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Short communication

Ion chromatographic procedures for analysis of total fluoride content in dentifrices

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Abstract

Monofluorophosphate (PO_3F^{-2}) and fluoride ions are commonly formulated into oral care products as an aid in the management of dental caries. The monofluorophosphate ion is not stable, and can expected to hydrolyze to yield phosphate and fluoride ions. Two ion chromatographic methods are presented for analysis of these ions. Depending upon the needs of the laboratory, the methods can be used to quantitate PO_3F^{-2} or simultaneously measure PO_3F^{-2} and fluoride.

Keywords: Fluoride; Fluorophosphates; Inorganic anions

1. Introduction

Monofluorophosphate (PO_3F^{-2}) and fluoride (F^-) are two ions of interest as anticaries agents in dentifrice preparations. During stability storage however, PO_3F^{-2} can be observed to hydrolyze to phosphate and fluoride ions. While ion selective electrode analysis is useful for analysis of fluoride in products, it would be convenient to measure F^- and PO_3F^{-2} simultaneously in aged oral care formulations. Described below are two methods for analysis of PO_3F^{-2} in a formulation. The first method is a rapid ion analysis column and is well suited for quality control laboratories conducting product release since fluorophosphate standards typically elute in less than 3 min. The second method requires a longer analysis time but offers the advantage of simultaneously quantitating the intact PO_3F^{-2} and the F^- hydrolysis product. This method is an improvement over the procedure reported by Talmage et al. [4] who were unable to retain the fluoride ion for measurement. The second method therefore allows for stability measurement of PO_3F^{-2} in a formulation and assessment of total fluoride content for the life of the product.

2. Experimental

2.1. Apparatus

The chromatograph was a Dionex 500DX module equipped with the Self Regenerating Suppressor and consisting of a GP40 gradient pump, ED40 detector and AS3500 autosampler (Dionex, Sunnyvale, CA, USA). The Dionex IonPac fast anion (10–32) column (System 1) was used to quantitate the PO_3F^{-2} ion in the rapid ion assay. The Sarasep AN1 (250× 4.6 mm) anion column with an AN1 standard guard column (System 2) (Metachem Technologies, Torrence, CA, USA) was used for evaluation of stability samples requiring quantitation of both the PO_3F^{-2}

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and fluoride ions. Data collection and peak measurement was accomplished using the Beckman CALS PeakPro software (Beckman Instruments, Allandale, NJ, USA).

2.2. Chromatographic conditions

The mobile phase for both systems separations consisted of 150 mg Na_2CO_3 in 1 l of deionized water. The pH was adjusted to 10.8±0.2 using 1 *M* NaOH. The detector sensitivity was 30 μS full scale and the self regenerating suppressor was set at 100 mA. The Fast Anion column flow-rate was 1.5 ml min^{-1} which gave a retention time of about 2.5 min for PO_3F^{-2}. The AN1 column flow-rate was 1.0 ml min^{-1}. The fluoride and PO_3F^{-2} eluted from the AN1 column in about 5 and 19 min, respectively. Injection volumes were 10 μl for fast anion column and 50 μl for the AN1 column. The mobile phases were continuously sparged with helium to avoid changes in pH during chromatography.

2.3. Reagents

All reagents used were ACS reagent grade. The sodium monofluorophosphate (SMFP) was obtained from Ozark–Manhoning Division of Pennwalt (Tulsa, OK, USA) and had an assay value of 98.3% by the USP assay procedure. The sodium fluoride was purchased from Aldrich (Milwaukee, WI, USA) and had a purity of 99.99%. The water used to prepare the mobile phase and sample solutions was purified by a Milli-RO4 system (Millipore, Bedford, MA, USA) and had a resistivity of a least 15 MΩ.

2.4. Standard preparation

A SMFP stock standard was prepared by dissolving 50 mg in 100 ml of deionized water. A 5-ml aliquot was then diluted to 100 ml to prepare the working standard. The sodium fluoride standard for stability sample analysis was prepared by dissolving 25 mg in 100 ml of deionized water. A 5-ml aliquot was then diluted to 100 ml. This solution was further diluted by taking a 5-ml aliquot and diluting to 100 ml. The working concentrations for the SMFP and NaF were 0.025 mg ml^{-1} and 0.625 μg ml^{-1}, respectively.

