Challenge
Accurate quantification of Ca, K, Mg and Na in electrolyte solutions

Solution
Determination of the analytes using F-AAS novAA 800 F

Intended audience
Research and quality control laboratories in the pharmaceutical industry

Quantification of Calcium, Potassium, Magnesium and Sodium in Pharmaceutical Solutions

Introduction

The determination of calcium (Ca), potassium (K), magnesium (Mg) and sodium (Na) in electrolyte solutions for e.g. intravenous therapy is a critical aspect of pharmaceutical quality control. These elements are vital electrolytes that play a fundamental role in maintaining the physiological functions of the human body, particularly in the regulation of fluid balance, stimulus transmission in nerve tracts, muscle function and cellular processes. Accurate quantification of these elements is therefore essential to ensure the safety, efficacy and consistency of electrolyte products.

In accordance with the guidelines of pharmacopoeias such as the United States Pharmacopeia (USP), the European Pharmacopeia (EP) and the British Pharmacopeia (BP), the determination of these elements is carried out using validated and standardized methods. Flame atomic absorption spectroscopy (F-AAS) is commonly used for this purpose due to its sensitivity, selectivity and robustness. The flame AAS technique provides accurate and reliable quantification of the elements.

Accurate determination of Ca, K, Mg and Na concentrations in electrolyte solutions is necessary not only to confirm compliance with regulatory specifications, but also to ensure that the solutions deliver the correct therapeutic dose. Variations in the concentrations of these elements can lead to serious clinical complications such as electrolyte imbalances. Therefore, using reliable analytical techniques such as F-AAS ensures that electrolyte solutions meet pharmaceutical standards, safeguarding patient well-being.

This application note describes how to determine the concentrations of calcium, potassium, magnesium and sodium in electrolyte solutions for intravenous therapy (IV) using the flame atomic absorption spectrometer (F-AAS)

novAA 800 F. Na and K were determined in emission and absorption modes, respectively. The AS-FD autosampler can be used for automated sample supply, including an automatic dilution function. The implemented software features enable full automation of the measurement procedure, including quality control. The ASpect CFR software extension offers functions such as electronic signatures and an audit trail, as well as variable rights assignment in user administration. This enables the determination of the analytes Ca, K, Mg and Na to be CFR Part 11-compliant.

Materials and Methods

Samples and reagents

- Electrolyte solution for intravenous therapy: sample 1-4
- Concentrated HNO_3 (62-65%, p.a.)
- Cesium and Lanthanum chloride solution (100 g/L CsCl, 100 g/L $LaCl_3$)
- Single element standards (Analyte concentration 1000 mg/L)

Sample preparation

Prior to measurement, the samples were diluted with ultrapure water and acidified with HNO_3. Then, the Cs/La solution was added. The acid concentration was 1% (v/v) HNO_3 (approximately 0.65% (w/w) HNO_3) in the diluted solution, with the addition of a 0.1% (v/v) Cs/La chloride solution (0.01% (w/w) CsCl or $LaCl_3$). Below is an example of how to dilute the samples:

To achieve a final volume of 50 mL, add approximately 10 mL of ultrapure water, 0.5 mL of concentrated nitric acid, and 0.5 mL of Cs/La solution (10% (w/w) of CsCl and $LaCl_3$). Add the sample to be diluted to this solution (see Table 1) and fill up to a final volume of 50 mL. It has proven effective to divide dilution factors higher than 150 into multiple-step dilutions.

Table 1 provides recommendations for the dilution factors of the electrolyte solution at typical concentrations of Ca, K, Mg and Na (Ca: 60–90 mg/L; K: 150–200 mg/L; Mg: 10–40 mg/L; Na: 3,000–3,500 mg/L). Different working ranges and dilution factors result depending on the selected wavelength and burner head position. Recommendations for stepwise dilution are also included.

Table 1: Recommended dilution factors in relation to method parameters

Element, line, burner head position	Dilution factor	Examples of dilution steps
Ca, 422 nm, 0°	50	Step 1: 50-fold
K, 766 nm, 0°	1,500	Step 1: 10-fold Step 2: 150-fold
K, 766 nm, 90°	150	Step 1: 150-fold
K, 404 nm, 0°	5	Step 1: 5-fold
Mg, 285 nm, 0°	250	Step 1: 10-fold Step 2: 25-fold
Mg, 285 nm, 90°	25	Step 1: 25-fold
Na, 589 nm, 0°	15,000	Step 1: 100-fold Step 2: 150-fold
Na, 589 nm, 90°	1,500	Step 1: 10-fold Step 2: 150-fold
Na, 330 nm, 0°	150	Step 1: 150-fold

Calibration

A typical procedure for monitoring the content of pharmaceutical products involves calibrating to a range of 0.7 to 1.3 times the expected value of the product in issue. At least three standards are used for calibration. Samples and standards should undergo the same reagent additions. In this application note, the measurement was calibrated using acid-stabilized, certified single-element standards. The calibration solutions had a concentration of 1% (v/v) HNO_3 (approximately 0.65% (w/w) HNO_3) and a Cs-La buffer concentration of 0.1% (v/v) (0.01% (w/w) CsCl or $LaCl_3$).

