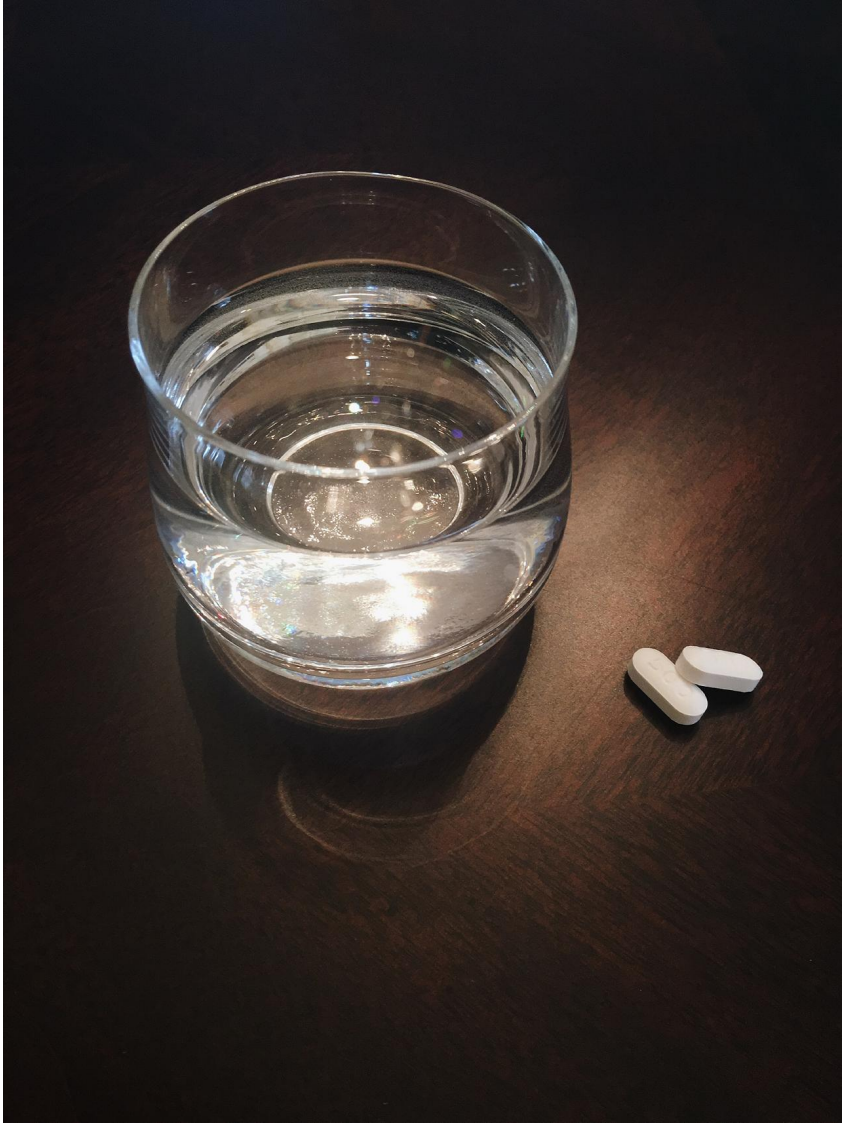

Application Note AN-S-397

IC assay for sodium chloride in sodium chloride tablets for solution

Method validations according to the U.S. Pharmacopoeia

Sodium chloride tablets are used to treat low sodium levels or to replenish electrolytes as prevention against heat cramps [1]. The quality of these tablets must adhere to strict requirements such as those addressed by the U.S. Pharmacopoeia (USP) to ensure their safety and compliance with the permitted levels of ingredients. For sodium chloride tablets, <USP29> specifies that the NaCl content must fall within 95–105% of the labeled amount.

