

Spectrophotometric determination of fluoride in dosage forms and dental preparations¹

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Abstract

The method is based upon the reaction between fluoride ions and the coloured complex of Fe(III) with methyl salicylate to form the stable, colourless hexafluoride complex of iron. The conditions of the method (pH, time and combination ratio) were studied and a standard curve was obtained for 0.01–0.08 mg NaF ml⁻¹, at 525 nm. A study was conducted on interference with complexing anions of Fe(III), cations that react with fluoride ions and with common ingredients of dosage forms and dental preparations. The method was validated and the results showed good precision (100.16 ± 2.33%) comparable with that of other analytical methods. Good results were obtained in the spectrophotometric determination of fluoride ions in a stomatological gel and in a toothpaste.

Keywords: Fe(III) methyl salicylate complex; Fluoride in gels and toothpaste; Fluoride in tablets; Fluoride-selective electrode; Indirect spectrophotometric method

1. Introduction

The biological role and importance of fluorides revealed by studies in recent decades have determined their use in prophylaxis and treatment of disease (especially in stomatology), by adding small quantities of fluorides to food (drinking water, milk or salt) as well as by their administration as tablets, toothpastes or locally applied gels.

The determination of fluorides continues to be a special concern for analysts [1–6] and the latest two issues of the FR (Farmacopeea Romana; Romanian Pharmacopoeia) propose new volumetric methods [7,8] because the results obtained with current methods are not satisfactory.

Among the methods used to determine fluoride ions in water, the best results were obtained with the spectrophotometric and potentiometric (with an F-selective electrode) methods [1,2,4,5,9]. A more accurate and accessible spectrophotometric method has been submitted for inclusion in the next issue of the FR.

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Table 1
Standard curve^a and spectrophotometric determination of NaF

Sample	NaF weighed ($\mu\text{g ml}^{-1}$)	Absorbance	NaF found		Statistical parameters
			$\mu\text{g ml}^{-1}$	%	
1	10	0.344	10.40	104.16	$\bar{x} = 100.162$ $n = 20; \alpha = 0.95; t = 2.09$
	10	0.344	10.40	104.16	
	21	0.317	19.80	94.04	Repeatability $s_r = 5.4$ $\text{RSD}_r = 5.39\%$
	21	0.216	19.30	92.06	
	21	0.322	21.80	103.96	
2	31	0.290	32.30	104.03	Reproducibility $s_R = 5.88$ $\text{RSD}_R = 5.87\%$
	31	0.287	31.00	100.00	
	31	0.284	29.80	95.96	95% Confidence limits $A = 100.162 \pm 2.33\%$
	31	0.287	31.00	100.00	
	31	0.288	31.40	101.34	
3	41	0.266	43.10	105.08	
	41	0.270	44.80	109.14	
	41	0.254	38.10	92.88	
	41	0.255	38.50	93.90	
	41	0.265	42.70	104.06	
4	83	0.162	79.30	95.48	
	83	0.167	81.30	97.99	
	83	0.169	82.20	98.99	
	83	0.185	88.80	107.02	
	83	0.169	82.20	98.99	

^a Each individual value is the mean of five measurements. Standard curve equation: $y = 0.31676 - 0.00203x$ ($r = -0.99319$).

The proposed method is an indirect spectrophotometric method and is based on the reaction of fluoride ions with the red-violet complex of Fe(III) with methyl salicylate and the formation of the colourless, more stable $[\text{FeF}_6]^{3-}$ complex, at pH 1–3.

2. Experimental and results

2.1. Apparatus

An Ultrospec III UV-Vis spectrophotometer (Pharmacia LKB, UK), an MV-84 pH meter (Cammann and Granert, Dresden, Germany) and an F-selective electrode, type 94-09 (Orion Research Inc., USA) were used together with 5 cm i.d. polyethylene Petri dishes. In the lid of each Petri dish was placed 0.1 ml of 0.5 M alcoholic NaOH; the alcohol evaporated when drying under vacuum.

