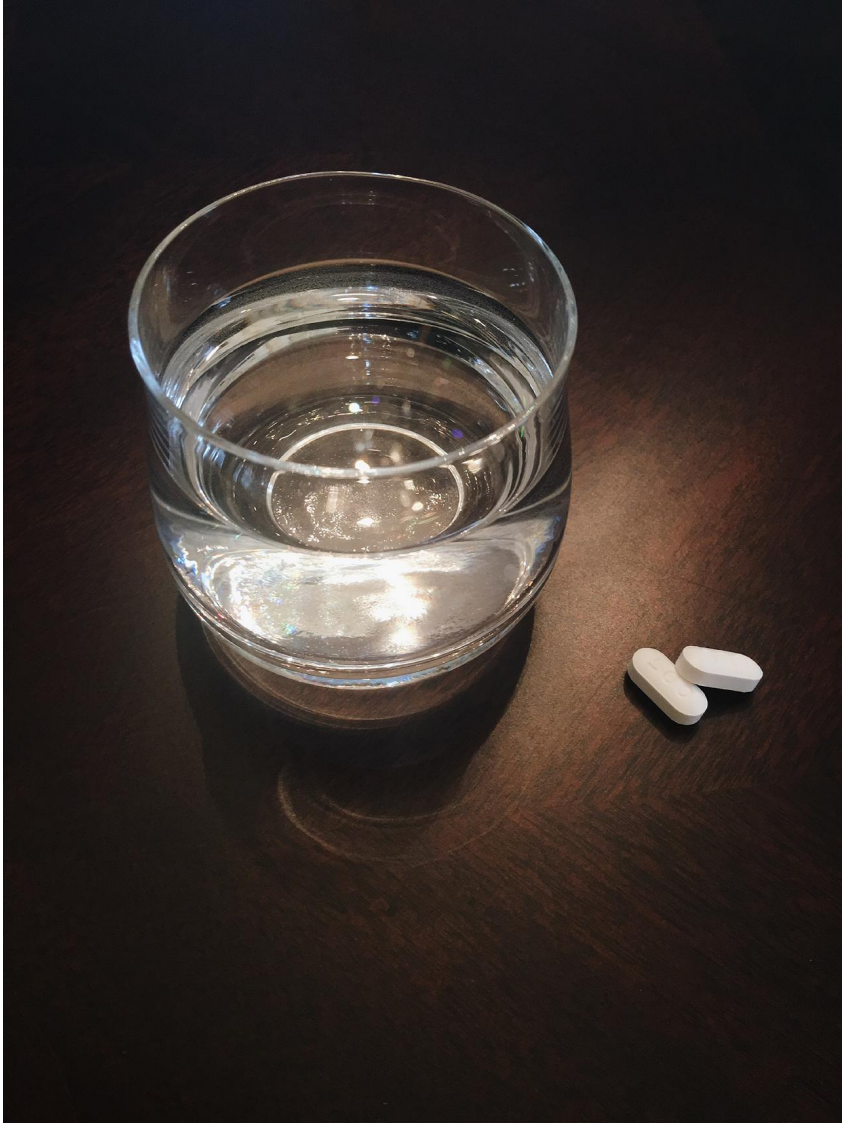

Application Note AN-S-397

溶液用化片中化的 IC(子色)

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).

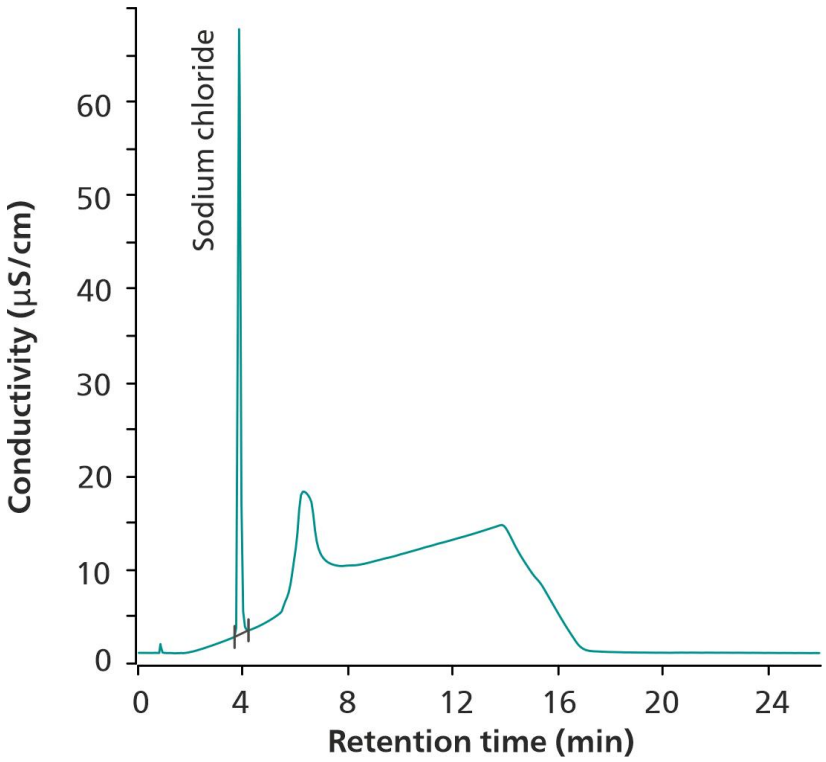

Figure 2. Chromatogram of chloride for sodium chloride tablets, USP («normal salt tablets for solution or oral use 1 gram») containing 101.35 µg/mL sodium chloride (101% recovery of the nominal concentration).