The USP has embarked on a global initiative to modernize many of their existing monographs. As an alternative to titration, ion chromatography (IC) with suppressed conductivity detection has been approved by the USP as a validated method to quantify chloride content in NaCl tablets for solution or oral use [2]. The Metrosep A Supp 17 - 150/4.0 column guarantees reliable separation of chloride and the potential impurity nitrite, while the Metrohm suppressor module (MSM) ensures low background noise. The presented IC method was validated following the USP General Chapter <1225>, Validation of Compendial Procedures [3].

SAMPLES AND SAMPLE PREPARATION

Sodium chloride tablets for oral use or solution (100 tablets, distributed by Consolidated Midland Corporation, Brewster, New York 10509 USA) with a labeled amount of 1 g NaCl were used for the qualification procedure. A sample stock solution of nominally 5 mg/mL NaCl was prepared as follows. Not less than 30 tablets were ground into a powder. Approximately 5 g of the powder was transferred into a 1000 mL volumetric flask and dissolved in approximately 50% of the final volume of ultrapure water (UPW) and then filled to the mark with UPW.
Out of the stock solution, the sample solutions with a nominal concentration of 100 µg/mL NaCl were prepared by dilution with UPW. Here, 10 mL of sample stock solution was transferred to a 500 mL volumetric flask, diluted to volume, and mixed well. A single point calibration with 100 µg/mL of USP Sodium Chloride RS in UPW was used.

Figure 1 Instrumental setup including a 940 Professional IC Vario with a binary high-pressure gradient and conductivity detection after chemical suppression (L), and an 889 IC Sample Center – cool (R). Cooling can prolong sample stability.

EXPERIMENTAL

The samples were injected directly into the IC (Figure 1) without any further sample preparation and analyzed according to the parameters stipulated in the USP monograph (Table 1). Chloride was separated from all other components (Figure 2) using a binary potassium hydroxide gradient (Table 2) on a Metrosep A Supp 17 - 150/4.0 column with packing material L91 – a certified alternative column for this method (Table 1). The conductivity signal was detected after chemical suppression.

Table 1. Requirements for IC method as per USP monograph «Sodium Chloride Tablets for Solution» [2].

Column with L91 packing	Metrosep A Supp 17 - 150/4.0
Flow rate	1.2 mL/min
Column temperature	35 °C
Injection volume	10 µL
Detection	Conductivity with suppression

Table 2. Eluent gradient profile as per USP monograph «Sodium Chloride Tablets for Solution». Solution A: 100 mmol/L KOH, and solution B: UPW [2].

Time (min)	Solution A (%)	Solution B (%)
0	5	95
12	70	30
15	5	95
24	5	95

RESULTS

The IC assay for sodium chloride content in sodium chloride tablets was validated according to USP General Chapter <1225>, Validation of Compendial Procedures [3]. Sodium chloride tablets, USP («normal salt tablets for solution or oral use 1 gram»), were analyzed for their chloride and nitrite content, and the accuracy of the sodium chloride determination was calculated as 101% (Figure 2).

Separation of chloride and nitrite peaks with the Metrosep A Supp 17 (L91) column achieved a resolution of >2 as required by USP definitions (Figure 3). All acceptance criteria were fulfilled, e.g., asymmetry (tailing factors) for the chloride and nitrite peaks were <2, or the relative standard deviation of standard solutions was <2.0% (n = 6) (Table 3).

