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Short communication

Potentiometric determination of monofluorphosphate in dentifrice: a critical discussion and a proposal for new improved procedures

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1. Introduction

It was shown that dentifrices containing fluoride ions can significantly contribute to caries prevention [1,2]. In the presence of F^-, the hydroxylfluorapatite $Ca_{10}(PO_4)_6(OH)_{2-x}F_x$, which is more resistant to acids than hydroxylapatite $Ca_{10}(PO_4)_6(OH)_2$, is sedimented on the tooth surface. As a result, the reconstitution of the tooth surface is much better and faster. The source of fluoride ions in dentifrices is sodium fluoride, tin fluoride, zinc fluoride, aminfluoride or sodium monofluorphosphate. The latter compound is the one used most frequently. It contains covalently bonded fluorine and releases usually about 6% of fluoride ions during the application of dentifrice by hydrolysis in the mouth. Sodium monofluorphosphate is used in various dentifrices which contain Ca^{2+} and Mg^{2+} insoluble salts as abrasives and the active fluoride ion can be lost as sparingly soluble CaF_2 or MgF_2. When Na_2FPO_3 is present, the F^- that disappeared is compensated by new F^- ions delivered by continuous hydrolysis of Na_2FPO_3 by dentifrice application in the mouth.

Since the difference between toxic and therapeutic concentrations of fluoride ions is rather small, an accurate and precise method for the determination of the fluoride source in dentifrice, like Na_2FPO_3 discussed here, is crucial.

Various methods, like potentiometry [1–4], gas chromatography [5,6], liquid chromatography [7], atomic absorption spectroscopy [8], titrimetry [9] and UV/Vis absorption spectroscopy [6], were applied for the determination of Na_2FPO_3 in dentifrices. Among them, the potentiometric method using F^- selective electrodes seems to be very suitable because it is simple, rapid and economical. However, inspection of the literature data

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reveals that the potentiometric procedures described have manifold disadvantages, which can cause insufficient precision and accuracy. The aim of this work was to analyse the characteristics of the potentiometric method and to point out factors influencing its accuracy and precision. A simple, rapid, accurate and precise procedures are proposed.

2. Experimental

2.1. Reagents and instrumentation

All reagents used were of analytical reagent grade from Kemika, Zagreb. Dentifrices were products of Pliva, Pharmaceutical, Chemical, Food and Cosmetic Industry, Inc., Zagreb, Croatia. Deionised water (<5 μS cm^{-1}) was used throughout.

A fluoride-selective electrode (ORION 94-09), reference Ag/AgCl electrode (ORION 94-01) and pH/mV meter (ORION 901) were used in all potentiometric measurements. Separation of phases was performed on a SANYO, Mistral 3000 centrifuge.

2.2. Procedures

2.2.1. Procedure I

To the suspension of dentifrice in water, obtained by dispersing 1 g dentifrice (weighed to the nearest 0.1 mg) in 20.0 ml of deionised water, 4.0 ml of 6 M HCl was added. Suspension was stirred and heated at 80°C on a water bath for 30 min, cooled at room temperature and diluted to 50.0 ml. The amount of fluoride was determined by direct potentiometric measurement. For potentiometric measurements a 1.0 ml aliquot of hydrolysed sample was mixed with 25.0 ml of TISAB buffer (1.0 M sodium chloride, 0.25 M acetic acid, 0.75 M sodium acetate, 0.001 M sodium citrate, pH 5.2 [12]) and finally water was added up to 50.0 ml. Standard solutions for calibration contained NaF (1×10^{-6}–1×10^{-2} M), as well as TISAB buffer and HCl in the same concentrations as the measuring samples described above.

2.2.2. Procedure II

The suspension of dentifrice in water, obtained by dispersing 1 g dentifrice (weighed to the nearest 0.1 mg) in 20.0 ml of deionised water, was stirred at room temperature with a magnetic stirrer for 10 min. The solid and liquid phase were separated by centrifugation at 3000 rpm for 10 min. After separation, the insoluble part was washed several times with deionised water, which was collected and added to the supernatant. To both, the supernatant and the insoluble part, 4.0 ml of 6.0 M HCl was added. The resulting mixtures were stirred at 80°C on a water bath for 30 min, then cooled and diluted to 100.0 ml. Aliquots of 2.0 ml were used for direct potentiometric measurements, which were performed in the same way as in Procedure I.

