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APPLICATION NOTE 72907

Determination of fluoride in tooth gel containing sodium fluoride

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Keywords

IonPac AS15-5µm column, toothpaste, USP Sodium Fluoride Gel monograph, USP<621>, OTC

Goal

To evaluate the Thermo Scientific™ Dionex™ IonPac™ AS15-5 µm column for the determination of fluoride in sodium fluoride tooth gel

Introduction

Fluoride occurs naturally in many foods and water. Fluoride helps prevent tooth decay by making the tooth more resistant to acid attacks from plaque bacteria. Thus, it is one of the common ingredients in tooth gels and mouth rinses. The US Food and Drug Administration (FDA) has approved the use of three fluorine-containing compounds in tooth gels: stannous fluoride, sodium fluoride, and sodium monofluorophosphate (MFP). Most over-the-counter (OTC) tooth gels contain 0.24% w/w sodium fluoride, while dentist-prescribed tooth gel contains up to 1.1% w/w sodium fluoride. It is important to carefully monitor the levels of sodium fluoride in tooth gels in order to evaluate the quality and stability of these samples. Several techniques have been used to determine fluoride, MFP, and other phosphates in dental care products, including gas chromatography (GC), ion-selective electrodes, ion chromatography (IC), and colorimetry.[1-3] The United States Pharmacopeia National Formulary (USP-NF) Sodium Fluoride Gel monograph describes a potentiometric titration method using ion selective electrode for the determination of fluoride.[4]

As part of the USP monograph modernization initiative, a revision to the Sodium Fluoride Gel monograph was proposed in Pharmacopeia Forum 44(4).[5] The proposal recommends replacing the current ion-selective

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electrode procedure with an IC based method for assaying fluoride present in sodium fluoride gel. Here we demonstrate that a Dionex IonPac AS15-5µm column[6] can be used to analyze tooth gel samples for the content of fluoride. Using this column, fluoride is separated from other anions using KOH eluent generated electrolytically with a Thermo Scientific™ Dionex™ EGC III KOH cartridge and detected by suppressed conductivity. Method performance is evaluated according to the system suitability requirements described in the monograph for the assay and the acceptance criterion set for sodium fluoride content in a tooth gel sample. Method ruggedness was evaluated by measuring the response of sodium fluoride standards and samples under the same conditions but on two separate columns.

Experimental

Equipment

Thermo Scientific™ Dionex™ ICS-5000⁺ system* including:

- Thermo Scientific™ Dionex™ ICS-5000⁺ SP/DP Pump module, P/N 079976
- Thermo Scientific™ Dionex™ ICS-5000⁺ EG Eluent Generator module with high-pressure degas module, P/N 075776
- Thermo Scientific™ Dionex™ ICS-5000⁺ DC Detector/ Chromatography module, P/N 075940
- Thermo Scientific™ Dionex™ AS-AP Autosampler, P/N 074925
- Thermo Scientific™ Dionex™ EGC III KOH Potassium Hydroxide Eluent Generator Cartridge, P/N 074532
- Thermo Scientific™ Dionex™ CR-ATC Continuously Regenerated Anion Trap Column, P/N 060477
- Thermo Scientific™ Dionex™ AERS 500 (2 mm) Anion Electrolytically Regenerated Suppressor, P/N 082541
- Thermo Scientific™ Chromeleon™ Chromatography Data System Software, Version 7.1
- Thermo Scientific™ Dionex™ Vial Kit, 10 mL Polystyrene with Caps and Blue Septa, P/N 074228

*This technique can be adapted for any Dionex IC system.

Reagents and standards

- Deionized (DI) water, Type I reagent grade, 18 MΩ-cm resistance or better
- Thermo Scientific™ Dionex™ Fluoride Standard (1000 mg/L), 100 mL (P/N 037158)
- USP Sodium Fluoride Reference Standard (RS), Sigma-Aldrich (P/N PHR1408)
- USP Sodium Acetate Reference Standard (RS), Sigma-Aldrich (P/N 1613407)

Preparation of solutions and reagents

100 µg/mL USP Sodium Fluoride RS stock solution

10 mg of USP Sodium Fluoride RS was accurately weighed and dissolved in 100 mL of DI water in a volumetric flask, sonicated for 1 minute, and mixed.

100 µg/mL USP Sodium Acetate RS Stock solution

10 mg of USP Sodium Acetate RS was accurately weighed and dissolved in 100 mL of DI water in a volumetric flask, sonicated for 1 minute, and mixed.

2 µg/mL USP Sodium Fluoride RS solution

2 mL of 100 µg/mL USP Sodium Fluoride RS Stock solution was added to a 100 mL volumetric flask and DI water was added up to the mark.

2 µg/mL USP Sodium Fluoride RS and 1 µg/mL USP Sodium Acetate RS mix

2 mL of 100 µg/mL USP Sodium Fluoride RS stock solution and 1 mL of 100 µg/mL USP Sodium Acetate RS stock solution were added in a 100 mL volumetric flask. Then DI water was added up to the mark. The standard solution was used as a system suitability standard to check the USP system performance criteria.

