Application note | 002344

Pharma

Determination of fluoride in sodium fluoride oral solution using carbonate/bicarbonate eluent

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Keywords

Dionex ICS-6000 HPIC system, Dionex IonPac AS22 column, Dionex ADRS 600 suppressor, ion chromatography, mouth rinse, mouthwash, dental

Goal

To develop a new method for the determination of fluorine in sodium fluoride oral solution using carbonate/bicarbonate eluent

Introduction

Fluoride is the active ingredient for anticavity mouth rinse products. Other components can be added into mouth rinse products, including sodium benzoate, sodium chloride, and disodium phosphate. Mouthwash containing 0.02–0.05% sodium fluoride can be purchased over the counter and used daily to prevent cavities (dental caries). Mouthwash manufacturers are required to determine the fluoride concentration in the final products. The determination of fluoride in oral solution using ion chromatography (IC) is described in the United States Pharmacopeia (USP) Sodium Fluoride Oral Solution monograph.[1]

The USP monograph method lists an L46 column set for the determination of fluoride in oral solution. The Thermo Scientific™ Dionex™ CarboPac™ PA1 column set belongs to this category and was reported to be the column used for this method.[2] An IC system was set up using a Dionex CarboPac PA1 column set and the same mobile phase and

chromatographic conditions as the USP monograph. However, we found the retention time of chloride is about 37 min, which is much longer than the expected time of 5 min reported in the USP monograph. The retention time of chloride remained around 37 min after extensive troubleshooting that included testing different column lots, mobile phase chemicals, and IC systems.

Thermo Scientific Application Note 002345 reports the development of a new method using a Thermo Scientific™ Dionex™ IonPac™ AS22 column with the same mobile phase as the USP monograph method. However, phosphate does not elute within the 10 min run time and elutes in the third injection after sample injection, though it does not interfere with fluoride determination.

In this application note, we developed a new method using the same column but with different mobile phase (eluent) conditions that are typical for both the column and IC methods with carbonate/bicarbonate eluents. The fluoride peak is still away from the water dip (column void volume), and phosphate elutes within 10 min. The method was validated for separation, calibration range, accuracy, and precision. The fluoride in three commercially available mouth rinse products was determined and compared with the labeled value.

Experimental

Equipment

- Thermo Scientific™ Dionex™ ICS-6000 HPIC system* including:
  - Dionex ICS-6000 DP Pump module
  - Dionex ICS-6000 DC Detector/Chromatography module with Conductivity Detector
  - Dionex AS-AP Autosampler with sample tray cooling, 250 µL sample syringe (P/N 074306), 1,200 µL buffer loop (P/N 074998), and 10 mL vial trays (P/N 074938)
- Thermo Scientific™ Chromeleon™ Chromatography Data System (CDS) Software, version 7.2.9

*This method can also be run on other Thermo Scientific™ Dionex™ systems

Consumables

- Thermo Scientific™ Dionex™ ADRS 600 Anion Dynamically Regenerated Suppressor, 4 mm (P/N 088666)
- Fisherbrand™ Narrow-Mouth field sample bottles, high-density polyethylene (HDPE), 125 mL, 250 mL sizes for storage of standards and samples (Fisher Scientific P/N 02-895A, B)

Reagents and standards

- Deionized (DI) water, Type 1 reagent grade, 18 MΩ·cm resistivity or better
- Sodium fluoride standard (USP P/N 1614002)
- Sodium chloride standard (USP P/N 1613804)
- Sodium benzoate standard (Fisher P/N AAA1594630)
- Thermo Scientific™ Dionex™ Phosphate standard, 1,000 mg/L (P/N 303172)
- Thermo Scientific™ Dionex™ AS22 Eluent Concentrate; Sodium Carbonate/Bicarbonate Concentrate (100X) (P/N 063965)

Samples

Three anticavity fluoride-containing mouthwashes were purchased from a local store.

Chromatographic conditions

Parameter	Value
Columns	Dionex IonPac AG22 (4 × 50 mm) guard column (P/N 064139) Dionex IonPac AS22 (4 × 250 mm) analytical column (P/N 064141)
Eluent	4.5 mM sodium carbonate and 1.4 mM sodium bicarbonate
Flow rate	1.5 mL/min
Injection volume	20 µL
Column temperature	30 °C
Detection	Suppressed conductivity
Suppressor	Dionex ADRS 600 (4 mm) suppressor, AutoSuppression recycle mode, 43 mA current
Detection/Suppressor compartment temperature	25 °C
Cell temperature	35 °C
Background conductance	~20 µS/cm
System backpressure	~2,300 psi (100 psi = 689.5 kPa)
Noise	<2 nS/cm
Run time	10 min

Preparation of solutions and reagents

Anions stock standard solutions

Stock standard solutions (1,000 mg/L) were prepared by dissolving the appropriate analyte amounts in 100 mL of DI water, according to Table 1.

