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THE STATE OF FLUORINE IN DENTIFRICE SYSTEMS

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Using ^{18}F in an adsorption and desorption technique and by means of chemical F analyses, it has been possible to establish a distribution pattern for F in dentifrice systems.

When a dentifrice is dispersed in water, parts of the F remain in the dentifrice in a) inactive form, or b) adsorbed form; parts are in solution, as c) ionic F^-, d) undissociated HF, or e) as complexed F; parts are present in the enamel surface presumably as f) CaF_2, or g) as $Ca_5(PO_4)_3F$, or h) as adsorbed complexes. Some F is possibly acquired by the enamel by means of i) exchange processes.

The results obtained compare reasonably well with theoretical expectations, indicating that the deposition of F in the enamel is a matter of physico-chemical *solubility.* The solubility product of fluorapatite seems to be a governing principle. No relationship was established between the fluoride ion concentrations (activities) and the uptake of F in the enamel. It was suggested that not only the chemical composition of a dentifrice but also its physical properties, are of importance for the behaviour of F in dentifrice systems.

An acidulated, NaF-containing dentrifrice has been found to possess superior parametric values as compared to Na_2PO_3F-containing dentifrices. A neutral, NaF toothpaste containing methylmetacrylate and liquid paraffin, retained 27 % of its F-content in the dentifrice phase whereas only 4 % was deposited in the enamel powder.

The cariostatic action of F-containing dentifrices is primarily dependent upon the availability of the fluorine for the enamel surface. This being the case two main problems are posed. First, fluorine must be liberated from the dentifrice under oral conditions. As shown by *Ericsson* (1961a), dentifrice ingredients such as carboxymethylcellulose, soap, lauryl sulphate, and glycerol may combine with the fluorine thereby presumably reducing the clinical effect. Above all, Ca-containing abrasives have a strong affinity for F. This difficulty has largely been overcome by avoiding such abrasives altogether, or by employing Ca-free metaphosphate as an abrasive, or by using

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combinations of F-compounds and abrasives which are reasonably compatible, e.g. SnF_2—Ca-pyrophosphate, Na_2PO_3F—Ca-carbonate.

Secondly, the F liberated from the dentifrice must be fixed unto the enamel and incorporated in the enamel apatite. It should be stressed that the fixation and the incorporation are separate and independent processes, which are influenced by the F-compound employed and the general composition of a toothpaste.

This paper reports studies on these two problems by means of ^{18}F and by chemical analyses of dentifrice systems.

MATERIAL AND METHODS

Seven F-containing dentifrices available on the Norwegian market were labelled I, II, III, IV, V, VI, and VII. Data relating to the chemical composition have been assembled in Table I. The amounts of F in the tubes as sold vary a great deal, although the F concentration is the same in all the brands, namely 0.1 %. Dentifrice III contains 0.025 % F.

With an exception for dentifrice I, the toothpastes under investigation also are sold in F-free varieties. After the study was well under way, information was provided by the manufacturers that the F-free varieties of dentifrices V and VII have a somewhat different chemical composition from the F-containing types, apart from the F content. The consequencies thereof will be discussed below.

The positron emitting radioactive ^{18}F was counted in a well-type scintillation detector with the samples in plastic tubes. The activity at the time of counting was of the order of 40,000—60,000 cpm/0.5 ml. The counts were corrected for background and decay (half-life 110 minutes).

The low-carrier radioisotope was added to the NaF-containing dentifrices. For the Na_2PO_3F-containing dentifrices monofluorophosphate was synthetized and labelled according to the procedures of *Ericsson* (1961b).

The fluoride ion activity was assessed by the Orion F^- electrode, with or without addition of acetate or citrate according to *McCann* (1968a). Total F was determined after separation by diffusion (*Taves*, 1968). A modification of this method enabled $PO_3F^=$ ions to be hydrolysed to F^- and orthophosphate.

Calcium was determined by atomic absorption. The pH was measured on the filtered (Munktell's Swedish Filter Paper No. OOH) and/or centrifuged solutions.

The adsorption and desorption experiments were performed under stirring in a waterbath held at a temperature of 37°C. The other experiments took place at room temperature in a rocking device.

Table I

Data relating to F-containing dentifrices

				Dentifrice			
Property	I	II	III	IV	V	IV	VII
Volume or weight of one tube as sold	90 ml	60 gm	100 gm	140 gm	140 gm	65 ml	75 gm
Density	1.10	1.34	1.35	1.52	1.38	1.37	1.38
F-compound in one tube, mg	219.0	132.7	55.3	1060.6	1060.6	674.3	567.4
		NaF			Na_2PO_3F		
F-amount in one tube, mg	99	60	25	140	140	89	75
Abrasive	None	Silica compound	Silica compound	$(NaPO_3)n$, $CaHPO_4$	$(NaPO_3)n$	?	$CaCO_3$
Detergent	Lauryl sulphate	None	None	Lauryl sulphate	Lauryl sulphate	?	Lauryl sulphate
Antienzymatic agent	None	None	None	Lauroyl sarcosinate	None	?	None
Binder	CMC*	Glycerol	Glycerol	Unspecified humectant	CMC*	?	CMC*, glycerol
Reaction in solution	Neutral	Acid	Acid	Neutral	Neutral	Alkaline	Alkaline
Special ingredients	Methyl metacrylate, liquid paraffin	Tartaric acid	Tartaric acid	Irish moss, benzoate, alumina	None	?	None

* CMC = carboxymethyl cellulose

RESULTS

Adsorption of F to the dentifrices

One litre of deionized water and 11.05 mg NaF or 37.9 mg Na_2PO_3F, both corresponding to 5 mg of F, were combined in plastic flasks. The radioactive isotope was incorporated as described above, and the T_0 countings were taken.

