

# Analysis of fluoride levels retained intraorally or ingested following routine clinical applications of topical fluoride products

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## Abstract

A variety of topical fluorides is now used clinically for the prevention and control of dental caries. It is essential for the dental profession to be fully aware of the relative retention rates of fluoride in saliva and thus its contact with the teeth. These may vary following the use of the different categories and concentrations of agents available and with different methods of use. It is also important to be aware of the amounts of fluoride ion ingested following use of the more concentrated forms and of the resultant elevation in total blood fluoride levels.

These parameters were investigated in a series of experiments involving human volunteer subjects using a variety of topical fluoride materials commercially available in Australia. Fluoride mouthrinses appeared to provide the highest salivary retention rates per dose of all forms of topical fluoride. Ingestion rates from concentrated gels were acceptable when effective evacuation methods were applied. The use of custom-made trays resulted in a reduction in amounts of fluoride ion ingested, though simple self-application by toothbrush of smaller quantities proved to be an effective alternative in terms of amount of fluoride ion retained in saliva per amount applied and ingested. None of the concentrated gels used resulted in elevations in total blood fluoride levels which were of concern in adults.

It is acknowledged that salivary retention rates of fluoride ion do not necessarily reflect the caries inhibitory effects of topical fluorides. However, these data provide some indication of possible advantages of some products and methods of application over others.

**Key words:** Fluoride, salivary retention, ingestion rates, blood fluoride elevation, clinical use.

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## Introduction

In the 35 years since topical fluoride materials have been in clinical use, there have been subtle but significant changes in recommendations as to how they might be most effectively used. Initially, the emphasis was on topical fluoride's role in preventing the development of carious lesions. However, in the last decade, there has been increasing recognition of topical fluoride's ability to enhance the remineralization of existing incipient carious lesions in enamel and on exposed root surfaces.<sup>1</sup> There is increasing evidence that even those at highest risk of caries development (those with severe xerostomia and those who through physical or psychological disability are unable to control dietary sucrose frequency and plaque accumulation effectively) can control this risk if topical fluorides are applied frequently and at certain minimal concentrations.<sup>2</sup> This increased utilization rate of concentrated fluoride gels, rinses or varnishes brings with it the need to ensure the risks of chronic toxicity or potential for fluorosis in children do not increase. Furthermore, there is evidence that frequent utilization of acidulated fluoride preparations can etch porcelain and glass ionomer cements.

Hence, it is necessary for every clinician to be thoroughly aware of the dosage and relative retention rates, possible levels of ingestion and potential toxicity or other damaging effects of all fluoride preparations used in dental offices or recommended for home application. This knowledge will permit clinicians to prescribe the safest and most dose-effective schedules of topical fluoride.

This study explored the relative salivary retention rates of a wide variety of topical fluoride materials available in Australia, applied in ways simulating those used clinically. The study also investigated the possible relative ingestion rates of some of the more concentrated preparations and the elevations in blood fluoride levels these may cause in adult patients.

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**Table 1. Materials and equipment used**

Material/equipment	Proprietary name	Manufacturer
Toothpastes		
Non-fluoride	Blackmore's Herbal and Mineral Toothpaste	Blackmore's Laboratories Ltd, Balgowlah, NSW, Australia
Containing Na <sub>2</sub> FPO <sub>3</sub> (1000ppm)	Colgate Fluorigard Minty Gel	Colgate Oral Care, Sydney, NSW, Australia
Mouthrinses		
Containing 100ppm F <sup>-</sup>	Dentamint	Colgate Oral Care, Sydney, NSW, Australia
Containing 250ppm F <sup>-</sup>	Colgate Dental Rinse	Colgate Oral Care, Sydney, NSW, Australia
Containing 1000ppm F <sup>-</sup>	Oral-B Fluorinse	Coopers Laboratories, Redwood City, CA, USA
Gels		
1.23% APF	Colgate Thixoflur Gel	Colgate Oral Care, Sydney, NSW, Australia
1.23% APF	Colgate Orofluor Gel	Colgate Oral Care, Sydney, NSW, Australia
2.2% NaF	Colgate Orofluor Neutral Gel	Colgate Oral Care, Sydney, NSW, Australia
Gel trays		
Commercial	Colgate	Colgate Oral Pharmaceuticals, NJ, USA
Custom-made	Scheu Dental Blank Trays	Scheu Dental, Iserlohn, Germany
Fluoride-specific electrode	Orion Model 96-09 Combination Fluoride Electrode	Orion Research Inc, Cambridge, MA, USA

## Materials and methods

### *Subject selection and preparation*

Volunteer students or staff of the Department of Dentistry, The University of Adelaide, or Adelaide Dental Hospital, underwent salivary flow rate tests and dental examinations. Only those volunteers who were in good dental health and whose salivary flow rate exceeded 0.7ml/min were selected to participate in the experiments.

