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FLUORIDES IN DENTIFRICES INVESTIGATIONS USING RADIOACTIVE FLUORINE

by

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There is ample evidence that a considerable part of the caries-preventive effect of fluorine is exerted through an uptake of fluoride ions in the enamel surface. A logical consequence of this concept is the direct local application of fluorides to the tooth surfaces, and it has even been questioned if systemic administration on the whole would be necessary to obtain the caries-preventive effect. It is well known that topical application of especially sodium and stannous fluorides has led to substantial caries reduction, although this effect seems to be rather limited in time.

Incorporation of fluorides in dentifrices has consequently been a lure to many workers in the field of fluorine and caries prevention. Theoretically, this form of administration would provide an ideal, repeated, nonsystemic, practically automatic application of fluorine. However, the clinical results have so far been disappointing with the exception of those obtained with a stannous fluoride-calcium pyrophosphate formula, and even the latter results have been somewhat inconsistent.

There has been speculation as to the cause of the negative results with dentifrices containing sodium fluoride. The fact that topical application of fluoride solutions has been most effective when performed after cleaning and drying the tooth surfaces might point to some hampering factor in the saliva. However, there are many proofs that fluoride is taken up by the enamel in salivary environment also (*Brudevold 1956, Yoon & al. 1958, Ericsson 1958 b*) and that this uptake may considerably increase

the resistance to caries (*Bibby & al.* 1955, *Hayes & al.* 1957, *Backer-Dirks* 1960, and others).

There are thus many indications that the daily use of fluorine in dentifrices would furnish an important protection of the enamel towards caries, provided that the fluorine is in a reactive form and the other ingredients compatible with the fluorine compound. The last-mentioned factors may have been the weak point of many dentifrice compositions which have been tested so far: it is well known that fluoride ions are taken up by calcium phosphate and calcium carbonate, the most commonly used abrasives of toothpastes.

In the investigation to be reported on, the radioactive fluorine isotope F^{18} has been utilized for studies *in vitro* of the compatibility of some fluorine compounds with different components of toothpastes, and the fluorine uptake by enamel surfaces and powdered enamel from water solutions of these fluorine compounds and from experimental pastes of promising composition.

Tests have also been carried out *in vivo* with fluoride-containing toothpastes labelled with F^{18} , in order to throw light on the fluoride retention following ordinary toothbrushing procedures. The tracer technique makes possible rapid and exact determination of the fluorine distribution on a micro-scale, which would only with difficulty or not at all be measurable by ordinary chemical analysis.

This investigation has been carried out partly as a screening for subsequent clinical tests.

THE SELECTION OF FLUORINE COMPOUNDS AND BASIC DENTIFRICE INGREDIENTS FOR THE TESTS

Sodium fluoride was tested as representing free fluoride ions without any specifically active cation.

Stannous fluoride, SnF_2 , was tested for the following reasons. Previous investigations have demonstrated a great uptake of fluoride in the enamel and a strong reduction of the solubility of the enamel on exposure to solutions of this compound *in vitro*. A considerable caries reduction has further been reported from several investigations using either topical application of stannous

fluoride solutions or incorporation of SnF_2 in a dentifrice with a calcium pyrophosphate abrasive. Our tests have been made especially with this abrasive.

The testing of stannous fluoride was somewhat less extensive than that of the other fluorine compounds owing to the great number of previous investigations which have been carried out with this substance (*Muhler* 1955, 1958 a, b, *Harris & Hester* 1959, and others).

Sodium monofluorophosphate, $\text{Na}_2\text{PO}_3\text{F}$, was tested mainly on the following grounds. Fluorine has been reported to be taken up by the enamel from solutions of this compound (*Santesson* 1957). $\text{Na}_2\text{PO}_3\text{F}$ has given caries reduction in animal experiments (*Shourie, Hein & Hodge* 1950, *Zipkin & McClure* 1951) and with topical application in children (*Hawes, Sonnes & Brudevold* 1954). The PO_3F ion is stable in solution at physiological pH values. CaPO_3F is much more soluble than CaF_2 and precipitation as calcium salt is thus not so imminent for solutions of monofluorophosphate as for alkali fluoride solutions. The toxicity of $\text{Na}_2\text{PO}_3\text{F}$ is much lower than that of NaF , when compared on the basis of the fluorine content. Finally, there are indications from preliminary clinical tests that fluorine is taken up by exposed cementum or dentine surfaces from solutions of $\text{Na}_2\text{PO}_3\text{F}$, with a desensibilizing effect on these surfaces.

The dentifrice ingredients tested in this investigation were selected mainly among those currently used in commercial preparations.

RADIOLOGIC METHODS

The production and purification of F^{18} has been described elsewhere (*Ericsson* 1958 a). F^{18} is distilled as SiF_6 , which is taken up in weak alkali or ammonia where practically complete hydrolysis to fluoride ions occurs. NaF and SnF_2 are labelled simply by mixing solutions of these salts with the distillate. The labelling of $\text{Na}_2\text{PO}_3\text{F}$ with F^{18} has been described by *Ericsson* (in press). In principle, it consists of labelling an NaF solution with F^{18} distillate taken up in ammonia, addition of a stoichiometric quantity of NaPO_3 , evaporation, and fusing the two salts to $\text{Na}_2\text{PO}_3\text{F}$ at $700^\circ\text{--}800^\circ$.

Counting was done in a well type scintillation detector with the samples in plastic tubes fitting into the well. Liquid samples were diluted to 2 ml in these tubes before counting.

All countings were timed on the minute and no counting exceeded 5 minutes. Recalculation of the counts to standard time was done using decay lines on semilog paper, drawn to fit the F^{18} half-life of 110 min. The mid-time of each counting period was used as point of departure for recalculation.

The counting error was below 1 per cent except in some cases of especially low uptake in tooth surfaces where it reached a maximum of 2.8 per cent.

THE FLUORINE UPTAKE BY INSOLUBLE ABRASIVES FROM SOLUTIONS OF THE FLUORINE COMPOUNDS

The following tests were carried out with abrasives that have been employed either in dentifrices or in polishing pastes used in dental practice.

In plastic centrifuge tubes were weighed up in duplo:

1. 2 grams of calcium carbonate C.P.
2. 2 " " tricalcium phosphate C.P.
3. 2 " " tricalcium phosphate C.P., heated¹⁾
4. 2 " " calcium pyrophosphate C.P.
5. 2 " " calcium pyrophosphate C.P., heated¹⁾
6. 2 " " sodium metaphosphate, insoluble²⁾
7. 2 " " pumice powder
8. 2 " " silica powder (SiO_2)
9. 2 " " silica gel (powder of precipitated H_2SiO_3)

6 ml F^{18} -labelled 20-mM sodium fluoride solution was pipetted into one of each pair of tubes and in one empty plastic tube (control).

In the same way, 6 ml F^{18} -labelled 20-mM sodium monofluorophosphate solution was pipetted in the duplicate tubes.

¹⁾ Heating was performed at about 900° for ½ hour.

²⁾ This salt was prepared by heating sodium dihydrogen orthophosphate at 315° for two hours.

The tubes were stoppered and shaken for 30 min. After brief centrifugation the supernatants were paper filtered and 0.1 ml aliquots of the filtrates analysed in the scintillation detector.

In a separate series 10-mM freshly prepared, F^{18} -labelled stannous fluoride in 0.1-M acetate buffer pH 5.0 was shaken in the same way with numbers 4, 5, 6 and 8 of the abovementioned abrasives. The resulting pH values were between 4.75 and 5.05, or in the range stated by *Muhler* to be ideal for a stannous fluoride dentifrice from the combined points of view of stability and solubility-decreasing effect on the enamel.

Results

The results are given in Table 1.

Table 1.

Activities remaining in solution after shaking 20-mM solutions of NaF and Na_2PO_3F or 10-mM solution of SnF_2 , all F^{18} -labelled, with different abrasives for 30 min.

Figures denote per cent of control.									
	CaCO ₃	Ca ₃ (PO ₄) ₂		Ca ₂ P ₂ O ₇		NaPO ₃	Pumice	Silica powder SiO ₂	Silica gel H ₂ SiO ₃
			heated		heated				
NaF	67.1	64.0	74.5	48.2	88.7	100.3	91.3	95.7	14.2
Na ₂ PO ₃ F	100.0	68.7	66.9	74.9	91.9	104.0	97.7	103.3	78.8
SnF ₂				21.5	89.2	94.5		88.0	

From sodium fluoride solution the loss of fluoride was very great to silica gel and quite substantial to the calcium salts, although heating of the calcium phosphates made these much less reactive. No fluoride was lost to sodium metaphosphate and very little to anhydrous silica powder. Stannous fluoride lost much more of its activity to unheated calcium pyrophosphate than did sodium fluoride, otherwise about the same.