Following this procedure 5 grams of F-free dentifrice were added to the flasks, the dentifrices I and II into the NaF solutions, and the dentifrices IV, V, VI and VII into the Na_2PO_3F solutions. Samples were removed for counting at intervals of 1, 3, 5, 10, 15, 20, 25, 30, 40, and 100 minutes.

Separating out the solid ingredients by means of filtration proved to be successful only in the case of dentifrice II, and partially so in the case of IV. For dentifrice I the filtration was ineffective. Centrifugation for two 10 minute periods at 4,000 rpm led to a marked improvement, although the supernatants were still somewhat cloudy. This especially applied to dentifrice I. The amounts of F assumed to be in solution are therefore somewhat too high for the dentifrices I, V, VI, and VII, but probably of the correct order for the dentifrices II and IV.

In an effort to determine if NaF and Na_2PO_3F have different adsorbing properties, dentifrice II was slurried in a $Na_2PO_3{}^{18}F$ containing solution.

Dentifrice VI is also sold in a F-free variety stated to contain Ca, probably in the form of calcium diphosphate. This dentifrice was included in the experiments, being labelled »VI-Ca».

The dentifrices IV, V, VI, and VII are hardly different among themselves (Table 2, second column). Attention must be given to the fact that the dentifrices V and VII are reported to contain about 40 % dicalcium phosphate.

The addition of a calcium compound to F-free dentifrice VI does not seem to affect the adsorption of fluoride from Na_2PO_3F appreciably.

It seems safe to conclude that dentifrice II adsorbs less fluoride, and dentifrice I more fluoride than the other toothpastes. *Birkeland* (1971) has reached the opposite conclusion. However, the fluoride ion concentration in slurries of dentifrices I and II cannot possibly be 938 ppm and 683 ppm, respectively, when 0.1 gm of toothpaste has been added to 25 ml of solution.

In the case of dentifrice II the adsorption of F from Na_2PO_3F is more pronounced than the adsorption from NaF (6 % and 1.3 %, respectively). However, the fact that the dentifrices I and II, both containing NaF, reveal the greatest difference, indicates that the nature of the added F-salt is not the decisive factor for the retention of F in a toothpaste.

Desorption of F from the dentifrices

In these experiments fluorine was leached from F-containing dentifrices into the slurry to which had been added low-carrier ^{18}F or labelled $Na_2PO_3{}^{18}F$. In other respects the experimental conditions are exactly the same as in the adsorption experiments.

We may conceive of these dentifrice systems as consisting of three compartments (Fig. 1). The ^{18}F may be present in the solution (A), remain in the dentifrice in an exchangeable form (B), or remain in the dentifrice in a non-exchangeable form (C). By a desorption approach the ^{18}F will be distributed

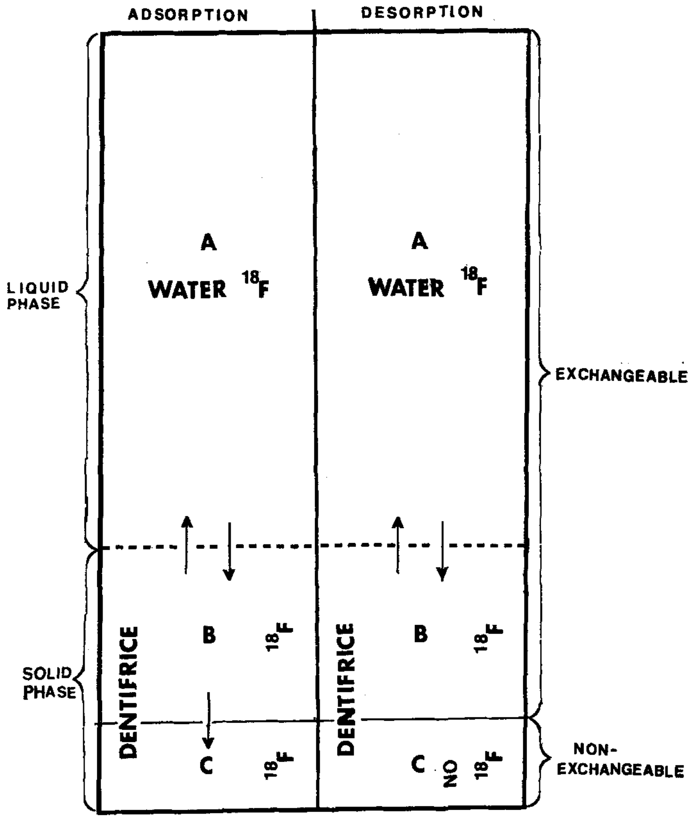

Fig. 1. Schematic representation of the distribution of ^{18}F in adsorption and desorption experiments.

between compartments A and B (»the exchangeable pool»), whereas compartment C will acquire no ^{18}F and thus is not affected.