All subjects were provided with non-fluoride toothpaste (Table 1) and asked to use it in the 18-hour period prior to each day's analyses. In addition, they were asked not to eat or drink fluoride ion-rich foods or beverages (for example, seafood or tea) prior to or during the experiments. Tests were carried out approximately one hour after breakfast.

Permission to carry out this study was obtained from The University of Adelaide Committee on the Ethics of Human Experimentation.

### *Topical fluoride agents*

The topical fluoride agents used, together with the concentrations of fluoride ion present, are shown in Table 1.

Concentrations of fluoride in all preparations were checked following chemical separation of fluoride using the Taves<sup>3</sup> method of acid hydrolysis, followed by measurement with a fluoride selective electrode, as described later. All fluoride ion concentrations conformed with those described by the manufacturers.

### *Methods of application*

Several modes of application of fluoride were studied.

#### *Dentifrice*

Fluoride application via a dentifrice was achieved in two ways. First, routine toothbrushing was carried

out, using either 1.5g (1.5mg F<sup>-</sup>), 0.5g (0.5mg F<sup>-</sup>) or 0.25g (0.25mg F<sup>-</sup>) per brushing, as weighed on a balance. Alternatively, the application of a 10mm length of toothpaste gel (containing 0.6mg F<sup>-</sup>) was squeezed on to a spatula and applied orally on to labial tooth surfaces and moved round by the tongue to coat remaining surfaces. This method has been used by many Adelaide clinicians as a cheap and readily applicable substitute for mouthrinse or gel application, particularly in the School Dental Service for older children who could not afford to purchase the more expensive products.

Toothbrushing was carried out for one minute, followed by rinsing with 20ml distilled, deionized water (DDW) for 15 seconds. With direct gel self-application, rinsing was not permitted until 30 minutes had elapsed. All applications were used at least 60 minutes after eating or drinking.

#### *Mouthrinses*

The selected mouthrinses were dispensed into 10ml aliquots and the subjects instructed to rinse for one minute. Rinsing with water was not permitted following use of the mouthrinse.

#### *Gels*

Gels were applied in commercial trays, custom-made trays or by toothbrush application.

When commercial trays were used, 5g of gel was used in each tray. Trays were placed and retained in subjects' mouths for four minutes, following brush cleaning (no dentifrice) and drying of teeth. Subjects were instructed to drool excess saliva and gel into a clean beaker during this time. After four minutes, trays were removed and placed in the beaker. Subjects were instructed to expectorate excess gel into the beaker for one further minute. Rinsing and

drinking were not permitted for 60 minutes after gel application.

Custom-made trays were prepared from stone casts of alginate impressions of subjects' dental arches. After brush cleaning (no dentifrices) and drying of teeth, the trays were filled with 2g fluoride-containing gel and kept in place for four minutes. Again, the subjects were instructed to drool excess saliva and gel into a clean beaker and to expectorate excess into the beaker for one minute after the trays were removed and also placed in the beaker. Rinsing and drinking were not permitted for at least 60 minutes after gel application.

#### *Toothbrush application of concentrated topical gels*

To save the cost of manufacturing custom trays for patients, clinicians recommend concentrated gels be painted directly on teeth, using a toothbrush. Subjects were instructed to paint, on the facial sides of their dental arches, two 'squeezes' of gel from 30ml plastic dispensing containers. A measured amount of 0.6g of gel containing 7.5mg F/subject was used. Subjects were then instructed to place the toothbrush containing unused gel into a clean beaker, and to expectorate excess gel into the beaker for one minute after application.