From sodium monofluorophosphate the loss of fluorine to calcium pyrophosphate and silica gel was less than from sodium fluoride solution.

The most striking result was the complete non-reactivity of sodium monofluorophosphate with solid calcium carbonate.

This was confirmed in repeated experiments, in some of which the concentration of sodium monofluorophosphate was increased up to 1-M. Repeated tests with 20-mM or 10-mM solutions, respectively, also gave essentially unchanged results for the other combinations of fluorine compounds and abrasives. This was also the case with widely varying grades of coarseness of anhydrous silica powder. However, when stannous fluoride solutions were shaken with different commercial preparations of calcium pyrophosphate — with or without previous heating of the abrasive — considerable variations were encountered, indicating a strong influence of the purity and crystal structure on the fluoride uptake.

THE FLUORINE UPTAKE BY ENAMEL POWDER AND INTACT ENAMEL SURFACES FROM SOLUTIONS OF DIFFERENT FLUORIDES

Of fundamental importance seems to be the fluorine uptake by the enamel from water solutions of the fluorine compounds that may be considered for use in dentifrices. This was tested with F^{18} -labelled solutions of sodium fluoride, sodium monofluorophosphate and stannous fluoride; the F^{18} uptake of both powdered and intact enamel was studied.

Comparison of sodium fluoride and sodium monofluorophosphate

First series

The solutions used had the following compositions.

- | | | |
|---|---|---|
| A | { | 20-mM F^{18} -labelled sodium fluoride |
| | { | 10-mM sodium chloride |
| B | { | 20-mM F^{18} -labelled sodium monofluorophosphate |
| | { | 10-mM sodium chloride |

The pH value of both solutions was adjusted precisely to 7.0 with hydrochloric acid or sodium hydroxide.

I. Powdered tooth enamel was prepared according to *Manly & Hodge* (1939). The fraction passing sieve No. 24 but not No. 40 was selected (mesh widths 0.25 and 0.15 mm, respectively). Duplicate 100 mg portions were shaken for 30 min in roundbot-

tomed plastic tubes with 2 ml aliquots of solution A and B, respectively. The tubes were kept standing in order to avoid loss of enamel powder when removing the stoppers.

The tubes were centrifuged, the supernatant suctioned off and the residue centrifuge washed with 3×4 ml distilled water. The activities of the enamel powders were then analyzed.

II. Homologous intact premolar teeth, extracted for orthodontic reasons and stored in thymol-saturated saline, were cleaned with soft brush and water, dried and washed with acetone. The roots and a 1 mm wide strip of the cervical enamel were covered with wax, which was carefully melted on to the enamel to seal along the cervical border.

The crowns of each tooth pair were exposed for one hour, without shaking or stirring, to 0.5 ml of solution A and B, respectively. Ten tooth pairs were thus exposed to the two solutions.

After the exposure the teeth were rinsed in running tap water for 1 minute, the wax was removed and the tooth crowns were separated from the roots with fissure burs. The crowns were then placed in standard position in plastic tubes for counting in the well type scintillator. Aliquots of solutions A and B, which had different F^{18} activities, were also counted and a factor was calculated to be applied to the analyzed F^{18} uptake ratios of tooth pairs and enamel samples in order to give the true ratios, (uptake from Na_2PO_3F): (uptake from NaF).

Results

The fluorine uptake by enamel powder and intact enamel surfaces is given in Tables 2 and 3, respectively.

Table 2.
Uptake of labelled fluorine by powdered enamel from solutions of sodium fluoride and sodium monofluorophosphate.

Activity of enamel powder		Uptake ratio $\frac{Na_2PO_3F}{NaF}$	Factor $\frac{NaF}{Na_2PO_3F}$	Uptake ratio $\frac{Na_2PO_3F}{NaF} \times \text{factor}$
Uptake from NaF	Uptake from Na_2PO_3F			
429,000	66,100	0.157	2.92	0.46
361,000	58,000			

Table 3.

Uptake of labelled fluorine by intact enamel surfaces from solutions of sodium fluoride and sodium monofluorophosphate.

Tooth pairs	Activities of tooth crowns		Uptake ratio	Uptake ratio
	Uptake from NaF	Uptake from Na ₂ PO ₃ F	$\frac{\text{Na}_2\text{PO}_3\text{F}}{\text{NaF}}$	$\frac{\text{Na}_2\text{PO}_3\text{F}}{\text{NaF}}$ x factor 1.68
1	22,500	2,410	0.107	0.180
2	8,890	1,155	0.130	0.218
3	11,450	1,880	0.164	0.276
4	24,900	2,160	0.087	0.146
5	16,400	1,850	0.113	0.190
6	46,000	3,390	0.074	0.124
7	13,500	1,660	0.123	0.207
8	19,000	3,210	0.169	0.284
9	25,200	3,640	0.144	0.242
10	16,500	3,900	0.236	0.396
				M = 0.226

The fluorine uptake by the enamel powder used in the experiment was thus not quite half as great from the sodium monofluorophosphate solution as from the equimolar sodium fluoride solution. The uptake by intact enamel surfaces from sodium monofluorophosphate was on the average not quite one quarter of the uptake by the homologous surfaces from sodium fluoride, without too large variation between tooth pairs.

Second series.

The difference between sodium fluoride and sodium monofluorophosphate was further tested in the following experiment. 1-ml volumes of 20-mM solutions of sodium fluoride and sodium monofluorophosphate, respectively, both labelled with F¹⁸ and kept at different pH values with 0.2-M acetate buffers, were shaken with 100 mg portions of enamel powder (sieve 24—sieve 40) for 30 min. The radioactive solutions were then removed and the enamel powder washed as described above, and the activity taken up by the enamel powder was determined with the scintillation crystal.

Results

The results appear in Fig. 1.

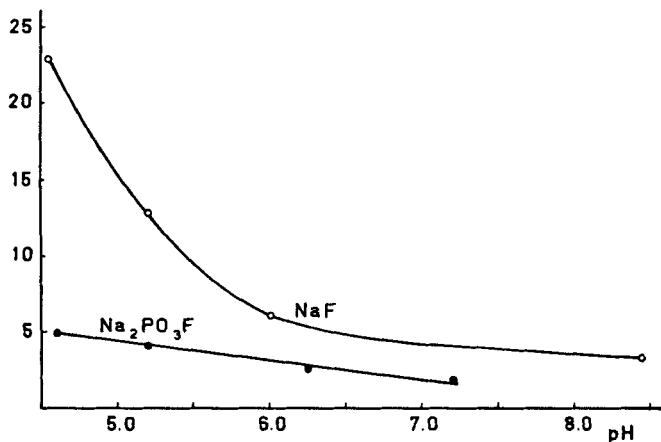


Fig. 1. F^{18} uptake by enamel powder from solutions of labelled NaF and $\text{Na}_2\text{PO}_3\text{F}$, respectively (per cent of solution activity).

It is seen that the enamel uptake of fluorine from sodium fluoride decreases sharply in the pH range 4.5—6.0, while the corresponding uptake from the monofluorophosphate shows only small variation in the same range. This points to some fundamental difference in the mode of reaction with the enamel of the two fluorine compounds. It also indicates that the uptake ratio $\text{Na}_2\text{PO}_3\text{F} : \text{NaF}$ of enamel surfaces might have been still lower than that given in Table 3, if the comparison had been made at a lower pH value.

Comparison of sodium fluoride and stannous fluoride

First series

Tests were also carried out to compare the fluoride uptake by the enamel from solutions of sodium fluoride and stannous fluoride, respectively. The first experimental series was performed with homologous tooth pairs only and not with enamel powder. It was thought that the precipitate forming in the stannous fluoride solution would contain an appreciable part of the F^{18} activity, which would be centrifuged down with the enamel powder and introduce a considerable error.

The sodium fluoride solution was the above-mentioned solution A. The stannous fluoride solution, called C, had the following composition.

$$C \left\{ \begin{array}{l} 10\text{-mM } F^{18}\text{-labelled stannous fluoride} \\ 10\text{-mM acetate buffer pH } 4.5 \end{array} \right.$$

The fluorine content was thus the same as in solutions A and B, and the ionic strength about the same. The pH value was adjusted to 4.5 because this was thought to be about the lowest pH that was practical for a toothpaste, and favourable for the fluoride uptake of the enamel.

Tests with six pairs of extracted homologous premolars were performed as described above with the exception that the roots were not separated from the tooth crowns before counting: it had been found that the wax covering effectively excluded any uptake of radioactive fluorine by the roots.

Solutions A and C had the same original activity. The precipitate forming in C was centrifuged down in a special portion after half the time of the tooth crown exposure, and the activity of the supernatant was determined in order to calculate a factor to correct for the difference between the two fluoride solutions.