2.2.3. Procedure ORION

To 10 g dentifrice (to the nearest 0.1 mg), 5 ml of concentrated HCl was added. The resulting mixture was stirred, left to stand over night and than NaOH was added to $5<\text{pH}<7$. The mixture was diluted to 250.0 ml with deionised water before analysis. The samples for potentiometric measurements contained 10.0 ml of the hydrolysed mixture, 90.0 ml of deionised water and 10.0 ml of TISAB III buffer. The fluoride content was determined by direct potentiometric measurements using standard solutions containing NaF and TISAB III buffer (Ch. Hüggli, ORION, personal communication).

2.3. Validity of the experimental procedures

Selectivity coefficient of the F^- electrode used to OH^- amounted to $K_{ij}^{\text{Pot}}=0.1$. The linear working range, slope, reproducibility and detection limit of the electrode were determined by measurements in standard NaF solutions, which contained TISAB buffer and HCl in the same amounts as the measuring samples. Linear range and detection limit of the electrode were 1×10^{-5}–1×10^{-1} M fluoride and 1×10^{-6} M fluoride, respectively. Reproducibility of the electrode expressed as the standard deviation of the mean value of the slope of the linear part of the calibration curve, obtained by measuring in the

above mentioned solutions during 3 months, was (-58.87 ± 0.34) mV ($n = 9$).

Precision of procedures for Na_2FPO_3 determination was expressed as standard deviation (SD) of data obtained by replicate performing of complete procedures, including weighing of sample, extraction, hydrolysis and potentiometric measurement. Deviation of the mean value of data obtained for Na_2FPO_3 content in the dentifrice from the specified value obtained by accurate weighing by the dentifrice manufacturer was taken as the measure for the accuracy of the procedures.

3. Results and discussion

Apart from a compound that liberates fluoride, a typical dentifrice contains water, insoluble calcium and/or magnesium salts (e.g. carbonates, various phosphates), sorbitol, glycerine, miscellaneous formulating agents like titan(IV) oxide, aromas, sodium lauryl sulphate, etc. Despite the complexity of dentifrices, fluoride-selective electrodes give satisfying results in the potentiometric determination of sodium, tin(II) and zinc fluoride [10–12]. However, procedures for the potentiometric determination of fluoride which originates in sodium monofluorphosphate are not sufficiently refined for quality control in the industrial production, or for clinical evaluation of the efficacy of dentifrices [1–4].

Heidbüchel tried to estimate the Na_2FPO_3 content in dentifrice from the fluoride released by spontaneous hydrolysis in a freshly prepared sample, proposing that 6% of Na_2FPO_3 was spontaneously hydrolysed [1]. However, liberation of fluoride from Na_2FPO_3 is dependent on time, temperature, Na_2FPO_3 concentration as well as on the content of other dentifrice components. It was shown that in some Na_2FPO_3 containing dentifrices even 12% of fluoride was spontaneously liberated [2]. Therefore, such procedure is characterised by low precision and accuracy. More precise and accurate determination of Na_2FPO_3 is possible after complete hydrolysis by acid. The problem in applying corresponding procedure arises from high salt concentrations after hydrolysis which can cause interferences and errors. Therefore, König even at an early stage stated that a fluoride-selective electrode was suitable only for qualitative analysis of Na_2FPO_3 in dentifrice, and recommended alternative methods like gas chromatography and spectrophotometry for quantitative determination [6]. In the following, it is shown that errors originating in interferences of salts present in high concentrations due to hydrolysis, as well as those originating in other sources (like loss of fluoride during dissolution of the sample, insufficient amount of hydrolysis reagent, ionic strength, pH value, etc.) can be avoided, without jeopardising the simplicity and velocity of the procedure.