2.5. Sample preparation

Approximately 1.5±0.2 g of a toothpaste sample was weighed into a 500-ml volumetric flask. The flask was filled with about 250 ml of deionized water, placed on a wrist action shaker until fully dispersed, then diluted to volume with water. The working concentration of SMFP in the sample preparation was approximately 0.025 mg ml^{-1}. Standard and sample solutions were filtered through a 0.45-μm Acrodisc CR PTFE filter (Gelman Sciences, Ann Arbor, MI, USA) prior to injection into the chromatograph.

3. Results and discussion

Previously, Talmage et al. [4] described a stability indicating ion chromatographic procedure for PO_3F^{-2}. The approach utilized a high pH carbonate mobile phase to shift the phosphate closer to pK_3 and resolve it from the divalent PO_3F. During method development with the fast anion and AN1 columns, optimal separation was achieved with 150 mg l^{-1} Na_2CO_3 and adjusting the pH to a range of 10.6–11.0. At pH values greater than 11.0 significant retention of phosphate ion could be expected resulting in longer sample run times. Conversely, too low a pH resulted in coelution of phosphate and monofluorophosphate. One difference observed between the two columns was the elution of saccharin from the Dionex column but not from the Metachem column. Despite extensive use of the Metachem column however, no significant change in separation or selectivity was observed until several hundred injections had been made.

A typical standard and sample chromatogram are presented in Fig. 1 for the analysis of PO_3F^{-2} using system 1. This column developed approximately 4000 theoretical plates for PO_3F^{-2} with a capacity factor of 1.3. The resolution between PO_3F^{-2} and SO_4^{-2} and PO_4^{-3} was typically greater than 1.5. Fig. 2 depicts typical chromatograms for standards and samples using system 2 to concurrently quantitate PO_3F^{-2} and F^- ions. This column typically developed approximately 6000 theoretical plates for fluoride and 5000 theoretical plates for PO_3F^{-2} with capacity factors of approximately 0.3 and 2.5, re-

