Challenge

Measure both the nutritional and toxic elemental content of cannabis and cannabis products with high sensitivity, precision, and accuracy.

Solution

A simple and effective method for routine analysis of cannabis and cannabis products using the PlasmaQuant MS ICP-MS analyzer and speedwave XPERT microwave digestion system.

Analysis of Trace Metals in Cannabis and Cannabis Products by ICP-MS

Introduction

In 1996, Proposition 215 was passed in California, which made the Golden State the first in the U.S. to allow for the medical use of cannabis. Today, medical cannabis is legal in 36 states, while 16 states including the District of Columbia allow its use for adult recreational consumption. Since the beginning of its legalization for medical and recreational use, investigation of toxic trace elements gained more and more interest to ensure the safety of cannabis and its products, like other food and drug products. Since a global guideline for the analysis of human consumption of cannabis and associated products does not exist, individual regulations and guidelines were created within the states that legalized the use of these products. For instance, the California Bureau of Cannabis Control states that laboratories shall investigate residual solvents and processing chemicals, pesticides, microbiological impurities, mycotoxins, water activity and moisture content, filth and foreign material, and heavy metals in cannabis and its related products.

Metallic elements have both beneficial and deleterious effects on human health due to their complex biochemistry. Human health can be improved by many metals for their nutritional and metabolic effects. Meanwhile, other metals can damage human health due to their toxic or carcinogenic effects. Hence, most states require analysis of the most toxic elements, As, Cd, Hg, and Pb in cannabis and cannabis products.

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Certain states, such as Maryland, go even further to require testing for Ag, Ba, Cr, and Se in addition to these "big four". As regulations keep evolving, it is likely that the number of metals requiring testing will increase and their acceptable concentrations will decrease. The analysis of minerals and additional trace elements will benefit the cannabis industry by providing more details about the nutrition, toxicity, and potential contamination of cannabis products.

Inductively coupled plasma mass spectrometry (ICP-MS) is commonly recognized as the prominent leader in elemental analysis due to its exceptional sensitivity, rapid sample throughput, and wide dynamic range. In this study, the PlasmaQuant MS ICP-MS analyzer was used to analyze 12 elements in a range of cannabis and cannabis-related products.

Materials and Methods

Sample Preparation

In this study, four different types of samples were analyzed. The samples included cannabis flowers, cannabis gummies, cannabis oil, and cannabidiol oil. For the preparation of the measurement solutions, 0.5 g of each sample was weighed and transferred into a microwave digestion vessel (DAK-100X) individually. 6 mL of HNO_3 (65%), 1.5 mL of H_2O_2 (30%), and 0.1 mL of a 100 ppm Au standard were added to each digestion vessel. The Au standard was used to stabilize Hg. All digestion vessels were carefully swirled and left under a fume hood for 20 min. Regardless of the sample matrix, all samples were then digested via the same digestion program (Table 1) using the speedwave XPERT microwave system. After completing the digestion and cooling to room temperature, the clear solution from each digestion vessel was further diluted to 50 mL with deionized water, along with the internal standards. Two certified reference materials (CRM), including one certified ground hemp (NSI Lab) and one certified hemp oil (Absolute Standard), were prepared using the same method to verify that the digestion was complete and to confirm the recovery of the analytes. One EnviroMAT™ Drinking Water CRM (SCP Science) was diluted 1,000-fold without digestion for analysis. It was used to verify the ICP-MS method's accuracy.

Table 1: Digestion program for microwave digestion

Step	T [°C]	P max. [bar]	Ramp time [min]	Hold time [min]
1	130	80	2	5
2	170	40	2	15
3	200	40	2	15
4	50	0	1	20

Instrumentation

A speedwave XPERT microwave digestion system with DAK-100X digestion vessels was used for sample preparation. All the analyses were performed using the PlasmaQuant MS with Teledyne Cetac ASX-560 autosampler. The detailed system configuration and operating conditions are shown in Table 2. The method specific parameters are given in Table 3.