Table 2 shows the concentration range of the calibration depending on the method parameters (wavelength and burner head position BHP) in absorption mode. Table 3 shows the equivalent data for emission mode (measurement without hollow cathode lamps). This working range should be adapted according to product characteristics and regulatory requirements. Figure 1 shows typical calibration curves for the respective method parameters graphically.

Table 2: Calibration concentrations used for the absorption mode

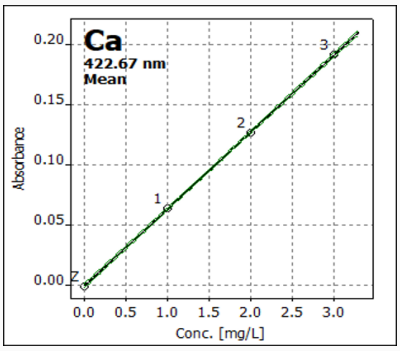
Standard	Concentration [mg/L]								
	Ca 422 nm BHP 0°	K 766 nm BHP 0°	K 766 nm BHP 90°	K 404 nm BHP 0°	Mg 285 nm BHP 0°	Mg 285 nm BHP 90°	Na 589 nm BHP 0°	Na 589 nm BHP 90°	Na 330 nm BHP 0°
Cal. 0	0	0	0	0	0	0	0	0	0
Std. 1	1	0.1	1	20	0.05	0.5	0.1	1	10
Std. 2	2	0.2	2	40	0.1	1.0	0.2	2	20
Std. 3	3	0.3	3	60	0.15	1.5	0.3	3	30

BHP: burner head position

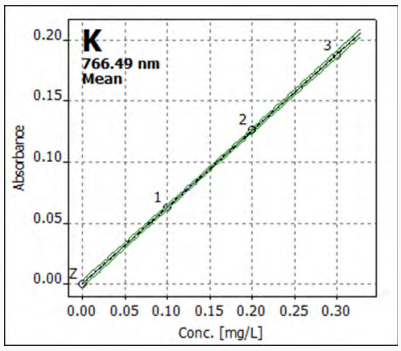
Table 3: Calibration concentrations used for the emission mode

Standard	Concentration [mg/L]		
	K 766 nm BHP 90°	K 404 nm BHP 0°	Na 589 nm BHP 90°
AutoMax	20	200	20
Cal. 0	0	0	0
Std. 1	1	10	1
Std. 2	2	20	2
Std. 3	3	30	3

BHP: burner head position



BHP 0°, Absorption,
Correlation $R^2_{(adj.)}$=0.99994



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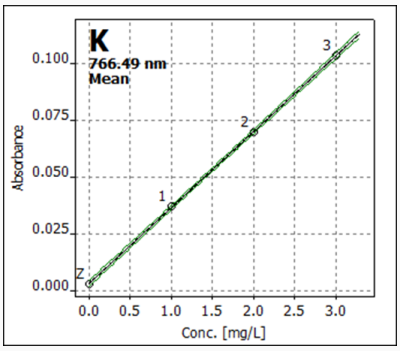

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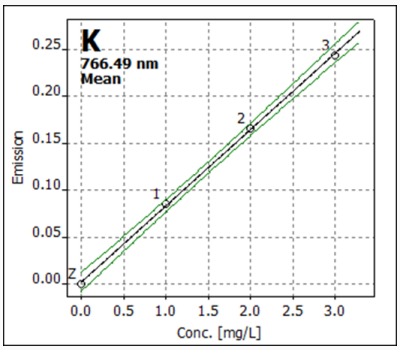

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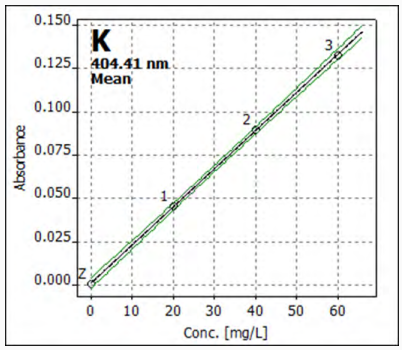

