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Determination Fluoride in Products for Oral Hygiene Using Flow-Injection (FIA) and Continuous Analysis (CA) with Home-Made FISE

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Pharmaceutical products for oral hygiene encompass several different formulations including toothpastes and pills. In these products, fluorides can be added in several different forms, such as sodium fluoride, sodium monofluorophosphate, tin fluoride, or in the form of different amines. This paper describes the potentiometric method with flow injection and continuous analysis for determination of hydrolysis of sodium monofluorophosphate and fluoride in the samples of toothpastes and pills. The measurements were performed in a home-made cell under appropriate flow conditions (2.86 mL min^{-1}, 0.2 mL samples, 10^{-6} M sodium fluoride and Ac-buffer pH=5.5). Na_2FPO_3 complete hydrolyzed at a concentration of 1×10^{-4} mol L^{-1} by addition of 1.0 mL 6.0 M HCl in the measurements with the FIA. Measurements carried out with CA shows that even after addition of 4.0 mL 6.0 M HCl does not come to a complete hydrolysis Na_2FPO_3. Obtained results show that in measurements performed with FIA errors ranged from 2.21 to 9.60 %, while errors are around 30% in the measurements with CA.

Keywords: Flow injection, continuous analysis, potentiometry, toothpaste, monofluorphosphate, fluoride

1. INTRODUCTION

Fluoride is an essential trace microelement for human health at low levels and is a potentially toxic element at higher levels [1]. The fluorine, which has the highest oxidation potential among all

elements, is mostly found in the form of fluorides. The fluoride and their compounds are mostly used in the synthesis of organic compounds, inorganic materials, drugs, enzyme inhibition, nuclear fuel reprocessing and polymers [2]. Pharmaceutical products for oral hygiene encompass several different formulations including toothpastes and mouthwash. [3]. Toothpaste is preparation for cleaning and polishing the surfaces of teeth. Dentifrices (toothpastes & toothpowders) usually contain mild abrasives for polishing, binding agents, sudsier (foaming agents), flavourings and humectants to prevent hardening on exposure to air. [4]. Fluorides are common ingredients in pharmaceutical products for oral hygiene due to their recognized effect in the prevention of tooth decay. Fluoride prevents early dental caries by several mechanisms. It reduces bacterial metabolism, especially glycolysis, thus reducing acid production and hence demineralization. Fluoride also helps control decay by enhancing remineralization and altering the tooth structure, making the surface less soluble. Fluorides may be added to toothpastes in several different forms, such as sodium fluoride (NaF), sodium monofluorophosphate (Na_2FPO_3), tin fluoride (SnF_2), or in the form of different amines. In most pharmaceutical products either NaF or Na_2FPO_3 is used as a source of fluoride ions. The main mechanism by which these differences may be explained is linked to different quantities of the liberated fluoride during dissociation of the salts. Namely, in aqueous solutions NaF is completely dissociated, whereas Na_2FPO_3 during its dissociation releases about 6% of the F^- [3]:

$$NaF \rightarrow Na^+ + F^- \quad (1)$$

$$Na_2FPO_3 \rightarrow 2Na^+ + FPO_3^{2-} \quad (2)$$

$$FPO_3^{2-} + OH^- \rightarrow F^- + HPO_4^{2-} \quad (3)$$

In toothpaste formulations, different polishing additives are normally added, and calcium carbonate is particularly popular. These salts can negatively reflect the stability of fluoride salts, reducing their concentration:

$$2F^- + CaCO_3(s) \rightarrow CaF_2(s) + CO_3^{2-} \quad (4)$$

The formed product (CaF_2) is sparingly soluble in the aqueous solutions, reducing the concentration of free fluorides [3].

Fluoride quantification, however, is limited to a few methods (fluoride ion-selective electrode (FISE), electroanalysis, flow injection analysis, gas chromatography, ion chromatography, capillary electrophoresis, and flame atomic absorption spectrometry). The most popular in this respect is fluoride ion selective electrode (FISE) introduced by Frant and Ross [5]. The use of the FISE as detector in continuous-flow (CA) and flow-injection analysis (FIA) has a great advantage over stationary measurements. This device has a membrane with single crystal of LaF_3 with high electrical conductance, good mechanical properties, wide fluoride concentration range response as well as an enhanced selectivity for fluoride ion [6]. The fluoride-selective membrane electrode is an ideal detecting device for the determination of fluoride using flow injection systems, especially due to the accuracy of the analytical information obtained. Fluoride-specific electrodes are commercially available and are sensitive over a wide temperature range (0-50^{o}C). It is well known that the limitation

of using ion-selective electrodes as detector systems are the limit of detection, influence of pH and selectivity of these devices [7]. Adjustment of pH with buffer is necessary because fluoride and hydroxide ions have the same valence and similar ion radius, so hydroxide ions can interfere in fluoride determination [3]. By using FIA systems, the selectivity of the electrode is improved due to the very short contact time of the interfering ions with the electrode membrane [7].

