Challenge

Analysis of heavy metals in cannabis with high sensitivity, precision and accuracy.

Solution

HR ICP-OES with exceptional sensitivity and industry leading high-resolution optical system for interference-free detection of metals.

Quantitative Analysis of Cannabis and Hemp with HR ICP-OES

Introduction

Cannabis and hemp are amongst the oldest crop plants with a history reaching back several millennia. Its first and main use was as textile fiber, which is still its main usage in textiles, ropes, insulation and waterproofing. A second use of cannabis and hemp is the field of food and drug for its nutritional value as well as its medical and recreational effects. Since the beginning of its legalization in 2014 for medical and recreational use, the investigation of toxic trace elements gained more interest to ensure the safety of cannabis products similar to other food and drug products. Since a global guideline for the analysis of hemp and cannabis products, dedicated for the consumption by humans is not yet existent, individual recommendations were created within the regions 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. Often local authorities define elements to be tested according to regulations of the FDA and the US EPA. In USP Chapter <232>, the elements As, Pb, Hg and Cd are classified to be the most toxic in pharmaceutical products. Hence, these "toxic four" are routinely analyzed in cannabis samples as well.

The determination of trace metals in plant materials is routinely done with optical emission spectroscopy with inductively coupled plasma (ICP-OES). However, the typically low trace levels of As, Pb, Hg and Cd require a high sensitivity of the analyzer. In this regard, common ICP-OES instrumentation often lacks the

detection power to securely analyze trace levels in the sub mg/kg range. Therefore, routine labs are often forced to employ the more sensitive ICP-MS technology or to use sensitivity enhancing accessories like an ultrasonic nebulizer (USN) in combination with ICP-OES.

In contrast to the above-mentioned solutions, the method described herein employs a high-resolution ARRAY ICP-OES, the PlasmaQuant 9100 Elite, which is able to achieve limits of detection in the sub µg/L range in a typical measurement solution of plant materials. Due to the long analytical zone of its plasma in combination with a counter gas technology and minimal loss of light throughout the optical path, the PlasmaQuant 9100 Elite offers a sensitivity which makes the use of complex and expensive sample feed accessories (such as USN) obsolete.

Materials and Methods

Sample and Reagents

For the preparation of the measurement solutions, 1 g of a dried plant material was accurately weighed and transferred into a microwave digestion vessel (PM 60). 5 mL of HNO_3, 1 mL of HCl and 1 mL of H_2O_2 were added to the vessel. The sample was then digested via the pre-installed "vegetables and leaves" digestion program (Table 1) using the TOPwave microwave system. After complete digestion and cooling to room temperature, the clear solution was filled up to 50 mL with deionized water, along with the addition of Au to stabilize Hg (200 µg/L Au in the final solution) and internal standard Tb. The common internal standard element Yttrium could not be used, as some samples contained a significant Y concentration. Terbium, which was not detected in any of the samples, was chosen as an internal standard instead.

Table 1: Digestion program for hemp sample

Step	T [°C]	Pmax [bar]	Ramp time [min]	Hold time [min]
1	150	40	5	5
2	200	40	5	15
3	50	0	1	20

Instrumentation

Instrument Settings

For the analysis, a PlasmaQuant 9100 Elite ICP-OES equipped with a standard sample introduction kit and an additional seaspray nebulizer was used in combination with a Teledyne Cetac ASX 560 autosampler. The detailed system configuration is shown in Table 2.

Table 2: Configuration of the PlasmaQuant 9100 Elite equipped with standard kit

Parameter	Specification
RF Power	1300 W
Plasma Gas Flow	12 L/min
Nebulizer Gas Flow	0.6 L/min
Auxiliary Gas Flow	0.5 L/min
Nebulizer	Seaspray, 0.4 mL/min, Borosilicate
Spray Chamber	Cyclonic spray chamber, 50 mL, Borosilicate
Injector	Quartz, inner diameter 2 mm
Outer Tube/Inner Tube	Quartz/Quartz
Pump tubing	PVC (black, black)
Sample Pump Rate	1 mL/min
Rinse/Read delay	45 s
Auto sampler	Teledyne Cetac ASX 560

Method Parameters

Table 3: Overview of method-specific evaluation parameters

Element	Line [nm]	Plasma view	Integration mode	Read time [s]	Evaluation			
					No. of pixel	Baseline fit, pixel no.	Polyn. degree	Correction
As	188.979	axial	peak	5	3	ABC [1]	auto	Tb
Cd	214.441	axial	peak	1	3	ABC	auto	Tb
Cr	267.716	axial	peak	1	3	ABC	auto	Tb
Hg	184.886	axial	peak	5	3	ABC	auto	Tb
Pb	220.353	axial	peak	5	3	ABC	auto	Tb
Tb	350.917	axial	peak	1	3	ABC	auto	-

[1] ABC = Automatic Baseline Correction

Calibration

Multi-element calibration standards were prepared with single element standards, Tb internal standard and Hg stabilizer in 10% (v/v) HNO_3 and 2% (v/v) HCl. Table 4 provides information in the concentration levels of the calibration standards and Figure 1 displays the according calibration functions.

