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Fluoride concentrations in whole saliva following use of fluoride tablets and a rinse

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Abstract

This clinical investigation is comprised of two studies. The first monitored the oral clearance of fluoride following the use of an oral rinse and two types of tablets: one that was chewed, swished, and swallowed, and another that was allowed to dissolve undisturbed at a specific site in the oral vestibule. Fluoride from the rinse and tablets exhibited similar rapid clearance patterns with a mean concentration of 1.2 ppm or less within 1 hr and returned to baseline concentrations within 24 hr. Data from the second study indicated fluoride was distributed unevenly to various areas of the mouth from the slowly dissolving undisturbed tablet. Information concerning oral clearance of fluoride may be used to rationalize various treatment regimens.

The frequent oral use of fluoride preparations has been shown to provide significant cariostatic effects. Two of the most popular vehicles are tablets and rinses (Driscoll 1974; Bruun et al. 1982; Horowitz and Heifitz 1986). Protection afforded the dentition by these preparations is primarily the result of cariostatic effects of saliva-borne fluoride (Larson et al. 1976; Ericsson 1977; Bruun et al. 1982). Consequently, several investigators have monitored the fluoride concentrations and clearance in whole saliva following use of fluoride tablets and rinses (Aasenden et al. 1968; Büttner et al. 1973; McCall et al. 1981; Bruun et al. 1982). However, relatively little information is available concerning the intraoral distribution of fluoride from tablets that are allowed to dissolve passively or undisturbed (Weatherell et al. 1984; Primosch et al. 1986).

This investigation measured the clearance of fluoride from the oral cavity following a single exposure to sodium fluoride supplied as: 1) a tablet that was chewed, swished, and swallowed, 2) a rinse, or 3) an experimental tablet designed to passively dissolve in 20 min. In addition, the distribution of fluoride was measured in eight areas of the oral cavity 5 min after complete dissolution of the undisturbed tablet.

Materials and Methods

Participants in both studies of this investigation were in good general and oral health. All treatments and saliva collections were made between 9–10 a.m. and at least one hour after food ingestion. Participants were instructed to brush their teeth as usual, but refrain from using a dentifrice or oral rinse containing fluoride for 24 hr prior to baseline collections and until the study was complete. The drinking water of the participants contained approximately 0.9 ppm fluoride.

In the first study, 3 men and 3 women (21–49 years of age) received each treatment on separate days during one week. Samples of unstimulated whole saliva were collected before and after each treatment. On the first day a slightly flavored tablet containing 1 mg of fluoride (Nafeen Chewable Fluoride Tablets, Lot Δ91022, Cooper Laboratories, Mountain View, CA 94043) was chewed for 30 sec, and the resultant fluoride/saliva mixture was swished around the mouth for an additional 20 sec and swallowed. Two days later, 10 ml of a rinse containing 0.2% sodium fluoride (approximately 9 mg of fluoride) was swished around the oral cavity for 60 sec, expectorated into a graduated tube and saved for later analysis. Twenty four hours later, the experimental tablet containing 1 mg of fluoride (Colgate Hoyt, Lot Δ79026-5A1, Canton, MA 02021) was placed under supervision in the buccal vestibule near the lower right first molar. It was allowed to dissolve undisturbed and the resultant fluoride-saliva solution swallowed reflexively.

Before each treatment, and on the following day prior to saliva collection, participants were instructed to rinse with 10 ml of distilled water. Unstimulated whole saliva was collected in polystyrene tubes during 5-min intervals. Samples were obtained immediately prior to treatment and 5, 15, 30 and 60 min after treatment, and again 24 hr later. All specimen containers were placed over chipped ice immediately after collection and stored at –70°C. Prior to analysis, the saliva samples were thawed

and clarified by centrifugation for 20 min at 2000 g and 4°C. The volume of the supernatant liquid was recorded and analyzed for fluoride using the method of Grön et al. (1968). The fluoride level was measured immediately after mixing an aliquot of supernatant with an equal volume of buffer (TISAB). Fluoride activity of the mixture was detected with a combination electrode (Orion 96-09, Orion Research Inc., Cambridge, MA 02139).