This is continuation of our previous investigations in products well used among population [8, 9], as well some theoretical approach for FISE being used [10].

This paper reports on the incorporation of a fluoride selective electrode in FIA and CA system for the determination of fluoride content in pharmaceutical products for oral hygiene (toothpaste and pills).

2. EXPERIMENTAL

2.1. Reagents

All reagents were prepared from analytical reagent grade chemicals unless specified otherwise and all the solutions were made up with ultra pure water. Ultra pure water was prepared by Millipore Simplicity, Millipore, USA.

A standard solution of 0.1 M sodium-fluoride has been prepared in a calibrated polypropylene flask. Solid sodium-fluoride had been previously dried at a temperature of 110 °C for 2h. A sodium fluoride stock solution was daily prepared by dissolving 4.1990g of sodium fluoride in 1000.0 mL of ultra pure water. Further concentrations of sodium-fluoride were prepared by diluting the standard solution by means of polypropylene flasks and pipettes.

Solution of sodium monofluorophosphate was prepared weighting 35.9875 g Na_2FPO_3 and dissolved in ultra pure water. To determine required amount of acid for the hydrolysis of sodium monofluorophosphate, in samples which containing 5.0 mL 1.0×10^{-2}, 1.0×10^{-1} and 1.0 mol L^{-1} sodium monofluorophosphate was added 1.0, 2.0 and 4.0 mL 6.0 mol L^{-1} HCl. The suspension was heated and stirred with a stirring hot plate at 100 °C for 30 min. After the samples were cooled to room temperature, ultra pure water was added to bring the volume to 50.0 mL. Before the potentiometric measurements, 5.0 mL of these hydrolyzed samples was diluted in 25.0 mL acetated buffer pH= 5.5 and finally the volume were completed to 50.0 mL with ultra pure water.

To prepare the samples with $CaCO_3$, 1.0 - 5.0 g $CaCO_3$ was weighed and transferred to a flask and added 5.0 mL of standard solution of NaF concentration 1.0×10^{-2} and 5.0×10^{-2} mol L^{-1} and 4.0 mL 6.0 mol L^{-1} HCl. The suspension was heated and stirred with a stirring hot plate at 100 °C for 30 min. After the samples were cooled to room temperature, ultra pure water was added to bring the volume to 50.0 mL.

Suspension of $CaCO_3$ and Na_2FPO_3 was prepared in the same manner.

Before the potentiometric measurements, 5.0 mL of these hydrolyzed samples was diluted in 25.0 mL acetated buffer pH= 5,5 and finally the volume was completed to 50.0 mL with ultra pure water.

2.2. Standard preparation

Five standard solutions contained 5.0 mL NaF (1.0×10^{-5} to 1.0×10^{-1} mol L^{-1}), 5.0 mL of 0.48 mol L^{-1} HCl, 25.0 mL acetated buffer pH= 5.5 and the volume were completed to 50.0 mL with ultra pure water.

Three standard solutions includes 5.0 mL NaF (1.0×10^{-4} to 1.0×10^{-2} mol L^{-1}), 1.0 mL of 0.48 mol L^{-1} HCl, 25.0 mL acetate buffer pH= 5.5 and the volume were completed to 50.0 mL with ultra pure water. Standard do not contain $CaCO_3$ because their quantity is not always known in toothpaste.

2.3. Preparation of toothpaste and pills samples

The toothpaste samples were randomly sampled and purchase from local supermarket has been investigated in this work. Fluoride content in these samples is 1450 ppm.

The samples have been prepared in two different ways:

1. Approximately 2.0 g of Aquafresh™ toothpaste (SmithKline Beecham Consumer Healthcare, Great Brittany) sample was weighed and suspended in 20.0 mL of ultra pure water (an ultrasonic bath was also used) and 4.0 mL 6.0 mol L^{-1} HCl was added to release fluoride ions completely. Suspension was heated and stirred with a stirring hot plate at 100^{o}C for 30 min. After the samples were cooled to room temperature, ultra pure water was added to bring the volume to 50.0 mL. Before the potentiometric measurements, 1.0 and 5.0 mL aliquot of hydrolysed samples was mixed with 25.0 mL acetate buffer and finally the volume was completed to 50.0 mL with ultra pure water.