Results

The correction factor (Soln. A): (Soln. C) was found to be 1.034, probably involving as much pipetting error as loss of activity of the SnF_2 solution to the precipitate (see below). The formation of the precipitate gave rise to the usual pH decrease of the stannous fluoride solution, in this case to 4.1 during the experiment.

The uptake of labelled fluoride by the enamel surfaces is given in Table 4.

The average ratio 1.07 does not deviate significantly from unity, implying about the same fluoride uptake from the acid stannous fluoride solution as from neutral sodium fluoride.

However, the distribution of the individual values was rather scattered, which might be thought to be due to some slight extraction damage found on some of the teeth on closer examination.

Table 4.

Uptake of labelled fluoride by intact enamel surfaces from solutions of sodium fluoride (A) and stannous fluoride (C). First series.

Tooth pair	Activities of tooth crowns		Uptake ratio $\frac{\text{SnF}_2}{\text{NaF}}$	Uptake ratio $\frac{\text{SnF}_2}{\text{NaF}}$ x factor 1.034
	Uptake from NaF	Uptake from SnF ₂		
1	29,000	18,800	0.629	0.650
2	14,200	19,900	1.401	1.449
3	11,100	19,900	1.793	1.854
4	21,000	24,990	1.190	1.230
5	28,600	18,600	0.650	0.672
6	33,000	17,900	0.542	0.560
				M = 1.07

Second series

A new test series was therefore performed with five pairs of homologous teeth, carefully selected to be free from caries and mechanical damage. Since it was found in subsequent tests that little F¹⁸ activity, or none at all, was lost with the precipitate (which largely consists of tin hydroxide) it was decided also to run tests with powdered enamel. The solutions of stannous and sodium fluoride and the technique employed were the same as described above.

Results

The results appear from Tables 5 and 6.

Table 5

Uptake of labelled fluorine from solutions of sodium fluoride and stannous fluoride.

Activity of enamel powder		Uptake ratio $\frac{\text{SnF}_2}{\text{NaF}}$
Uptake from NaF	Uptake from SnF ₂	
133,000	240,000	1.96
126,000	267,000	

Table 6.

Uptake of labelled fluorine by intact enamel surfaces from solutions of sodium fluoride and stannous fluoride. Second series.

Tooth pairs	Activities of tooth crowns		Uptake ratio $\frac{\text{SnF}_2}{\text{NaF}}$
	Uptake from NaF	Uptake from SnF ₂	
1	7,210	19,500	2.70
2	14,500	24,700	1.64
3	8,700	13,460	1.54
4	9,950	22,700	2.28
5	15,517	26,700	1.72
			M = 1.98

A second test with powdered enamel, performed in the same way with labelled solutions of SnF₂ and NaF, gave as the result an uptake from SnF₂ that was 1.59 times the uptake from NaF.

It thus appears from the majority of the tests that the fluorine uptake by the enamel is greater from weakly acid solutions of stannous fluoride than from neutral solutions of sodium fluoride having the same fluorine concentration.

Influence of soluble dentifrice ingredients on fluorine uptake by enamel powder and intact enamel surfaces

First series

Soluble dentifrice ingredients may be thought to influence the fluoride uptake of the enamel surfaces by changing the viscosity, the wetting capacity, the pH value or other qualities of the dentifrices. To test this supposition, 300-mM neutral solutions were prepared of F¹⁸-labelled sodium fluoride and sodium monofluorophosphate, respectively, and mixed with solutions of common dentifrice ingredients to the following final concentrations.

- 1 a. 100-mM NaF, water (control)
- 2 a. " " , 0.1 % carboxymethyl cellulose
- 3 a. " " , 50 vol. % glycerol
- 4 a. " " , 2 $\frac{2}{3}$ % soap (Sapo albus)
- 5 a. " " , 2 $\frac{2}{3}$ % sodium lauryl sulphate
- 6 a. " " , $\frac{2}{3}$ -saturation of sodium bicarbonate (about 9.2 %).

A corresponding series 1 b—6 b contained similar concentration of $\text{Na}_2\text{PO}_3\text{F}$, with otherwise the same components.

Duplicate 3 ml portions of each solution were pipetted into round-bottomed plastic tubes, each containing 100 mg standardized enamel powder (sieve 24—sieve 40). The tubes containing the enamel powder and the solutions were treated as described in the preceding section.

The uptake by macroscopically intact enamel surfaces was studied in the following way.

Homologous, intact extracted premolars were prepared and exposed as described above. During the preparative work the enamel surface was protected with a piece of rubber tubing. Three pairs of teeth were thus exposed to each pair of solutions, containing NaF and $\text{Na}_2\text{PO}_3\text{F}$, respectively.

After the exposure the teeth were rinsed and freed from the wax as described and the activities were determined with the scintillation detector.

Second series

After it was learnt that sorbitol is gradually replacing glycerol as a binding substance in toothpaste manufacturing, an experiment was made in order to compare the effect of these two substances. About 47 % w/w sorbitol solution was used, the viscosity of which is very close to that of the 50 % v/v glycerol solution. The experiment was performed with powdered enamel and intact enamel surfaces according to the technique described above with the following exception:

Three pairs of homologous tooth crowns were exposed to the NaF-glycerol and NaF-sorbitol solutions, respectively. Three pairs were exposed to $\text{Na}_2\text{PO}_3\text{F}$ -glycerol and $\text{Na}_2\text{PO}_3\text{F}$ -sorbitol, respectively. Finally, three pairs were exposed to NaF-water and $\text{Na}_2\text{PO}_3\text{F}$ -water, respectively. Closest comparison could thus be made between the effects of the two binding substances in this series.

Results

First series

The results of the enamel powder experiments are given in Fig. 2. The duplicate tests agreed within 10 % with the exception of the NaF-soap test (22 % difference). The ratio, (% uptake from $\text{Na}_2\text{PO}_3\text{F}$): (% uptake from NaF) was 0.21 for the water controls, 0.55 for the soap solutions, and 0.32—0.36 for the other solutions.

The uptake by the tooth surfaces is given in Fig. 3. The ratio, (% uptake from $\text{Na}_2\text{PO}_3\text{F}$): (% uptake from NaF) varied between 0.19 and 0.69 for the individual tooth pairs, and the variations within each group of three tooth pairs exposed to corresponding

ACTIVITY OF 100mg ENAMEL POWDER,
% OF ACTIVITY OF 0.1ml SOLUTION.

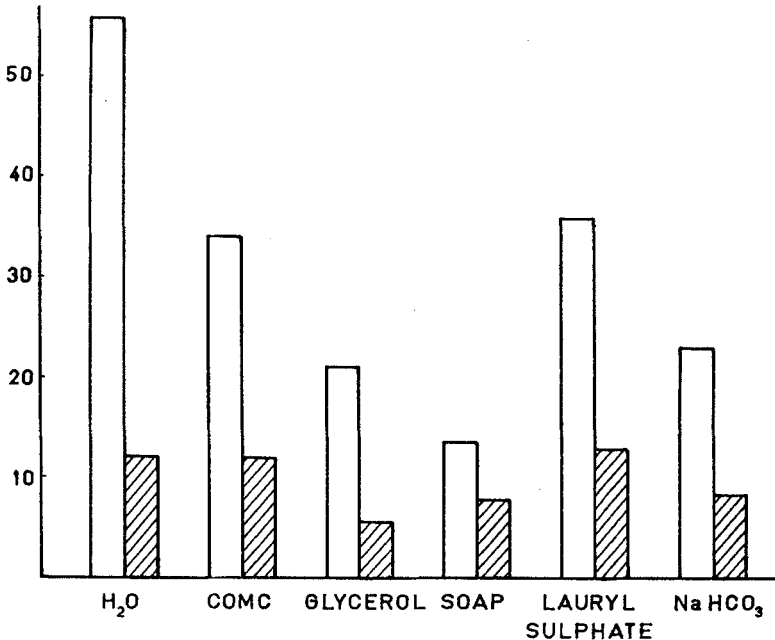


Fig. 2. F^{18} uptake by powdered enamel from labelled solutions of NaF (open columns) and $\text{Na}_2\text{PO}_3\text{F}$ (striated columns) containing different soluble ingredients.

COMC = carboxymethyl cellulose.