Sample solution

83.34 mg of tooth gel sample (containing 0.24% w/w sodium fluoride) was accurately weighed and dissolved in 100 mL of DI water. The solution was vortexed for 2–3 min and then filtered through a 0.2 µm filter before injection.

Chromatographic conditions

Table 1. Chromatographic conditions

System:	Dionex ICS-5000+ system
Column:	Dionex IonPac AS15 3.0 mm × 150 mm, 5 µm (P/N 057594) Dionex IonPac AG15 3.0 mm × 30 mm, 5 µm (P/N 057597)
Eluent:	5 mM KOH
Column temp.:	30 °C
Eluent source:	Dionex EGC III KOH (P/N 074532)
Flow rate:	0.5 mL/min
Injection volume:	20 µL
Loop overfill factor:	5
Detection:	Suppressed conductivity
Suppressor type:	Dionex AERS 500 2 mm (P/N 082541)
Suppressor mode:	Recycle
Suppressor current:	7 mA
Run time:	23 min
Background conductivity:	0.15–0.2 µS
Baseline noise:	0.2–0.3 nS

Results and discussion

A revision of the assay of sodium fluoride gel is propsed in USP Pharmacopeia Forum (PF) 44(4). This proposal describes an IC method for assaying fluoride in a sodium fluoride gel, replacing the current ion-selective electrode procedure. The IC method uses a 4.0 mm × 25 cm; 4.6 µm L91 packing column. Here we demonstrate that a Dionex IonPac AS15-5 µm (3.0 mm × 15 cm) column can be used as an alternative column for fluoride assay in the USP Sodium Fluoride Gel proposed monograph revision. The Dionex IonPac AS15-5 µm column is a hydroxide-selective, strong anion-exchange column consisting of ethylvinylbenzene cross-linked with 55% divinylbenzene and grafted with smaller particles containing alkanol quaternary ammonium ions. The selectivity of the Dionex IonPac AS15 column was designed to retain fluoride well out of the water dip (system dip) and to separate common anions and low molecular weight organic acids. Figure 1 displays the chromatogram of a 2 µg/mL USP Sodium Fluoride RS analyzed using the chromatographic conditions listed in Table 1. Fluoride was separated from other anions using 5 mM KOH eluent generated electrolytically. The retention time (RT) of fluoride is 7.42 min. According to USP Sodium Fluoride gel monograph revision (USP PF 44(4)), the relative RTs for the fluoride and acetate ions are 1.0 and 1.3, respectively. Figure 2 shows the chromatogram of a 2 µg/mL USP Sodium Fluoride RS and 1 µg/mL USP Sodium Acetate RS mix. The relative RTs for fluoride and acetate were 1.0 and 1.32, respectively. As per the system suitability requirement described in the monograph, the run time should be not less than (NLT) 3 times the retention time of fluoride. The run time for our method is 23 min, thus meeting the requirement.

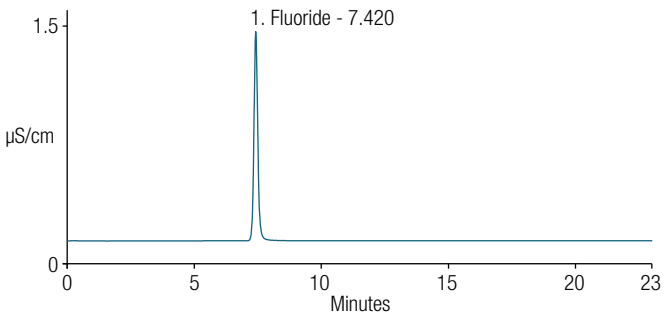

Figure 1. Chromatogram of the standard solution (2 µg/mL USP Sodium Fluoride RS)

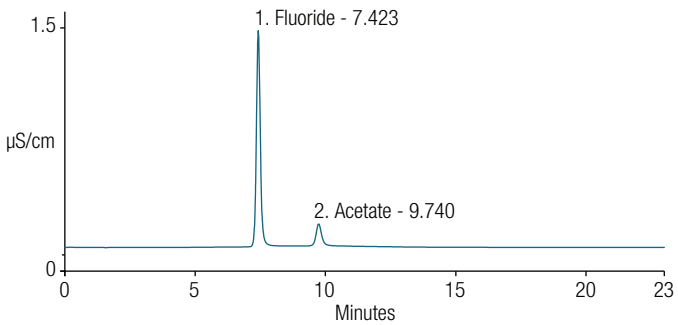

Figure 2. Chromatogram of the system suitability solution (2 µg/mL USP Sodium Fluoride RS and 1 µg/mL USP Sodium Acetate RS mix)

As per USP General Chapter <621>[7], when the particle size of the column is changed, the flow rate may require adjustment because smaller-particle columns will require higher linear velocities for the same performance (as measured by reduced plate height). Flow rate changes for both a change in column diameter and particle size can be made by:

$$F2 = F1 \times [\{(dc2)^2 \times dp1\}/\{(dc1)^2 \times dp2\}]$$

where F1 and F2 are the flow rates for the original and modified conditions, respectively, dc1 and dc2 are the respective column diameters, and dp1 and dp2 are the particle sizes.