2. A two gram of toothpaste sample was suspended in 20.0 mL of ultra pure water and suspension was stirred at room temperature with a magnetic stirrer for 10 min. The solid and liquid phases were separated by centrifugation for 10 min. After centrifugation, solution was separated from the precipitate and transferred in a volumetric flask with 4.0 mL 6.0 mol L^{-1} HCl and steps were performed in the same way as in procedure 1. The precipitate was washed several times with ultra pure water, which was collected and added to solution. In the same way, the precipitate was treated. Aliquots of 2.0 and 10.0 mL were used for potentiometric measurements.

Except for samples of toothpaste determination of fluoride concentration was performed in pills - "FLUONATRIL" (Belupo, Croatia). The FLUONATRIL pills samples were taken from local pharmacies. Analysis of samples was carried out with different amounts of pills samples of 0.0490 g to 0.490 g.

2.4. Instrumentation

The flow injection and continue flow system used in this work consists of peristaltic pump (Minipuls 2, Gilson, France) fitted with silicon rubber tubing with a diameter of 2.0 mm i.d. and an injection valve (V-100, Tecator, Sweden). The output of the injection valve is connected to the home made design flow cell with FISE. The reference electrode used in the experiment was an Orion 90-02 single-junction reference electrode. Potentiometric data were captured at room temperature by a

millivoltmeter (Model MA 5741, Iskra, Ljubljana, Slovenia) attached to a personal computer. The example FIA system developed for determination of fluoride is shown schematically in Figure 1.

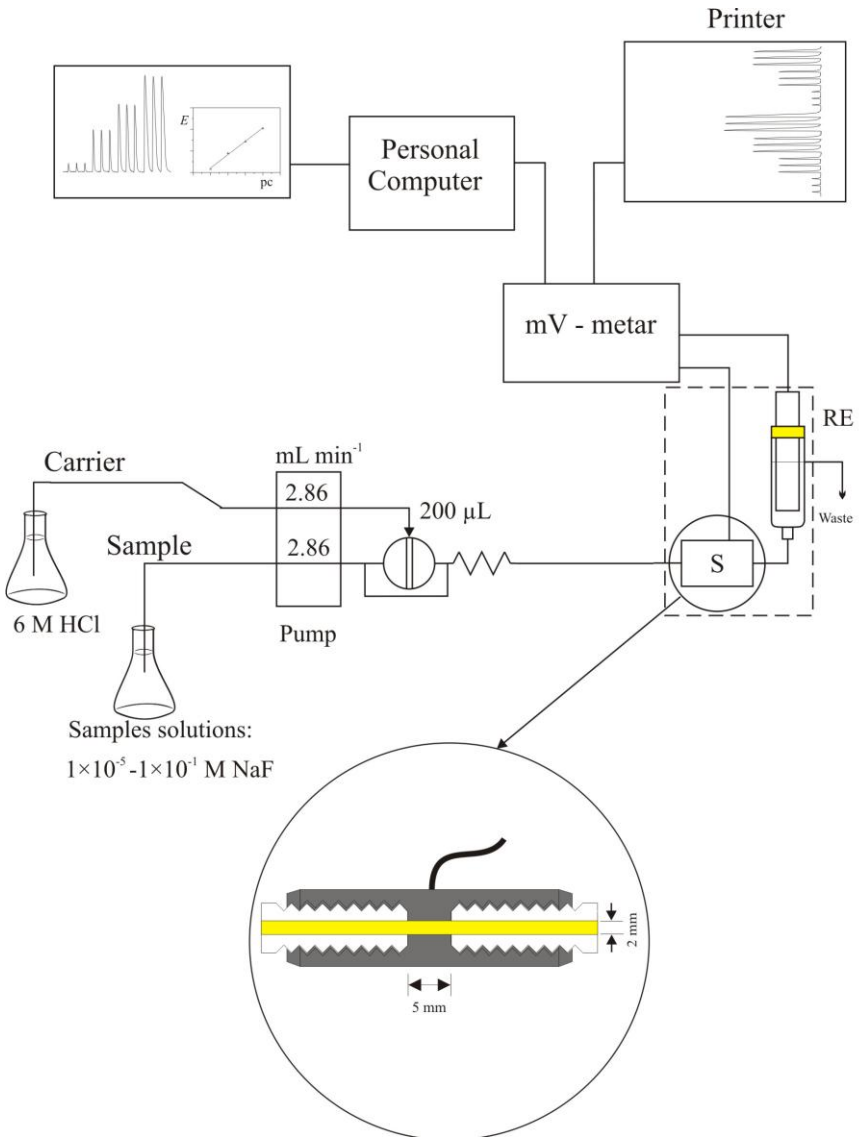

Figure 1. Manifold of FIA system for potentiometric determination of fluoride. Same apparatus was used for CA experiment but without injection valve

2.5. Procedure

The carrier solution was pumped through a two-position injection valve, and a peristaltic pump was used to change the flow in the single-line flow manifold. While one loop served as the carrier stream, a sample was drawn through the other loop at the same flow rate.