### **Experimental design**

#### *Salivary retention of fluoride from dentifrices and mouthrinses*

Brushing with a dentrifice was carried out as described above using the equivalent of 1.5, 0.5 or 0.25g of paste. Mouthrinsing with a fluoride-containing rinse was also performed as described above using the equivalent of 0.02, 0.05 and 0.2 per cent sodium fluoride.

Six subjects participated in each of these tests. Unstimulated saliva samples were taken for five minutes at time points corresponding to immediately prior to brushing or rinsing; immediately following brushing or rinsing; or at 20, 40, 60, 120, 180 and 300 minutes after brushing or rinsing was completed.

Subjects were requested not to have morning tea until after the 60-minute salivary samples were taken and to continue with normal work activities. Salivary samples were kept at 4°C until all were ready for fluoride ion separation and analysis.

#### *Salivary retention of fluoride from gels*

Salivary retention of fluoride from gels was monitored over a seven-hour period using the following protocols: (1) a four-minute professional application of acidulated phosphate fluoride (APF) gel using commercial trays, as previously described; (2) a four-minute professional application of APF gel using custom-made trays; (3) a four-minute

professional application of NaF Gel using commercial trays; (4) self-application of APF gel with a toothbrush; (5) spatula-to-mouth application of 0.6g sodium monofluorophosphate toothpaste gel, with intraoral spreading around the teeth, using the tongue, as described previously.

Six subjects participated in each of these tests. Unstimulated salivary samples were taken for five-minute periods as in the previous experiment, except that one extra sample was collected for each subject at seven hours following gel application.

#### *Estimation of amounts of fluoride ion ingested during and following fluoride application*

During gel application subjects were required to drool excess saliva and gel into clean beakers. After application, each tray or brush was also placed in the beaker and subjects were then asked to expectorate excess gel into these beakers for one minute. This procedure was intended to simulate the normal clinical routine of professional or self-gel application and to collect all gel not retained in the mouth for each subject. Amounts of gel used in each case were carefully weighed and it was assumed all gel, which was not collected in the beakers, would eventually be swallowed.

A volume of 500ml of deionized distilled water was added to the beakers to cover all appliances used and shaken vigorously for two hours to form a solution of all remaining fluoride ion.

The amount of fluoride present in the beaker from each subject in each experiment was calculated and subtracted from the original amount used, to indicate the probable amount swallowed during the application process, and retained in saliva or adsorbed to the mucous tissues. It was recognized that the amount retained in the saliva or attached to the oral tissues would be only slowly released and eventually swallowed.

#### *Total blood fluoride elevation following gel application*

Three volunteers participated in this experiment. Prior to the tests, each volunteer had a butterfly catheter placed in a suitable forearm vein and the catheter was retained for the five hours of the tests, small amounts of heparin being used to inhibit clotting within the catheter.

The gels were applied as follows: 5g APF gel applied professionally in commercial trays for four minutes; strips containing 0.5g of APF gel self-applied by toothbrush to the facial surfaces of both arches; and one subject only swallowed 10mg fluoride ion prepared in the form of a NaF solution.

Venous samples of 3ml blood were taken prior to gel application, immediately following, and at 15, 30, 45, 60, 120, 180 and 300 minutes following gel application. To inhibit clotting, each tube contained

**Table 2. Mean salivary fluoride levels (ppm) at varying times following use of fluoride dentifrice or mouthrinse**

Time (min)	Mouthrinse			Toothpaste		
	0.022%	0.05%	0.2%	0.25g	0.5g	1.5g
Base	0.046±0.025	0.028±0.028	0.038±0.019	0.039±0.039	0.036±0.0214	0.037±0.021
0	13.856±5.364	30.911±12.21	133.939±64.227	1.372±0.9	2.627±4.7	4.700±1.95
20	0.396±0.206	0.865±0.319	6.941±3.167	0.126±0.059	0.175±0.214	0.214±0.125
40	0.166±0.059	0.256±0.083	3.309±2.216	0.065±0.026	0.077±0.082	0.082±0.025
60	0.097±0.044	0.185±0.089	1.794±0.918	0.057±0.029	0.056±0.072	0.072±0.022
120	0.038±0.019	0.153±0.125	0.845±0.526	0.063±0.056	0.039±0.092	0.092±0.102
180	0.031±0.018	0.08±0.108	0.667±0.537	0.048±0.045	0.033±0.041	0.041±0.017
300	0.025±0.016	0.032±0.032	0.229±0.224	0.025±0.019	0.023±0.044	0.044±0.024

0.5ml heparin solution. Samples were kept in ice until fluoride separation could be carried out. The venous blood collection was carried out by medical nursing staff of the Oral and Maxillofacial Surgery Unit of the South Australian Dental Service, adhering to full infection control procedures.