If the F incorporated in the dentifrice is freely exchangeable, the per cent activity in solution would be independent of whether equilibrium is approached from below or from above.

If part of the F in the dentifrice is bound in some non-exchangeable way, the per cent activity in solution would be higher in desorption than in adsorption experiments.

The third possibility, i.e. the per cent activity in solution is lower in desorption than in adsorption experiments, must mean that incorporating F in a dentifrice in some way increases its adsorbing properties. Table II (third column) shows that this third possibility does not apply.

Table II

Per cent ^{18}F activity in dentifrice-water systems
The figures are the means of at least 7 values with a maximum S.D. of 2.1 %

		% ^{18}F in supernatant		% distribution of ^{18}F		
				Exchangeable F		Non-exchangeable F
Dentifrice,	F-compound	Adsorption approach*	Desorption approach**	In slurry supernatant	In dentifrice phase	In dentifrice phase
I.	NaF	73.0	88	73	10	17
II,	NaF	98.7	98	99	1	0
II,	Na$_2$PO$_3$F	94.0	—	—	—	—
III,	NaF	98.7	100	99	1	0
IV,	Na$_2$PO$_3$F	88.4	90	88	10	2
V.	Na$_2$PO$_3$F	87.1	93	87	7	6
VI,	Na$_2$PO$_3$F	91.6	94	91	6	3
VI-Ca,	Na$_2$PO$_3$F	90.9	—	—	—	—
VII,	Na$_2$PO$_3$F	88.0	89	88	11	1

* ^{18}F labelled F-compound (≈ 5 mg F) added to solution with which 5 gm of F-free dentifrice was equilibrated.

** Na^{18}F or Na$_2$PO$_3$^{18}F added to solution in equilibrium with 5 gm fluoridated dentifrice (≈ 5 mg F).

According to the calculated distributions of ^{18}F in Table II, a substantial part of the F in dentifrice I, and smaller amounts in the Na$_2$PO$_3$F dentifrices, are present in non-exchangeable form. It should be noted that the F-free varieties of dentifrices V and VII are reported to contain $CaHPO_4 \cdot 2H_2O$, which would have the effect of reducing the adsorption activities thereby leading to an overestimation of non-exchangeable F.

The observed differences do not seem to be related to the nature of the two F-salts employed. An explanation must primarily be sought in the compositional formulas of the dentifrices, where especially the acid reaction of dentifrices II and III, and the special ingredients of dentifrice I attract attention (Table I).

Adsorption of dentifrice fluoride to pulverized dental enamel

Equilibrating solutions were prepared by adding the radioisotope to 1 litre of deionized water. The activity, determined at time zero, was 78,000 cpm/ml. Thirty ml were pipetted into vials each containing 2 gm of the dentifrice to

Table III

Comparison of activity values after filtration and centrifugation
Two grams of dentifrice equilibrated in 30 ml water for 30 minutes. 78,000 cpm added to each ml initially

Dentifrice, F-compound	Filtration	Centrifugation	Difference %
I, NaF	76,700 cpm/ml	73,300 cpm/ml	4
II, NaF	75,000 cpm/ml	73,600 cpm/ml	2
III, NaF	73,200 cpm/ml	70,000 cpm/ml	4
IV, Na_2PO_3F	86,700 cpm/ml	69,000 cpm/ml	20
V, Na_2PO_3F	76,700 cpm/ml	60,000 cpm/ml	22
VI, Na_2PO_3F	82,000 cpm/ml	67,000 cpm/ml	18
VII, Na_2PO_3F	75,000 cpm/ml	63,000 cpm/ml	16

Arithmetic mean and standard error of filtration values: 77,900 ± 1800 cpm/ml

be tested. The fluoride in the dentifrices was then leached out by agitating the vials for 30 minutes.

Portions of the slurries were filtered or centrifuged. The results of the activity determinations in the filtrates and supernatants, all corrected to time zero, are given in Table III. The mean of the filtration values, 77,900, S.E. 1,800 cpm, indicates that filtration is not effective in separating out slurried dentifrices.

In general, more fluoride was centrifuged out in these experiments than in the centrifugation experiments of Table II. This finding must evidently be explained by the fact that different solid/solution ratios were employed (5 gm/l in Table II versus 2 gm/30 ml in the present case).

The one exception is dentifrice I. The 27 % adsorption of dentifrice I in Table II was obtained after repeated centrifugations, whereas in the present case dentifrice I was centrifuged just once.

Duplicate samples of the equilibration solution were taken out for calcium determination, and another duplicate 4 ml portion was added to round-bottomed counting vials containing 100 mg of pulverized enamel. These enamel powders were taken from the same batch with a standardized particle size between sieve 24 and sieve 40.

After equilibrating for 30 minutes under continuous agitation, the vials were centrifuged, and 2 ml of the supernatant transferred to another set of plastic tubes for counting. The pH and the calcium content were determined.