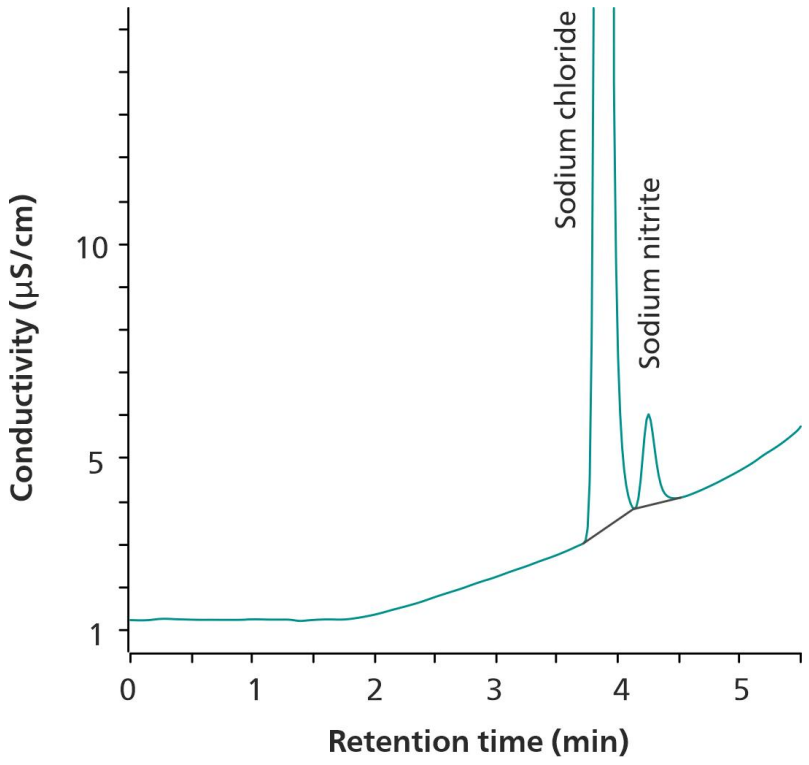

Figure 3. Chromatogram for a system suitability solution of the USP reference standards sodium chloride (Cat. No. 1613804) and sodium nitrite (Cat. No. 1614454), containing 100 µg/mL sodium chloride and 8.0 µg/mL sodium nitrite.

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] *〈1225〉 Validation 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

940 Professional IC Vario ONE/ChS/PP/HPG 是智能型 IC 器,有**化学抑制**、**蠕**用于抑制器再生,以及**二元高梯度**。 可使用 942 Extension Modul 将其展至四元梯度系。 器可使用各分和方法。

典型的用范:

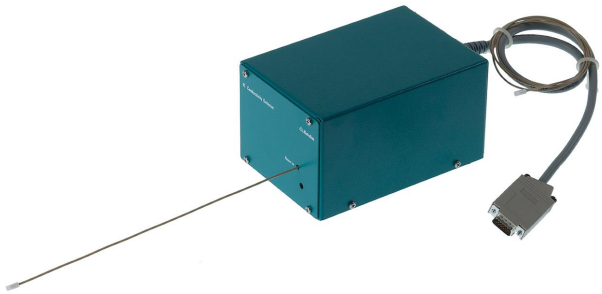
- 梯度用,用于子定,化学抑制

889 IC Sample Center – cool

889 IC Sample Center – cool 自化解决方案也用于品量少的情况。与 889 IC Sample Center 相比,它具有冷却功能,因此是用于生物化学相域或定性差的品的最佳自器。

Metrosep A Supp 17 - 150/4.0

分柱 Metrosep A Supp 17 - 150/4.0 是子定的最佳,要求在境温度下具有高分率和短分。最高 1.4 mL/min 的流速最佳定效果提供了可能。Metrosep A-Supp-17 柱具有很好的性价比。



IC Conductivity Detector

用于智能型子色的智能型高性能器。卓越的温度定性,受保的器端子板内的整个信号理程以及最新一代的DSP(数字式信号理)均能保量的精性。功于工作范,无需行范更(也不是自行)。

MSM-HC A

用于所有 MSM-HC(高容量万通抑制器模)的子色的抑制器