Test blank containers of 0.5ml heparin were also tested for fluoride content along with blood samples.

#### *Fluoride ion separation and analysis*

Fluoride ion separation from all salivary, gel, mouthrinse and toothpaste samples and from whole blood was carried out using the Taves<sup>3</sup> closed acid hydrolysis technique. This technique used hexamethyldisiloxane (HMDS) as the transport for the volatile HF formed during acid hydrolysis into a fluoride sink within this closed chamber, resulting in a 98 per cent recovery rate. A fluoride specific electrode was used to measure fluoride concentrations (Table 1).

### **Results**

#### ***Salivary retention of fluoride from dentifrices and mouthrinses***

Table 2 shows the concentration of total fluoride ion retained in saliva at selected times following use of varying amounts of dentifrice and differing concentration mouthrinses. These data and data from experiments recording salivary retention of fluoride from gels and fluoride ingestion represent mean and standard deviations from six subjects.

The data from these experiments indicate the retention rate of fluoride in saliva from toothpastes was roughly proportional to the amount used, although wide differences between subjects immediately following brushing point to the individual variability of this amount. Likewise, the amount of fluoride retained in saliva following mouthrinse use was also roughly proportional to the concentration of fluoride ion in the original mouthrinse preparation.

It is interesting to note that salivary fluoride levels remained well above baseline amounts for two hours after a full brush of paste was used. When mouthrinse containing similar concentrations of fluoride as toothpaste was used (1,000ppm), retention continued for a much longer period and rates were still significantly elevated for most subjects after five hours. Even the 0.05 per cent (250ppm F<sup>-</sup>) fluoride mouthrinse was retained much longer than occurred following brushing with a full head of paste. This was obviously because the subjects did not rinse following the use of mouthrinse, though all had morning coffee after the 60-minute sample of saliva was collected.

#### ***Salivary retention of fluoride from gels***

The concentrations of total fluoride ion present in saliva following use of acidulated and neutral concentrated gels and toothpaste gels used as a gel/mouthrinse are presented in Table 3 and Fig 1.

**Table 3. Mean salivary fluoride levels (ppm) at various times after application of gels using differing methods**

Time (min)	5g APF gel in commercial tray	2g APF gel in custom tray	5g NaF gel in commercial tray	0.5g APF gel applied with toothbrush	0.6g dentifrice gel self-applied with spatula
Base	0.038±0.023	0.041±0.018	0.043±0.032	0.029±0.026	0.03±0.013
0	173.34±105.38	169.17±55.07	208.61±72.05	56.24±27.95	6.83±2.09
20	26.52±9.80	18.89±6.22	15.99±5.53	34.64±8.89	0.99±0.63
40	17.14±8.82	10.08±2.59	7.77±4.71	6.95±4.44	0.42±0.33
60	9.26±3.79	6.01±1.38	5.42±3.49	4.70±2.50	0.38±0.22
120	5.26±2.24	3.89±1.90	1.62±0.78	1.74±1.66	0.30±0.28
180	4.07±1.77	3.69±0.39	0.78±0.69	1.14±1.24	0.18±0.04
300	1.14±0.50	1.49±0.53	0.41±0.31	0.45±0.24	0.16±0.06
420	1.16±0.30	1.39±0.03	0.18±0.17	0.242±0.19	0.18±0.09