The residue enamel was washed with 3×4 ml deionized water before the activities were measured. It had previously been ascertained that the enamel

Table IV

Data from equilibrating enamel powder in supernatants from dentifrice slurries
100 mg enamel powder equilibrated in 4 ml supernatants for 30 minutes

		Calcium			
Dentifrice, F-compound	Final (Ca) mM	dissolved μg	precip. μg	% ^{18}F counts in enamel powder	pH in supernatant
II, NaF	3.375	532	—	17	3.75
III, NaF	2.875	452	—	14	3.85
V, Na_2PO_3F	0.100	8	—	12	6.20
IV, Na_2PO_3F	0.250	8	—	11	6.45
VII, Na_2PO_3F	2.000	—	80	9	8.90
VI, Na_2PO_3F	4.200	—	248	7	9.10
I, NaF	0.150	4	—	6	6.45

containing tubes gave a satisfactory geometric balance during the counting procedure. The total counts in the 4 ml of equilibrating solution and in the 100 mg of enamel powder, agreed closely to the number of counts added.

In Table IV the dentifrices have been arranged in descending order according to the per cent ^{18}F adsorbed into the enamel. It is suggestive that the uptake of ^{18}F increases with decreasing pH, the one exception being dentifrice I.

Since the radioisotope has been added as low carrier NaF in these experiments, the uptake values in principle only reflect the movement of the F^- ion and not necessarily the behavior of $PO_3F^=$ and similar complex ions. Therefore, the possibility exists that the uptake of total fluoride has been underrated as far as the Na_2PO_3F containing dentifrices are concerned.

The pre-equilibrated solutions of dentifrices I, II, III, and V contained trace quantities of calcium which may stem from impurities or may be referred to the uncertainties involved in analyzing for these minute amounts. Some of the calcium reported to be present in dentifrices IV and VII (Table I), and apparently also in dentifrice VI, has been leached out into the equilibrating solutions. In the case of dentifrices VI and VII substantial amounts of calcium were reprecipitated.

The F fractions in the liquid phase of dentifrice systems

Approximately 0.4 grams of the dentifrices were suspended in 40 ml of deionized water and agitated for one hour. After centrifugation at 13,000 rpm

Table V

F fractions in ultracentrifuged dentifrice supernatants
Values in ppm units

Dentifrice, F-compound	pH in supernatant	F-electrode in H_2O (F^-)*	F-electrode in Citrate	F-electrode in Acetate	Diffusion and hydrolysis. Total F
			Dissociable F		
I, NaF	6.8	11.5	12.0	13.5	11.3
II, NaF	3.7	5.6	8.6	8.7	9.6
III, NaF	3.7	1.4	2.9	2.3	2.9
IV, Na_2PO_3F	7.3	0.7	0.8	0.7	9.9
V, Na_2PO_3F	6.4	0.8	0.9	0.9	11.5
VI, Na_2PO_3F	9.2	1.6	1.8	1.9	8.1
VII, Na_2PO_3F	9.0	1.9	2.0	2.2	8.0

* The fluoride ion concentration is put equal to the fluoride ion activity.

for 20 minutes the pH was determined and ten parts of the supernatant were mixed with one part of either H_2O, or acetic acid buffer, or citrate acid buffer.

In the H_2O solutions the F electrode measures the actual F^- activity directly. In the buffered systems the electrode is assumed to estimate the total concentration of originally dissociated and undissociated fluoride. Lastly, total F including complex forms such as $PO_3F^=$, may be determined after diffusion and hydrolysis.

Table V shows that the total F concentrations in the NaF containing dentifrices I, II, III are essentially the same whether the determinations are carried out by diffusion and hydrolysis or by means of the F^- electrode in buffered solutions. As would be expected, the F^- electrode reading in H_2O is only about half of that of the buffered solutions in the case of the acid II and III dentifrices. Note that dentifrice III only contains 250 ppm fluoride (Table I).

The absolute amounts of F involved in these experiments were determined in three ways: by assessing the amounts in solution from the diffusion-hydrolysis values of Table V, by carrying out chemical analyses of the dentifrices themselves (diffusion-hydrolysis), and by calculating from the reported F content of the dentifrices.

Table VI indicates that the F concentration of a dentifrice may vary considerably around the theoretical content of 0.1 % (for dentifrice III the theoretical content is 0.025 %). These chemical data confirm the earlier

Table VI

F analyses of the dentifrice systems
Approximately 0.4 gm of dentifrice added to 40 ml of solution. Ultracentrifugation

	F-amount added			
Dentifrice, F-compound	from dentifrice composition* mg	from chemical analysis mg	F-amount in 40 ml solution mg	Per cent F dissolved
I, NaF	0.4146	0.5783	0.4520	78
II, NaF	0.4140	0.4037	0.3840	95
III, NaF	0.0996	0.1052	0.1160	~100
IV, Na_2PO_3F	0.3966	0.5215	0.3960	76
V, Na_2PO_3F	0.4135	—	0.3600	(87)
VI, Na_2PO_3F	0.4012	0.4694	0.3240	70
VII, Na_2PO_3F	0.3922	0.3914	0.3240	81

* 0.025 % F in dentifrice III, 0.1 % in the others.

radioactive findings that only small amounts of fluoride remain attached to the acid dentifrices II and III. Approximately 20 % of the fluoride in dentifrice I is not being leached out. For the Na_2PO_3F containing dentifrices considerably more F is centrifuged out by the ultracentrifugation employed in the experiments of Table VI than by the less rigorous separation used for the data of Tables II and III.