In assessing procedures for potentiometric determinations it is useful to break down Na_2FPO_3 analysis into three steps: extraction of Na_2FPO_3 by dispersing of dentifrice in water (Section 3.1), hydrolysis of dissolved Na_2FPO_3 in the presence of acid (Section 3.2) and measurement of released fluoride using a selective electrode (Section 3.3).

3.1. Quantitative extraction of total Na_2FPO_3 content

Since Na_2FPO_3 is water soluble, it is easily extracted into the water. Consequently, in most of the procedures described in the literature, total Na_2FPO_3 is analysed in the soluble part of toothpaste after extraction and removal of the insoluble part.

However, the stability of Na_2FPO_3 in dentifrice depends on its age and composition. During the ageing of dentifrice, Na_2FPO_3 is partly hydrolysed to fluoride which may react with Ca^{2+} and/or Mg^{2+} liberated from abrasives to form sparingly soluble salts [2]. The conversion of Na_2FPO_3 into insoluble fluoride is dependent on the kind of abrasive and on other dentifrice components. It takes place when the solubility of abrasive in the toothpaste is greater than a solubility of CaF_2. (It should be kept in mind that the solubilities of abrasives and of CaF_2 vary dependent on pH, ionic strength, on concentration of common ions, etc.) As a consequence, the quantitative transfer of total fluorine from paste into the water solution is sometimes difficult to achieve. Some au-

Table 1
Percentage of total fluorine in the insoluble part of dentifrice dependent on the time of extraction of dentifrice with water[a]

Extraction time (stirring of dentifrice suspension) (min)	F in the insoluble part (%)
10	5.3
30	5.4
60	5.3
120	5.4
240	5.4
240 (heating at 60°C)	6.8

[a] After extraction, the insoluble part of dentifrice was separated from the solution, treated by acid and analysed using a F^- selective electrode according to procedure II. Total expected content (expressed as 100% F) was 0.10 g of fluorine in 100 g of dentifrice.

thors suggest heating and stirring of dentifrice suspension in water for 0.5–4 h to achieve quantitative extraction [1,3,9]. In fact, such procedures are time consuming and inefficient, when the above mentioned reactions take place. Table 1 shows that the amount of undissolved fluorine remains constant regardless of the stirring time and even increases by heating of the dentifrice suspension in water. Non-quantitative extraction of fluorine causes errors in the determination of total Na_2FPO_3 in water solution after separation and discharging of the insoluble part of dentifrice [1,3,9].

However, quantitative extraction can be achieved in a short time by the addition of acid. In this way, the extraction and hydrolysis of Na_2FPO_3 are carried out in one step. Simultaneously, the fluoride originating in sparingly soluble salts, eventually formed during the ageing of toothpaste, is also extracted into water. After 30 min, 98–100% of total fluorine is converted to water soluble F^-, which can be analysed directly in the hydrolysed solution (see Sections 2.2.1 and 2.2.3). Attention should be paid to the concentrations of the measuring samples. The Na_2FPO_3 concentration and the amount of abrasives should not exceed a critical level, because above this level the fluoride liberated by Na_2FPO_3 hydrolysis and Ca^{2+} released from abrasives by acid treatment may form precipitate even under this acidic condition. Table 2 illustrates errors in the determination of Na_2FPO_3 caused by the presence of calcium salts. Experiments were carried out on model samples containing Na_2FPO_3 and calcium carbonate. The liberated fluoride was measured using a fluoride-selective electrode after total hydrolysis with HCl had been made, without separation of the insoluble sample part. In model samples, the critical level was achieved at the Na_2FPO_3 (fluoride) concentration of 1×10^{-4} M and at amounts of 4×10^{-3} mol $CaCO_3$ added in 1 l of the solution. In the case of the ORION procedure, this critical level can be exceeded (e.g. measuring samples of the Pliva dentifrice 'Superfresh', contained in addition to 2×10^{-4} M fluoride, 1×10^{-2} mol total calcium from abrasives in one litre of the solution) and errors are possible. Such errors can be completely avoided if the sample is properly diluted before hydrolysis, like in procedure I (Section 2.2.1). With procedure I, maximum amounts of fluoride and Ca^{2+} in measuring samples originating in most toothpaste