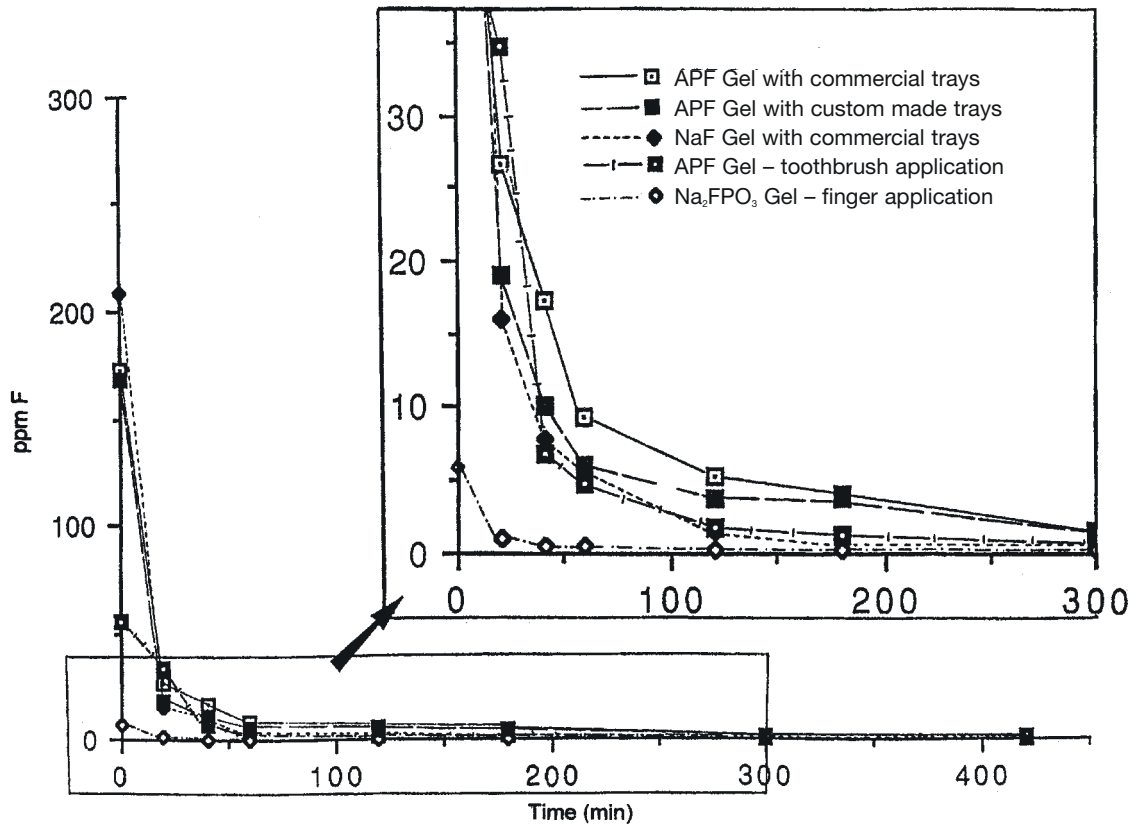


Fig 1. – Salivary fluoride (ppm) retained in saliva following application of topical gels using a variety of methods against time (min).

The initial amount of fluoride ion retained in saliva (Table 3) following the use of concentrated acidulated or neutral gels did not vary significantly whether commercial or custom-made trays were used. Retention rates were still very high seven hours after application for the acidulated gels, though considerably less for NaF gel. The use of even low quantities, for example, 0.6g, in a self-application brushing technique resulted in surprisingly high retention rates per amount of fluoride used when compared with that from the much higher amounts, for example, 2 or 5g, used in trays. After 20 minutes, retention rates were similar to those from use of 10 times the amount of NaF gel in a commercial tray and very comparable with the use of larger amounts of 1.23 per cent APF gel in either commercial or custom trays. Even at seven hours, the retention rate

was comparative. It is acknowledged that the use of trays may prove more comfortable for some patients and limit the spread of gel in the oral cavity. However, where cost is a factor or where trays are not liked by patients, it is useful to know this simple method provides such good retention rates.

Use of a centimetre ribbon of toothpaste gel as a self-applied tongue-smear alternative provided a salivary retention rate less than from the concentrated gels in proportion to the amounts of fluoride ion applied. Even so, it appeared to have a superior retention rate in the short and long term compared with twice the amount of toothpaste used with a normal brushing technique. This does not indicate it was an alternative to toothbrushing, the necessity for plaque removal by the latter being

Table 4. Ingestion of fluoride from topical fluoride gels applied by a variety of methods