DISCUSSION

From the data presented in Tables II, IV, and V it is possible to draw up a rough distribution pattern of the F in the tested dentifrice systems. In Fig. 2 the dentifrices have been arranged in the order of the F uptake in the enamel powders, which presumably would bear some relationship to the efficiency of the toothpastes as fluoridating vehicles.

F remaining in the dentifrices

It has been amply demonstrated that the fluoride ion will react with and be inactivated by Ca-containing abrasives such as $CaCO_3$, $CaHPO_4 \cdot 2H_2O$, and $Ca_2P_2O_7$, possibly through the formation of CaF_2. None of the NaF containing dentifrices (I, II, III) contain such Ca compounds.

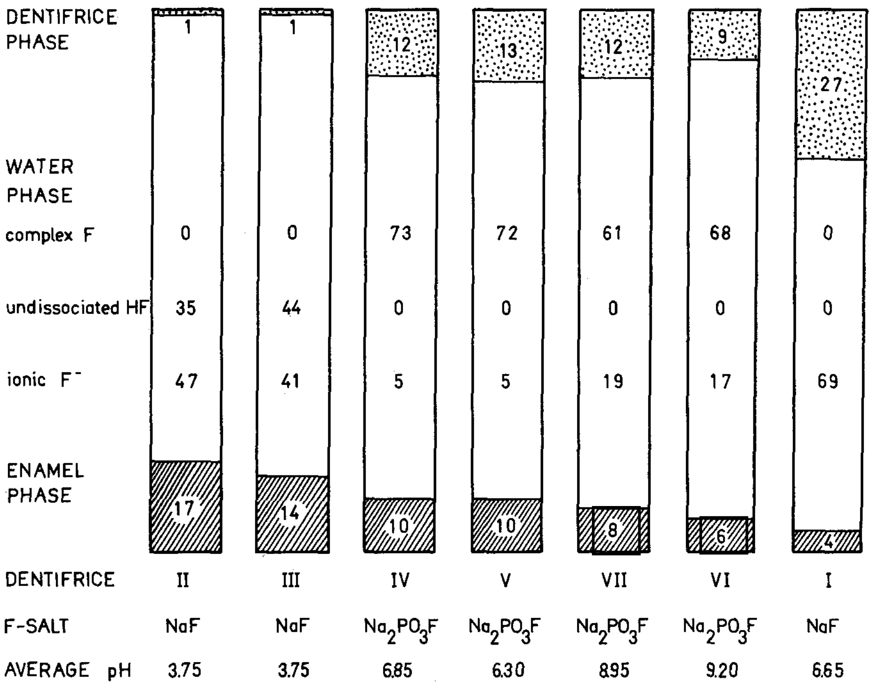

Fig. 2. Distribution of ^{18}F in dentifrice systems. Per cent values.

Complex ions such as $PO_3F^=$ are much less reactive than F^-, and would not be expected to react to any large extent with $(NaPO_3)_n$ which is an ingredient of dentifrices IV and V. The calcium carbonate of dentifrice VII would probably combine with monofluorophosphate only to the extent that the $PO_3F^=$ ion undergoes a hydrolytic cleavage (*Ericsson*, 1961a). It should be noted that the non-exchangeable F of Table II har probably been somewhat overestimated as regards dentifrices V and VII (*vide supra*).

The fact that heating tricalcium phosphate and calcium pyrophosphate substantially reduces the retention of F both from NaF and Na_2PO_3F (*Ericsson*, 1961a), proves that the inactivation and the adsorption to the dentifrice are not simply questions of a chemical union, e.g. formation of CaF_2. Heating will undoubtedly influence the crystal size and thereby the specific surface with definite consequences for processes like chemisorption and physical adsorption. The efficiency of a fluoridated dentifrice therefore cannot be evaluated in terms of its chemical composition alone.

The most interesting observation made is the very high retention of fluoride in dentifrice I, especially as compared to the similar NaF-containing dentifrices II and III. The latter dentifrices consist for a greater part of silica compounds (Table I). *Ericsson* (1961a) found that silica powder (SiO_2) retained about 4—5 % of added fluoride and silica gel (H_2SiO_3) around 85—86 %. This difference indicates that the physical state, and not just the chemical nature of the additives, is of importance for retaining F in a dentifrice.

In the case of dentifrice I, even the most generous allowance for combination of F to the carboxymethyl cellulose, the lauryl sulphate and the acrylic particles present (Table I), cannot explain the 27 % retention. *Koch* (1967) reported that some 4 % of the added F could be bound to the acrylic particles.

From the experiences of the present study it seems that the acrylic particles and possibly the liquid paraffin of dentifrice I add to the viscosity of the system in such a way as to act as diffusion-limiting barriers for the free movement of the fluoride ion. From this point of view the distinction between exchangeable F and non-exchangeable F would be somewhat arbitrary, since these two fractions might reflect different rates of diffusion, the ions in the »inactive» part being buried deeper in the gel than the ions of the »adsorbed» part.