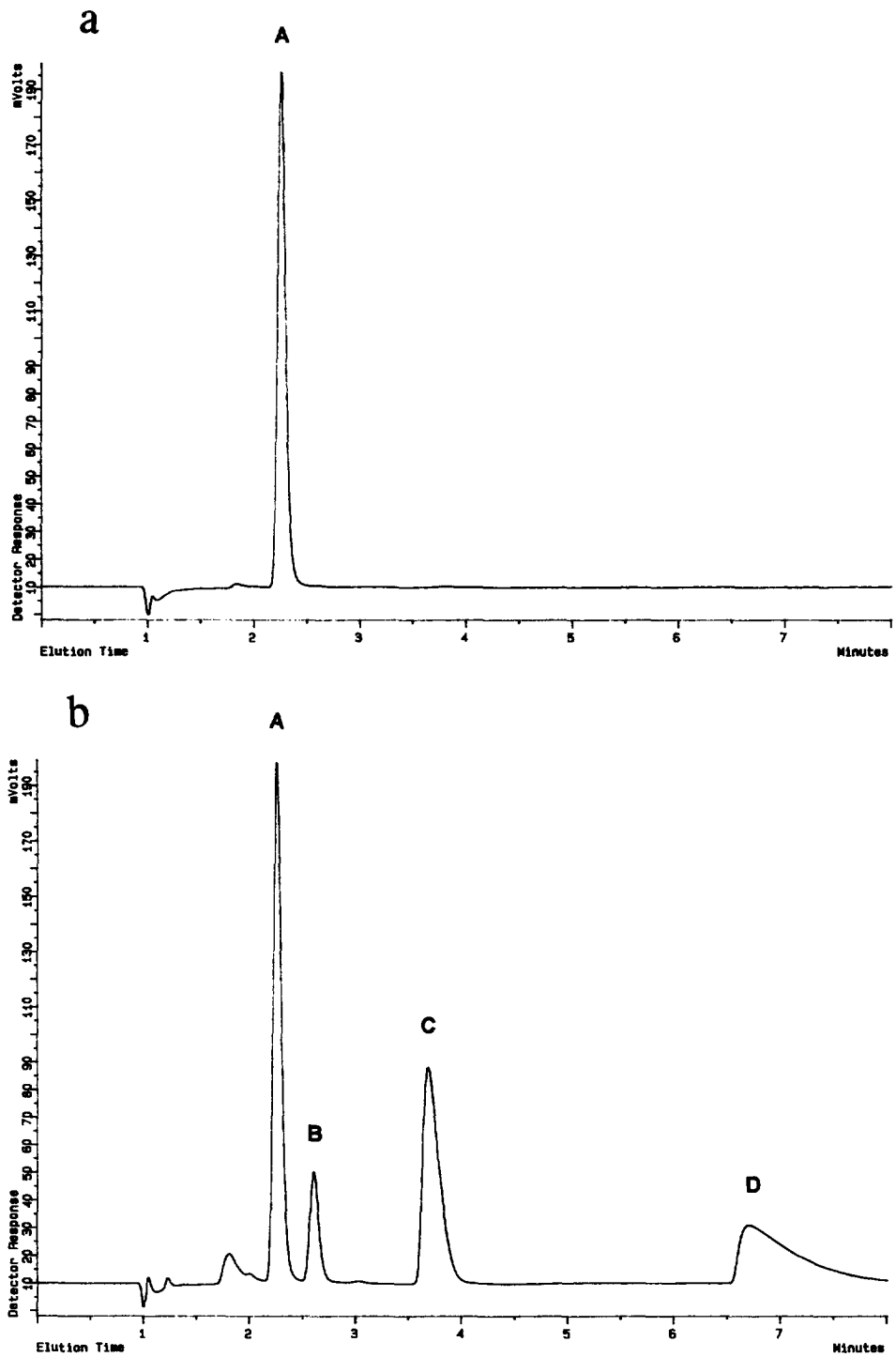

Fig. 1. Chromatograms of (a) sodium monofluorophosphate standard and (b) dentrifice sample using Dionex fast anion (10–32) column. Peaks: A=monofluorophosphate; B=sulphate; C=phosphate; D=saccharin. Conditions: fast anion column using 150 mg l^{-1} Na_2CO_3 (pH 11.0) and flow-rate of 1.5 ml min^{-1}.