Table 4: Concentration of calibration standards

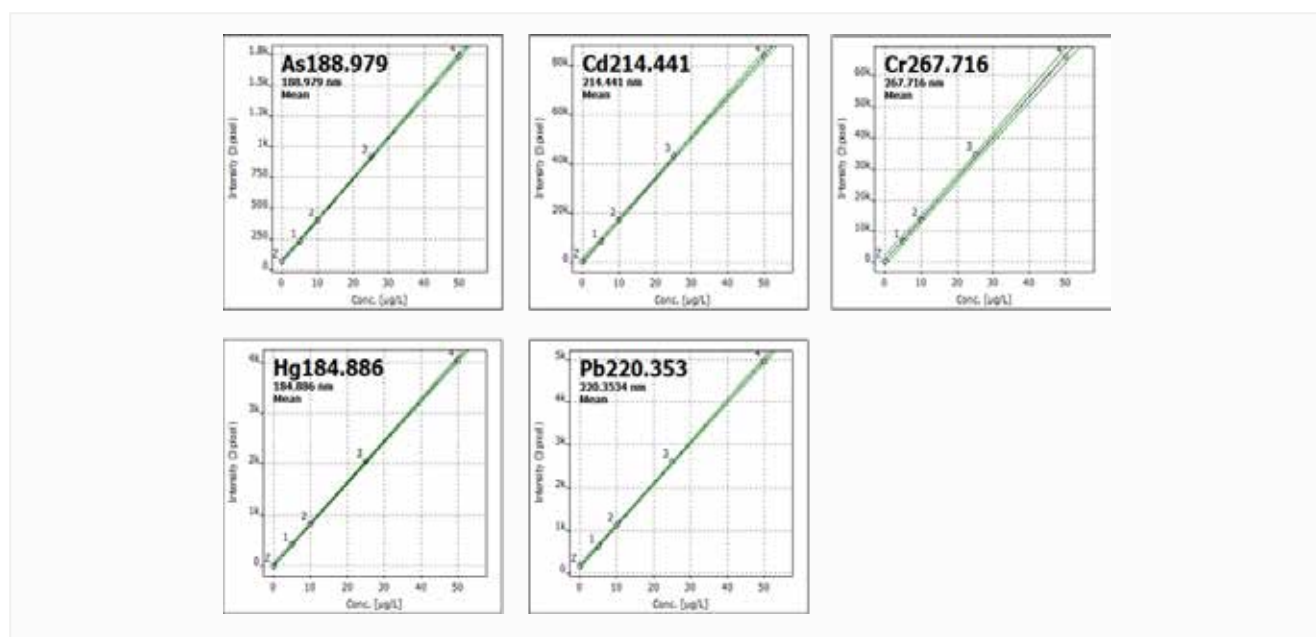| Element	Unit	Cal.0	Cal.1	Cal.2	Cal.3	Cal.4	Correlation coefficient
As	µg/L	0	5	10	25	50	0.9997
Cd	µg/L	0	5	10	25	50	0.9995
Cr	µg/L	0	5	10	25	50	0.9986
Hg	µg/L	0	5	10	25	50	0.9997
Pb	µg/L	0	5	10	25	50	0.9997

Figure 1: Calibration data

Results and Discussion

The targets for inhalable and all other cannabis products as defined by the California Bureau of Cannabis Control are stated in Table 5. With the applied dilution factor 50, the target limits in the actual measurement solution are in a range of 2 to 60 µg/L. The achieved method detection limits (MDLs) (see Table 5) are well below the stated limits and therefore allow for a secure determination of the trace metal contents of As, Hg, Pb, Cr, and Cd. A further reduction of the MDLs can be achieved by applying a lower dilution factor (e.g. 20).

Table 5: Limits of heavy metal concentrations in solid samples and measurement solutions, MDLs of PlasmaQuant 9100 Elite

Element	Limit of all inhalable cannabis products		Limit for other cannabis products		Method detection limit
	Sample [µg/g]	Measurement solution[1] [µg/L]	Sample [µg/g]	Measurement solution[1] [µg/L]	Sample [µg/g]
As	0.2	4	1.5	30	0.034
Cd	0.2	4	0.5	10	0.002
Cr	n.d.	n.d.	n.d.	n.d.	0.006
Hg	0.1	2	3.0	60	0.009
Pb	0.5	10	0.5	10	0.024

[1] dilution factor: 50

Method validation in terms of accuracy and sensitivity was performed by spike recovery tests at the regulation target levels. Table 6 shows the results for one digestion of hemp sample and spiked sample. The spike levels were 10 µg/L for all elements. All spike recoveries are within ± 7% of the added amounts, further validating the methodology.