This concept of the role played by the physical consistency for a mechanical entrapping of the F, would fit in with the observation that dentifrices II and III (1 % retention) could easily be prepared to give water-clear solutions. The dentifrices IV, V, VI, and VII (retention figures from 9 % to 13 %) tended to remain somewhat cloudy, whereas dentifrice I (27 % retention) retained its creamy appearance in spite of undergoing repeated separating procedures.

Birkeland (1971) reported activity values of 1620 ppm and 630 ppm F^- in the water phase of dentifrices I and II, respectively. However, these values would correspond to activity coefficients far greater than unity as calculated from the fluoride ion concentrations he found. The difficulties involved in employing the F^- electrode directly in a dentifrice are considerable and do not seem to have been solved.

F in solution

The activity coefficients have in the present dilute systems been put equal to unity so that no distinction is made between »activity» and »concentration».

With a view to influencing the enamel surface it would theoretically be advantageous that the solubilized F should be present as the fluoride ion, F^-.

However, Fig. 2 does not indicate any relationship between the amount of ionic fluoride and the uptake of F in the enamel powders.

The chemical state of solubilized F is dependent upon three factors: a) the nature of the compounds itself, b) the pH, and c) the ionic strength of the solution.

a): Monofluorophosphate seems largely to be present as $PO_3F^{=}$ in the solutions, the per cent figures in Fig. 2 ranging from 61 to 73. In the NaF systems no complexing seems to have taken place. From this point of view, the addition of NaF to a dentifrice would be preferable to the addition of Na_2PO_3F.

b): The partition of solubilized F is clearly pH dependent. At a pH of 6.45—6.80 (dentifrice I) all the fluoride is ionized, whereas at a pH of 3.70—3.80 (dentifrices II and III) only about half of the added fluoride is present in dissociated form. In the Na_2PO_3F systems a comparison of dentifrices IV and V versus dentifrices VI and VII indicates that about 3—4 times more ionized fluoride is present at a pH of 8.90—9.20 than at a pH of 6.20—7.30. For the purpose of producing F^- ions, a neutral reaction would therefore seem to be preferable in a NaF dentifrice and a alkaline reaction in a Na_2PO_3F dentifrice.

c): In general, an increased ionic strength will lead to lower pK values, and thereby to increased ionic concentrations. At the same time the activity coefficients will decrease entailing relatively lower ionic activities in the dentifrice systems. It is impossible to decide what the net results of these opposing processes will be.

The above considerations have little impact on the present, very dilute solutions. Under *in vivo* conditions, however, the partition in the liquid phase may be significantly different from that given in Fig. 2. Therefore, great caution should be exercised in giving the presented results a practical and clinical application.

It is interesting that Fig. 2 indicates that dentifrice III, with 250 ppm F, gives several times more free ionic fluoride in solution than do the Na_2PO_3F-containing dentifrices with 1000 ppm F. The uptake in the enamel is also greater for dentifrice III. These findings would indicate the possibility that the F content of present-day dentifrices could be reduced without affecting their clinical usefulness.

F in the enamel powders

In principle, the uptake figures of Fig. 2 reflect only the deposition of fluoride ion. The Na_2PO_3F-containing dentifrices IV, V, VI, and VII may therefore have been somewhat under-rated in this respect, since the F would presumably deposit as $PO_3F^=$ in these cases. Moreover, *Grøn et al.* (1971) have shown that Na_2PO_3F is easily washed away by water. On the other hand, these same authors have also found that hydroxyapatite exerts a catalytic action on the hydrolysis of Na_2PO_3F, releasing F^- ions.

The very low uptake from dentifrice I is astonishing, considering the high concentration of ionic fluoride present in this system. *Pohto et al.* (1971) found little difference in fluoride uptake by enamel surfaces from dentifrice I and a commercial $Na_2PO_3F-CaCO_3$ dentifrice, in spite of the many times greater F^- concentration of the former. It may be that the acrylic particles and the liquid paraffin specific to dentifrice I, act as a protective cover on the enamel.

The high per cent of fluoride acquired by the enamel powder from the acid dentifrices II and III is in harmony with earlier findings. *Brudevold et al.* (1963) observed that a low pH furthered the uptake. *Mellberg et al.* (1967) found that deciduous enamel acquired greater amounts of F from an acid gel than from a neutral gel, both containing 1.1 % NaF. *Ericsson* (1961a) proved that this pH dependence of F deposition is not so pronounced for Na_2PO_3F as for NaF. *Grøn et al.* (*loc. cit.*) found that the catalytic property of hydroxyapatite for Na_2PO_3F was more active at a pH of 5.0 than at a pH of 7.0. In the absence of hydroxyapatite, Table V suggests that the splitting of the $PO_3F^=$ takes place more readily at an alkaline reaction (dentifrices VI and VII versus dentifrices IV and V). Even at a neutral pH, however, NaF has been found to be a more efficient source of F for dental mineral than Na_2PO_3F (*Ingram*, 1968). Thermodynamic considerations of the $CaO-CaF_2-P_2O_5-H_2O$ system would explain the relatively inefficient uptake of fluoride by dental enamel from alkaline solution (*Duff*, 1971).