2.2. Reagents

$\text{Fe}(\text{NH}_4)(\text{SO}_4)_2 \cdot 12 \text{H}_2\text{O}$ (Reactivul București), methyl salicylate (FR Xth edn.), ethyl alcohol 95% (v/v) (FR Xth edn.), NaF (Merck), HNO_3 (Merck), NaOH (Merck) and HClO_4 70% (w/w) (Merck) were used.

2.3. Solutions

2.3.1. Solution A

0.10000 g NaF was weighed into a 100 ml calibrated volumetric flask, dissolved in distilled water and diluted to 100 ml with distilled water.

2.3.2. Solution B

To 200 ml of 10^{-2} M Fe(III) solution were added 350 ml of 1% methyl salicylate solution and 300 ml of ethyl alcohol 95% (v/v) and the mixture was diluted to 1000 ml with distilled water.

Table 2
Influence of foreign ions on the spectrophotometric determination of fluoride

Interferent ion	Critical concentration ($\mu\text{g ml}^{-1}$)	Interferent ion	Critical concentration ($\mu\text{g ml}^{-1}$)
Acetic acid	1000	KCl (NaCl)	150 (230)
Oxalic acid	10	KNO ₃	200
Citric acid	5	Al ³⁺	22
Lactic acid	5	Ca ²⁺	80
Na ₂ S ₂ O ₃	15	Mg ²⁺	1358
NaHCO ₃	37	CaCO ₃ (suspension)	5000
Na ₂ CO ₃	63	MgCO ₃ (suspension)	5000
Na ₂ HPO ₄	7	Mg stearate (suspension)	No interference

2.3.3. 10^{-2} M Fe(III)

9.6442 g of FeNH₄(SO₄)₂·12 H₂O or 5.6000 g of Fe₂(SO₄)₃·9 H₂O was dissolved in \approx 300 ml of distilled water and 50 ml of 1 M HNO₃ and the solution was diluted to 1000 ml with distilled water.

2.3.4. 1% Methyl salicylate solution

5 g of methyl salicylate (or 4 ml) was dissolved in 95% (v/v) ethyl alcohol and diluted to 500 ml with the same solvent.

2.3.5. TISAB II (total ionic strength adjustment buffer; Orion Research Inc.)

In \approx 500 ml of H₂O in a 1 l beaker was dissolved 57 ml of CH₃COOH, 58 g of NaCl and 1 g of CDTA. The solution was cooled and adjusted to pH 5.0–5.5 with 5 M NaOH. The solution was cooled to room temperature, transferred to a 1 l volumetric flask and diluted to volume with distilled water.

2.3.6. 0.5 M alcoholic NaOH

1 g NaOH was dissolved in 20 ml of distilled water. The solution was cooled and diluted to 50 ml with 95% (v/v) ethyl alcohol.

2.4. Determination of the standard curve (spectrophotometric method)

2.4.1. Variation of the absorbance with wavelength and time

Fe(III) ions reacted with methyl salicylate in a

hydroalcoholic medium to form a red–violet complex which has a maximum absorbance a 525 nm. At pH 1–3, with a slight excess of 1% methyl salicylate solution (ratio of Fe: methyl salicylate = 1:3) the absorbance of the complex was stable for 10 min–2 h, with only very little change even after 24 h.

2.4.2. Variation of the absorbance with concentration

In each of a number of 25 ml calibrated flasks 10 ml of solution B was mixed with a different volume (0.25–2.00 ml) of solution A; the mixture was stirred gently and diluted to 25 ml with distilled water. After 15 min the absorbance was measured at 525 nm and 1 cm polyethylene cells against distilled water. The results are given in Table 1.

2.4.3. Influence of foreign ions

Successive dilutions were made to establish the concentrations over which the absorbance of the [Fe(MetSal)₃] complex was significantly modified (Table 2).