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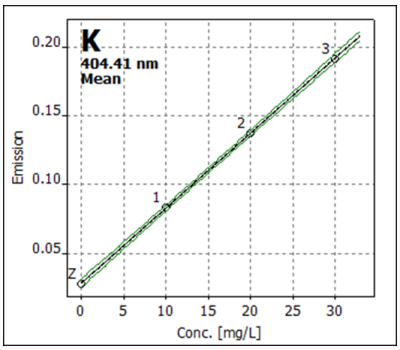

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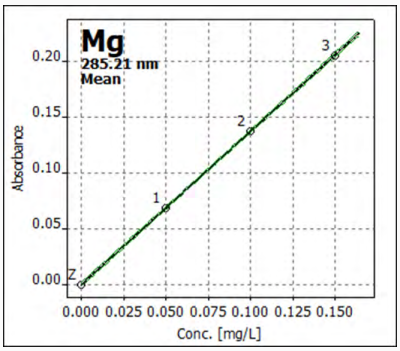

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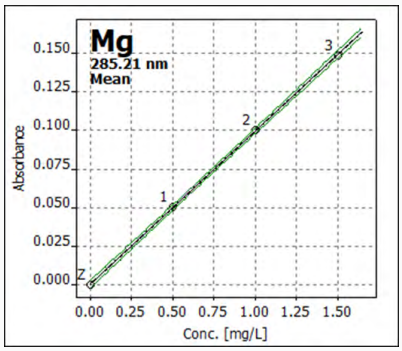

BHP 90°, Absorption,
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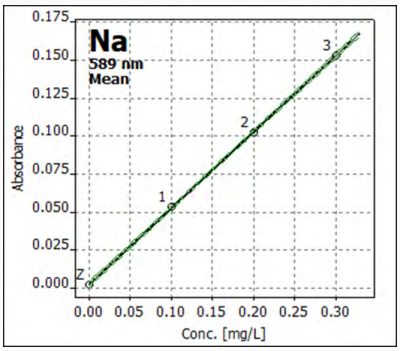

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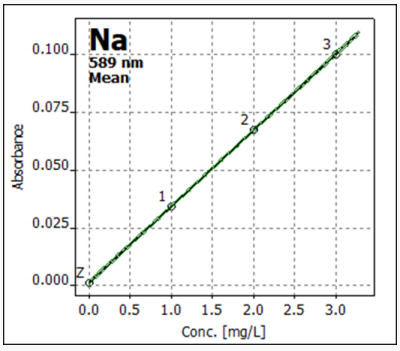
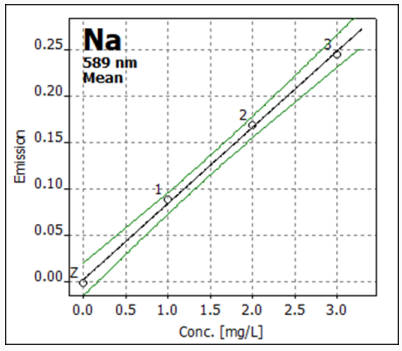
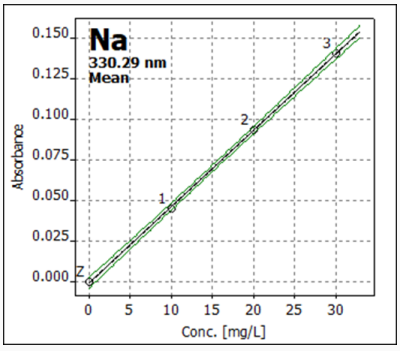


BHP 90°, Absorption,
Correlation $R^2_{(adj.)}$=0.99994



BHP 90°, Emission,
Correlation $R^2_{(adj.)}$=0.998



BHP 0°, Absorption,
Correlation $R^2_{(adj.)}$=0.9996

BHP: burner head position

Figure 1: Typical calibration functions

Instrument settings

To increase measurement precision, we recommend a waiting time of 10 to 15 minutes with the lamp activated and the flame ignited. Any potential variation in HCL intensity can be compensated for using the spectrometer's dual-beam mode. In emission mode, a burn-in time of 10 to 15 min is recommended as well.

Table 4 shows the general device parameters used for the application note presented. Table 5 shows the recommended optical method settings, and the flame conditions used. Depending on the method chosen, different flame and optical settings must be used. These parameters are set and controlled fully automatically by software.