Ericsson (1963, 1967), *Ingram* (1968), and *Simpson* (1968) have indicated that monofluorophosphate may be incorporated as such in the apatite lattice. Another explanation for the initial deposition and the eventual incorporation of F might be sought in the precipitation of CaF_2 or $Ca_5(PO_4)_3F$.

Diagram 1 represents a plane cut through a three-dimensional model of the solubilities of some Ca-phosphates. The ions involved (Ca^{++}, $PO_4^{\equiv}$, F^-) are at their stoichiometric concentrations, and the pH is the free variable. It is seen that the $S.P._{CaF_2}$ is, in general, determinant for the deposition at pH values below 5.5, and the $S.P._{Ca_5(PO_4)_3F}$ for systems with pH's above 5.5.

A rough estimation of the ionic products of CaF_2 and $Ca_5(PO_4)_3F$ may be

Table VII

Estimated ionic products of calcium fluoride and fluorapatite

Dentifrice F-compound	Ca mM	P* mM	F^- mM . 10^3	pH	p(I.P.) CaF_2	p(I.P.) $Ca_5(PO_4)_3F$	Uptake in enamel**
II, NaF	3.375	1.995	1.645	3.75	14.0	53.7	17 %
III, NaF	2.875	1.695	0.360	3.80	15.4	54.0	14 %
IV, Na_2PO_3F	0.250	0.030	0.275	6.45	16.7	57.4	10 %
V, Na_2PO_3F	0.100	0.030	0.275	6.20	17.1	60.1	10 %
VII, Na_2PO_3F	2.000	—	0.665	8.90	14.4	—	8 %
VI, Na_2PO_3F	4.200	—	0.595	9.10	14.8	—	6 %
I, NaF	0.150	0.015	2.415	6.45	16.1	63.5	4 %

* 0.6 × dissolved calcium

** Per cent of total amounts of F added.

made from the equilibration experiments with the powdered enamel. The Ca^{++} and the pH values are taken from Table IV directly. Assuming that total P is equal to 0.6 × dissolved Ca, the concentration of trivalent phosphoric groups would be:

$$(PO_4^{\equiv}) = \frac{K_2K_3}{(H^+)^2 + (H^+)K_2 + K_2K_3} \cdot 0.6 \times \text{Ca dissolved,}$$

where $K_2 = 10^{-7.165}$ and $K_3 = 10^{-12.180}$ (*Bjerrum and Unmack*, 1929).

The concentration of ionized fluoride is calculated from the 2 grams of dentifrice added to the systems and the distribution figures of Fig. 2.

Table VII shows that all the systems have ionic products of CaF_2 which are lower than the accepted values of the solubility product of this salt, namely 10^{-10}—10^{-12}. However, the ionic products of fluorapatite compare favourably with the uptake % in the enamel powders. According to a solubility product of fluorapatite of 10^{-58}—10^{-60}, the acid dentifrices are strongly supersaturated, the dentifrices IV and V lie just on the borderline of saturation, whereas dentifrice I is undersaturated. It is not possible to calculate any ionic product of $Ca_5(PO_4)F$ for the dentifrices VI and VII by the methods employed. It is a possibility that the enamel powders have acquired some fluoride by the mode of an OH^-—F^- exchange.

The question of whether CaF_2 or $Ca_5(PO_4)_3F$ is formed, cannot be unequivocally answered. Under stoichiometric conditions which are seldom realized in practice, the formation of CaF_2 is favoured at pH's below 5.5,

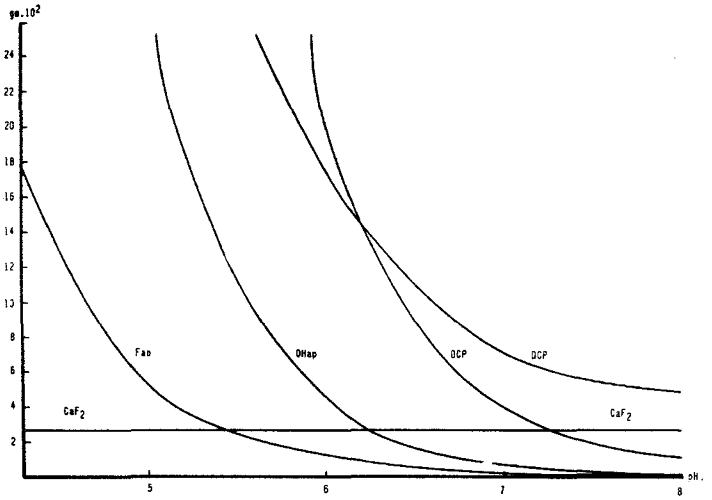

Fig. 3. The calculated solubilities (gm/l) for various calcium phosphates and calcium fluoride. The effect of varying the pH. Ionic strength 0.0.

and the formation of $Ca_5(PO_4)_3F$ above this value (Fig. 3). Structurally, CaF_2 is much less complicated than $Ca_5(PO_4)_3F$, which undoubtedly will influence the kinetics of the formation. *Wei and Forbes* (1968) have observed that CaF_2 is formed when enamel powders are exposed to acid F-solutions for one hour. However, intact enamel exposed to similar solutions for 24 hours, showed only an apatite diffraction pattern.