2.5. Determination of the standard curve (potentiometric method)

The AOAC Official Method 984.37 (Fluoride in Drug Tablets and Solutions) [9] was used. The results are given in Table 3.

Table 3
Standard curve for the potentiometric determination of NaF

Run	Standard concentration ($\mu\text{g ml}^{-1}$)	Potential (mV)	Sample concentration ^a		Statistical parameters
			($\mu\text{g ml}^{-1}$)	%	
1	11.51	55.3	10.62	92.24	$\bar{x} = 100.158$ $n = 30$; $\alpha = 0.95$; $t_x = 2.04$
	23.02	35.5	23.47	101.97	
	34.53	25.5	35.04	101.49	
	46.04	17.5	48.29	104.89	
	92.98	3.0	86.34	93.76	
2	10.66	54.7	10.88	102.02	Repeatability $s_r = 4.9$ (%) $\text{RSD}_r = 4.89\%$ Reproducibility $s_R = 5.05$ (%) $\text{RSD}_R = 5.04\%$
	21.33	37.8	21.41	100.36	
	32.00	27.0	33.00	103.13	
	42.66	20.5	42.82	100.37	
	85.33	2.5	88.09	103.23	
3	10.79	55.0	10.75	99.59	95% Confidence limits $A = 100.158 \pm 1.205\%$
	21.58	35.3	23.66	109.65	
	32.37	26.8	33.27	102.77	
	43.16	19.5	44.57	103.27	
	86.32	2.2	89.15	103.28	
4	10.13	56.8	10.00	98.69	
	20.26	40.0	19.60	96.75	
	30.39	29.0	30.46	100.23	
	40.52	26.0	34.35	84.77	
	81.04	3.8	83.61	103.18	
5	10.19	57.8	9.60	94.26	
	20.38	39.0	20.40	100.11	
	30.57	28.5	31.08	101.65	
	40.75	20.5	42.82	105.08	
	81.51	7.6	71.80	88.09	
6	10.23	55.7	10.45	102.13	
	20.46	37.9	21.32	104.21	
	30.69	28.3	31.33	102.07	
	40.92	21.8	40.65	99.33	
	81.84	3.8	83.61	102.17	

^a Calculated for each determination from the standard curve equation: $y = 114.25416 - 57.46413 \log x$ ($r = -0.99718$).

2.6. Determination of sodium fluoride in tablets

Samples of 0.2000 g of powdered tablets were placed in calibrated flasks (100 ml for spectrophotometry and 25 ml for potentiometry), dissolved in distilled water and diluted to the mark with distilled water. From the suspensions obtained dilutions were prepared directly (potentiometry) or after filtration through a quantita-

tive dry filter (spectrophotometry). For potentiometry, volumes of 2–6 ml were diluted to 25 ml in calibrated flasks; for spectrophotometry, volumes of 5–15 ml were diluted to 100 ml in calibrated flasks with distilled water. Then, the appropriate procedures described in Sections 2.4.2. (spectrophotometry) and 2.5 (potentiometry) were carried out. The results are given in Table 4.

Table 4
Spectrophotometric (a) and potentiometric (b) determination of NaF (mg per tablet) in Osofluor tablets (ICCF Cluj-Napoca) (a)

Sample	Run				Statistical parameters
	1	2	3	4	
1	24.56	24.88	26.69	25.34	$\bar{x} = 24.86$ mg per tablet $n = 20$; $\alpha = 0.95$; $t_{\alpha} = 2.09$ $A = 24.86 \pm 0.78$ mg per tablet
2	23.08	25.30	26.34	26.39	
3	23.97	24.67	25.34	24.77	
4	23.64	24.67	24.97	25.79	Repeatability $s_r = 0.77$ mg per tablet
5	24.57	25.29	24.97	24.60	$RSD_r = 3.10\%$
Mean	23.96	24.96	25.66	25.36	Reproducibility $s_R = 1.09$ mg per tablet $RSD_R = 4.41\%$