Table 6: Results and spike recoveries for the analysis of hemp samples

Element	Hemp sample		Spiked Hemp Sample[2]	Instrument Detection Limit
	Sample [µg/g]	Measurement Solution[1] [µg/L]	Recovery [%]	Measurement Solution[1] [µg/L]
As	0.17	3.44	100	0.67
Cd	0.02	0.43	93	0.04
Cr	0.09	1.76	98	0.12
Hg	< LOD	< LOD	103	0.17
Pb	0.11	2.29	93	0.48

[1] dilution factor: 50
[2] spike level: 10 µg/L

Result consistency was investigated by analyzing two different emission lines for each element. Even lines with a high risk of spectral interferences, such as the Cd/As line pair at 228.8 nm, can be used for correct quantification, since they are base-line separated by the high-resolution optics of the PlasmaQuant 9100 Elite (Figure 2).
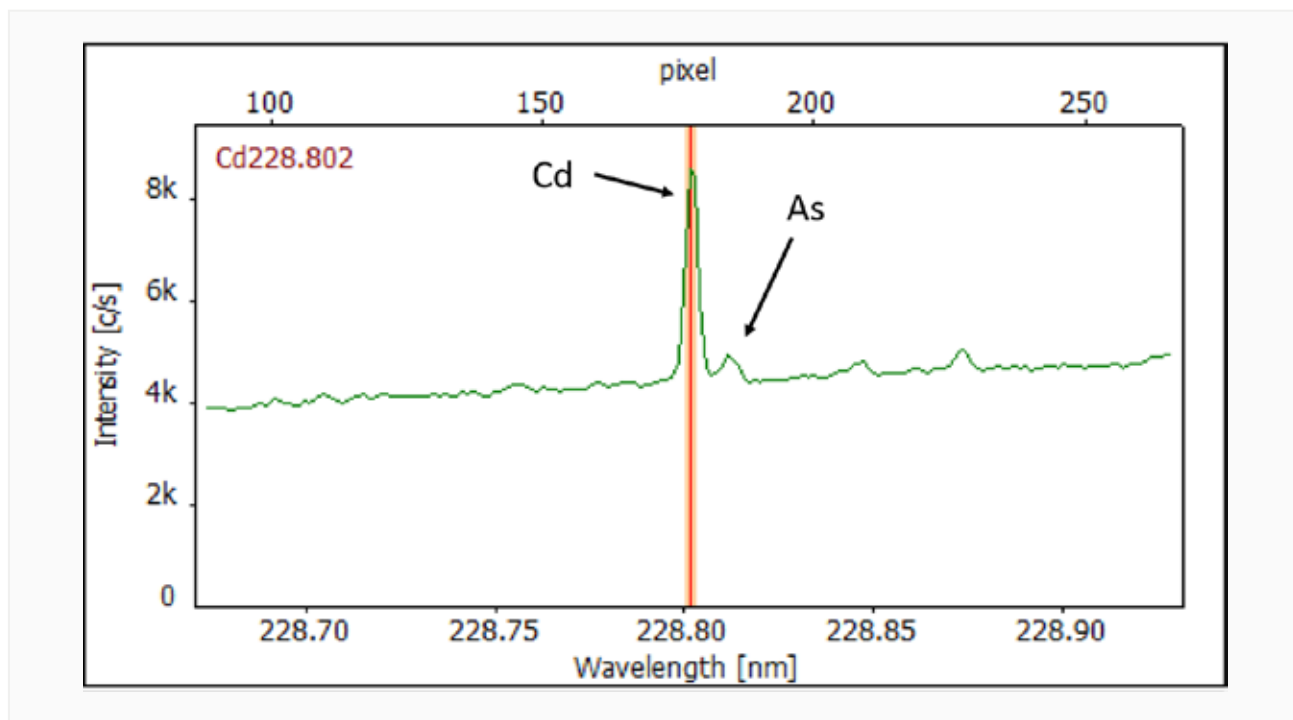
Figure 2. As-recorded spectrum of Cd/As line pair at 228.8 nm with base-line seperation for interference-free quantification

Conclusion

The analysis of trace metals in cannabis and hemp products by ICP techniques has become a routine task for laboratories in the food and pharmaceutical industry. The methodology presented herein uses a highly sensitive HR-ARRAY ICP-OES, the PlasmaQuant 9100 Elite, with a standard sample introduction system to securely determine trace concentrations of Arsenic, Cadmium, Mercury, Lead and Chromium.

Due to PlasmaQuant 9100 Elite's high spectral resolution (2 pm @ 200 nm), an interference-free analysis of all investigated elements is possible. Thus, time-consuming data analysis of multi-line evaluation becomes obsolete. The PlasmaQuant 9100 Elite delivers results of highest confidence by single line evaluation in a routine task such as cannabis analysis.

The achieved method detection limits in the low µg/kg range are well below the target limits defined by local authorities and can be achieved with a standard sample introduction system (pneumatic nebulizer, cyclonic spray chamber). A further reduction of the MDLs would be possible by applying less dilution to the measurement solutions, the use of a hydride system (As, Hg) or the use of a highly sensitive ultrasonic nebulizer (USN). However, especially the use of an USN comes along with a higher complexity of operating the instrument as well as with significantly higher initial investment cost. For this reason, the focus of this study was to evaluate the possibilities of a standard setup for ICP-OES as a robust, reliable, easy to use and cost-efficient solution for the analysis of trace metals in cannabis and hemp samples. Additionally, the PlasmaQuant 9100 Elite represents a feasible alternative to ICP-MS instrumentation for the analysis of cannabis and hemp.