In the CA, the background solution was first pumped, then the peristaltic pump was stopped and the flow was exchanged with sample solution, which was being pumped until a constant potential was achieved. After establishing a stable potential again to stop the flow tube and transferred to a basic solution. The procedure is repeated for all samples.

The carrier solution was sodium fluoride, at a concentration 1.0×10^{-6} with acetated buffer pH=5.5.

The linear working range, slope, reproducibility and detection limit of the electrode were determined by measurements in standard NaF solutions, which contained acetated buffer and HCl in the same amounts as the measuring samples. The accuracy of the method was checked by recovery experiments. The calculated percentage recoveries were excellent in all cases ranging between 98.1 and 99.4%.

3. RESULTS AND DISCUSSION

Based on the literature citation [11], in this paper investigated the possibility of determining fluoride in products for oral hygiene with FIA and CA system with a detector homemade FISE [12].

The response characteristics and selectivity coefficients of the fluoride selective electrode incorporated into the conduits of the FIA and CA systems were evaluated under optimum running conditions (Figure 2). Calibration curves both for FIA and CA show very good agreement with Nerstian slope for monovalent ions, 58.543 and 58.873, respectively.

By using data acquired from calibration curves, it was possible to calculate limit of detection (LOD) and quantification (LOQ) of fluoride ions for applied FIA and CA methods.

Table 1. Calculated values of LOD and LOQ for FIA and CA

	FIA/mol L^{-1}	CA/mol L^{-1}
LOD	9.84×10^{-5}	9.44×10^{-6}
LOQ	1.06×10^{-4}	1.21×10^{-5}

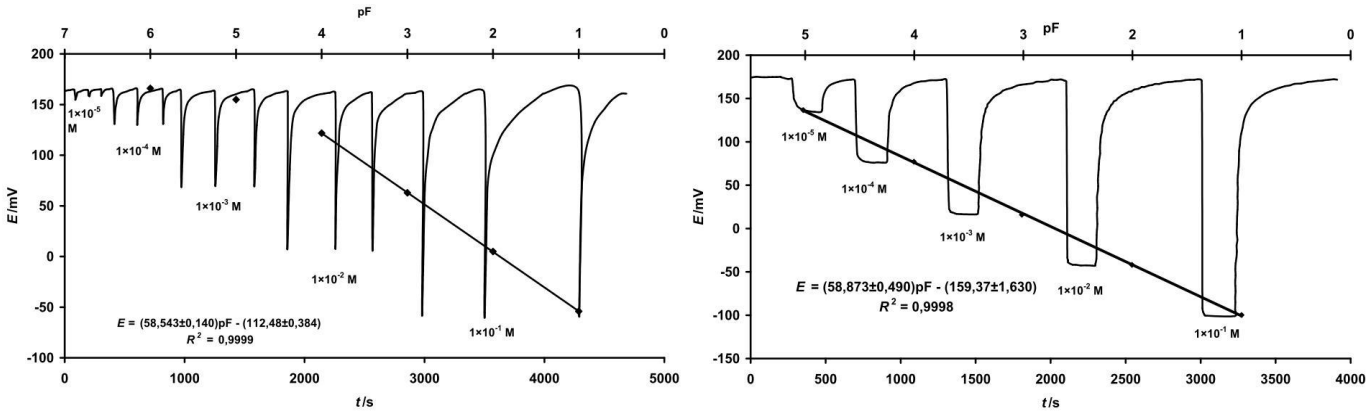

Figure 2. Calibration curves obtained for FISE in FIA and CA. Standard solution NaF, *c*(NaF)= 1×10^{-6} mol L^{-1}, Ac-buffer pH=5.5, samples NaF, *c* = $1\times10^{-}1$ to 1×10^{-5} mol L^{-1}.

In defining LOD, multiple criteria can be applied. The sensitivity of a certain analytical method is determined by the lowest analyte concentration that can be reliably determined in statistically acceptable limits [3].