(b)

Run	Sample			Mean	Statistical parameters
	1	2	3		
1	26.13	26.66	25.54	26.44	$\bar{x} = 25.30$ mg per tablet $n = 24$; $\alpha = 0.95$; $t_{\alpha} = 2.06$ $A = 25.30 \pm 0.63$ mg per tablet
2	25.15	25.64	25.77	25.52	
3	25.51	25.63	25.36	25.50	
4	24.17	26.06	25.67	25.30	Repeatability $s_r = 0.52$ mg per tablet
5	26.13	25.64	25.87	25.88	$RSD_r = 2.09\%$
6	25.17	23.90	24.75	24.60	Reproducibility $s_R = 0.82$ mg per tablet
7	24.37	25.58	24.85	24.93	$RSD_R = 3.25\%$
8	23.87	24.16	24.73	24.25	

2.7. Determination of sodium fluoride in a stomatological gel

Samples of 1.0000 g of gel were placed in a 100 ml calibrated flask and diluted to the mark with distilled water. Different volumes of this solution (2–6 ml for spectrophotometry and 5–10 ml for potentiometry) were diluted to 100 ml and the appropriate procedures described in Sections 2.4.2. (spectrophotometry) and 2.5 (potentiometry) were carried out. The results are given in Table 5.

2.8. Determination of sodium fluoride in a toothpaste

Samples of 1.0000–10.0000 g of toothpaste were stirred in a beaker with 50 ml of distilled water and the suspension was transferred to a 100 ml calibrated flask. Determination of the fluoride was achieved by direct measurement of the potential (as in Section 2.5) or by measurement of the absorbance after microdiffusion (see below). After the diffusion technique was complete, the lid was washed 4–5 times, with 1 ml of distilled water

Table 5
Fluoride determination in Elmex gel (Ciba International Ltd., Switzerland)

Spectrophotometric method			Potentiometric method			
Sample	NaF (%)	% vs. \bar{x}	Sample	Run (NaF (%))		
				1	2	3
1	3.20	102.09				
2	2.74	80.75	1	3.24	3.39	3.36
3	3.26	104.97	2	3.24	3.29	3.36
4	3.21	102.28	3	3.41	3.54	3.41
5	3.24	104.04	4	3.41	3.46	3.38
6	3.28	105.85	5	3.16	3.23	3.36

$\bar{x} = 3.15\%$	$\bar{x} = 3.35\%$
$n = 6; \alpha = 0.95; t_{\alpha} = 2.57$	$n = 15; \alpha = 0.95; t_{\alpha} = 2.14;$
	$A = 3.35 \pm 0.025\%$
Repeatability	Repeatability
$s_r = 0.205 (\%)$	$s_r = 0.094 (\%)$
$RSD_r = 6.52\%$	$RSD_r = 2.82\%$
$A = 3.15 \pm 0.21\%$	
	Reproducibility
	$s_R = 0.098 (\%)$
	$RSD_R = 2.92\%$

each time, and the washings were transferred to a 25 ml calibrated flask which contained 10 ml of solution B; the solution was diluted to the mark with distilled water, and the procedure described in Section 2.4.2. was carried out. The results are given in Table 6.

2.8.1. Microdiffusion technique (after Hanocq [1])

In a Petri dish (prepared as in Section 2.1) were placed 2 ml of suspension and 4 ml of HClO_4 70% (w/w); the mixture was quickly covered with the lid and kept in a drying oven at 60–65°C for 6½ h.