In the second study, the pattern of fluoride distribution in the oral cavity from an undisturbed slowly dissolving tablet was assessed in 6 males (12-16 years of age). Samples of oral fluid were obtained using borosilicate glass filter discs (Millipore 47005, Millipore Corp., Bedford, MA 01730). The fluoride content of the filters had been reduced from approximately 1 ppm to less than 0.01 ppm by soaking them in 50 ml of 1N HC104 for 30 min. Each filter was placed within a filter holder (Swinnex 47, Millipore Corp.), then rinsed with 250 ml of distilled water and 10 ml of 95% ethanol. The filters were allowed to dry in an oven at 80°C for 30 min. Discs 6 mm in diameter were cut from the filter, placed in capped polystyrene vials, and weighed.

Before the slowly dissolving experimental tablet was administered, discs were placed 3 mm apical to the free gingival margin at 8 sites in the mouth of each subject for 5 min. Discs were positioned on the buccal gingiva near the 4 first molars, on the midline labial gingiva of the maxilla and mandible, and on the lingual gingiva near each mandibular cuspid. The discs were returned to their coded vials and reweighed. Participants were instructed to let the tablet dissolve undisturbed. The oral fluids at the 8 sites again were sampled with filter discs, beginning 5 min after the tablet had dissolved completely (approximately 25 min after placement). All discs were stored at -10°C until analysis. The weight increase of each sample was used to calculate the volume of oral fluid absorbed by the disc. An equal volume of TISAB and 2.5 ml of distilled water were added and mixed thoroughly with a micropipette tip. A 0.3 ml aliquot of the mixture was put on a cover slip and placed in contact with the fluoride combination electrode sensor for 1 min. This was done once to exercise the sensor and 3 more times for recording. The fluoride level was computed from the logarithmic mean of the final 3 millivolt readings. The sensor was calibrated using the same procedures.

Fluoride clearance curves were plotted on graph paper, and the area under the curve (AUC) computed for each treatment and expressed in square mm. Mean differences were detected with a one-way analysis of variance and compared using the method of Tukey (Dixon and Massey 1957).

Results

All 3 regimens in the first study demonstrated the highest mean fluoride levels in the salivary samples collected 5 min after treatment (Table 1). The chew, swish, and swallow tablet imparted 7.5 ppm; the slowly dissolving tablet 12.9 ppm; and the rinse 43.4 ppm. The coefficient of variation for each treatment at most samplings was approximately 0.5. Within 24 hr after each treatment, the fluoride concentration in whole saliva returned to baseline levels (0.02–0.03 ppm). The mean rate of unstimulated whole saliva flow rate was 0.53 ml/min with a standard deviation of 0.27.

TABLE 1. Mean Levels of Fluoride in Whole Saliva Obtained at Various Time Intervals Following Three Treatment Regimens

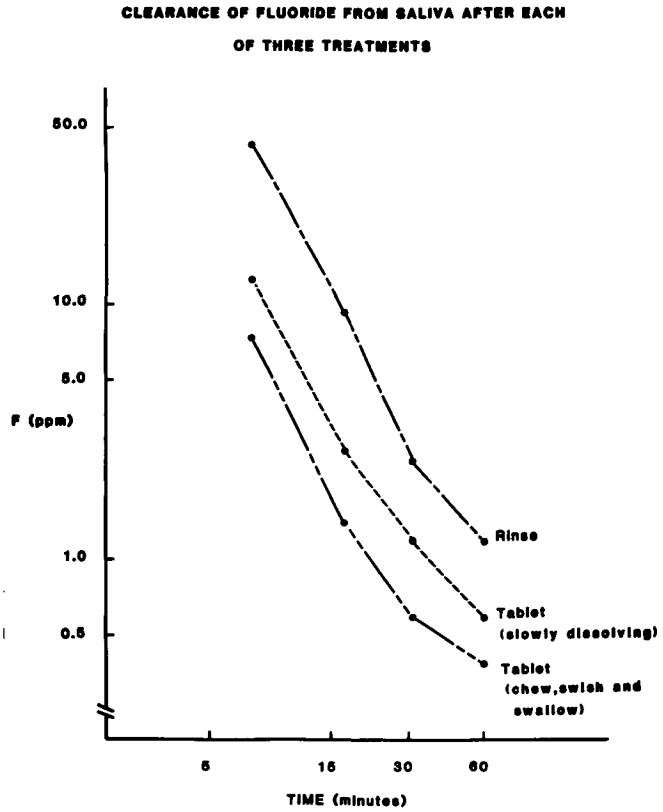
		Mean Fluoride Levels (ppm) Min after treatment*				
Treatment	*Baseline*	*5*	*15*	*30*	*60*	*24 hr*
Tablet (chew, swish, and swallow)	0.04	7.5	1.4	0.6	0.4	0.03
Tablet (dissolved undisturbed)	0.03	12.9	2.7	1.2	0.6	0.02
Rinse	0.02	43.4	9.5	2.5	1.2	0.03

* Coefficient of variation ~0.5, N = 6.