Table 2
Determination of Na_2FPO_3 in model samples containing $CaCO_3$ and Na_2FPO_3 after complete hydrolysis with HCl

c (Na_2FPO_3) added (mol l^{-1})	Amounts of $CaCO_3$ added (mol l^{-1})	c (F^-) measured (mol l^{-1})	Relative error (%)
2.00×10^{-5}	1.0×10^{-3}	1.99×10^{-5}	−0.5
2.00×10^{-5}	2.0×10^{-3}	2.03×10^{-5}	1.5
2.00×10^{-5}	4.0×10^{-3}	1.99×10^{-5}	−0.5
1.00×10^{-4}	4.0×10^{-3}	9.89×10^{-5}	−1.1
1.00×10^{-4}	2.0×10^{-2}	9.38×10^{-5}	−6.2
1.00×10^{-4}	4.0×10^{-2}	5.79×10^{-5}	−42.1
5.00×10^{-4}	4.0×10^{-2}	1.45×10^{-4}	−71.0

formulations were 2.1×10^{-5} mol fluoride and 1.2×10^{-3} mol Ca^{2+} in 1 l of the solution, i.e. they were below the range of interferences. The fluoride concentration in measuring samples according to procedure I is still in the measuring range of the electrode enabling accurate and precise potentiometric analysis.

The extraction can be carried out without the addition of acid provided both, the insoluble and the soluble parts are treated with acid and analysed after separation (procedure II, Section 2.2.2). Since Na_2FPO_3 is in the soluble part and the abrasives are in the insoluble part, a possible reaction of fluoride from hydrolysed Na_2FPO_3 with complexing ions (Ca^{2+}, Mg^{2+}), released from abrasives during acid treatment is avoided. Such analysis takes longer, but is very accurate and precise. Additionally, it gives the information about the amount of Na_2FPO_3 which is converted to insoluble fluoride during ageing. The procedure is suitable for clinical investigations in which the processes taking place during the ageing of toothpaste are monitored.

3.2. Hydrolysis of Na_2FPO_3

The hydrolysis of Na_2FPO_3 follows the ionisation of the salt in aqueous solution and protonation of FPO_3^{2-}. Excess of acid is known to catalyse hydrolysis [13]. Therefore, an excess of acid should be added. Most authors use HCl as hydrolysis reagent [1,3,4,6], but in some cases the excess of acid applied is not sufficient [1,3].

Table 3 presents the results evaluating the amount of liberated fluoride in dependence on the acid to monofluorphosphate ratio. Hydrolysis was carried out by addition of various volumes of 6 M HCl to 5.0 ml of Na_2FPO_3 solution and heating for 30 min at 80°C. This corresponds to the conditions applied most frequently. The released fluoride was measured with a fluoride-selective electrode. The table shows that at least a 400-fold excess of HCl was necessary for complete hydrolysis.

Table 3
Fluoride liberated during acid hydrolysis of monofluorphosphate at various mol ratios of HCl and Na_2FPO_3[a]

c (Na_2FPO_3) (mol l^{-1})	v (6M HCl) (ml)	n (HCl) / n (Na_2FPO_3)	Liberated fluoride[b] (%)
1.0	2.0	2.4	37.1
	4.0	4.8	65.8
1.0×10^{-1}	1.0	12	91.3
	2.0	24	94.5
	4.0	48	97.0
1.0×10^{-2}	1.0	120	97.8
	2.0	240	98.7
	4.0	480	100.1

[a] Heating for 30 min at 80°C; c (HCl), 6M; v (Na_2FPO_3), 5.0 ml.
[b] Each value is the mean of two independent measurements.

3.3. Potentiometric measurement of fluoride

The potentiometric procedures developed for dentifrices containing NaF and SnF_2 can be utilised for the determination of fluoride liberated by acid hydrolysis [10–12]. Direct potentiometric measurement can be successfully applied under the following conditions:

- the pH of the sample has to be between 5.2 and 5.5 in order to avoid interferences from OH^- and conversion of F^- to HF and HF_2^-
- the standards and unknowns must have the same ionic strength
- interferences of ions which form complexes or precipitates with fluoride must be avoided.

