Application Note AN-S-376

药用氟化钠凝胶中的氟化物

Method validation according to the U.S. Pharmacopoeia

Fluoride is a mineral that is naturally found in water and some foods. It has been proven to strengthen the enamel of the teeth and protect them from decay [1]. However, exposure to too much fluoride can cause dental fluorosis, a condition that affects the appearance of the teeth. Therefore, it is important to monitor the amount of fluoride in dental care products such as gels and toothpastes.

Sodium fluoride gel is a beneficial product that effectively helps prevent cavities (caries). As specified by the authoritative United States Pharmacopeia – National Formulary (USP-NF) Monograph «Sodium Fluoride Gel» [2], ion chromatography (IC) with suppressed conductivity detection is a reliable method to measure fluoride and impurities in sodium fluoride gel.

This study validates an IC method using a Metrosep A Supp 16 - 250/4.0 column and a hydroxide eluent, which meets the USP-NF criteria. Fluoride is separated from chloride and other contaminants in gel toothpaste with high accuracy and precision. The IC method has been validated according to USP General Chapters <621> Chromatography [3] and <1225> Validation of Compendial Procedures [4].

SAMPLE AND STANDARD PREPARATION

Commercial gel toothpaste was diluted to a known concentration of approximately 2 µg/mL sodium fluoride (NaF). Here, 1.585 g of a gel toothpaste containing 331.5 mg NaF/100 g was diluted in 500 mL ultrapure water (UPW). The solution was sonicated for 10 minutes and further diluted 1:8.8 with UPW. Afterwards, the diluted solution was filtered using 0.2 µm pore size filters. The nominal sodium fluoride concentration for these samples was 1.19 µg/mL.

No additional sample preparation is required.

The standard solutions and the system suitability solutions are prepared from the respective 1000 µg/mL certified standards by dilution with UPW. For the assay, the standard solution is obtained by diluting a sodium fluoride solution to 2 µg/mL. The system suitability solution contains 2 µg/mL sodium fluoride and 1 µg/mL sodium acetate. For the impurity test, the standard solution consists of 0.2 µg/mL sodium chloride in UPW. The system suitability solution for the impurity test contains 1 mg/mL sodium fluoride and 1 µg/mL sodium chloride in UPW.

EXPERIMENTAL

Samples and standard solutions were directly injected into the IC using a 919 IC Autosampler plus (**Figure 1**).

Figure 1. Instrumental setup including a 930 Compact IC Flex, 919 IC Autosampler plus, and an 800 Dosino for automatic regeneration of the Metrohm Suppressor Module (MSM).

Fluoride was separated from acetate and chloride by using a potassium hydroxide eluent and the Metrosep A Supp 16 column (column material L91, **Table 1**). The analytes were quantified by evaluating their conductivity signal after chemical suppression.

The calibration was performed using a single 2.0 µg/mL sodium fluoride standard injected six times. The sample was analyzed in duplicate.

Table 1. Requirements for IC method as per USP Monograph «Sodium Fluoride Gel» [2].

Column with L91 packing	Metrosep A Supp 16 - 250/4.0
Eluent	15 mmol/L potassium hydroxide
Flow rate	1.0 mL/min
Temperature	40 ° C
Injection volume	20 µL
Detection	Conductivity with suppression

RESULTS

The IC assay for fluoride content was validated according to the USP Monograph «Sodium Fluoride Gel» [2]. Suitability requirements for resolution, tailing factor, and relative standard deviation were fulfilled (**Table 2**).

Table 2. Suitability requirements for the fluoride assay.

Parameter (assay)	Actual	USP requirement	Status
Resolution F^- /acetate	5.9	NLT 1.5	Pass
Tailing factor	1.1	NMT 2.0	Pass
RSD fluoride (%, n=5)	0.52	NMT 0.73	Pass

Commercial gel toothpaste samples were analyzed for their sodium fluoride content and the results showed the concentration at 104% of the label claim (**Figure 2**). The recovery of fluoride for the sample analysis was within the USP acceptance criteria of 90–110%.

