

Fluoride in OTC Products by Ion Chromatography

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PURPOSE

Fluoride is commonly used in dental products to help prevent tooth decay. Fluoride products are intended to prevent the formation of cavities and when present in high concentrations are regulated by 21 CFR 355. Three fluoride compounds used in Over-the-Counter (OTC) anti-caries dental products are sodium fluoride, stannous fluoride and sodium monofluorophosphate (MFP). The assay of fluoride in these active ingredients and finished formulations are determined by manual titration, or by ion-selective electrodes. As a part of USP's global monograph modernization initiative, an alternative selective and sensitive method has been developed and validated – ion chromatography (IC). The proposed IC method can also be used for the identification test as an alternative to the wet chemistry method. Fluoride-based monographs that are currently being modernized using ion chromatographic methods are shown in Figure 1.

METHOD

An ion-selective electrode (ISE) has a specific shelf-life and requires periodic calibration to guarantee accurate results. Electrode fouling and response change over time are additional limitations of ISE. Ion chromatography, on the other hand, is well-suited for the separation of mono and divalent anions, and organic acids in the presence of complex sample matrices such as OTC dental products. A Metrosep A Supp 16 250/4.0 mm column with L91 packing was identified as the most suitable for the separation of monoatomic anions such as fluoride. The method for fluoride assay in sodium fluoride gel was developed and validated using 15mM potassium hydroxide as the mobile phase. A modified mobile phase containing a combination of sodium carbonate and sodium hydroxide was used and Metrosep A Supp1 with L46 packing was used for an equivalent column study in a sodium fluoride oral solution.

RESULTS

A Metrosep A Supp 16 250/4.0 mm column with L91 packing was used for fluoride assay procedures for USP monograph modernization of sodium fluoride API, impurities in sodium fluoride, sodium fluoride tablet, sodium fluoride gel, and sodium monofluorophosphate. The results of the column equivalency study for the sodium fluoride oral solution are summarized in Table 1. The separation of fluoride is well resolved from chloride in the resolution solution (Figure 2), and from organic impurities in two OTC drug products from Listerine (Figure3) and Colgate oral solution (Figure4).

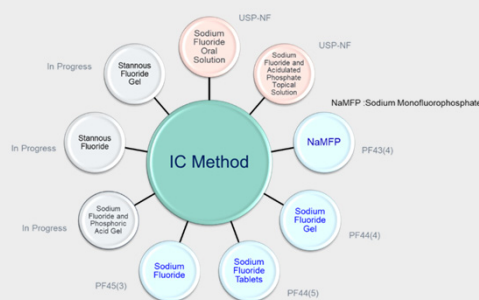


Figure 1: Fluoride Monographs currently being modernized using Ion Chromatography

DATA

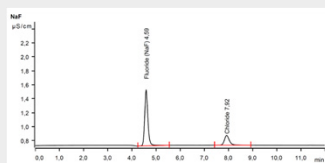


Figure 2: System suitability solution for Sodium Fluoride Oral Solution

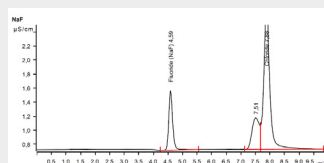


Figure 3: Sample - Fluoride in Listerine Cuidado Total

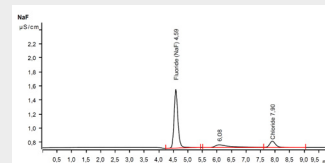


Figure 4: Sample - Fluoride in Colgate Plax Ice Infinity

Sodium Fluoride Oral Solution as per USP - Summary Table			
Parameters	Metrohm	USP Monograph	Status
Eluent	150 mg/L of anhydrous sodium carbonate and 1.0 mL/L of 1 N sodium hydroxide in water.	150 mg/L of anhydrous sodium carbonate and 1.0 mL/L of 1 N sodium hydroxide in water.	✓
System Suitability Solution	1.0 ug/mL of USP sodium fluoride RS and 0.5 ug/mL of USP sodium chloride RS in water	1.0 ug/mL of USP sodium fluoride RS and 0.5 ug/mL of USP sodium chloride RS in water	✓
Sample Solution	Nominally 1.1 ug/mL of sodium fluoride from a portion of oral solution in water	Nominally 1.1 ug/mL of sodium fluoride from a portion of oral solution in water	✓
Detection	Conductivity with suppression (MSM+MCS)	Conductivity with suppression	✓
Column	Metrosep A Supp 16—250/4.6 (SN 12008533) Metrosep A Supp 16—Guard/4.6 (SN 06207007)	L46 Column 4.0 mm x 250 mm; 10 um packing Guard 4.0 mm x 50 mm; 10 um packing	✓
Flow Rate	1.0 mL/Min	1.0 mL/Min	✓
Injection Volume	20 µL	20 µL	✓
Run Time	NLT 2x fluoride peak Fluoride (4.6) Run time - 10 min	NLT 2x fluoride peak	✓
Column Temperature	Room temperature	Not mentioned	✓
System Suitability (n=6)			
Resolution	11.4	NLT 1.5 between fluoride and chloride peak	✓
Tailing Factor	1.2	NMT 2.0 for fluoride peak	✓
Relative Standard Deviation	1.3%	NMT 2.0% for fluoride ion	✓
Listerine Cuidado Total (Lot#2967B02)			
Mean Sample Recovery: Duplicate	98.7	90.0%-110.0%	✓
Sample Preparations			
Colgate Plax Ice Infinity (Lot#8294BR122AH15:13)			
Mean Sample Recovery: Duplicate	98.8	90.0%-110.0%	✓
Sample Preparations			

Table 1: Sodium Fluoride Oral Solution column equivalency data

INSTRUMENT

- Metrohm 940 Professional IC Vario
- Detection: Conductivity Detection after Sequential Suppression
- Column Temperature: 30° C
- Flow Rate: 1.0 mL/min
- Injection Volume: 20 µL
- Eluent : 150 mg/L of anhydrous sodium carbonate and 1.0 mL/L of 1 N sodium hydroxide in water.
- Column: Metrosep A Supp 16-250/4.6, packing L46



Fig 5. Ion Chromatography Instrument used for Fluoride Assay in OTC Products

CONCLUSION

A single IC procedure for fluoride assay and identification in sodium fluoride oral solutions was developed and tested for column equivalency. A Metrosep A Supp 16 250/4.0 mm column with L91 packing is suitable for the separation of fluoride from the rest of the impurities in sodium fluoride and other oral formulations. Divalent cations such as calcium, added as EDTA salt does not affect the suppressor. Chemical regeneration ensures that the divalent cations are completely removed and offers highly reproducible method performance. A single chromatographic method for assay and identification simplifies the overall QA/QC workflow. The addition of Metrohm inline ultrafiltration helps protect the analytical column and enhances column life and performance.

Metrohm USA, Inc¹, United States Pharmacopeia²
Colgate and Listerine were not involved in this study.

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