Calculated values are given in Table 1 by using next formulae:

$$\mathrm{LOD} = \frac{3\sigma}{s} \qquad \mathrm{LOQ} = \frac{10\sigma}{s} \tag{5}$$

s – slope of calibration curve; σ – standard deviation of slope

The hydrolysis of Na_2FPO_3 follows the ionisation of the salt in aqueous solution and protonation of FPO_3^{2-}. Hydrolysis was carried out by addition of various volumes of 6.0 M HCl to Na_2FPO_3 solution with different concentrations. The released fluoride was measured with a fluoride selective electrode. Stable potential is slowly established at higher concentrations of Na_2FPO_3, however, everything occurs within five minutes (Figure 3).

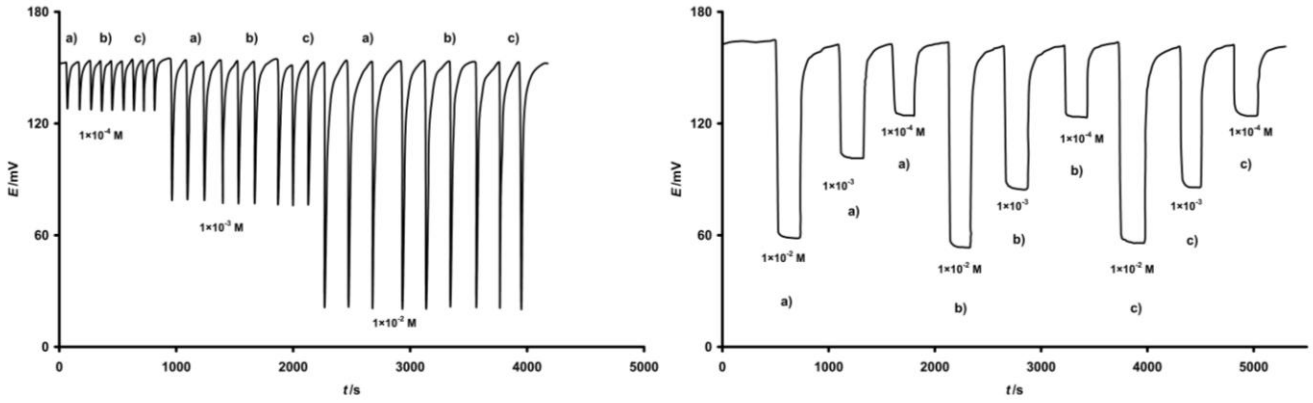

Figure 3. FISE response to Na_2FPO_3 in FIA and CA experiment. Standard solution Na_2FPO_3, $c(Na_2FPO_3) = 1\times10^{-5}$ mol L^{-1}, samples Na_2FPO_3, $c = 1\times10^{-3}$, 1×10^{-2} and 1×10^{-1}; with HCl, c(HCl); a) 0.12, b) 0.24, and c) 0.48 mol L^{-1}.

Na_2FPO_3 complete hydrolyzed at a concentration of 1×10^{-4} mol L^{-1} by addition of 1.0 mL 6.0 M HCl in the measurements with the FIA. Measurements carried out with CA shows that even after addition of 4.0 mL 6.0 M HCl does not come to a complete hydrolysis of Na_2FPO_3. Namely, hydrolysed only 69.86 % Na_2FPO_3 (Table 2). Measuring with classical potentiometry obtained that Na_2FPO_3 hydrolysed 79.97%. Previous studies with classical potentiometry [11] have shown that complete hydrolysis of Na_2FPO_3 occurs after addition of 4.0 mL 6.0 M HCl.

Na_2FPO_3 is partly hydrolysed to fluoride which may react with Ca^{2+} liberated from toothpastes to form sparingly soluble salts. It takes place when the solubility of abrasive in the toothpaste is greater than solubility of CaF_2. Therefore, if CaF_2 formed on plaque-free enamel is an important factor responsible for the anticaries effect of professionally applied topical fluoride treatments, fluoride

released from CaF_2 should be found in the fluid of newly formed plaque, where it could significantly inhibit enamel demineralization. The minimum concentration of fluoride required for CaF_2 formation is not well known and may depend on whether calcium is available from plaque fluid or only through dissolution of the dental hard tissue [13]. Correlation between F^- and CaF_2 and their impact on the demineralization of tooth enamel investigated Tenuta et al.[14].