The rinse provided significantly higher concentrations of fluoride for the entire test period (AUC) than either of the tablets, which delivered statistically equivalent concentrations of systemic fluoride ($P < 0.05$). However, the slowly dissolving tablet group exhibited mean fluoride concentrations which were numerically intermediate for each sampling interval.

The pattern of oral fluoride clearance was similar and rapid for each of the test agents, resulting in levels of 1.2 ppm or less after 60 min (Table 1). A roughly linear relationship was observed between the logarithm of the fluoride concentrations and the logarithm of time (Fig 1, see top of next page). The expectorated oral rinse from each participant was analyzed for fluoride content. Although the findings varied, the mean intraoral fluoride retention was 1 mg (12%). The correlation (r) of the whole saliva flow rate to fluoride concentration was inconclusive: baseline (r = -0.39), chew, swish, and swallow (r = -0.24), slowly dissolving tablet (r = -0.15), and rinse (r = 0.74).

In the second study, the fluoride from the undisturbed slowly dissolving tablets was found to be unevenly distributed throughout the oral cavity (Table 2, see bottom of next page). Much of the fluoride remained near the dissolution site with the lowest levels diffusing to the opposite quadrants from the tablet placement. The mean flow rate for unstimulated saliva was 0.54 ml/min with a standard deviation of 0.27. This was similar to that noted in the first study of this investigation.



Discussion

The essentially linear relationship between the logarithms of fluoride concentration and time during the first hour was remarkably similar to the result reported by Aasenden et al. (1968). They tested clearance of fluoride delivered as a 0.2% rinse, and topical applications of 0.05% and 1.2% fluoride. In the present study, the fluoride concentration returned to baseline within 24 hr. The mean baseline concentrations (0.02–0.04 ppm fluoride) observed also were similar to those reported previously for children and adults consuming fluoridated drinking water (Yao and Grön 1970).

The unstimulated salivary flow rate at baseline and following fluoride treatment was in accord to that previously reported (Brawley et al. 1940; Aasenden et al. 1968; Turtola 1977). No consistent trend appears to exist between the flow rate and fluoride concentration of saliva before fluoride treatment. The salivary flow rate was unassociated with the AUCs following the rinse or tablet procedures. Surprisingly, the correlation coefficients were positive, with only that of the flow rate and the rinse AUC approaching significance ($r = 0.74$). Many factors governing oral clearance may have obscured the relationship of salivary flow rate and fluoride retention in the oral fluids, including swallowing volume and frequency (Dawes 1983). It would be desirable to evaluate this relationship in a larger population using a multifactorial approach.

Despite the rapid decrease in fluoride level following treatment, the samples taken 60 min post-treatment still were 10–60 times higher than those observed at baseline and probably persisted for several hours. Büttner et al. (1973) reported that fluoride tablets containing 1 mg of fluoride, when swallowed, elevated the fluoride levels in serum and ductal saliva for at least 8 hr. Furthermore, dental plaque, which concentrates fluoride from its milieu, returns some of it to the oral fluids. This reservoir presumably provides much of the caries protection noted following the use of fluoride tablets and rinses.

When comparing the fluoride levels provided by the two types of tablets, the sampling schedule should be considered. In the present study, oral fluids were collected after the tablets had cleared the mouth to avoid disturbing their dissolution. Compared with the chew, swish, and swallow tablet, the slowly dissolving tablet had been in the mouth an additional 20 min at each of the sampling intervals. Therefore, it is presumable that the slowly dissolving tablet had imparted more fluoride to the oral cavity than did the chew, swish, and swallow tablet, even though their areas under the curve are statistically equivalent.

