	99	100	97	104	89	100	95	98	106	105	110	100	90
Butter	Mean value	n.d.	0.0435	0.595	0.0108	0.0201	n.d.	n.d.	0.0428	0.150	0.104	0.202	n.d.	n.d.	n.d.	n.d.	n.d.	4.8
	RSD (n = 3)	---	3.08	1.18	**8.49**	**12.44**	---	---	**9.44**	1.28	1.36	**12.73**	---	---	---	---	---	1.38
Fortified butter	Mean value	6.10	6.84	136	6.48	6.06	121	601	5.65	115	6.22	6.34	5.94	6.40	6.55	6.40	6.19	118
	RSD (n = 3)	**5.88**	1.58	0.20	0.51	2.43	0.84	0.88	0.99	1.23	0.26	2.47	0.25	0.64	1.03	**6.32**	3.40	0.90
Recovery (%)		98	109	108	104	97	97	96	90	92	98	98	95	102	105	102	99	91
Hard candy	Mean value	n.d.	0.0574	0.579	n.d.	0.290	0.813	n.d.	n.d.	0.464	0.0625	n.d.	0.00490	n.d.	n.d.	n.d.	0.193	2.04
	RSD (n = 3)	---	4.57	2.02	---	4.33	4.15	---	---	0.88	0.35	---	2.31	---	---	---	2.43	0.70
Fortified hard candy	Mean value	6.85	6.80	136	6.62	6.54	128	621	6.29	136	6.07	5.88	6.20	6.27	6.52	6.87	6.63	138
	RSD (n = 3)	**5.24**	2.11	1.01	0.54	3.89	0.66	**6.30**	**8.83**	0.07	0.37	2.86	0.34	0.37	2.69	**5.32**	2.80	0.53
Recovery (%)		110	108	108	106	100	102	99	101	108	96	94	99	100	104	110	103	109
Hop	Mean value	n.d.	0.313	306	0.0602	1.91	20.9	1240	0.117	172	0.626	10.2	1.30	n.d.	0.212	0.326	2.04	108
	RSD (n = 3)	---	2.53	1.88	2.68	3.86	1.00	3.53	1.78	1.51	3.14	1.48	2.55	---	2.25	5.31	0.70	1.43
Fortified hop	Mean value	4.20	6.20	422	6.15	8.27	136	1820	6.68	308	7.2	16.6	7.89	6.21	5.82	7.15	8.47	220
	RSD (n = 3)	**19.01**	0.84	1.69	1.73	0.94	1.54	4.82	2.07	1.28	0.75	1.21	1.27	1.68	1.97	3.30	1.29	1.06
Recovery (%)		**67**	94	93	97	102	92	93	105	109	105	102	105	99	90	109	103	90

- The low recovery of Ag (67%) for the hop sample might be due to 1). Ag was absorbed onto precipitates and removed from the solution by filtration, and 2). high amount of chlorine presents in hop sample that readily form precipitates with Ag and was removed from the solution by filtration.
- Table 4 shows concentrations of target elements in raw materials. All matrices contain high amounts of Mn and Zn, and negligible amounts of Ag, As, Hg, and Pb. Cookie, chocolate, gummy bear and hops contain high amount of Fe, Cu, Mn and Ni.

Table 4. Concentrations of elements (in ng/g matrix) for raw materials, back-calculated for dilution and ~500 mg initial mass of matrices

	Ag	As	Ba	Cd	Cr	Cu	Fe	Hg	Mn	Mo	Ni	Pb	Pd	Sb	Se	V	Zn
Cookie	n.d.	14.4	892	8.87	150	2390	11456	18.8	3967	89.4	236	13.0	n.d.	n.d.	54.3	27.9	6644
Chocolate	n.d.	9.56	6576	244	940	11604	53152	8.52	11253	217	5092	12.4	7.02	n.d.	60.3	44.5	25698
Gummy bear	n.d.	27.3	126	n.d.	17.4	1789	2526	4.54	123	n.d.	42.7	2.92	32.0	2.20	17.9	27.5	1146
Olive oil	n.d.	n.d.	99.3	n.d.	n.d.	n.d.	n.d.	7.10	26.8	1.20	24.2	2.79	n.d.	1.15	n.d.	n.d.	328
Butter	n.d.	6.82	93.4	1.69	3.15	n.d.	n.d.	6.72	23.5	16.3	31.7	n.d.	n.d.	n.d.	n.d.	n.d.	753
Hard candy	n.d.	9.11	91.9	n.d.	46.0	129	n.d.	n.d.	73.7	9.92	n.d.	n.d.	n.d.	n.d.	n.d.	30.6	324
Hops	n.d.	50.1	48960	9.63	306	3344	198400	18.7	27520	100	1632	208	n.d.	33.9	52.2	326	17280

Conclusions

- Complex matrices of cannabis-based products can be digested with microwave digestion system, and analyzed with the Shimadzu ICPMS-2030 to assess the levels of heavy metals in those cannabis-based products.
- Shimadzu ICPMS-2030 coupled with AS-10 autosampler and Labsolutions ICPMS software provides excellent sensitivity, precision, accuracy, tolerance and fast time response to meet and exceed compliance with regulations on heavy metals in complex matrices of cannabis-based products.

References

- "Analysis of heavy metal contaminants in cannabis flower using the Shimadzu ICPMS-2030", Shimadzu application note.
- "Standard test method for analyses of trace elements in cannabis by inductively coupled plasma – Mass spectrometry", ASTM draft test method.