Table 1. Masses of compounds used to prepare 100 mL of 1,000 mg/L ion standards

Analyte	Compound	Amount (mg)
Fluoride	Sodium fluoride (NaF)	221.0
Chloride	Sodium chloride (NaCl)	164.9
Benzoate	Sodium benzoate (NaC_6H_5COO)	119.0

Fluoride calibration standard solution

Fluoride calibration standard solutions were prepared by diluting the 1,000 mg/L stock solutions with DI water. Five levels of calibration standard (0.1, 0.25, 0.5, 0.75, and 1 mg/L) were used in this study to investigate if the fluoride concentration of the USP monograph (0.5 mg/L) is within the linear range.

System suitability solution

The USP monograph lists 1.0 µg/mL of USP Sodium Fluoride RS and 0.5 µg/mL of USP Sodium Chloride RS in water as the system suitability solution. This corresponds to 0.45 mg/L fluoride and 0.30 mg/L chloride. This system suitability solution mixture was prepared by diluting the fluoride and chloride stock solutions with DI water.

Four anions mixture solution

An anions mixture solution (fluoride 0.5 mg/L, chloride 0.5 mg/L, benzoate 10 mg/L, and phosphate 5 mg/L) was prepared to investigate the separation of fluoride from other common anions found in oral mouth rinse samples.

Eluent preparation

For fast, reliable eluent preparation, the ready-to-dilute Dionex AS22 Eluent Concentrate; Sodium Carbonate/Bicarbonate Concentrate saved time and eliminated potential contamination and preparation error. The eluent was prepared by diluting the concentrate 100-fold with DI water.

Results and discussion

Separation

The Dionex IonPac AS22 columns are designed for compliance monitoring of inorganic anions in accordance with United States Environmental Protection Agency Methods 300.0 (A) and 300.1 (A). The selectivity of the Dionex IonPac AS22 column was optimized to retain fluoride well out of the water dip (a dip in the baseline at the column's void volume) while separating common anions with an isocratic mobile phase.[4]

Phosphate is listed as an ingredient in all three oral rinse products and benzoate is listed as an ingredient in sample #1. Figure 1 shows the separation of four anions (fluoride, chloride, benzoate, and phosphate) using a Dionex IonPac AS22 column with a run time of 10 min. Fluoride is away from the water dip, and it is well separated from chloride.

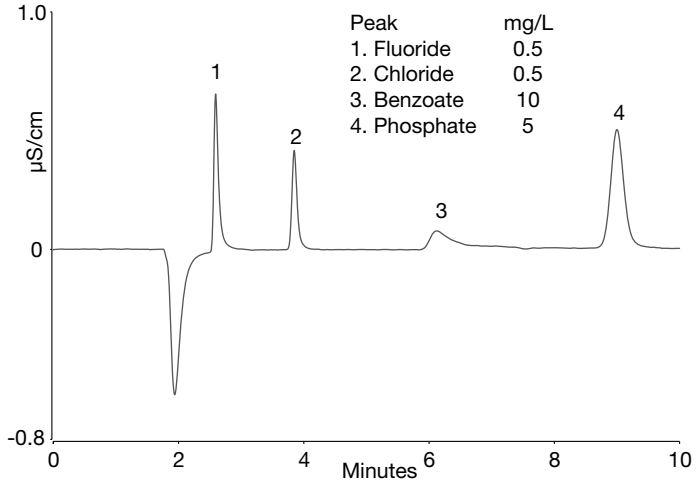

Figure 1. Separation of four anions

The USP monograph uses a system suitability standard of 1.0 µg/mL of USP Sodium Fluoride RS and 0.5 µg/mL of USP Sodium Chloride RS in water to evaluate resolution, tailing factor, and relative standard deviation. The separation reported here passes USP specifications as shown in Table 2.

Table 2. System suitability

Parameter	Required	Found
Resolution	NLT = 1.5	8.8
Tailing factor	NMT = 2.0	1.8
RSD %	NMT = 2	0.33

Method linearity

The USP monograph method calculates the percentage of fluoride in a sample using one calibration level of 1.1 µg/mL sodium fluoride standard, which is equivalent to 0.5 mg/L fluoride. To ensure 0.5 mg/L fluoride is in the method's linear range, the linearity of fluoride was investigated in the concentration range of 0.1–1 mg/L. Figure 2 shows the calibration curve; the coefficient of determination (r^2) is 0.9999 using linear fitting, which suggests an excellent fit between the experimental data and the linear calibration model.