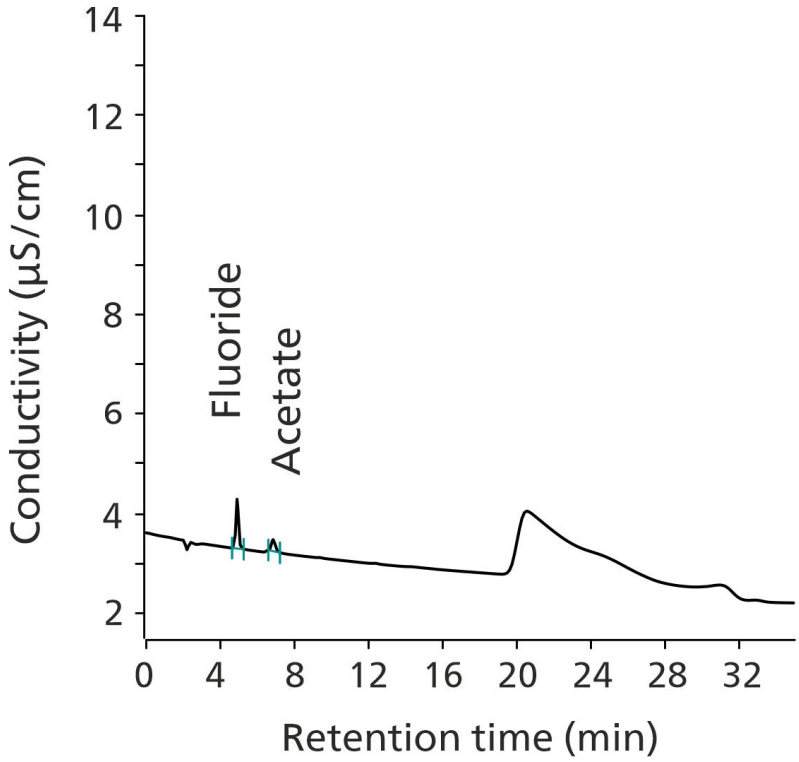

Figure 2. Chromatogram of a commercial toothpaste sample containing 1.24 µg/mL sodium fluoride (104% of the label claim).

When performing the impurity tests for potential contamination with chloride, the IC method showed excellent compliance with the USP requirements (Table 3).

Table 3. Suitability requirements for the chloride impurity in sodium fluoride gel.

Parameter (impurity)	Actual	USP requirement	Status
Resolution F^- /Cl^-	7.7	NLT 4	Pass
RSD fluoride (%, n=5)	4.2	NMT 5	Pass
S/N ratio Cl^-	>740	NLT 20	Pass

概要

The presented IC method complies with the USP General Chapters <621> and <1225> [3,4]. It is suitable to determine sodium fluoride in gels containing sodium fluoride according to the USP Monograph «Sodium Fluoride Gel» [2].

REFERENCES

1. Yeung, C. A. A Systematic Review of the Efficacy and Safety of Fluoridation. *Evid Based Dent* **2008**, *9* (2), 39–43. https://doi.org/10.1038/sj.ebd.6400578.
2. *Sodium Fluoride Gel*; Monograph; U.S. Pharmacopeia/National Formulary: Rockville, MD. https://doi.org/10.31003/USPNF_M3947_02_01.
3. *〈621〉 Chromatography*; General Chapter; U.S. Pharmacopeia/National Formulary: Rockville, MD. https://doi.org/10.31003/USPNF_M99380_01_01.
4. *〈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

930 Compact IC Flex Oven/ChS/PP/Deg

930 Compact IC Flex Oven/ChS/PP/Deg 是智能型 Compact IC 仪器,带有**柱加热炉**、**化学抑制**和**蠕动泵**用于抑制器再生,以及内置的**脱气装置**。 该仪器可使用各种分离和检测方法。

典型的应用范围:

- 使用化学抑制和电导检测进行阴离子测定
- 用离子排斥色谱法和反向抑制测定有机酸

919 IC Autosampler plus

919 IC Autosampler plus 满足实验室内处理中等样品量的要求。使用该仪器,可实现万通产品的各种离子色谱分析自动化。

800 Dosino

800 Dosino 驱动头,带有可用于智能型加液单元的读/写硬件设备。带固定电缆。