Table 2: System configuration and operating conditions of the PlasmaQuant MS

Parameter	ICP-MS Setting
RF power	1300 W
Plasma gas flow	9.0 L/min
Nebulizer gas flow	1.0 L/min
Auxiliary gas flow	1.5 L/min
Nebulizer	Standard concentric nebulizer
Spray chamber	Scott double-pass spray chamber, cooled to 3°C
Sample Pump rate	15 rpm
Pump tubing	PVC (black, black)
Rinse/Read delay	45 s
Auto-sampler	Teledyne Cetac ASX-560
Stabilization delay	10 s
Scans per replicate	20 (peak hopping, 1pt/peak)
Replicates per sample	5
Dwell time	20 ms (10 ms for Ba, Hg, Pb, Sb)

Table 3: Overview of method-specific parameters

Element	Parameters		
	Mass	Internal Standard	Gas mode
Ag	107	Y^{89}	He
As	75	Y^{89}	H_2
Ba	137	Tb^{159}	No gas
Cd*	114	Tb^{159}	He
Cr	52	Sc^{45}	He
Cu	65	Sc^{45}	He
Hg	202	Bi^{209}	No gas
Ni	60	Sc^{45}	He
Pb	206,207,208	Bi^{209}	No gas
Sb	121	Tb^{159}	No gas
Se	78	Y^{89}	H2
Zn*	68	Y^{89}	H2

*isotopes chosen for optimal LOD, some states' regulations recommend different isotopes.

Calibration

Calibration standards were prepared by mixing single element standards and internal standards in a diluent of 1 % (v/v) HNO_3 and 200 µg/L Au. A summary of the calibration data, including calibration standards' concentration, instrument detection limits (IDLs) and correlation coefficients (R^2) is shown in Table 4. All analytes' correlation coefficients (R^2) are higher than 0.9998, which demonstrates excellent linearity in the calibration range. Representative calibration curves for the highly toxic heavy metals As, Cd, Hg, and Pb are given in Figure 1.