Table 4: General instrument parameters

Parameter	Specification
Device	novAA 800 F
Burner type	50 mm
Flame type	Air/acetylene
Measuring time	5 x 5s
Rinsing solution	1% (v/v) HNO_3

Table 5: Method settings

Element and meas. mode	Wavelength [nm]	Slit [nm]	Current HCL [mA]	Acetylene flow rate [L/h]	Burner height [mm]	Background correction
Ca Absorption	422.7	1.2	3	55 (+75)*	5	None
K Absorption	766.5 404.4	0.8	4	45	5	None
K Emission	766.5 404.4	0.2	-	55	11	None
Mg Absorption	285.2	1.2	1.5	45	5	D_2
Na Absorption	303.3 589.0	0.8	3	50	6	None
Na Emission	589.0	0.2	-	55	12	None

*Auxiliary oxidant

Results and Discussion

This application note presents the results of an analysis of four typical electrolyte solutions for intravenous therapy. Table 6 shows the results of the measurements taken to determine the concentrations of the elements Ca, K, Mg and Na. The relative standard deviation (RSD) listed is based on measurement replicates. The measurement parameters were chosen so that the solutions could be diluted automatically by the AS-FD autosampler after the samples had been pre-diluted manually (dilution factor 25).

The user software complies with CFR part 11 (electronic signatures, audit trail, user management and FDA certificate), enabling automation of the measurement process. If quality limits are exceeded for parameters such as the relative standard deviation, the regression quality of the calibration ($R^2_{(adj)}$) and the content of the control samples, selected reactions can be triggered. These reactions can include automatically repeating the measurement, performing a recalibration and stopping the measurement at the user's request, among others. These exceptional functions allow the equipment presented to process the sample automatically.

Table 6: Measurement results of the determination of Ca, K, Mg and Na in electrolyte solution

Sample	Element	Dilution factor	Method setting	Measured value [mg/L] (RSD)
Sample 1	Ca	50	422 nm, 0°, Absorption	65 (0.24%)
	K	150	766 nm, 90°, Emission	169 (0.08%)
	Mg	25	285 nm, 90°, Absorption	17.2 (1.1%)
	Na	1,500	589 nm, 90°, Emission	3,260 (0.15%)
Sample 2	Ca	50	422 nm, 0°, Absorption	82 (0.20%)
	K	150	766 nm, 90°, Absorption	290 (0.04%)
	Mg	25	285 nm, 90°, Absorption	22.3 (0.45%)
	Na	1,500	589 nm, 90°, Absorption	4,080 (0.1%)
Sample 3	Ca	50	422 nm, 0°, Absorption	94.2 (0.56%)
	K	150	766 nm, 90°, Absorption	166 (0.76%)
	Mg	25	285 nm, 90°, Absorption	19.4 (0.43%)
	Na	150	330 nm, 0°, Absorption	3,786 (0.5%)
Sample 4	Ca	50	422 nm, 0°, Absorption	79.6 (0.52%)
	K	150	766 nm, 90°, Absorption	160 (1.1%)
	Mg	25	285 nm, 90°, Absorption	20.1 (0.46%)
	Na	150	330 nm, 0°, Absorption	3,981 (0.76%)

Summary

The novAA 800 F flame atomic absorption spectrometer enables precise quantification of the elements Ca, K, Mg and Na in electrolyte solutions for intravenous therapy or other solutions used in the pharmaceutical industry in compliance with regulations. Together with the AS-FD autosampler, the analytes can be measured automatically after just one dilution step. The selection of different method parameters such as primary and secondary spectral lines in absorption or emission mode as well as the burner head rotation (0°-90°) allow maximum flexibility for the user. In combination with the CFR Part 11 compliant user software and its automation functions, maximum measuring convenience is generated.

Figure 2: novAA 800 F

Recommended device configuration

Table 7: Overview of devices, accessories, and consumables

Article	Article number	Description
novAA 800 F	812-08000-2	Atomic absorption spectrometer with flame technology
AS-F	810-60500-0	Autosampler for flame AAS
AS-FD	810-60501-0	Autosampler with auto-dilution for flame
Sample rack 139 position	810-60503-0	Sample tray with 129 positions for 15mL vials and 10 positions for 50mL vials
Sample rack 54 position	810-60502-0	Sample tray 54 positions for 50 mL vials
Burner head 50 mm	810-60057-0	Burner head for acetylene/nitrous-oxide or acetylene/air flame
HCL Ca	480-450.009C	Coded HCL Ca Coded Hollow Cathode Lamp Calcium (Ca)
HCL K	480-450.041C	Coded HCL K Coded Hollow Cathode Lamp Potassium (K)
HCL Mg	480-450.031C	Coded HCL Mg Coded Hollow Cathode Lamp Magnesium (Mg)
HCL Na	480-450.052C	Coded HCL Na Coded Hollow Cathode Lamp Sodium (Na)
FDA 21 CFR Part 11 Compliance	810-60152-0	Software module for FDA 21 CFR Part 11 software compliance of ASpect LS

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Version 1.0 · Author: HoSi
en · 09/2025
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