Observed fluoride values at the initial baseline probably were influenced by fluoride-containing dentifrices used prior to the study. Saliva samples were taken at the same time of day to avoid the effects of circadian rhythms on salivary flow and fluoride content (Dawes 1975; Mirth et al. 1982). Consistency may have been promoted by removal of sediment known to contain

TABLE 2. Fluoride Distribution From an Undisturbed Slowly Dissolving Tablet to the Whole Saliva in Various Areas of the Mouth Five Min After Completion of Treatment

	Fluoride (ppm)	
Areas Sampled	*Mean*	*Standard Deviation*
Maxillary right first molar (buccal)	5.86	8.29
Maxillary central incisors	5.80	11.07
Maxillary left first molar (buccal)	3.58	4.30
Mandibular left first molar (buccal)	2.50	3.75
Mandibular central incisors	10.18	9.29
Mandibular right first molar (buccal)*	30.43	30.73
Mandibular right cuspid (lingual)	10.77	21.02
Mandibular left cuspid (lingual)	1.45	2.73

* Tablet site.

rich deposits of plaque-associated fluoride (Yao and Grön 1970). Analytic accuracy was assured by frequent calibration of the electrode and occasional reanalysis of a salivary sample using silane-mediated diffusion for fluoride isolation. The remarkably consistent salivary flow rate probably exerted little effect on the fluoride detected in the resultant sample. Ductal saliva would have exhibited a lower fluoride concentration (Yao and Grön 1970) than the whole saliva of the current study, because whole saliva is actually an oral fluid containing soluble non-salivary constituents of plaque and crevicular fluid.

The systemic exposure to fluoride was comparable for each of the three modalities used in the present investigation. The tablets containing 1 mg of fluoride were ingested, whereas the rinse was expectorated with about 1 mg of fluoride being retained and presumably swallowed. When considered on a weekly basis, tablets would be expected to provide substantially more systemic fluoride because tablets are consumed daily, whereas rinses of this concentration generally are used weekly. However, rinses and tablets similar to those used in this study often provide comparable levels of protection (Bruun 1982). Thus, rinses result in a more favorable systemic dose/cariostatic response ratio. The dose response also favors the rinse when considering the concentration of fluoride in the oral fluids over time expressed as area under the curve. The AUC ratios are as follows: rinse = 5.2; slowly dissolving tablet = 1.7; chew, swish, and swallow tablet = 1. Unfortunately, once fluoride is ingested, only a small percentage is subsequently secreted into the saliva.

The intraoral distribution of fluoride varies considerably among treatment modalities. Oral rinses and tablets that are chewed actively or sucked provide a better distribution of fluoride than do tablets that are allowed to dissolve passively (Primosch et al. 1986; Weatherell et al. 1986). Primosch's (1986) limited study reported similar findings to those which we obtained at 8 intraoral sites, indicating slow fluoride dispersion from a passively dissolving tablet.

Despite the sluggish diffusion of fluoride noted by this and other studies, several investigators have reported that slowly dissolving tablets afford good protection to the teeth against dental caries (Stephen and Campbell 1978).

Delivering and maintaining an active agent at its site of action is an important therapeutic principle. The caries protection provided by slowly dissolving tablets would be expected to improve if the dissolution sites are varied, thereby providing a more homogeneous dispersion of fluoride. Also, expectoration of a fluoride rinse apparently removes most, but not all, fluoride from the oral cavity. These findings illustrate the need for understanding the pharmacokinetics of various fluoride regimens in order to rationalize their preferred application.

The informed consent of all study participants, or their parents (when a minor participated), was obtained after the nature of the procedures and the possible discomforts and risks had been fully explained.

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Sealants underused

Only 7.6% of American schoolchildren have dental sealants on their teeth, according to survey results announced by the National Institute of Dental Research (NIDR).

Nearly 40,000 children were examined during the 1986-87 school year. The results of the survey showed that in New England, the Southwest, and the Northwest, 12% or more of the children studied had sealants placed. In the Northeast, Midwest, and Southeast, slightly more than 5% of children had them. In urban and suburban areas, 8% of children had sealants, compared to 6.3% in rural areas.

Officials at NIDR expressed surprise at the low rate of sealant usage, since research has found them to be completely safe, highly effective, and economical in preventing tooth decay.

The chewing surfaces of children's teeth are the most susceptible to decay and the least protected by fluorides. The NIDR surveyors found that two-thirds of all cavities occur in these areas of the tooth, where pits and fissures trap food particles and bacteria.

Sealants can last as long as 10 years. The cost of applying a sealant to one tooth is approximately $10-$15, and a growing number of insurance companies reimburse sealant application, according to the American Dental Association's most recent data.

Dental sealant resource kit available

Studies on the efficacy and cost effectiveness of dental sealants are available in a "Dental Sealant Resource Kit" available from the ADA's Council on Community Health, Hospital, Institutional and Medical Affairs.

Single copies of the kit are available by calling 312-440-2862.