ACTIVITY OF 3 TOOTH CROWNS,
% OF ACTIVITY OF 0.1ml SOLUTION

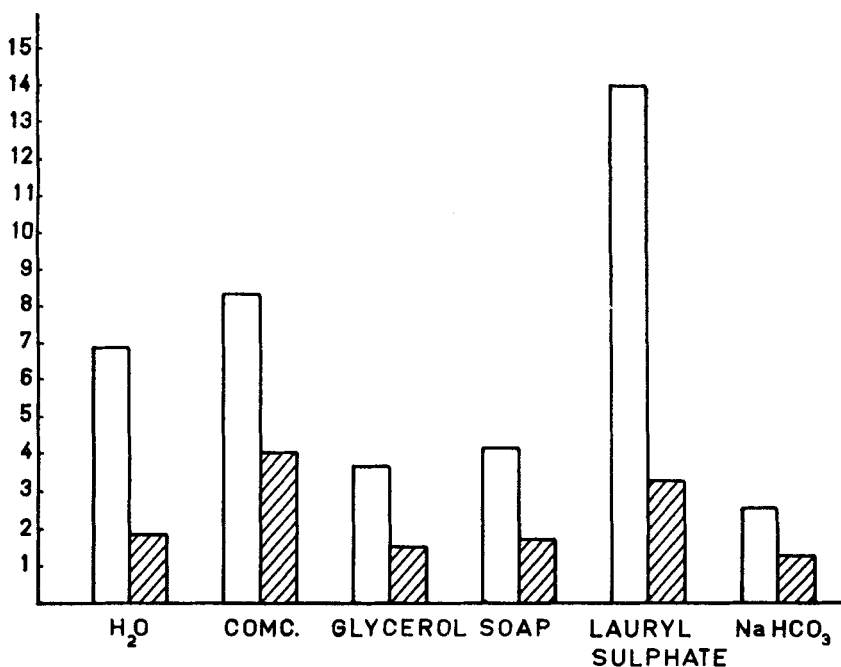


Fig. 3. F^{18} uptake by homologous tooth pairs from labelled solutions of NaF (open columns) and $\text{Na}_2\text{PO}_3\text{F}$ (striated columns) containing different soluble ingredients.

Each pair of columns gives the results obtained with three pairs of homologous teeth. COMC = carboxymethyl cellulose.

solutions was also considerable. However, the general trend of the influence of the tested soluble substances is seen to be the same for the intact enamel as for the enamel powder.

Second series

The results of the enamel powder experiments are given in Fig. 4. In this series, too, the duplicate tests agreed within 10 % with the exception of the NaF -glycerol test (20 % difference). The ratio, (% uptake from $\text{Na}_2\text{PO}_3\text{F}$) : (% uptake from NaF) was 0.54—0.59 for all three solutions.

The uptake by the tooth surfaces is given in Fig. 5. The ratios, (% uptake from NaF -sorbitol solution) : (% uptake from NaF -glycerol solution) were 0.47, 0.78, 0.80 for the individual tooth

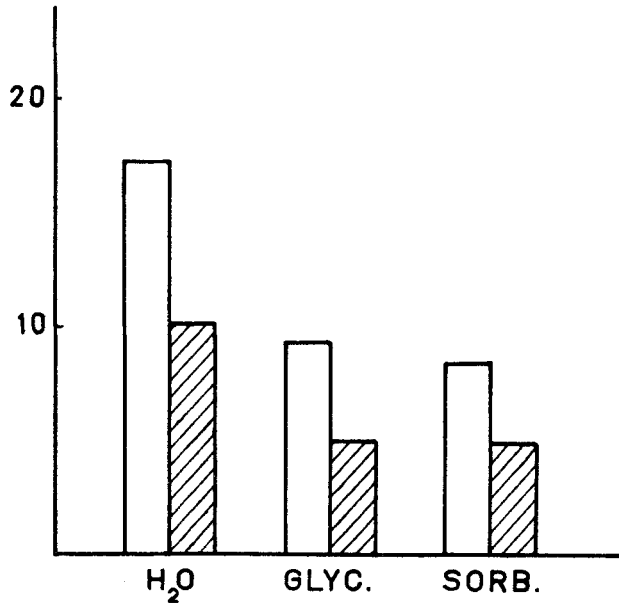


Fig. 4. F^{18} uptake by powdered enamel from labelled solutions of sodium fluoride (open columns) and sodium monofluorophosphate (striated columns) containing glycerol or sorbitol.

Ordinate graduated as in Fig. 2.

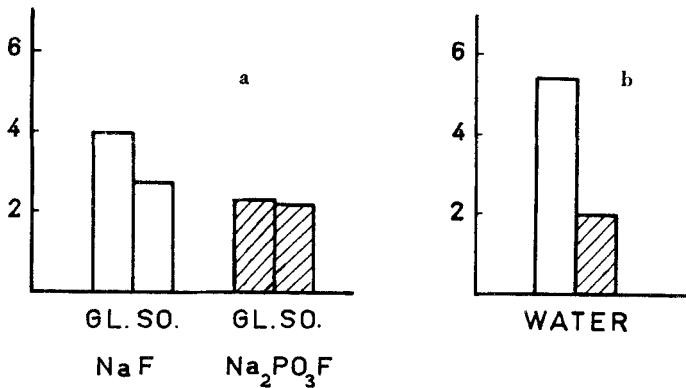


Fig. 5. a) F^{18} uptake by homologous tooth pairs from labelled solutions of sodium fluoride and sodium monofluorophosphate containing either glycerol (GL.) or sorbitol (SO.).

b) F^{18} uptake by homologous tooth pairs from solutions used in (a), without addition of glycerol or sorbitol.

Each pair of columns gives the results obtained with three pairs of homologous teeth. Ordinate graduated as in Fig. 2.

pairs. The corresponding ratios, (% uptake from $\text{Na}_2\text{PO}_3\text{F}$ -sorbitol): (% uptake from $\text{Na}_2\text{PO}_3\text{F}$ -glycerol) were 0.75, 1.02, 1.08.

It is evident that glycerol reduces the fluorine uptake from both NaF and $\text{Na}_2\text{PO}_3\text{F}$ solutions, which is not, or not so much, the case with carboxymethyl cellulose. Sorbitol has an even more reducing effect on the enamel fluoride uptake than glycerol. Soap reduces the uptake, which is not, or not appreciably, the case with sodium lauryl sulphate. Sodium bicarbonate, finally, reduces the fluorine uptake, especially from sodium fluoride solution.

THE UPTAKE OF LABELLED FLUORINE BY INTACT ENAMEL SURFACES
AND POWDERED ENAMEL FROM TOOTHPASTE COMPOSITIONS
CONTAINING NaF, SnF_2 OR $\text{Na}_2\text{PO}_3\text{F}$

In order to test the effect of the three fluorine compounds under conditions more closely resembling those occurring in ordinary toothpastes the following tests were carried out. Simplified diluted pastes composed according to Table 7 were shaken in plastic tubes for 30 min immediately after mixing. They were then centrifuged and the decanted supernatant centrifuged a second time.

Table 7.
Composition of test pastes.

Labelled fluoride	Abrasive	Binder	Detergent	Additional fluid
NaF, 5 ml 125-mM	NaHCO_3 , 5.5 g	Carboxyme- thyl cellu- lose 0.15 g	Na-lauryl- sulphate 0.2 g	Water 5 ml
SnF_2 , 5 ml 62.5-mM*)	$\text{Ca}_2\text{P}_2\text{O}_7$, 5.5 g**)	"	"	Acetate buffer 5 ml 0.2-M*)
$\text{Na}_2\text{PO}_3\text{F}$, 5 ml 125-mM	CaCO_3 , 5.5 g	"	"	Water, 5 ml

*) pH adjusted to 4.5 in one series, 5.5 in another series.

**) The calcium pyrophosphate used was a pure commercial preparation without special heating. The mixing was done with free access of air, thus providing the most unfavourable conditions possibly to be expected in large-scale manufacturing.

The activities of the supernatants were determined and compared with the activities of the labelled solutions of fluorine compounds, which formed a part of the corresponding pastes. A measure of the possible loss of labelled fluorine to the insoluble ingredients was thus obtained.

The uptake of labelled fluorine by intact tooth surfaces from the three supernatants was measured in the following way. Homologous premolar pairs were prepared and exposed as described above. Three pairs of intact teeth were thus exposed to NaF and SnF₂; three pairs were exposed to NaF and Na₂PO₃F; and three pairs to SnF₂ and Na₂PO₃F, respectively. This arrangement was of course due to the fact that triplicate homologous teeth do not exist.

After exposure the teeth were treated and their F¹⁸-activities analyzed as described above.

For tests on the uptake of labelled fluorine by enamel powder the supernatants of the test toothpastes were diluted with equal parts of distilled water. Duplicate 1 ml aliquots of each diluted supernatant were pipetted into round-bottomed plastic tubes, each of which contained 100 mg enamel powder (sieve No. 24—sieve No. 40, see above). The tubes were shaken in an upright position for 30 min, followed by centrifugation, decantation and centrifuge-washing with 3×4 ml distilled water. The activities of the enamel powder batches were then analyzed in the scintillator where the plastic tubes fitted into the well.