Table 2. Results of hydrolysis Na_2FPO_3 for FIA and CA

		c (Na_2FPO_3) in standard solution (mol L^{-1})					
		1.00		1.00×10^{-1}		1.00×10^{-2}	
		c (Na_2FPO_3) in dilute solution (mol L^{-1})					
		1.00×10^{-2}		1.00×10^{-3}		1.00×10^{-4}	
	V (HCl)	*c measured (hydrolysed F^-) (mol L^{-1})*	% hydrolysed F^-	*c measured (hydrolysed F^-) (molL^{-1})*	% hydrolysed F^-	*c measured (hydrolysed F^-) (molL^{-1})*	% hydrolysed F^-
FIA	1.00	3.654×10^{-3}	36.53	6.092×10^{-4}	60.92	1.041×10^{-4}	102.4
	1.00	3.625×10^{-3}	36.25	5.768×10^{-4}	57.68	1.036×10^{-4}	103.6
	2.00	5.768×10^{-3}	57.68	6.561×10^{-4}	65.61	1.056×10^{-4}	105.6
	2.00	5.723×10^{-3}	57.23	6.409×10^{-4}	64.09	1.069×10^{-4}	106.9
	4.00	5.273×10^{-3}	52.73	6.261×10^{-4}	62.61	1.012×10^{-4}	101.2
	4.00	5.131×10^{-3}	51.31	5.997×10^{-4}	59.97	1.016×10^{-4}	101.6
CA	1.00	3.023×10^{-3}	30.27	2.509×10^{-4}	25.08	6.668×10^{-5}	66.67
	1.00	3.099×10^{-3}	30.98	2.422×10^{-4}	24.22	6.799×10^{-5}	67.98
	2.00	4.087×10^{-3}	40.86	6.595×10^{-4}	65.95	6.959×10^{-5}	69.59
	2.00	4.087×10^{-3}	40.86	6.699×10^{-4}	66.98	6.987×10^{-5}	69.86
	4.00	3.594×10^{-3}	35.93	6.294×10^{-4}	62.93	6.668×10^{-5}	66.67
	4.00	3.579×10^{-3}	35.79	6.318×10^{-4}	63.18	6.694×10^{-5}	66.93

The indicated connection F^- and CaF_2 have resulted justification of addition $CaCO_3$ in products for dental care. Therefore, Ca^{2+} which composed in products for oral hygiene interfere with the determination of fluoride with FISE. Table 3 present the result of determination fluoride in the model samples containing $CaCO_3$ with Ac-buffer pH=5.5

In model samples, the critical level for FIA was achieved at the fluoride concentration of 1×10^{-4} mol L^{-1} and at amounts of 0.1 g $CaCO_3$ added in solution. For CA the critical concentration and amounts of $CaCO_3$ is the same but error is much higher. All errors are negative, which is in agreement with previous studies performed with classical potentiometry [11].

Tables 4 and 5 show results of repeated analysis of fluoride in the dentifrice "Aquafresh" by FIA and CA after hydrolysis. Two procedures were applied (Section 2.3).

In the samples prepared in the first mode, error between the expected and measured concentrations of fluoride ions in measurements performed with FIA ranged from 2.21 to 9.60 %, while errors are around 30% in the measurements with CA. However, in the samples prepared in the

second mode errors are significantly higher than 30%, in the measurements performed with FIA and CA. Analysis performed with classical potentiometry [10] showed better applicability of second method, however this determination referred only on Na_2FPO_3.

Table 3. Determination of fluoride in the model samples containing $CaCO_3$ with Ac-buffer pH=5.5

	Amounts of $CaCO_3$ added / g	E / mV	expected $c_e(F^-)$/ mol L^{-1}	measured $c_m(F^-)$/ mol L^{-1}	c_m - c_e / mol L^{-1}
FIA	0.1	131.9	1×10^{-4}	8.90×10^{-5}	2.3×10^{-6}
	0.1	105.3	5×10^{-4}	2.51×10^{-4}	-2.18×10^{-4}
	0.2	134.4	1×10^{-4}	8.07×10^{-5}	-1.04×10^{-5}
	0.2	132.1	5×10^{-4}	8.83×10^{-5}	-4.0×10^{-4}
	0.3	133.4	1×10^{-4}	8.39×10^{-5}	-5.6×10^{-6}
	0.3	132.8	5×10^{-4}	8.59×10^{-5}	-4.07×10^{-4}
	0.4	136.2	1×10^{-4}	7.52×10^{-5}	-1.29×10^{-5}
	0.4	136.7	5×10^{-4}	7.38×10^{-5}	-4.12×10^{-4}
	0.5	132.5	1×10^{-4}	8.69×10^{-5}	-8.5×10^{-6}
	0.5	135.1	5×10^{-4}	7.85×10^{-5}	-4.11×10^{-4}
CA	0.1	90.8	1×10^{-4}	5.51×10^{-5}	-4.49×10^{-5}
	0.1	49.0	5×10^{-4}	2.81×10^{-4}	-2.19×10^{-4}
	0.2	106.8	1×10^{-4}	2.95×10^{-5}	-7.05×10^{-5}
	0.2	96.2	5×10^{-4}	4.46×10^{-5}	-4.55×10^{-4}
	0.3	101.8	1×10^{-4}	3.59×10^{-5}	-6.41×10^{-5}
	0.3	98.6	5×10^{-4}	4.06×10^{-5}	-4.59×10^{-4}
	0.4	99.0	1×10^{-4}	4.00×10^{-5}	-5.99×10^{-5}
	0.4	100.0	5×10^{-4}	3.85×10^{-5}	-4.62×10^{-4}
	0.5	100.6	1×10^{-4}	3.80×10^{-5}	-6.24×10^{-5}
	0.5	99.9	5×10^{-4}	3.89×10^{-5}	-4.61×10^{-4}