Calculations for flow rate adjustment:

$$F2 = 1 \times [(9 \times 4.6)/(16 \times 5)]$$
$$F2 = 1 \times (41.4/80)$$
$$F2 = 0.52 \text{ mL/min}$$

Thus, we used a 0.5 mL/min flow rate instead of 1 mL/min. The resolution between the fluoride and acetate is 6.75 (calculated by the chromatography software using the USP formula). The asymmetry of the fluoride peak is 1.11 (calculated by the chromatography software using the USP formula). Table 2 shows that the method using the Dionex IonPac AS15-5µm column meets the the system suitability requirement described in the proposed monograph.

Method ruggedness was evaluated by measuring the response of sodium fluoride standards and samples under the same conditions but on two separate columns. The RTs of fluoride ion on two columns were found to differ by ~0.7%; i.e., 7.39 min on Column 1 and 7.34 min on Column 2. The USP monograph system suitability and assay acceptance criteria (90–110%) were met by both columns. Tables 2 and 3 list the USP system suitability requirements and the USP assay acceptance criterion, respectively.

Sample analysis

Most OTC tooth gels contain 0.24% w/w sodium fluoride but the dentist-prescribed tooth gels contain 1.1% w/w sodium fluoride. We bought fluoride tooth gel sample (containing 0.24% sodium fluoride) from a local store and analyzed the sample using the conditions listed in Table 1. Figure 3 displays the chromatogram of the sample solution prepared as described in the monograph and Table 3 displays the results of the assay. We could not obtain the 1.1% product, but we do not anticipate a problem analyzing that product.

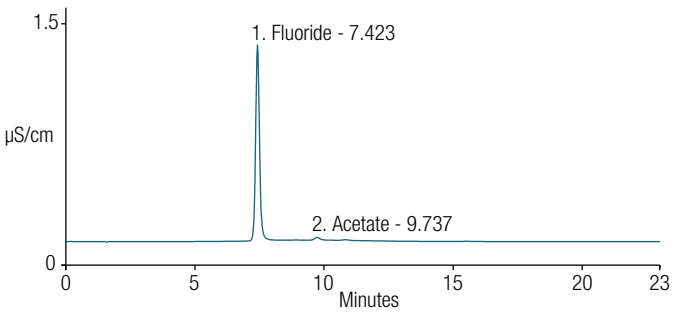

Figure 3. Chromatogram of fluoride tooth gel sample solution

Table 2. System suitability requirements

USP System Suitability	Requirement	Column 1	Column 2
RT (Fluoride)	n.a	7.42	7.37
RT (Acetate)	n.a	9.74	9.67
Relative RT (Fluoride = 1)	1 and 1.3	1 and 1.32	1 and 1.32
Resolution (Fluoride and Acetate)	NLT 1.5	6.65	6.67
Tailing Factor (Fluoride)	NMT 2	1.11	1.12
Relative Standard Deviation (RSD)	NMT 2.0	Area RSD - 0.79 RT RSD - 0.03	Area RSD - 0.66 RT RSD - 0.05

Table 3. Assay of sodium fluoride gel

	r_u (µS*min)	r_s (µS*min)	C_s (µg/mL)	C_u (µg/mL)	Result (%)	USP Acceptance Criterion (%)
Column 1	0.2248	0.2327	2.02	2.01	97.1	90.0–110.0
Column 2	0.2262	0.2349	2.02	2.01	96.8	90.0–110.0

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USP Sodium Fluoride gel assay acceptance criterion

The percentage of the labeled amount of sodium fluoride (NaF) in the portion of gel taken is calculated as follows:

$$\text{Result} = (r_u/r_s) \times (C_s/C_u) \times 100$$

r_u = peak response of the fluoride ion from the *Sample solution*

r_s = peak response of the fluoride ion from the *Standard solution*

C_s = concentration of USP Sodium Fluoride RS in the *Standard solution* (µg/mL)

C_u = nominal concentration of sodium fluoride in the *Sample solution* (µg/mL)

Conclusion

In this application note, we demonstrated that the sodium fluoride assay of sodium fluoride gel in the proposed USP monograph could be successfully performed using the Dionex IonPac AS15-5µm column. Our results show that the Dionex IonPac AS15-5µm column can be used as an alternative column for this assay using modified conditions allowed by USP <621>. Two separate columns were evaluated for method ruggedness. Both columns passed the system suitability requirements set in the USP monograph and delivered results showing the fluoride tooth gel sample passed the assay acceptance criterion.

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