Table 4: Calibration data

| Element	Cal 1 conc. [µg/L]	Cal 2 conc. [µg/L]	Cal 3 conc. [µg/L]	Cal 4 conc. [µg/L]	Cal 5 conc. [µg/L]	IDL [µg/L]	R^2
Ag	0.5	1	5	20	50	0.0011	0.9998
As	0.5	1	5	20	50	0.0066	1.0000
Ba	0.5	1	5	20	50	0.0009	1.0000
Cd	0.5	1	5	20	50	0.0017	1.0000
Cr	0.5	1	5	20	50	0.0168	1.0000
Cu	0.5	1	5	20	50	0.0065	1.0000
Hg	0.5	1	5	20	-	0.0049	0.9999
Ni	0.5	1	5	20	50	0.0056	1.0000
Pb	0.5	1	5	20	50	0.0002	1.0000
Sb	0.5	1	5	20	50	0.0260	0.9999
Se	0.5	1	5	20	50	0.0463	1.0000
Zn	0.5	1	5	20	50	0.0193	0.9999
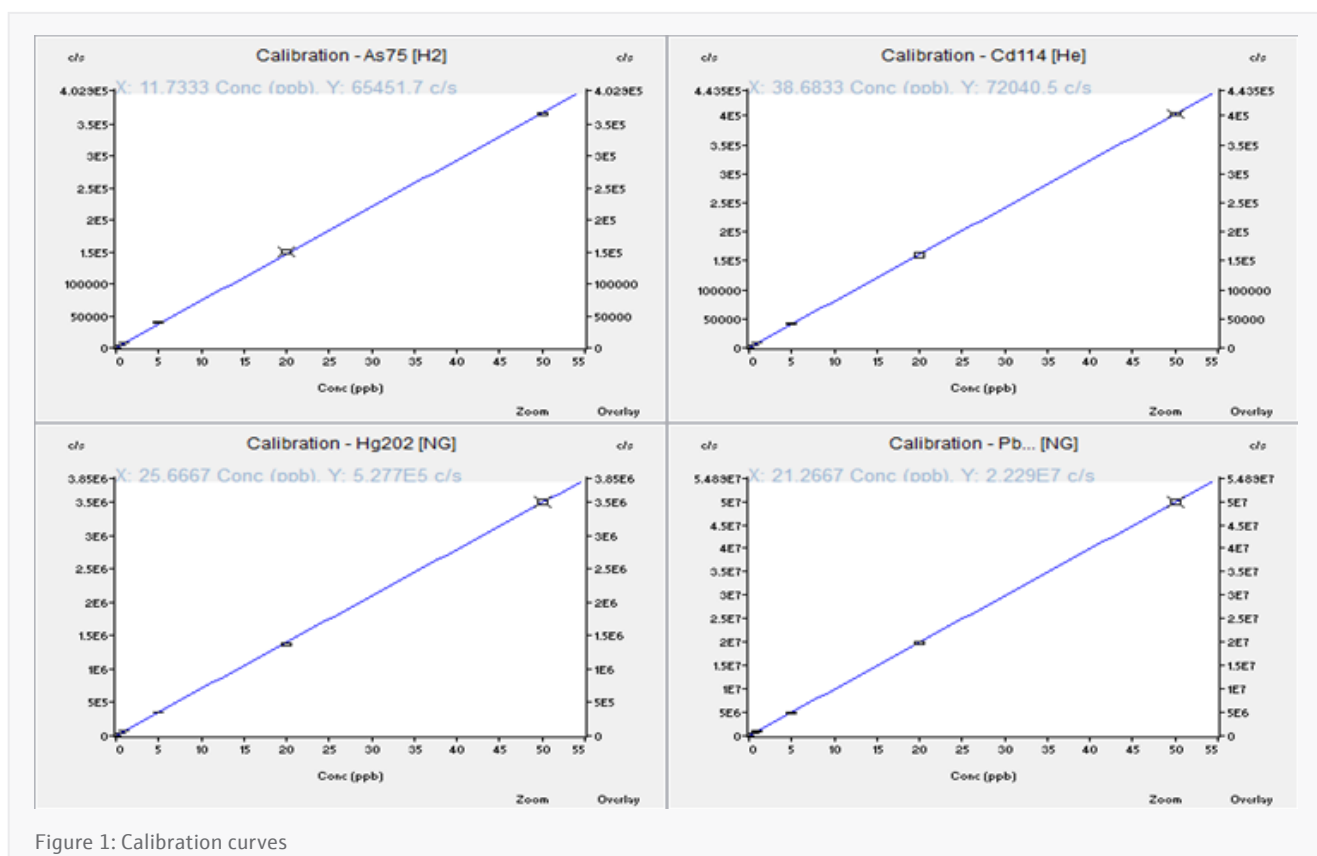
Figure 1: Calibration curves

Results and Discussion

Toxic metals are one of several possible contaminants in cannabis and cannabis products. The key metals of interest are As, Cd, Hg, and Pb. These elements are regulated by most states. Analysis for additional elemental contaminants, such as Ag, Ba, Cr, Cu, and Se, is required by some states like New York and Maryland. Table 5 lists acceptable limits for hazardous metals of inhalable and all other cannabis products in Maryland and New York. The achieved method detection limits (MDLs) are far below state-level limits and therefore allow for a reliable determination of the trace metal contents.

Table 5: Action level for cannabis products in Maryland and New York, and MDLs of the Plasma Quant MS

Element	Maryland limits for all cannabis products [µg/g]	New York action level for all other cannabis products* [µg/g]	New York action level for all inhalable cannabis products [µg/g]	MDL [µg/g] (100x dilution)
Ag	1.4	-	-	0.0001
As	0.4	1.5	1.5	0.0006
Ba	60	-	-	0.00009
Cd	0.4	0.5	0.2	0.0002
Cr	0.6	1100	110	0.0017
Cu	-	300	30	0.0007
Hg	0.2	3	0.3	0.0005
Ni	-	20	2	0.0006
Pb	1	0.5	0.5	0.00002
Sb	-	120	2	0.00008
Se	26	-	-	0.0005
Zn	-	4000	4000	0.0002

*New York regulates elemental limit values in µg/dose. Values were converted to µg/g based on typical dosage.