Table 4. Determination of fluoride in toothpaste samples prepared in a first mode - dilution with Ac - buffer, pH = 5.5

	E / mV	mL solution for dilution	expected $c_e(F^-)$/ mol L^{-1}	measured $c_m(F^-)$/ mol L^{-1}	c_m - c_e / mol L^{-1}
FIA	151.4	1	4.57×10^{-5}	5.01×10^{-5}	4.39×10^{-6}
	153.2	1	4.57×10^{-5}	4.47×10^{-5}	-1.01×10^{-6}
	152.8	1	4.57×10^{-5}	4.43×10^{-5}	-1.41×10^{-6}
CA	105.3	1	4.52×10^{-5}	3.13×10^{-5}	-1.39×10^{-5}
	105.4	1	4.52×10^{-5}	3.12×10^{-5}	-1.40×10^{-5}
	104.9	1	4.52×10^{-5}	3.18×10^{-5}	-1.34×10^{-5}

Table 5. Determination of fluoride in toothpaste samples prepared in a second mode – dilution with Ac - buffer, pH = 5.5

	E / mV	mL solution for dilution	measured $c_m(F^-)$/ mol L^{-1}		c_m - c_e / mol L^{-1}
FIA	161.1 (PS) 148.7 (SP)	2	2.85×10^{-5} 4.62×10^{-5}	total: 7.47×10^{-5}	2.96×10^{-5}
	160.2 (PS) 148.5 (SP)	2	2.95×10^{-5} 4.65×10^{-5}	total: 7.60×10^{-5}	3.09×10^{-5}
	160.2 (PS) 148.5 (SP)	2	2.95×10^{-5} 4.65×10^{-5}	total: 7.60×10^{-5}	3.09×10^{-5}
	162.4 (PS) 135.7 (SP)	10	2.71×10^{-5} 7.67×10^{-5}	total: 1.04×10^{-4}	-1.26×10^{-4}
	162.4 (PS) 135.2 (SP)	10	2.71×10^{-5} 7.67×10^{-5}	total: 1.04×10^{-4}	-1.26×10^{-4}
	161.0 (PS) 134.9 (SP)	10	2.86×10^{-5} 7.91×10^{-5}	total: 1.08×10^{-4}	-1.22×10^{-4}
CA	107.9 (PS) 66.9 (SP)	2	2.83×10^{-5} 1.40×10^{-4}	total: 1.68×10^{-4}	1.24×10^{-4}
	107.9 (PS) 66.1 (SP)	2	2.83×10^{-5} 1.44×10^{-4}	total: 1.72×10^{-4}	1.28×10^{-4}
	107.3 (PS) 66.7 (SP)	2	2.90×10^{-5} 1.41×10^{-4}	total: 1.70×10^{-4}	1.26×10^{-4}
	172.7 (PS) 157.4 (SP)	10	2.26×10^{-6} 4.11×10^{-6}	total: 6.37×10^{-6}	-2.17×10^{-4}
	173.5 (PS) 157.4 (SP)	10	2.19×10^{-6} 4.11×10^{-6}	total: 6.30×10^{-6}	-2.17×10^{-4}
	173.2 (PS) 156.2 (SP)	10	2.22×10^{-6} 4.31×10^{-6}	total: 6.53×10^{-6}	-2.16×10^{-4}

*PS = pure solution
SP = solution of the precipitate

c_e for FIA : for 2 mL = 4.51×10^{-5} mol L^{-1}
for 10 mL = 2.30×10^{-4} mol L^{-1}
c_e for CA : for 2 mL = 4.45×10^{-5} mol L^{-1}
for 10 mL = 2.23×10^{-4} mol L^{-1}

Considering the results obtained in our research, FIA is more sensitive method for determination the concentration of fluoride in samples of toothpaste.

Except for samples of toothpaste determination of fluoride concentration was performed in pills - "FLUONATRIL" (Belupo, Croatia) (Table 6).