Method of gel application	Amount of F initially used (mg)	Amount of F retrieved (mg)	Amount presumed ingested (total) (mg)	Amount accounted for by salivary retention over 7h (mg)
5g APF 1.23% gel in commercial tray	62.5	56.4	6.1	3.5
2g APF 1.23% in custom tray	24.6	21.1	3.5	2.4
5g NaF 2.2% gel in commercial tray	50.2	45.9	4.3	1.9
0.5g APF 1.23% gel applied with toothbrush	6.18	4.38	1.8	0.9
0.6g dentifrice gel self-applied with spatula	0.62	0.32	0.3	0.1

**Table 5. Mean total blood fluoride concentrations (ppm) up to five hours following APF gel application and controlled ingestion**

Time (min)	Method 1*	Method 2†	Method 3‡
0.00	0.040 (0.01)	0.035 (0.01)	0.020
+15	0.038 (0.02)	0.032 (0.02)	0.035
+30	0.038 (0.04)	0.038 (0.03)	0.070
+45	0.050 (0.06)	0.040 (0.02)	0.170
+60	0.070 (0.03)	0.050 (0.02)	0.160
+120	0.080 (0.04)	0.035 (0.01)	0.050
+180	0.050 (0.03)	0.036 (0.01)	0.052
+300	0.052 (0.02)	0.038 (0.02)	0.045

\*5g APF gel in commercial tray for four minutes.

†0.5g APF gel self-applied in strips by toothbrush to facial surfaces of both arches.

‡10mg of fluoride ion prepared as NaF solution swallowed by one subject only.

critical to prevention. These data serve only to provide comparison in retention rates from all methods of topical fluoride use, in order to help the clinician formulate the most effective combinations of use for a particular patient.

### Fluoride ingestion

Table 4 shows the initial amounts of fluoride ion applied in each method in the experiment recording salivary retention of fluoride from gels, the amounts retrieved by drooling excess into the beaker, by expectoration for one minute following completion of the application and the amount still attached to the article of application (tray or toothbrush). By subtraction of this amount from that originally used, the estimated amount of fluoride ion which would eventually be swallowed was calculated. This amount included that adsorbed to the soft tissues of the mouth, retained in saliva and any swallowed during the application process. Amounts of fluoride ion present in the saliva over the seven hours of the experiment were estimated by computer analysis of

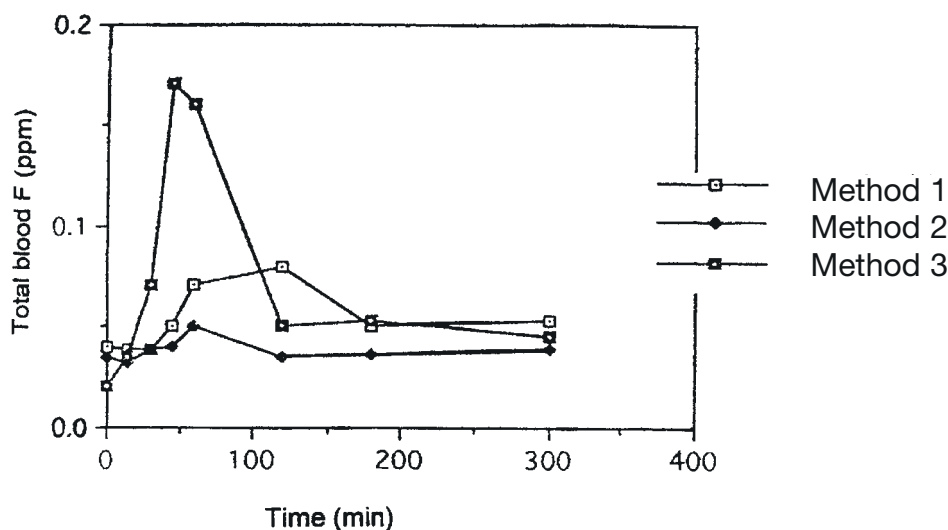
the area under each curve of declining retention rate (Fig 1). It was assumed the majority of fluoride to be ingested which was not accounted for by this figure was swallowed during the application process.

### Fluoride levels in blood following gel application

Total blood fluoride levels resulting from application of 5g of 1.23 per cent APF gel in a commercial tray, in three subjects, with careful evacuation and expectoration of excessive gel following application, reached a mean peak of 0.07ppm, and remained in this vicinity for approximately 100 minutes (Table 5, Fig 2). Gel self-application by brushing resulted in total blood fluoride concentrations which were barely detectable above baseline. The ingestion by one subject of 10mg fluoride ion resulted in a peak of approximately 0.17ppm blood fluoride concentration for a very short period of time, quickly reducing to the plateau level retained following use of the 5g of APF gel.

