Challenge
Accurate quantification of Al in electrolyte solutions

Solution
Quantification of metals using graphite tube technology with Zeeman background correction

Intended audience
Research and quality control laboratories in the pharmaceutical industry

Quantification of Aluminum in Electrolyte Solutions

Introduction

Electrolyte solutions and solutions for intravenous therapy (IV) are essential components of modern medicine. They are used to supply fluids, electrolytes and active substances to patients. They are particularly useful for treating volume deficiency and electrolyte imbalances, and for administering medication. Their high purity and pharmaceutical quality are crucial for patient safety as they enter the bloodstream directly, meaning they must meet the highest contamination control standards.

Although aluminum has no immediate toxicological relevance in typical concentrations, the quantitative determination of aluminum in electrolyte solutions is primarily carried out for regulatory and quality assurance reasons. This is because of the potential for accumulation in vulnerable patient groups, particularly newborns and patients with impaired kidney function. Additionally, the analysis ensures compliance with pharmacological limits and controls possible contamination from production processes or primary packaging materials.

Graphite furnace atomic absorption spectrometry (GF-AAS) is a well-established, sensitive and reliable method for determining aluminum. It can detect trace concentrations in the low µg/L range, making it particularly suitable for analyzing complex matrices. The method's high selectivity and precision allow even the lowest aluminum contents to be reliably quantified, ensuring compliance with regulatory requirements. Essential for correct and precise determination are Zeeman background correction, a furnace design based on the STPF (stabilized temperature platform furnace) concept, and transversely-heated graphite tubes.

This application note describes the determination of aluminum in electrolyte solutions for IV using GF-AAS with the ZEEnit 650P or ZEEnit 700P. The AS-GF autosampler performs automated sample handling, including automatic dilution or spiking of the sample and reagent addition.

The existing functions of the user software enable the entire measurement process, including quality control, to be fully automated. The ASpect CFR software extension offers functions such as electronic signatures, an audit trail and variable rights assignment in user management, enabling compliance with 21 CFR Part 11.

Materials and Methods

Samples and reagents

- Electrolyte solution for intravenous therapy
    - Concentrate
    - Ready to use solutions
    - Process solution
- Concentrated HNO_3 (62-65%, p.a.)
- Pd-modifier solution (10 g/L), alternatively Pd standard solution (1 g/L, ICP standard)
- Ca standard solution (1 g/L ICP standard)
- Certified single element standard for aluminum (1,000 mg/L)

Sample preparation

The samples can be used for measurement either undiluted or diluted. Diluting the sample reduces the effects of the matrix that may occur during measurement. It is recommended that a solution of 0.5 (v/v) HNO_3 is used as a diluent. If lower sample dilutions are required due to specified limit values, the aluminum recovery rate (RR) should be determined by spiking the sample. If the recovery rate is outside the tolerance range (i.e. less than 80% or greater than 120%), the standard addition or addition calibration method should be used instead.

Calibration

Standard method:

In this method, solutions with known concentrations of the analyte are used for calibration. It is suitable for diluted samples or electrolyte solutions with low matrix content. Common regulations, such as the European Pharmacopoeia, stipulate that calibration should be performed using at least three standards and a blank value. Calibration should be performed from the detection limit up to 120% of the limit value. This application note presents a working range of 0–25 µg/L Al (see Table 1). 0.5% (v/v) HNO_3 is used as the diluent and blank value. A typical calibration within the specified range is shown in figure 1.

Method of addition:

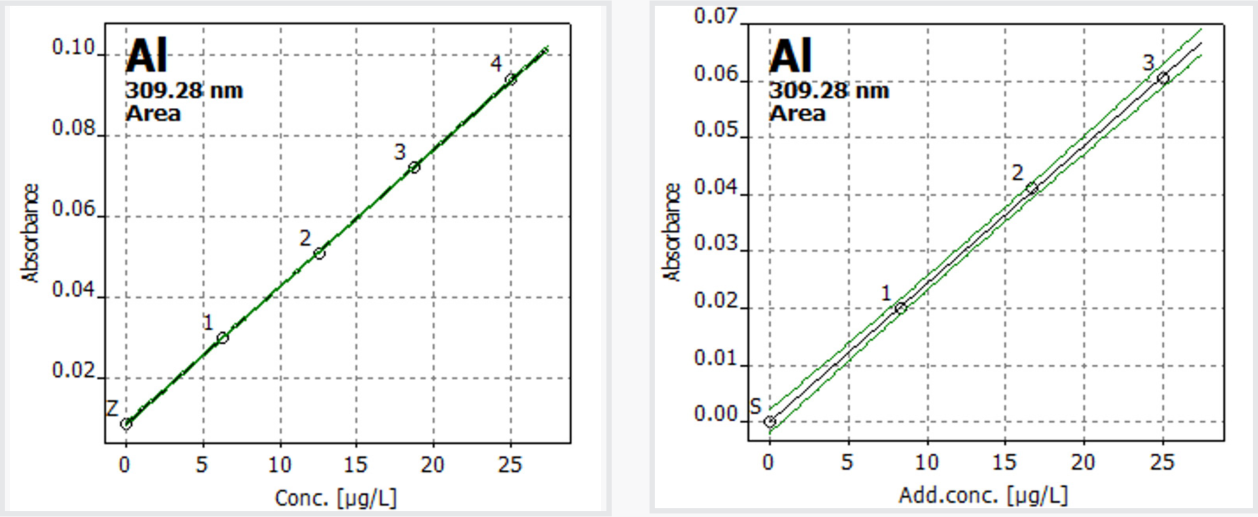
Using this procedure, the original concentration of the sample is obtained by performing a regression analysis on a series of mixtures prepared by adding known amounts of the analyte to aliquots of the sample. The resulting calibration line is extrapolated to its intersection with the x-axis, which corresponds to the negative of the sample's initial concentration. If the recovery rate of aluminum in the sample solution is outside the tolerance range (European Pharmacopoeia 80–120%), the method of addition needs to be used with at least three spiked sample aliquots (spiking with blank solution, standard 1 and standard 2). An insufficient recovery rate is often caused by the sample matrix and can be improved by diluting the sample. However, if the limit value required is so low that it is not possible to dilute the sample, the standard addition method can compensate for the matrix influence. The AS-GF autosampler can perform the method of addition fully automatically. For this application, injecting 15 µL of the sample (standard or the blank) into the graphite tube has proven effective. A typical calibration in the specified range is shown in table 1 and figure 1.

Method of addition calibration:

The method of addition calibration is a special feature. If samples with a similar matrix composition are to be quantified, this procedure can eliminate the need for subsequent addition steps (spiking the sample). A standard addition performed previously serves as the calibration of the procedure.

Table 1: Concentrations used for calibration

Standard	Concentration [µg/L]	
	Standard procedure	Method of addition
Cal. 0	0	0
Std. 1	6.25	8.33
Std. 2	12.50	16.70
Std. 3	18.75	25.00
Std. 4	25.00	



Procedure: Standard, correlation $R^2 = 0.99994$

Procedure: Method of addition, correlation $R^2 = 0.99994$

Figure 1: Characteristic calibration functions

Instrument settings

Determining the concentration of aluminum in an electrolyte solution is an analytical challenge that can only be accomplished correctly and precisely using high-performance graphite furnace systems with Zeeman background correction and transversely-heated graphite tubes. Table 2 lists the device type used for this application note, along with the relevant parameters.

Table 3 shows the temperature time program used. It is essential that the sample dries slowly and steadily (steps 1 to 4). Due to the presence of glucose or lactose in electrolyte solutions, air ashing (steps 5 and 6) helps to minimize the background during the measurement. The salt components of the sample are reduced in the subsequent pyrolysis step, an effective temperature range is between 1,200 and 1,500 °C. If a high background signal occurs during the measurement, this pyrolysis step should be extended. The sample should be measured at 2,450–2,500 °C, as this is the temperature range at which the signal intensity is at its maximum.