Result shows better applicability of FIA where the errors were within the limits under 10%, except for the sample of 10 pills where the error was higher. It is necessary to say that at low concentrations of fluoride ($<10^{-5}$ mol L^{-1}) error is higher because it is the concentration that is the limit of sensitivity of the electrode. But, a change in the potential of only 4 mV in FIA causes an error in the

concentration of 17.81%. Errors in measurements with CA are in the range of 17.87% to 40.09%. These values correlate to those obtained previously [3, 10].

Table 6. Determination of fluoride concentration in the samples "FLUONATRIL" pills (Belupo, Croatia) - dilution with Ac buffer pH = 5.5

	number of pills	mL solution for dilution	E / mV	expected $c_e(F^-)$ / mol L^{-1}	measured $c_m(F^-)$ / mol L^{-1}	$c_m - c_e$ / mol L^{-1}
FIA	1	1	148.4	5.26×10^{-6}	5.10×10^{-6}	-1.64×10^{-7}
	1	5	145.8	2.63×10^{-5}	2.52×10^{-5}	-1.10×10^{-6}
	2	1	145.9	1.05×10^{-5}	1.07×10^{-5}	2.19×10^{-7}
	2	5	139.8	5.26×10^{-5}	5.16×10^{-5}	-1.04×10^{-6}
	4	1	143.3	2.11×10^{-5}	2.07×10^{-5}	-4.00×10^{-6}
	4	5	131.4	1.05×10^{-4}	1.01×10^{-4}	-4.22×10^{-6}
	8	1	139.7	4.21×10^{-5}	4.22×10^{-5}	1.00×10^{-7}
	8	5	125.0	2.11×10^{-4}	2.06×10^{-4}	-5.00×10^{-6}
	10	1	139.3	5.26×10^{-5}	4.47×10^{-5}	-7.93×10^{-6}
	10	5	121.3	2.63×10^{-4}	1.15×10^{-4}	-1.48×10^{-4}
CA	1	1	156.1	5.26×10^{-6}	4.32×10^{-6}	-9.41×10^{-7}
	1	5	122.9	2.63×10^{-5}	1.58×10^{-5}	-1.06×10^{-5}
	2	1	143.9	1.05×10^{-5}	6.95×10^{-6}	-3.57×10^{-6}
	2	5	105.1	5.26×10^{-5}	3.15×10^{-5}	-2.11×10^{-5}
	4	1	124.9	2.11×10^{-5}	1.46×10^{-5}	-6.47×10^{-6}
	4	5	86.1	1.05×10^{-4}	6.62×10^{-5}	-3.91×10^{-5}
	8	1	107.6	4.21×10^{-5}	2.86×10^{-5}	-1.35×10^{-5}
	8	5	67.8	2.11×10^{-4}	1.35×10^{-4}	-7.55×10^{-5}
	10	1	102.0	5.26×10^{-5}	3.56×10^{-5}	-1.70×10^{-5}
	10	5	62.5	2.63×10^{-4}	1.66×10^{-4}	-9.72×10^{-5}

4. CONCLUSIONS

In this paper, results of simultaneous potentiometric measurement (FIA and CA) of fluoride content in pharmaceutical products for oral hygiene (toothpaste and pills) are presented. Since the concentration of fluoride in the pharmaceutical products for oral hygiene in the concentration range of 10^{-3} to 10^{-4} mol L^{-1}, the proposed ISE-FIA and ISE-CA system seems to be suitable as a reliable low cost analyser especially in the manufacturing of toothpaste. Obtained results show that in measurements performed with FIA errors ranged from 2.21 to 9.60 %, while errors are around 30% in the measurements with CA. Moreover, Ca^{2+} which composed in products for oral hygiene interfere with fluorides which are determined with FISE. In measurements performed with FISE achieved complete hydrolysis Na_2FPO_3 with addition of 1.0 mL 6.0 mol L^{-1} HCl, while measurements carried

out with CA shows that even after addition of 4.0 mL 6.0 M HCl does not come to a complete hydrolysis Na_2FPO_3.

Taking into consideration the toxicity of fluorides, more strict control of fluoride content in pharmaceutical product for oral hygiene is proposed.

Measuring performed potentiometrically using a fluoride selective electrode is simple and inexpensive. Possible matrix effects can be easily eliminated by the addition of Ac buffer. As a low cost, low maintenance (especially with the low cost fluoride selective electrode as detector) reliable analyser, the ISE-FIA and ISE-CA system should be particularly attractive for the determination of the fluoride in the pharmaceutical products for oral hygiene.

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