These conditions are fulfilled by proper dilution of samples and the use of total ionic strength adjustment buffer, TISAB. Additionally, as high excesses of acid are necessary for total hydrolysis of Na_2FPO_3, it is reasonable to add acid in corresponding amounts to the standards. The TISAB buffer is capable of adjusting the ionic strength of so prepared standards as well as of properly diluted samples to the same value. Most authors make a mistake when neutralising the excess of HCl with NaOH after hydrolysis (see e.g. Section 2.2.3) [1–4]. Neutralisation of the excess of HCl with NaOH after hydrolysis should be avoided because the resulting high concentrations of salts in the sample solution can overcome the ionic strength compensation capacity of the buffer. In the properly diluted samples, the pH value still remains in the required range.

3.4. Results of analysis of Na_2FPO_3 in dentifrice by two suggested procedures

Table 4 shows the results of repeated analyses of Na_2FPO_3 in the Pliva dentifrice 'Superfresh' with a high content of calcium salts by direct potentiometric measurement after hydrolysis. The dentifrice contained 0.76% Na_2FPO_3, 18.5% $CaCO_3$ and 10% $CaHPO_4 \cdot 2H_2O$, corresponding to 5.28×10^{-5} mol g^{-1} Na_2FPO_3 and 2.42×10^{-3} mol g^{-1} Ca^{2+}. In the case of the content of Na_2FPO_3 the producer guaranteed a value of (0.760 ± 0.001)%. Accordingly, the fluoride and calcium amounts in measuring samples were 2.1×10^{-5} mol F^- and 9.7×10^{-4} mol Ca^{2+} per 1 of the solution. Two procedures were applied. In the first procedure (Section 2.2.1), the extraction and hydrolysis of Na_2FPO_3 were performed in one step and the liberated fluoride was determined directly in the hydrolysed solution. In the second procedure (Section 2.2.2), the extraction of Na_2FPO_3 from dentifrice into the water, separation of phases and hydrolysis were carried out successively. The phases were hydrolysed and analysed after separation. The relative standard deviations in the applied procedures were 4.5% (procedure I) and 1.8% (procedure II), which in both cases was very good precision for direct potentiometric measurement. The insoluble part of dentifrice was analysed in both procedures. When it was analysed separately (procedure II), higher precision and accuracy were achieved. Both procedures were easily repeatable, unlike to the potentiometric procedures described in the literature [1–3]. Our analysis of the same dentifrice following the procedures of Heidbüchel [1] and Friedman [3] gave results characterised by a systematic error of 5–50%. Systematic errors up to 10% were noted if the procedure suggested by ORION was applied.

Table 4
Analysis of Na_2FPO_3 in dentifrice using a fluoride-selective electrode[a]

Procedure	w (Na_2FPO_3), measured, mean value %	Standard deviation ($n = 10$) %
I	0.75	0.03
II	0.76 (insoluble: 0.04; soluble: 0.72)	0.01

[a] Content of Na_2FPO_3 in dentifrice was specified to be (0.760 ± 0.001)% (w/w); number of measurements in each procedure, $n = 10$.

In terms of accuracy, precision and simplicity, the two procedures suggested in this work fully satisfied the requirements for quality control in view of clinical application. The disadvantages of the methods for the potentiometric Na_2FPO_3 determination described in the literature, like loss of the fluoride during dissolution of the sample [1,3], insufficient amount of hydrolysis reagent [1,3], and errors originating from inadequate ionic strength or pH [1–4] are completely avoided in the procedures described here. Our procedures are simpler compared with the potentiometric procedure including the step of separation of fluoride from the dentifrice by hexamethyldisiloxane diffusion [4].

Compared with alternative methods, like GC, HPLC, spectrophotometry and AAS [5–8], the precision of the potentiometric method is as high or even higher and less time consuming. Due to the achieved characteristics, potentiometric method should be the method of choice for the assessment of dentifrice quality with regard to Na_2FPO_3, except when characterisation of Na_2FPO_3 reactions in biological fluids is required, where other methods, like HPLC, are more informative.

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