The possible advantages of an acid reaction for the deposition of fluoride may primarily be referred to the fact the dental enamel loses considerable amounts of calcium and phosphorus at the low pH's. These amounts will furnish an additional supply of ions for the reprecipitation of the more stable F salts, especially when the reaction returns to neutrality. Under *in vivo* conditions, the discomplexing of soluble calcium aggregates at acid reactions will also denote a fresh supply of ions for the precipitation processes. It seems that in the oral cavity the stable phase will eventually be fluorapatite (*McCann*, 1968b).

In vivo applications and relation to clinical studies

The chemical nature and the physical properties of the saliva and the dental plaque will supposedly modify the results obtained in the present simplified systems, so as to lead to distribution patterns quite different from those given in Fig. 2. For one thing, *Ericsson* (1967) has shown that monofluorophosphate is enzymatically hydrolysed in the mouth, releasing F^- ions.

A comparison between laboratory and clinical findings is also hampered by the fact that present-day caries-statistical technics are hardly so refined that true quantitations, and thereby true, clinical comparisons, can be made between the various dentifrices.

The value of Na_2PO_3F as a caries-prophylactic agent when employed in dentifrices, has been reported in many papers (*Finn & Jamison*, 1963; *Naylor & Emslie*, 1967; *Fanning et al.*, 1968; *Frankl & Alman*, 1968; *Mergele*, 1968a and 1968b, *Møller et al.*, 1968; *Thomas & Jamison*, 1968; *Volpe*, 1968). On this basis it may be considered that the figures obtained for dentifrices IV, V, VI, and VII in the present study have some practical-clinical significance; an uptake % of approximately 10 (Fig. 2) would be sufficiently high to make itself appear clinically.

Two propositions would then follow:

a) the dentifrices II and III with an uptake % of 17 and 14, respectively, should be more effective than the Na_2PO_3F dentifrices, and

b) dentifrice I, uptake % of 4, should be less effective.

As to the first proposition, *Torell & Ericsson* (1965) among others have shown that a NaF-containing dentifrice has cariostatic properties. The effectiveness is probably increased by acidifying the paste (*Grøn & Brudevold*, 1967). A dentifrice containing NaF, H_3PO_4, and $(NaPO_3)_n$ has been maintained to possess superior anticariogenic qualities (*Brudevold & Chilton*, 1966; *Peterson & Williamson*, 1968). The same formula applied in solution or in gel has in a number of clinical studies proved to be most successful (*Brudevold et al.*, 1963; *Wellock & Brudevold*, 1963; *Pameijer et al.*, 1963; *Wellock et al.*, 1965; *Szwejda et al.*, 1967; *Bryan & Williams*, 1968; *Cartwright et al.*, 1968; *Horowitz*, 1968, 1969; *Ingraham & Williams*, 1970, *Horowitz & Doyle*, 1971). Several of these authors have claimed that the acidulated NaF solutions are superior to SnF_2 solutions. *Heifetz et al.* (1970) found that dental enamel acquired significant amounts of fluoride from acidulated phosphate-NaF solutions and prophylaxis pastes, whereas this was not the case when stannous fluoride solutions and pastes were employed. The caries prevention action of stannous fluoride itself has been referred to the general acidity of this salt and not so much to any possibly specific effect from the Sn^{++} ion (*Grøn & Brudevold*, 1967).

As a whole, the studies mentioned give some support to the clinical implications of the present laboratory findings, namely that the acid NaF-containing dentifrices II and III show the greatest F-uptake in enamel powders. These dentifrices do not contain H_2PO_3, which would indicate that the acid reaction *per se*, without the presence of added phosphorus, might be of value.

As to the second proposition, i.e. the presumably lesser effectiveness of dentifrice I, this result is definitely at variance with *Koch's* (1967) clinical study of this dentifrice. He reported statistically significant reductions of up to 63.8 %.

However, *Koch's* thesis contains some conspicuous inconsistencies. A few examples:

11 year old children of the baseline examination (his Table 6B) had an average DF-tooth of	11.87
11 year old children who had been using dentifrice I for the preceding two years (Tables 6A and 12A), had an average DF-tooth of at least	11.32
11 year old children who had been using fluoride-free dentifrice I for the preceding two years (Tables 6A and 12A), had an average DF-tooth of at least	13.26

These figures show that children using the F-containing dentifrice I had hardly improved their caries status, whereas children using the fluoride free dentifrice I had 12 % more DF-teeth than children not participating in the study.

	Test group	Control group
The caries increment between the 11. and 12. year after use of dentifrice I for 1 year was	3.80 surfaces	6.58 surfaces
The caries increment between the 11. and 12. year after use of dentifrice I for 2 years was	4.20 surfaces	8.45 surfaces

These figures from Koch's Table 12 show that the annual increment increased approximately 11 % after prolonged use of F-containing dentifrice I, and with 28 % after prolonged use of fluoride free dentifrice I.

It might be argued that the large differences reported by *Koch* are caused by a recorded caries increase in the placebo groups rather than by a caries decrease in the test groups. The tenor of this argument would not be contradictory to the low uptake % observed for dentifrice I in the present study.

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