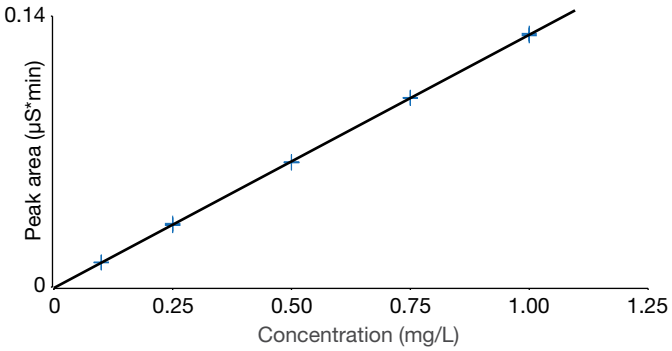

Figure 2. Fluoride calibration curve

Sample analysis

The USP monograph specifies sample solution as follows: "Nominally 1.1 µg/mL of sodium fluoride from a portion of Oral Solution in water." This corresponds to a fluoride concentration of 0.5 mg/L. The sample was diluted to approximately 0.5 mg/L fluoride according to the active ingredients label (Table 3).

Figure 3 shows the chromatograms of three oral rinse samples with a run time of 10 min. Fluoride is always resolved from the water dip and well separated from chloride. Benzoate is found in sample #1, as expected from the product label. All three oral rinse samples contain phosphate. Chloride is not found in sample #3.

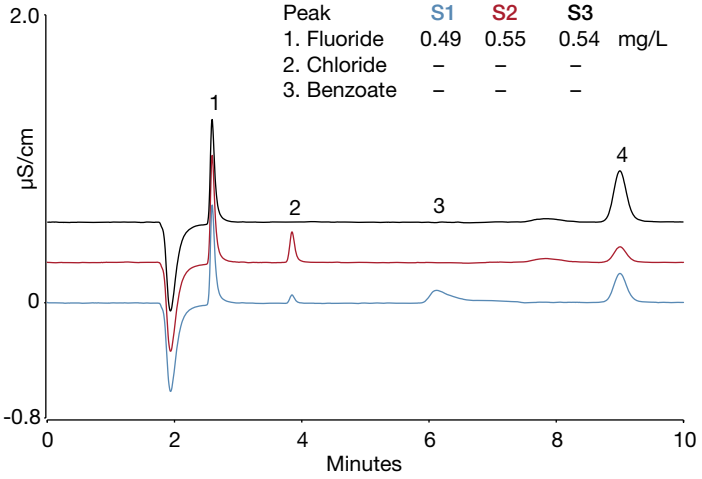

Figure 3. Fluoride determination of three oral rinse samples

The USP monograph uses a one-point calibration to calculate the fluoride amount in samples as shown below.

Result = (Ru/Rs) × (Cs/Cu) × 100

Ru = peak response of fluoride from the sample solution

Rs = peak response of fluoride from the standard solution

Cs = concentration of USP Sodium Fluoride RS in the standard solution (µg/mL)

Cu = nominal concentration of sodium fluoride in the sample solution (µg/mL)

Table 4 summarizes sample results using one-point calibration and a calibration curve, respectively. Results show that the fluoride concentrations calculated by the two methods are similar, suggesting that one-point calculation is accurate for this analysis. All three samples pass the USP acceptance criteria of 90%–110%.

Method accuracy and precision

Method accuracy was evaluated by determining the recovery of fluoride spiked into the oral rinse sample at concentrations ranging 20% to 50% of the original amount. Table 5 summarizes the analyte recoveries for the three oral rinse samples. Analyte recoveries were 90–110%.

Method precision was determined by triplicate injections of the 0.5 mg/L fluoride standard on three separate days. The calculated peak area precision varied 0.33% with retention time precision <0.15%.

Table 3. Preparation of samples to achieve approximately 0.5 mg/L fluoride

Sample	Sample description	Active ingredient (sodium fluoride) labeled %	Convert label to fluoride conc. (mg/L)	Dilution fold	Fluoride conc. (mg/L) after dilution
1	Alcohol free for children	0.05	226.2	450	0.503
2	Alcohol free for adults	0.02	90.5	180	0.503
3	With alcohol for adults	0.02	90.5	180	0.503

Table 4. Fluoride in oral rinse sample

Sample	Labeled value (mg/L)	Measured (one point method, mg/L)	Recovery (%)	Measured (Calibration curve method, mg/L)	Recovery (%)
1	226.2	228	101	226	100
2	90.5	92.8	103	92.0	102
3	90.5	95.7	106	94.9	105

Table 5. Recovery of fluoride spiked in oral rinse sample

	Spike level 1			Spike level 2		
Sample	Amount found (mg/L)	Amount added (mg/L)	Recovery (%)	Amount found (mg/L)	Amount added (mg/L)	Recovery (%)
1	0.50	0.1	100	0.50	0.25	106
2	0.51	0.1	107	0.51	0.25	107
3	0.53	0.1	96	0.53	0.25	96

Conclusion

This application developed a new method for the determination of fluoride in oral rinse products using carbonate/bicarbonate eluent. The method demonstrates excellent accuracy and precision for fluoride in commercially available oral rinse samples and, therefore, can be used as a quality control method by oral rinse manufacturers.

References

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4. Thermo Scientific Dionex IonPac AS22 column manual. https://assets.thermofisher.com/TFS-Assets/CMD/manuals/Man-065119-IC-IonPac-AS22-Fast-Man065119-EN.pdf

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