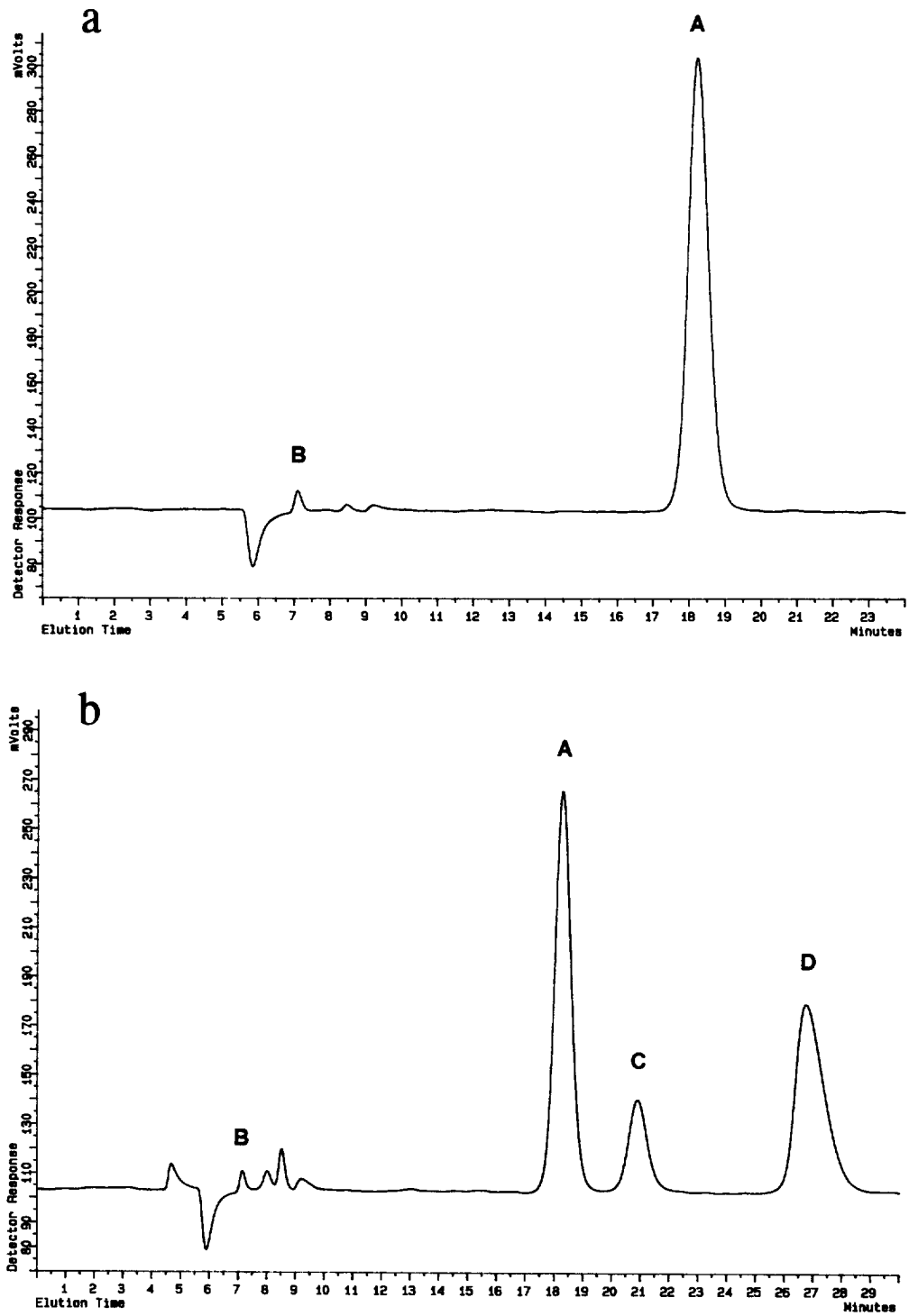

Fig. 2. Chromatograms of (a) sodium monofluorophosphate standard and (b) dentrifice stability sample using AN1 column. Peaks: A=monofluorophosphate; B=fluoride; C=sulphate; D=phosphate. Conditions: AN1 column using 150 mg l^{-1} Na_2CO_3 (pH 11.0) and flow-rate of 1.0 ml min^{-1}.

spectively. The resolution factor for the 'water dip' and the fluoride ion is typically >2 and between PO_3F^{-2}, SO_4^{-2} and PO_4^{-3}>2.5. The tailing factor for the analytes on both systems is observed to be <1.5.

Suitability of the methods for PO_3F^{-2} and F^- analysis was demonstrated by conducting the following validation experiments. Detector linearity was determined over the range of 0.012–0.036 mg ml^{-1} for PO_3F^{-2} for both systems and 0.1–1.0 μg ml^{-1} for fluoride on the AN1 column. The correlation coefficients were found to be better than 0.999 for the ions on both columns. Chromatographic reproducibility was established by injecting standard solutions of PO_3F^{-2} and F^- five times and measuring the peak areas.

The relative standard deviations obtained were as follows: PO_3F^{-2} on fast anion column, 0.29%, on AN1 column, 1.16% and fluoride on AN1 column, 0.50%.

Analytical accuracy (recovery) of each method was determined by spiking placebo toothpaste with PO_3F^{-2} and F^- and conducting the assays as described above. Approximately 1.5 g of placebo toothpaste was spiked with an aqueous preparation of PO_3F^{-2} by accurately pipetting aliquots of stock PO_3F^{-2} to give final concentrations of 20.0, 25.0 and 31.2 μg ml^{-1} representing 80, 100, or 120% of the target level in the sample preparation. Fluoride recovery was performed over the range 15, 30, 45, 60, 75 and 90 ppm which represented the levels anticipated to form in a product from hydrolysis of PO_3F^{-2} at room temperature shelf life. All recovery studies for PO_3F^{-2} and F^- were conducted in triplicate. The recoveries for PO_3F^{-2} and fluoride ranged from not <98.3% to not >101.3% for both ions on either the fast anion or AN1 columns with relative standard deviations <1.5%. Analytical precision was ascertained by preparing a sample of dentifrice six times and conducting the PO_3F^{-2} and fluoride assays described above. The relative standard deviation for six sample preparations for the PO_3F^{-2} assay precision using system 1 was 0.36%. For system 2 results were 0.83% for the PO_3F^{-2} and 1.68% for fluoride.

4. Conclusion

Both assay systems described exhibit the ruggedness required for high volume use in industrial manufacturing and stability analysis laboratories. Periodically, the columns will require clean up using the manufacturers instructions to maintain performance. The methods represent improvements over prior reported techniques to quantitate ions considered important in the management of dental caries. The fast anion column offers the advantage of rapid sample analysis time for PO_3F^{-2} when the levels of fluoride ion are not required. Conversely, the AN1 column offers the power of concurrently quantitating both ions in order to assess the stability of the PO_3F^{-2} in an oral care formulation. For further background reading, see Refs. [1–3,5].

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