Results

The supernatants of the NaF and Na₂PO₃F pastes retained the total F¹⁸ activity of the liquid phase of the pastes. The supernatants of the SnF₂ pastes adjusted to pH 4.5 and 5.5 contained 10.0 and 22.8 per cent, respectively, of the original activity of the liquid phase.

The F¹⁸ uptake by powdered enamel and homologous teeth appears from the diagrams Figs. 6 and 7.

The following main conclusions may be derived from the results.

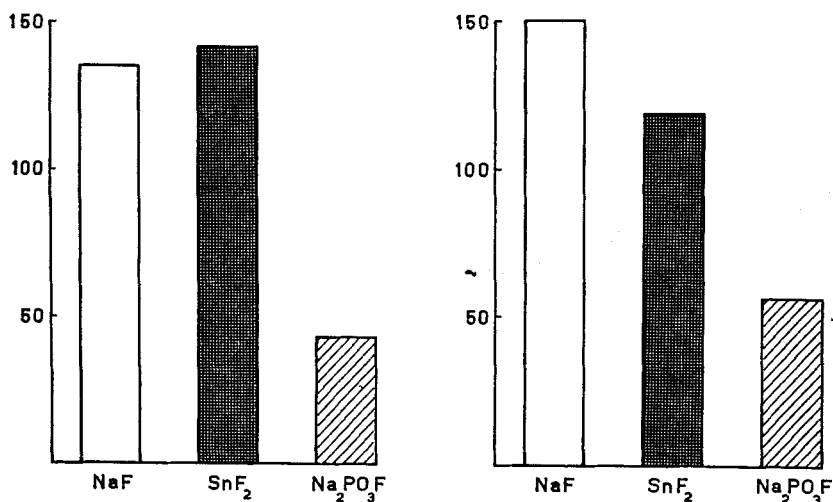


Fig. 6. F^{18} uptake by powdered enamel from toothpastes containing labelled fluorides.

Left diagram: pH of SnF_2 paste = 4.5. Right diagram: pH of SnF_2 paste = 5.5.

Ordinates denote uptake as promille of original activities of 0.1 ml liquid phase of the pastes.

1. There was no loss of fluorine from the liquid phase of the pastes containing NaF and $\text{Na}_2\text{PO}_3\text{F}$.
2. Most of the fluorine of the liquid phase of the paste containing SnF_2 was rapidly lost, especially at the lower pH value.
3. When calculated as a fraction of the total fluorine content of the pastes the uptake by enamel powder was of about the same order from SnF_2 and NaF , and about three times greater than the uptake from $\text{Na}_2\text{PO}_3\text{F}$.
4. When calculated as a fraction of the fluorine remaining in the supernatant the uptake by enamel powder was far greater from SnF_2 than from NaF , and about three times greater from NaF than from $\text{Na}_2\text{PO}_3\text{F}$. The difference between SnF_2 and the two other compounds was especially striking at the lower pH value.

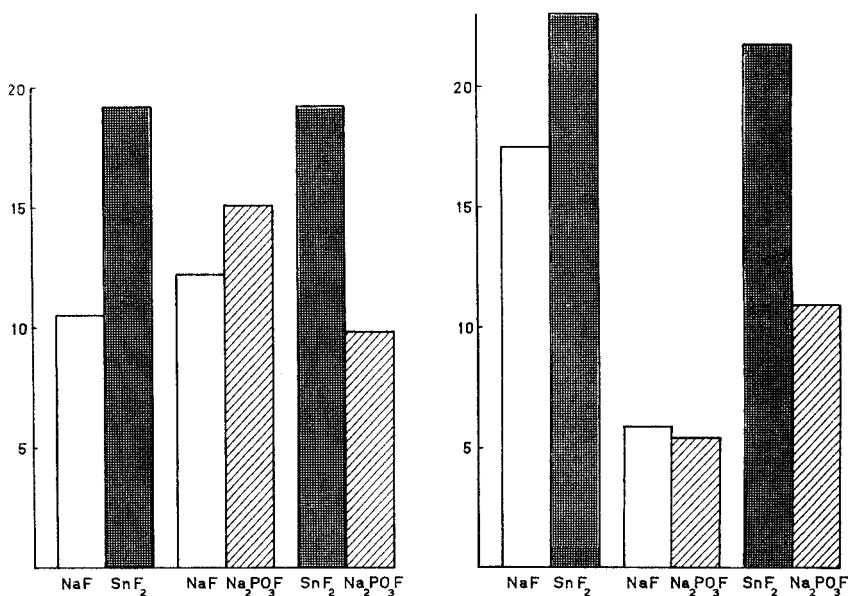


Fig. 7. F^{18} uptake by homologous tooth pairs from toothpastes containing labelled fluorides.

Left diagram: pH of SnF_2 paste = 4.5. Right diagram: pH of SnF_2 paste = 5.5.

Ordinates denote average uptake by tooth crowns as promille of original activities of 0.1 ml liquid phase of the pastes. Each pair of columns gives the results obtained with three pairs of homologous teeth.

- The differences between homologous teeth regarding uptake of labelled fluorine generally went in the same direction as found with powdered enamel. However, the differences between $\text{Na}_2\text{PO}_3\text{F}$ and the other two compounds were much less pronounced than found with the enamel powder.

THE DISSOLUTION OF CALCIUM AND PHOSPHORUS FROM ENAMEL POWDER BY SOLUTIONS OF DIFFERENT FLUORIDES

The results reported above demonstrate that sodium monofluorophosphate is inferior to sodium fluoride and stannous fluoride as regards the *quantity* of fluorine taken up by the enamel. However, this does not necessarily mean that the fluoro-

phosphate is also inferior as regards protection of the enamel against carious dissolution. From previous investigations with stannous fluoride and sodium fluoride it is evident that the crystal and molecular changes brought about in the enamel surface are of great importance for this protection.

Analysis of the liberation of calcium and phosphate ions from the enamel through the action of the fluorine compounds seemed to be a convenient method of obtaining some information on this action. The following experiments were designed to test the dissolution of calcium phosphate from the enamel through the action of the different fluorides.

1. Dissolution of calcium and magnesium

100 mg portions of powdered enamel (sieve 24—sieve 40) were shaken for 30 min. in stoppered centrifuge tubes with 5 ml volumes of 0.1-M $\text{Na}_2\text{PO}_3\text{F}$ and 0.1-M NaF , respectively, each *in duplo*. The tubes were centrifuged and the supernatants removed by careful suction. 2 ml aliquots were titrated for $\text{Ca} + \text{Mg}$ using an EDTA method.

The results appear in Table 8. It is seen that the dissolution of calcium and magnesium was about 25 % higher in sodium fluoride than in sodium monofluorophosphate solution.

Table 8.

Calcium and magnesium dissolved from enamel powder by solutions of $\text{Na}_2\text{PO}_3\text{F}$ and NaF , respectively.

Solution	Ca + Mg in solution, mM/l	
$\text{Na}_2\text{PO}_3\text{F}$	0.71	0.74
NaF	0.89	0.96

2. Dissolution of phosphate

A. Dissolution of P^{32} from P^{32} -treated enamel powder

100 mg portions of enamel powder (sieve 24—sieve 40) were shaken in 4 round-bottomed plastic centrifuge tubes with 0.5 ml volumes of P^{32} -labelled 0.005-M phosphate buffer pH 7.0 for 1

hour. After shaking, 5 ml distilled water was added to each tube, which was then centrifuged, decanted and centrifuge-washed with 3×5 ml water.

The tubes were dried at 95°C , after which the activities taken up by the enamel powder were determined.

5 ml 0.1-M $\text{Na}_2\text{PO}_3\text{F}$ was pipetted into two of the tubes and 5 ml 0.1-M NaF into the other two. The tubes were stoppered, shaken for 30 min. and centrifuged. 2.1 ml portions of the supernatants were analyzed in the scintillation detector.

The results appear in Table 9. It is seen that considerably more of the labelled phosphate was liberated from the enamel powder by the sodium fluoride than by the sodium monofluorophosphate solution.

Table 9.

P^{32} dissolved from enamel powder by solutions of $\text{Na}_2\text{PO}_3\text{F}$ and NaF , respectively.