In terms of accuracy, recovery tests of three CRMs were performed. Table 6 shows certified concentrations, measured concentrations, and recovery rates of three CRM samples. The diluted EnviroMAT™ Drinking Water CRM (SCP) was used to verify the ICP-MS method's accuracy. The recoveries for all the certified elements present in the drinking water CRM were excellent, ranging from 98-107% (Table 6). One certified ground hemp (NSI Lab) and one certified hemp oil (Absolute Standard) were analyzed to verify the analysis procedure. Table 6 shows that all recoveries of the hemp and hemp oil were within ±7% of the certified values.

One cannabis flower sample and three cannabis products including cannabis gummies, cannabidiol (CBD) oil, and cannabis oil, were analyzed in this study. Their results are given in Table 7. All the concentrations of the analytes are well below the action levels.

Table 6: Results of three CRMs

Element	EnviroMAT™ Drinking Water CRM			Ground hemp CRM			Hemp oil CRM		
	Certified conc. [mg/L]	Measured conc. [mg/L]	Recovery [%]	Certified conc. [µg/g]	Measured conc. [µg/g]	Recovery [%]	Certified conc. [µg/g]	Measured conc. [µg/g]	Recovery [%]
Ag	-	-	-	-	-	-	-	-	-
As	10.4	10.192	98	10	9.388	94	10.8	10.368	96
Ba	8.25	8.288	100	-	38.856	-	-	0.159	-
Cd	2	1.981	99	10	10.361	104	10.1	9.797	97
Cr	13	13.960	107	-	0.146	-	-	0.030	-
Cu	16.5	17.043	103	-	16.326	-	-	0.290	-
Hg	-	0.078	-	10	9.732	97	10.2	10.404	102
Ni	20.3	21.147	104	-	0.775	-	-	0.239	-
Pb	4.04	4.021	100	10	10.417	104	10.1	9.393	93
Sb	11.7	12.046	103	-	0.017	-	-	0.009	-
Se	59.4	60.307	102	-	0.056	-	-	0.027	-
Zn	43.5	46.083	106	-	85.176	-	-	2.098	-

Table 7: Results of cannabis flower, cannabis gummies, CBD oil and cannabis oil

Element	Cannabis flower Measured conc. [µg/g]	Cannabis gummies Measured conc. [µg/g]	CBD oil Measured conc. [µg/g]	Cannabis Oil Measured conc. [µg/g]
Ag	0.016	<LOD	0.001	0.002
As	0.026	0.096	0.013	0.001
Ba	0.659	0.139	0.048	0.148
Cd	0.025	<LOD	<LOD	0.002
Cr	0.079	0.109	0.114	0.064
Cu	23.3	0.303	0.201	0.495
Hg	0.002	0.097	<LOD	0.009
Ni	0.760	0.058	0.107	0.234
Pb	0.005	0.013	0.018	0.061
Sb	0.003	0.004	0.001	<LOD
Se	0.024	<LOD	0.023	<LOD
Zn	117	10.4	0.751	6.72

LOD: limit of detection

Conclusion

The analysis of trace metals in cannabis and cannabis-based products by ICP-MS has become a routine task for laboratories in the food and pharmaceutical industry. The PlasmaQuant MS and speedwave XPERT are well suited for the sample preparation and determination of trace elements in cannabis and cannabis-based products. In the presented method, the achieved method detection limits are well below the regulatory and guideline levels defined by local authorities. Sample preparation and analysis methods were validated by the good recovery results of three CRMs. A range of cannabis and cannabis-based products were analyzed by the presented method.

The PlasmaQuant MS includes unique and patented technologies that significantly lower running costs and increase ease-of-use without compromising performance. These include the Eco Plasma, the only plasma system that runs on <11.5 L/min of argon gas without compromising plasma robustness or analyte sensitivity. The integrated Collision Reaction Cell (iCRC) is a powerful yet simple to use interference management system that removes spectroscopic interferences on essential analytes, including As, Cr, Cu, and Se.