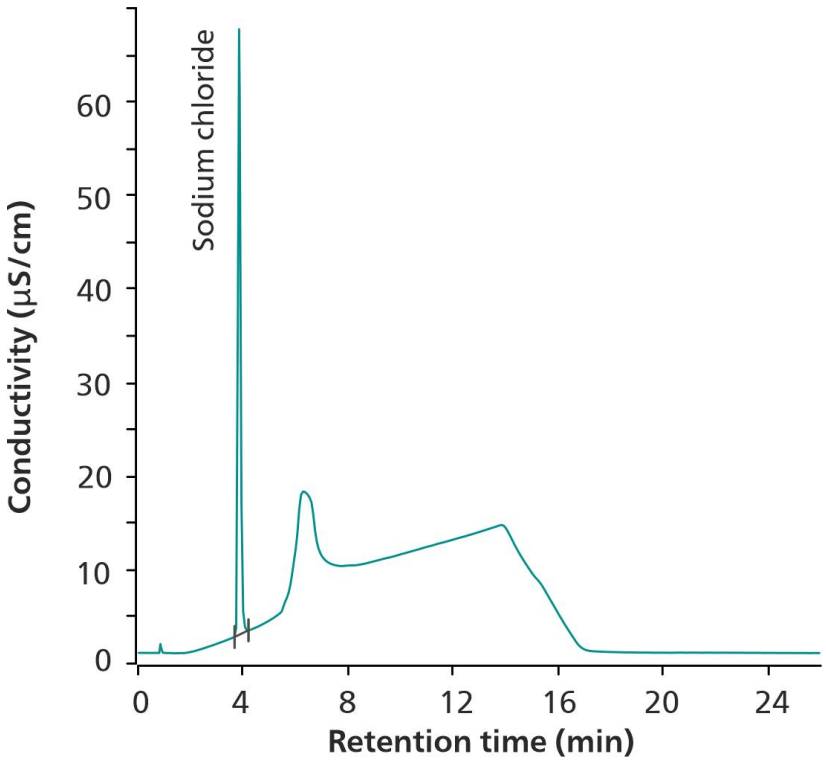

Figure 2. Chromatogram of chloride for sodium chloride tablets, USP («normal salt tablets for solution or oral use 1 gram») containing 101.35 µg/mL sodium chloride (101% recovery of the nominal concentration).

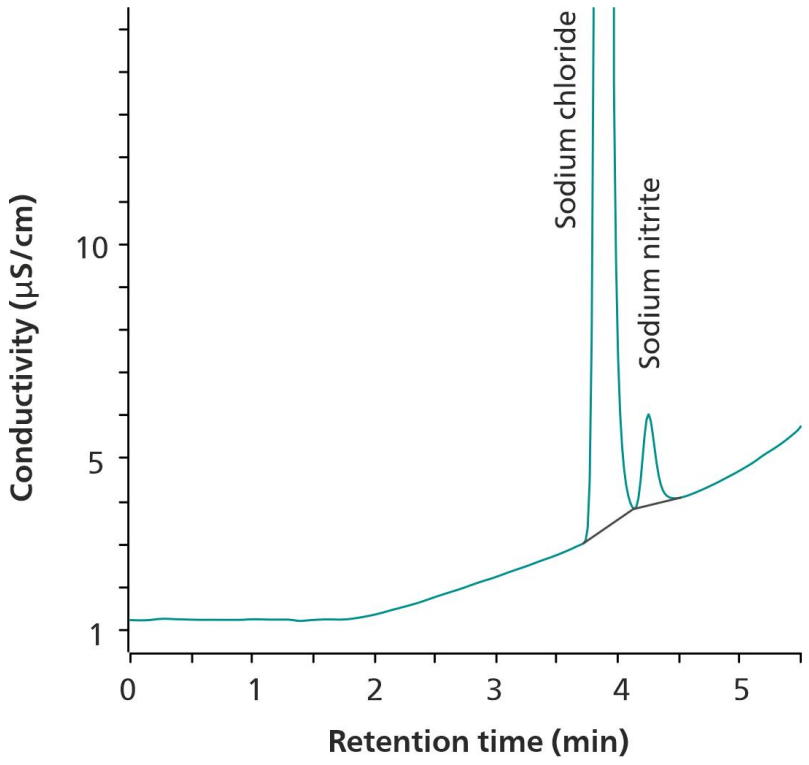

Figure 3. Chromatogram for a system suitability solution of the USP reference standards sodium chloride (Cat. No. 1613804) and sodium nitrite (Cat. No. 1614454), containing 100 µg/mL sodium chloride and 8.0 µg/mL sodium nitrite.

Table 3. Selected performance characteristics.