Solution	Activity of enamel powder P	Activity of 2.1 ml supernatant S	S/P
$\text{Na}_2\text{PO}_3\text{F}$	305,244	6,109	0.020
	272,713	5,084	0.019
NaF	249,152	9,095	0.037
	276,368	8,903	0.032

B. Dissolution of active atoms, mainly P^{32} , from neutron activated enamel powder

Enamel powder of the same particle size as in the previous experiment was neutron activated at about $5.5 \times 10^{11} \text{ n} \cdot \text{cm}^{-2} \cdot \text{sec}^{-1}$ for 4 days. The decay curves as obtained with the scintillation crystal with 1 mm Cu filter (bremsstrahlung) approached the P^{32} slope after about 6 days. The following experiment was performed after this time: --

Exactly 100 mg activated enamel powder was weighed into each of 5 ordinary centrifuge tubes. Into the tubes were pipetted:

- 1) 5 ml 0.1-M $\text{Na}_2\text{PO}_3\text{F}$
- 2) 5 ml 0.1-M NaF
- 3) 5 ml 0.05-M SnF_2 (freshly prepared)
- 4) 5 ml 0.1-M Na_2SO_4
- 5) 5 ml dist. water

The fluorine compounds were thus compared at equal fluorine concentrations; sodium sulphate was included in the series owing to its close chemical similarity to the monofluorophosphate.

After shaking for 30 min the tubes were centrifuged and 1 ml volumes of the supernatants were analyzed in the scintillator.

The results are given in Table 10. It is seen that the solutions liberated activated ions from the enamel powder in the following order: $\text{NaF} > \text{Na}_2\text{PO}_3\text{F} > \text{Na}_2\text{SO}_4 > \text{H}_2\text{O} > \text{SnF}_2$.

Table 10.

Liberation of active atoms (mainly P^{32}) from neutron activated enamel powder by different solutions.

Solution	Activity of 1 ml solution, c/min.
$\text{Na}_2\text{PO}_3\text{F}$	4,275
NaF	5,248
SnF_2	1,061
Na_2SO_4	3,617
H_2O	2,400

To sum up, the dissolution of calcium + magnesium ions and phosphate ions from the enamel powder was consistently greater on treatment with a sodium fluoride solution than on treatment with an equimolar sodium monofluorophosphate solution.

The liberation of phosphate ions from the enamel on treatment with stannous fluoride was remarkably low. The most probable explanation of this finding is the low solubility of tin phosphate.

THE RETENTION OF FLUORIDE FOLLOWING TOOTHBRUSHING WITH FLUORIDE-CONTAINING DENTIFRICES

For a safe dosage of fluorine compounds in dentifrices it is necessary to have sufficient knowledge of the quantity of fluorine that is retained when the dentifrices are used in the ordinary

way. Tests were therefore carried out with fluorine-containing toothpastes, the fluorine compounds of which were labelled with F^{18} . The composition of the toothpastes is given in Table 11. Labelling was performed as described under Radiologic Methods.

Table 11.
Composition of toothpastes used in retention tests. Average quantities used for toothbrushing.

	Fluoride-abrasive combination		
	NaF-NaHCO ₃	SnF ₂ -Ca ₂ P ₂ O ₇	Na ₂ PO ₃ F-CaCO ₃
Fluorine compound	0.2	0.4	0.8
Abrasive	50	40	40
Glycerol	10	10	10
Sodium lauryl sulphate	1.9	2.0	2.0
Carboxymethyl cellulose	1.7	1.4	1.4
Flavouring agents	1.45	1.45	1.45
Water	ad 100	ad 100	ad 100
Average quantity used	0.696 g	0.484 g	0.617 g

After thorough mixing of the ingredients the pastes were filled into ordinary toothpaste tubes which were lacquered inside. Weighed samples for analysis of the paste activities were taken from the tubes before and after the portions used by the subjects.

The pastes were tested on different days. 10 subjects brushed their teeth according to their customary technique with about 2 cm portions of each paste ejected from the tube. These portions were weighed with the brushes, which had been weighed in advance. The average weight of the portions used is given in Table 11. Every subject collected the rinsings in a beaker into which the rinsings of the brush were also emptied. The rinsings were thoroughly homogenized, their volume was measured and duplicate 2 ml samples were taken for radiometric analysis.

From some of the subjects the urine produced up to 4 hours after the toothbrushing was collected, the volume was determined and duplicate samples analysed for F^{18} in the same way as the rinsings.

The percentages of F^{18} applied in the toothpaste portions that were recovered in the rinsings or the urine were calculated.

Results

Table 12 gives the average and maximum figures for the quantities retained. The differences between the three toothpastes were not statistically significant. The urine counts were all below 20 per cent of the background; the highest count, still with a large error, corresponded to a 4-hour excretion of about 4.3 % of the F^{18} content of the toothpaste portion used.

Table 12.
Retention of F^{18} from toothpastes containing labelled fluorides.

	Fluoride-abrasive combination		
	NaF-NaHCO ₃	SnF ₂ -Ca ₂ P ₂ O ₇	Na ₂ PO ₃ F-CaCO ₃
Per cent retention, M of 10 subjects	8.1	12.1	5.7
max.	33.7	35.4	19.6

The quantity of these toothpastes to give a retention of 1 mg of fluorine per day would be 8.5—16.4 grams or 17—26 ordinary portions when calculated on the basis of average retention, 2.9—4.8 grams or 4—8 portions when calculated on the basis of the maximum retention found.

DISCUSSION

The experiments have demonstrated wide variations among the different insoluble abrasives tested as regards absorption of fluorine from solutions containing fluoride ions or monofluorophosphate ions. The great variability of the fluorine uptake by calcium pyrophosphate from solutions of stannous fluoride deserves special attention.

A notable finding is also the complete compatibility of calcium carbonate with fluorine as monofluorophosphate; the explanation may be the inadaptability of the monofluorophosphate ion to the crystal lattice of the carbonate.

However, factors other than the reactivity with fluorine also influence the choice of abrasives. Silica and pumice may for example have an unsuitable degree of hardness. Sodium meta-

phosphate is reported to be mechanically very suitable (*Van Huisen & Boyd* 1952) but has been little used in dentifrices, apparently in part owing to the risk of transformation into soluble metaphosphate with its well-known calcium-sequestering property. Calcium carbonate, finally, is one of the best established insoluble abrasives, generally in the form of natural or precipitated chalk.

Much work has been spent by *Muhler* and collaborators in the search for suitable abrasives for a dentifrice containing stannous fluoride. From our tests it is evident that even calcium pyrophosphate, regarded by the *Muhler* group as the most suitable abrasive for a stannous fluoride toothpaste, may rapidly bind the greater part of the fluorine in stannous fluoride if the pyrophosphate is not of the ideal quality.

Soluble abrasives have often been advocated on the assumption that insoluble toothpaste ingredients would have an irritating effect in the gingival pocket. No scientific support seems to exist for this assumption, but from the point of view of non-reactivity with fluoride ions a soluble abrasive as for example sodium bicarbonate would be suitable. However, our tests showed a reduced uptake of fluoride, or fluorine from monofluorophosphate, by dental enamel from solutions that were saturated with sodium bicarbonate.

The experiments reported have further shown that soap, glycerol and sorbitol all reduce the uptake of fluorine from sodium fluoride and sodium monofluorophosphate. This finding may help to explain some of the negative results in previous clinical tests with fluorine-containing dentifrices. There was little or no reduction of the fluoride uptake with sodium lauryl sulphate and carboxymethyl cellulose.

From our tests it appears that the uptake of fluorine by powdered enamel and intact enamel surfaces is considerably lower from solutions of sodium monofluorophosphate than from comparable solutions of sodium fluoride, especially at pH values below 6. A notable exception is the uptake from the liquid phase of the dentifrices by homologous tooth surfaces, which was about the same from both compounds.

The quantities of calcium and phosphorus that were liberated from the enamel on treatment with $\text{Na}_2\text{PO}_3\text{F}$ were less than with

NaF. This may be due either to a lower reaction rate with the PO_3F ion or a special mode of reaction of this ion with the enamel phosphate. It may be mentioned in this connection that treatment of powdered enamel or enamel surfaces with $\text{Na}_2\text{PO}_3\text{F}$ results in an uptake of phosphorus simultaneously with fluorine although to a less extent; this was found in experiments with P^{32} , F^{18} -labelled $\text{Na}_2\text{PO}_3\text{F}$ (technique: *Ericsson*, in press). This, however, still does not answer the question of the mode of action of the PO_3F -ion.

Previous findings on the solubility-decreasing effect of monofluorophosphate are also of interest in this connection. *Haydon & al.* (1951) found a reduction of the solubility of hydroxy apatite by 20—320 ppm $\text{Na}_2\text{PO}_3\text{F}$, which was lower than the reduction obtained with NaF at the lower levels of fluoride but higher at the higher fluoride levels, in spite of the fact that the fluoride uptake was always less from $\text{Na}_2\text{PO}_3\text{F}$. *Burnett* (1955) found a solubility decreasing effect on dentine by 2 % $\text{K}_2\text{PO}_3\text{F}$ which as a rule was somewhat less than that obtained with NaF. *Hein & al.* (1951) found a similar caries reduction in animal experiments from $\text{Na}_2\text{PO}_3\text{F}$ as from NaF, and *Hawes & al.* (1954) obtained a 20—30 % reduction of human dental caries by topical application of $\text{Na}_2\text{PO}_3\text{F}$.