### Discussion

There is concern regarding the ingestion rates of dentifrices by young children,<sup>4</sup> and current practice is to recommend parental supervision to ensure only a 'pea-sized' amount of dentifrice is used. Even though the subjects in this case were young adults, it is interesting to note retention rates of fluoride ion in saliva following use of dentifrice are roughly proportional to quantity used. Even though use of reduced quantities of dentifrice by children is appropriate, whether there is a corresponding significant reduction of oral retention rates in such cases and whether there is a corresponding reduction in preventive effectiveness are questions that need to be asked. The small size of the oral



**Fig 2.** – Mean total blood fluoride concentrations (ppm) up to five hours following APF gel application and controlled ingestion.

cavity and reduced ability to rinse excess paste in young children may still result in much greater retention levels in such cases.

In formulating a program for a patient, it is important to know the comparative dose/retention rate for all types, concentrations and methods of application of available topical fluoride materials. Of interest was the greater level of retention of fluoride ion in saliva following the use of mouthrinses compared with dentifrices. When compared with the use of concentrated gels, mouthrinses provide a good comparative dose/retention rate for the amount of fluoride ion introduced into the oral cavity.

Among the methods used for gel application, the results indicated duration of retention of NaF gel was much less than acidulated gels at approximately the same concentration. The relative effectiveness of both types of gels needs to be further investigated *in vivo* and *in vitro*.

The results indicated the amount of gel presumably swallowed was reduced significantly by use of a custom-made tray, even with effective evacuation to minimize swallowing. When the amount of fluoride accounted for by salivary retention figures was calculated using the area under the curves in Fig 1, it appeared the amount of gel swallowed during the application process was within acceptable limits for all methods used. It must be remembered that a certain amount of fluoride is retained adsorbed to the oral mucosa, to the teeth and in plaque,<sup>5</sup> though these amounts will diminish as they are slowly released into saliva and then swallowed.

The data from ingestion studies of gel use were surprising and tended to be contrary to those from previous studies by other workers. In his studies, Ekstrand<sup>6</sup> found much higher amounts of gel fluoride were swallowed. However, Ekstrand did not use evacuation procedures, the subjects swallowing all excess gel from the trays.

The total blood fluoride levels following commercial tray application of 1.23 per cent gel were relatively low. This was presumably due to slow release from the ingested gel over a two-hour period. It has been stated that 0.9-1ppm of fluoride in plasma represents a toxic dose level in adults.<sup>6</sup> The mean levels obtained from the three subjects were well below this concentration (0.07ppm). The resultant spike of increase in total blood fluoride was consistent with that obtained in other studies, indicating this method produced reliable data.<sup>7</sup> Following gel application using a custom tray, it was originally intended to record blood fluoride levels. However, the results from use of a commercial tray were so low, it was decided there was little benefit in this further knowledge, considering the invasive nature of the test.

Despite this evidence, it is important dental practitioners use methods which ensure minimal ingestion and maximum retention of fluoride ion, especially in the young and the elderly. It is also important that adequate instruction in the safest methods of self-application be given to each patient, including a practice session in the dental office. It is recognized that salivary retention rates do not necessarily equate with enamel uptake and storage or final preventive effectiveness. Even so, this measure should provide some initial concept of relative effectiveness.

The extensive prescription of topical fluorides by dental practices requires all staff to know the precise dosage rates, probable toxic potential and outcomes of use of such agents. As demonstrated, some methods are more dose-effective than others, yet some methods and materials are more acceptable to patients than others. A thorough knowledge of comparative retention and ingestion rates will enable the dental practitioner to determine those methods or combination of methods which may prove most effective and safe.

## Conclusions

Although previous studies have sought to determine fluoride retention rates following utilization of mouthrinses, dentifrices or gels available abroad,<sup>8,9</sup> this study provides a comprehensive analysis of the comparative retention rate following use of dentifrices, mouthrinses or gels commonly available in Australia. The study also provides estimates of ingestion rates and blood fluoride levels associated with the use of concentrated gels and substantiates the safety of these gels in normal adults when safe clinical procedures are followed.

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