2.9. Validation of the method

In order to validate the method the linearity, accuracy and precision (repeatability and reproducibility) of the analytical results have been evaluated [10]. The results of the statistical evaluation are given in Tables 1–6

3. Discussion

As one can see from Table 1 the Lambert–Beer law was followed in the concentration range 10–80 $\mu\text{g NaF ml}^{-1}$; the correlation coefficient of the straight line was -0.99319 . It is interesting that for the spectrophotometric method, the value of the absorbance decreases while the F-concentration increases; this explains the negative value of the correlation coefficient. A semilogarithmic curve describes the variation of the potential with the F-concentration; for the potentiometric method, the linear range is 10^{-5} – 10^{-1} M (0.4 $\mu\text{g ml}^{-1}$ –4.2 mg ml^{-1}) which is much larger than the range 2.5×10^{-4} – 2×10^{-3} M (10–80 $\mu\text{g ml}^{-1}$) for the spectrophotometric method.

The results of the determination recalculated in both cases, by interpolation on the corresponding regression standard curves (Tables 1 and 3), present good reproducibility and demon-

Table 6
Fluoride determination in Colgate Dual Fluoride toothpaste (Colgate Palmolive Romania Ltd.)

Spectrophotometric method		Potentiometric method				
Sample	NaF (mg per 100 g)	Sample	Run, NaF (mg per 100 g)			
1	88.00	1	101.85	103.08	108.36	105.36
2	104.00	2	99.98	94.89	103.52	90.32
3	115.00	3	88.68	88.32	96.56	90.94
4	96.72	4	84.66	81.66	97.94	92.60
5	101.43	5	97.28	94.59	93.07	95.99
6	98.99	6	79.16	78.53	99.07	98.26
$\bar{x} = 100.69$ mg per 100 g		$\bar{x} = 94.36$ mg per 100 g				
$n = 6; \alpha = 0.95; t_{\alpha} = 2.57$		$n = 24; \alpha = 0.95; t_{\alpha} = 2.06$				
Repeatability		Repeatability				
$s_r = 8.89$ (mg per 100 g)		$s_r = 7.57$ (mg per 100 g)				
RSD _r = 8.83%		RSD _r = 8.02%				
$A = 100.69 \pm 3.81\%$		Reproducibility				
		$s_R = 8.1$ (mg per 100 g)				
		RSD _R = 8.59%				

strate that the accuracy of the proposed method complies with the FR Xth edition recommendations for spectrophotometric methods.

The most serious interference problems, as can be seen in Table 2, are generated by a series of organic anions with complexing properties and by phosphate, which is a usual component of toothpaste. Aqueous suspensions of several sparingly soluble ingredients present in tablets of the drug as well as toothpaste have been studied: CaCO₃, MgCO₃, MgO and magnesium stearate. The magnesium stearate is an excipient, present in nearly all tablets, which does not interfere with the spectrophotometric method for fluoride. In contrast, the combinations of calcium and magnesium, with their low water solubility, can create problems in the case of toothpaste, where they can be found in large amounts together with NaHCO₃ and phosphates; this means that the fluorides have to be separated by different procedures.

Very good results have been obtained in the determination of NaF in Osofluor tablets containing 25 mg NaF per tablet (ICCF Cluj-Napoca) (Table 4). The values obtained in the spectrophotometric determinations are comparable to those obtained by potentiometry with respect to accuracy as well as precision (repeatability and repro-

ducibility); the proposed method is much faster and more convenient than the compendial method.

Good results have been obtained in the determination of fluoride in Elmex gel (Ciba International Ltd., Switzerland) (Table 5); the sensitivity, accuracy and precision of the spectrophotometric method are comparable to those of the potentiometric method.

The determination of fluoride in toothpaste, Colgate Dual Fluoride (Colgate Palmolive Romania Ltd.), after separation by the microdiffusion technique, led to results with statistical parameters that are less favourable but which can be improved (Table 6).

4. Conclusions

An indirect spectrophotometric method is proposed for the determination of fluoride at concentrations of 10–80 $\mu\text{g ml}^{-1}$ with 95% confidence limits of $\pm 3\%$; the accuracy complies with the FR Xth edition recommendations.

The method has been used successfully to determine directly NaF in water, tablets and stomatological gels and with less favourable results in

toothpaste; the results have been validated and compared to those obtained by the potentiometric method with a fluoride-selective electrode.

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