Performance characteristics	Acceptance criteria	Results
Resolution	Resolution between the chloride and nitrite peaks is NLT 2.0	2.07
Tailing factor	Tailing factors (asymmetry) for the chloride and nitrite peaks are NMT 2.0	1.25 and 1.35 respectively
Repeatability	Relative standard deviation for the chloride peak in the standard solution is NMT 2.0% for six replicates	0.039%
Accuracy	Average % recovery should be 95.0–105.0% of the manufacturer's CoA value	101%

CONCLUSION

Ion chromatographic analysis of sodium chloride using the Metrosep A Supp 17 separation column qualified as a USP-validated approach for the quantification of sodium chloride in sodium chloride tablets for solution or oral use. The Metrosep A Supp 17 column contains the alternative packing material L91 approved for the USP monograph «Sodium Chloride in Sodium Chloride Tablets for Solution or Oral Use». Beside the chloride content, nitrite impurities can also be accurately determined in the same analysis.

REFERENCES

[1] Anastasiou, C. A.; Kavouras, S. A.; Arnaoutis, G.; et al. Sodium Replacement and Plasma Sodium Drop During Exercise in the Heat When Fluid Intake Matches Fluid Loss. *Journal of Athletic Training* **2009**, *44* (2), 117–123. https://doi.org/10.4085/1062-6050-44.2.117.

[2] *Sodium Chloride Tablets for Solution*; Monograph; U.S. Pharmacopeia/National Formulary: Rockville, MD. https://doi.org/10.31003/USPNF_M76140_02_01.

[3] *1225Validation of Compendial Procedures; General Chapter*; U.S. Pharmacopeia/National Formulary: Rockville, MD. https://doi.org/10.31003/USPNF_M99945_04_01.

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CONFIGURATION

940 Professional IC Vario ONE/ChS/PP/HPG

The 940 Professional IC Vario ONE/ChS/PP/HPG is the intelligent IC instrument with **chemical suppression**, a **peristaltic pump** for suppressor regeneration and **binary high-pressure gradient**. It can be extended with the 942 Extension Modules to up to a quaternary gradient system. The instrument can be used with any separation and detection methods.

Typical areas of application:

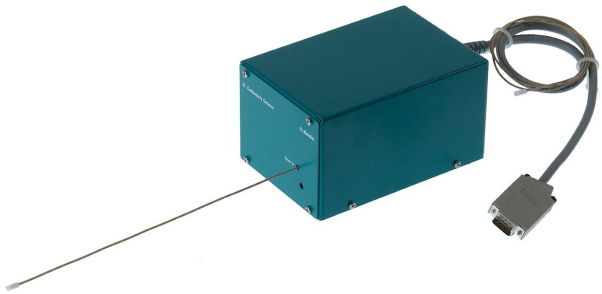
- Gradient applications for anion determinations with chemical suppression

889 IC Sample Center – cool

The 889 IC Sample Center – cool is the appropriate automation solution when you have only a very small amount of sample. In comparison with the 889 IC Sample Center, it possesses in addition a cooling function and is thus the ideal sample changer for biochemically relevant or thermally unstable samples.

Metrosep A Supp 17 - 150/4.0

The Metrosep A Supp 17 - 150/4.0 separation column is the column of choice for anion determinations that require good separating efficiency and short separation times at room temperature. The maximum flow rate of 1.4 mL/min then also makes it possible to optimize the determination. The Metrosep A-Supp-17 columns convince with their good price-performance ratio.



IC Conductivity Detector

Compact and intelligent high performance conductivity detector for intelligent IC instruments. Outstanding temperature stability, the complete signal processing within the protected detector block and the latest generation of DSP – Digital Signal Processing – guarantee the highest precision of the measurement. No change of measuring ranges (not even automatic ones) is required, due to the dynamic working range.

MSM-HC Rotor A

Suppressor rotor for all IC instruments with MSM-HC (Metrohm Suppressor Module with high capacity)