Table 2: General instrument parameters

Parameter	Specification
Device	ZEEnit 650P / 700P
Tube type	PIN-plattform
Modifier solution	Pd (1 g/L)
	Ca (0.5 g/L)
Background correction	Zeeman (0.8 T)
Rinsing solution	1% (v/v) HNO_3

Table 3: Used temperature time program

Step	Name	Temp. [°C]	Ramp [°C/s]	Hold [s]	Time [s]	Gas	
						Int.	**Add.**
1	Drying	80	6	20	28.3	Min	Stop
2	Drying	95	3	25	30.0	Min	Stop
3	Drying	110	5	15	18.0	Max	Stop
4	Drying	220	7	1	16.7	Max	Stop
5	Pyrolysis	575	50	20	27.1	Stopp	Max
6	Pyrolysis	575	0	18	18.0	Max	Stopp
7	Pyrolysis	1,200	75	18	26.3	Min	Stopp
8	Pyrolysis	1,250	50	5	6.0	Max	Stopp
9	AZ*	1,250	0	6	6.0	Stopp	Stopp
10	Atomize	2,450	1,500	3	3.8	Stopp	Stopp
11	Clean	2,500	500	4	4.1	Max	Stopp

* AZ: Autozero

Results and Discussion

This application note examines typical samples of electrolyte solutions. These included concentrates, ready-to-use solutions for intravenous therapy, and used process solution.

Table 4 shows the sample type, the dilution factor used, and the measurement results for aluminum determination. The standard deviation (SD) is based on repeat measurements of the samples.

Depending on the composition of the electrolyte solution concentrate and the resulting matrix concentration, the accuracy of the measurement can be affected. Samples with low salt and additive concentrations can be accurately determined without dilution or with minimal dilution. However, for samples with a higher matrix load, dilution by a factor of 10 to 50, or the use of the method of addition, is necessary for an analytically valid analysis. The limit of detection of the system is 0.3 µg/L and less (limit of quantification ≤1 µg/L).

Table 4: Measurement results of the determination of Al in electrolyte solution

Sample	Dilution factor	Calibration type	Recovery rate	Measured value [µg/L] (SD)	
Concentrate 1	20	Standard	67%	< LOD	
	50	Standard	107%	< LOD	
	10	Method of addition	106%	< LOD	
Concentrate 2	20	Standard	96%	< LOQ	
	50	Standard	109%	< LOD	
	10	Method of addition	111%	< LOQ	
Concentrate 3	1	Standard	117%	2.68	±0.25
	1	Method of addition	107%	2.67	±0.37

Sample	Dilution factor	Calibration type	Recovery rate	Measured value [µg/L] (SD)	
Electrolyte for IV 1	1	Standard	109%	6.20	±0.23
	1	Method of addition	111%	6.73	±0.52
Electrolyte for IV 2	10	Standard	102%	291	±2.0
	5	Standard	109%	310	±19
Process solution	1	Standard	103%	< LOD	
	1	Method of addition	101%	< LOD	

SD: standard deviation, LOD: limit of detection, LOQ: limit of quantification

Summary

The ZEEnit 650P and ZEEnit 700P graphite tube atomic absorption spectrometers enable the compliant and precise quantification of aluminum in electrolyte solutions in the pharmaceutical industry. The ZEEnit series' powerful design enables optimum measurement precision and accuracy while offering maximum ease of use thanks to automated hardware and software.

Samples with low to medium salt and reagent concentrations can be analyzed for aluminum content using the standard calibration procedure. Samples with a high matrix concentration should be analyzed using the method of addition or diluted prior to measurement.

Figure 2: ZEEnit 650P

Recommended device configuration

Table 5: Overview of devices, accessories, and consumables

Article	Article number	Description
ZEEnit 650P	813-0650P-2-K	Graphite furnace AAS with Zeeman background correction
ZEEnit 700P	813-0700P-2-K	Flame- and graphite furnace AAS with Zeeman background correction
Graphite tube, platform	407-152.314	Graphite tubes with PIN-platform -pyrolytically coated (10 pieces)
Chiller, 50 Hz	810-60053-0	Software-controlled cooling system (50 Hz power supply)
Chiller, 60 Hz	810-60052-0	Software-controlled cooling system (60 Hz power supply)
Al-HCL	480-450.001C	Coded hollow cathode lamp aluminum
FDA 21 CFR Part 11 software	810-60152-0	Software module for FDA 21 CFR Part 11 compliance

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