From all these data it seems reasonable to draw the tentative conclusion that sodium monofluorophosphate should give caries reduction when incorporated in a reactive form in a toothpaste. The magnitude of this effect can only be assessed in clinical tests. The present investigation also indicates that several toothpaste components may influence the clinical effect.

Our tests with equivalent solutions of sodium fluoride and stannous fluoride gave as a rule greater uptake by the enamel of labelled fluoride from stannous fluoride than from sodium fluoride. This is in agreement with the findings of *Hatton & al.* (1955) but in apparent contradiction of the findings reported by *Brudevold & al.* (1956) and *Cooley & al.* (1958). Differences in the experimental conditions may perhaps explain the inconsistent results (Table 13).

In spite of the great loss of fluorine from stannous fluoride to the abrasive used in our toothpaste tests the fluoride uptake by

Table 13.

Fluoride uptake by dental enamel from solutions of NaF and SnF₂, respectively.

Comparison of experimental methods and results.

Authors	Tissue preparation	NaF solution		SnF ₂ solution		Uptake
		conc.	pH	conc.	pH	
<i>Hatton & al</i>	Powd. enamel	2—50 μg F/ml	7.8—6.4	same as NaF	5.0—3.1	Greater from SnF ₂
<i>Brudevold & al</i>	Intact enamel	0.01 % F	6.0	0.01 % F	3.7	Slightly greater from NaF
<i>Cooley & al</i>	Chips of enamel	0.2-M	natural	0.1-M	natural	Greater from NaF
<i>Present author</i>	Intact enamel. Powd. enamel	20-mM	"	10-mM	4.1	Greater from SnF ₂

the enamel was notably high from this compound. Still more remarkable was the low liberation of phosphorus from the enamel by treatment with SnF₂, probably owing to the low solubility of tin phosphate; tin is known to be taken up at the same time as fluoride (*Brudevold & al.* 1956, *Cooley* 1960).

As regards the indications for clinical testing obtained from these studies the following may be concluded:

Sodium fluoride deserves to be tested in toothpastes containing abrasives that do not combine with fluoride. The selection of abrasives is a technical problem that merits further study.

Sodium monofluorophosphate should be tested in a toothpaste containing calcium carbonate as abrasive. The addition of this fluorine compound to chalk pastes for polishing fillings and rough tooth surfaces also appears strongly indicated. Such polishing involves the removal of a microscopic part of the surface layer of the tooth. Since the surface layer of the enamel is less soluble than the subsequent layers (*Brudevold & Little* 1951, *Isaac & al.* 1958), polishing is liable to expose less protected enamel layers to caries attack, often in pronouncedly caries-prone areas. A corresponding effect may be visualized for denuded

cementum and dentine surfaces. This should be counteracted by the incorporation in polishing pastes of substances known to reduce the solubility of the tooth's mineral salts. Sodium monofluorophosphate appears ideal for this purpose since it can be combined at a high concentration with chalk, a well established polishing agent.

Stannous fluoride with its remarkable protective action on the enamel appears worthy of use as an ingredient of toothpastes. The discoloration of tooth areas showing incipient dissolution, which has been reported in some clinical cases (*Shapiro & Hood* 1956, *Muhler* 1957, *v. Ehrenheim* 1959), appears to be a minor problem limited to cases of unsatisfactory oral hygiene. This possible side effect should, however, be closely watched. In addition to calcium pyrophosphate other abrasives seem to deserve testing in combination with stannous fluoride, such as silica (*Segreto & al.* 1959).

Sodium lauryl sulphate can be used as a detergent in fluorine-containing toothpastes, and the desired viscosity can be attained with advantage by carboxymethyl cellulose while the glycerol or sorbitol content should be as low as possible; some glycerol or sorbitol apparently has to be added to most toothpastes to preserve their consistency and prevent them from drying up if the tubes are left open.

Some previous authors have studied the retention of fluoride and/or the urinary excretion following the use of fluoride-containing dentifrices or mouthwashes. Their data are summarized in Table 14 together with our own results.

While the urinary fluoride excretion was below or on the borderline of detection according to all the tests, there is considerable variation of the figures for total retention. Differences regarding age of the subjects, preparations used and modes of application may account for at least part of this variation.

With any of the retention figures the continuous daily use of dentifrices containing about 1 mg fluorine per gram may be regarded as safe. As regards the acute toxicity, even if a small child could eat a whole tube of dentifrice (50—75 g) its life would not be in danger. Such consumption, however unlikely to occur, should still be prevented.

Table 14.

Fluorine retention and/or excretion with the urine following the use of fluoride-containing dentifrices or mouthwashes (round figures).

Authors	Subjects	F-preparation	Mode of application	Retention, % of F in portion	Excretion, % of F in portion
<i>Bossert & Dunning</i> 1945	Adults	0.1% NaF solution	2 min. mouthrinse, 25 ml 3 » » » » »	Average 3-9% » 5-11%	—
<i>Eichter & al.</i> 1945	4 years— adults	Toothpaste, 2 mg F/g	Single toothbrushing, customary technique	{ » 20% Max. 43%	—
<i>Winkler & al.</i> 1953	11-15 years	» , 0.15% NaF	» » »	{60% of soluble F {30% » total F	—
<i>Schweinsberger & Muhlner</i> 1956, 1957	11-12 years 2-5 »	» , 0.4% SnF ₂ » » »	Routine use » » »	—	Excretion not increased
<i>Hellström</i> 1960	Adults 5-15 years	0.1% NaF* soln., 15 ml » » » , 10 ml	1 min. mouthrinse, 15 ml » » » , 10 ml	Average 30% » 19%	<1.5%/4 hours <4% / »
<i>Present author</i>	Adults	3 toothpastes, each contg. 1 mg F*) /g	Single toothbrushing, customary technique	{ » 6-12% Max. 20-35%	<5% / »

*) F¹⁸-labelled

SUMMARY

F¹⁸-labelled sodium fluoride, sodium monofluorophosphate and stannous fluoride were utilized for *in vitro* studies of the uptake of fluorine by dental enamel from solutions of these compounds, and the influence of toothpaste abrasives and soluble toothpaste ingredients on this uptake. The experiments were carried out with powdered enamel and intact enamel surfaces of homologous extracted teeth. The fluoride retention following toothbrushing was also studied using toothpastes containing F¹⁸-labelled fluorides.

Considerably less fluorine was taken up by the enamel from Na₂PO₃F than from NaF (neutral solutions), and generally more from SnF₂ (solution pH 4.1—4.5) than from neutral NaF solution. With decreasing pH value the fluorine uptake by enamel powder from NaF was greatly increased, from Na₂PO₃F only very moderately.

From NaF and Na₂PO₃F solutions no fluorine was lost to the abrasive sodium metaphosphate, and very little to silica powder (SiO₂) and pumice powder. The loss of fluorine from both compounds to tricalcium phosphate and calcium pyrophosphate was substantial, although reduced when these abrasives had been heated.

NaF lost about as much fluorine to calcium carbonate as to calcium orthophosphate, while Na₂PO₃F, even in 1-M concentration, lost no fluorine to calcium carbonate.

SnF₂ solutions lost small amounts of fluorine on shaking with sodium metaphosphate and anhydrous silica. The loss to calcium pyrophosphate showed great variations and was minimized by using a pure preparation of pyrophosphate that had been heated to 900°—1,000° C.

Glycerol, sorbitol, soap and sodium bicarbonate all reduced the fluorine uptake by dental enamel, both from NaF and Na₂PO₃F, while carboxymethyl cellulose and sodium lauryl sulphate caused no such reduction.

Tests were performed with simplified toothpaste compositions containing carboxymethyl cellulose, sodium lauryl sulphate and one of the fluoride-abrasive combinations, NaF — NaHCO₃, SnF₂ — Ca₂P₂O₇ or Na₂PO₃F — CaCO₃. The fluorine uptake by dental

enamel was of the same order from SnF_2 as from NaF in spite of the loss of the greater part of the fluorine of SnF_2 to the calcium pyrophosphate used; the uptake from $\text{Na}_2\text{PO}_3\text{F}$ was clearly lower.

In the treatment of enamel powder with solutions of these fluorine compounds, more calcium, magnesium and phosphorus was dissolved by NaF than by $\text{Na}_2\text{PO}_3\text{F}$, and much less phosphorus was dissolved by SnF_2 than by the two other compounds.

Clinical tests with three specially composed toothpastes containing NaF , SnF_2 or $\text{Na}_2\text{PO}_3\text{F}$ gave an average retention in the body of about 6—12 per cent of the fluoride content, the maximum retention being about 35 per cent. It can be calculated from these results that a toothpaste containing 0.1 per cent fluorine can be used several times daily with a total retention of less than 1 mg F/day.

The discussion deals with the indications obtained from these studies for clinical testing of fluoride toothpastes.

Acknowledgement

This investigation was financially supported by the Swedish Medical Research Council.

RÉSUMÉ

FLUOR EN PÂTES DENTIFRICES

INVESTIGATIONS AVEC LE FLUOR RADIOACTIF F^{18}

Les fluorures de sodium et d'étain (II) et le monofluorophosphate de sodium, tous marqués de F^{18} , ont été utilisés pour des études *in vitro* sur l'incorporation du fluor de solutions de ces combinaisons dans l'émail dentaire et sur l'influence sur cette incorporation d'abrasifs et de substances solubles de dentifrices. Les expériences ont été exécutées avec de l'émail pulvérisé et des surfaces intactes d'émail de dents homologues extraites. La rétention de fluor au brossage des dents a été étudiée avec des pâtes dentifrices contenant des fluorures marqués de F^{18} .

L'émail a incorporé notamment moins de fluor venant de $\text{Na}_2\text{PO}_3\text{F}$ que de NaF (tous les deux en solution neutre). En général, l'émail a absorbé plus de SnF_2 (pH de solution 4,1—4,5) que de NaF en solution neutre. Avec un pH diminuant l'absorp-

tion de fluor du NaF par l'émail pulvérisé a fortement augmenté, celle du $\text{Na}_2\text{PO}_3\text{F}$ ne montrant qu'une augmentation limitée.

Rien du fluor des NaF et $\text{Na}_2\text{PO}_3\text{F}$ ne fut perdu à l'abrasif métaphosphate de sodium et très peu aux poudres de silice (SiO_2) et de pierre ponce. La perte de fluor des deux combinaisons aux ortho- et pyrophosphate de calcium était notable même si un chauffage préalable la réduisait.

NaF a perdu autant de fluor au carbonate de calcium qu'à l'orthophosphate de calcium, tandis que $\text{Na}_2\text{PO}_3\text{F}$, même à concentration molaire, n'a perdu aucun fluor au carbonate.

Les solutions de SnF_2 ont perdu de petites quantités de fluor par agitation avec du métaphosphate de sodium ou avec de l'anhydride de silice. La perte de fluor au pyrophosphate de calcium a beaucoup varié et a été réduite au minimum par l'emploi d'une préparation pure de pyrophosphate chauffé à 900° — 1.000° C.

La glycerine, le sorbitol, le savon et le bicarbonate de sodium ont tous réduit l'incorporation du fluor des NaF et $\text{Na}_2\text{PO}_3\text{F}$ dans l'émail, tandis que la carboxyméthylecellulose et le laurylsulphate de sodium n'ont pas causé de réduction.

Des épreuves ont été faites avec des dentifrices simples contenant de la carboxyméthylecellulose, du laurylsulphate de sodium et un des combinaisons fluorure — abrasif suivantes: NaF — NaHCO_3 , SnF_2 — $\text{Ca}_2\text{P}_2\text{O}_7$, $\text{Na}_2\text{PO}_3\text{F}$ — CaCO_3 . L'incorporation du fluor de SnF_2 dans l'émail dentaire était du même ordre que celle de NaF en dépit de la perte de la plus grande partie du fluor de SnF_2 à l'abrasif employé; l'incorporation de fluor du $\text{Na}_2\text{PO}_3\text{F}$ était nettement plus basse.

En traitant l'émail pulvérisé avec des solutions des trois combinaisons de fluor, une plus grande quantité du calcium, du magnésium et du phosphore de l'émail fut dissoute par NaF que par $\text{Na}_2\text{PO}_3\text{F}$. Beaucoup moins de phosphore fut dissous par SnF_2 que par les deux autres combinaisons.

Des épreuves cliniques avec trois pâtes dentifrices spécialement composées et contenant NaF, SnF_2 ou $\text{Na}_2\text{PO}_3\text{F}$ ont amené une rétention moyenne dans le corps d'environ 6—12 p. c. du fluor et d'environ 35 p. c. au maximum. Partant de ces résultats on peut calculer qu'une pâte dentifrice contenant 0.1 p. c. de fluor peut être utilisée plusieurs fois par jour avec une rétention totale inférieure à 1 mg F par jour.

La discussion traite, entre autres choses, des indications obtenues de ces études pour des épreuves cliniques de dentifrices fluorés.

ZUSAMMENFASSUNG

FLUOR IN ZAHNPASTEN

UNTERSUCHUNGEN MIT HILFE DES RADIOAKTIVEN FLUORISOTOPS F^{18}

Natriumfluorid, Natriummonofluorophosphat und Stannofluorid, alle F^{18} -markiert, wurden für Studien in vitro benutzt, um die Fluoraufnahme des Zahnschmelzes und deren Beeinflussung durch Schleifmittel und lösliche Bestandteile von Zahnpasten zu beleuchten. Die Versuche wurden mit pulverisiertem Schmelz und mit intakten Schmelzflächen extrahierter homologer Zähne ausgeführt. Die Fluorretention beim Zähnebürsten wurde mit Zahnpasten studiert, die F^{18} -markierte Fluoride enthielten.

Aus Na_2PO_3F -Lösung wurde bedeutend weniger Fluor vom Schmelz aufgenommen als aus NaF-Lösung (beide von neutraler Reaktion). Aus SnF_2 -Lösung wurde bei pH 4,1—4,5 im allgemeinen mehr Fluor aufgenommen als aus neutraler NaF-Lösung. Mit sinkendem pH-Wert wurde die Fluoraufnahme des pulverisierten Schmelzes aus NaF stark, aus Na_2PO_3F nur mässig erhöht.

NaF- und Na_2PO_3F -Lösungen verloren kein Fluor zum Schleifmittel Natriummetaphosphat und sehr wenig zu Kieselsäureanhydrid und Bimsstein. Die Fluorverluste zu Trikalziumphosphat und Kalziumpyrophosphat waren aus beiden Lösungen bedeutend, wenn auch durch Heizung der Schleifmittel reduziert.

NaF verlor etwa gleichviel Fluor zum Kalziumkarbonat wie zum Kalziumorthophosphat, während Na_2PO_3F auch in 1-M Konzentration kein Fluor zum Kalziumkarbonat verlor.

Lösungen von SnF_2 verloren kleine Fluormengen beim Schütteln mit Natriummetaphosphat oder Kieselsäureanhydrid. Die Verluste zum Kalziumpyrophosphat schwankten erheblich und wurden durch Anwendung reiner, bis auf 900° — 1.000° C erhitzter Präparate stark reduziert.

Glycerin, Sorbitol, Seife und Natriumbikarbonat reduzierten alle die Fluoraufnahme des Zahnschmelzes sowohl aus NaF als

aus $\text{Na}_2\text{PO}_3\text{F}$, während Carboxymethylzellulose und Natriumlaurylsulphat keine Reduktion bewirkten.

Teste wurden mit vereinfachten Zahnpasten durchgeführt, die ausser Carboxymethylzellulose und Natriumlaurylsulphat eine der folgenden Fluorid-Schleifmittelkombinationen enthielten: $\text{NaF} - \text{NaHCO}_3$, $\text{SnF}_2 - \text{Ca}_2\text{P}_2\text{O}_7$, $\text{Na}_2\text{PO}_3\text{F} - \text{CaCO}_3$. Die Fluorid-Aufnahme des Schmelzes aus SnF_2 war der gleichen Größenordnung wie die aus NaF , obgleich der grössere Teil des Fluorinhaltes des SnF_2 an das benutzte Pyrophosphat verloren ging. Die Aufnahme aus $\text{Na}_2\text{PO}_3\text{F}$ war bedeutend niedriger.

Bei der Behandlung des Schmelzpulvers mit NaF - und $\text{Na}_2\text{PO}_3\text{F}$ -Lösungen wurde mehr Kalzium, Magnesium und Phosphor durch NaF als durch $\text{Na}_2\text{PO}_3\text{F}$ vom Schmelz ausgelöst. Viel weniger Phosphor wurde durch SnF_2 als durch die anderen Verbindungen ausgelöst.

Klinische Versuche mit drei besonders komponierten Zahnpasten, die NaF , SnF_2 oder $\text{Na}_2\text{PO}_3\text{F}$ enthielten, ergaben eine durchschnittliche Retention im Körper von etwa 6—12 % des Fluorinhaltes; die maximale Retention war etwa 35 %. Aus diesen Resultaten kann berechnet werden, dass eine Zahnpaste, die 0,1 % Fluor enthält, mehrmals täglich benutzt werden kann, ohne dass die totale Retention 1 mg F/Tag erreicht.

Die Diskussion erörtert u.a. die Anhaltspunkte, die diese Studien für die klinische Prüfung von Fluoridzahnpasten gegeben haben.

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