Sealing of Developmental Pits and Fissures: II. Fluoride Release from Flexible Fissure Sealers

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A fluoride-releasing polyurethane adhesive coating was found to be effective in reducing the acid solubility of enamel in vitro and the incidence of carious lesions of rat molars in vivo; this indicates that the coating would be an efficient topical fluoride system for application to developmental pits and fissures and all other surfaces of teeth.

An investigation of a potentially anticariogenic system was undertaken in the present study; this system was a polyurethane-based formula that contained fluoride salts for coating all surfaces of teeth, including pits, fissures, and interproximal surfaces. Physical and chemical properties of the polyurethane material have been reported previously.[1] Both in vitro and animal experiments were conducted.

The polyurethane material was formulated to release fluoride to the enamel surface and to maintain the released fluoride on the enamel surface for an extended period, of 24 hours to 30 days. This topical system was designed to provide improved caries resistance properties to all surfaces. Evidence that a long-term topical fluoride application is far more effective in providing caries resistance to enamel than conventional short-term (4 to 12 minute) application is derived from various sources.[2,3] The principal evidence is that with long-lasting topical agents, there is an increased formation of caries resistant fluorapatite.[4,5] In short-term applications, the major deposit left on enamel is believed to be calcium fluoride (CaF_2). This type of fluoride is leached away rapidly in the first 24 hours.[4–6] Conversion of CaF_2 to fluorapatite apparently increases with time and is achieved by topical fluoride systems in which the fluoride is isolated from the oral environment for at least 16 to 24 hours.[4,5]

In the initial phase of this study, it was decided to evaluate several of the clinically proven fluorides to determine the most suitable for incorporation in the polyurethane polymer. Stannous fluoride (SnF_2) was not considered because of its known instability[7] and propensity for staining teeth.[8–10] Moreover, in preliminary tests, it was found that SnF_2 dissolved only slowly in aqueous solutions. Disodium monofluorophosphate (Na_2PO_3F) was considered because of evidence that this fluoride is effective in formation of true fluorapatite, probably because of the contribution of both the fluoride and PO_4 ions of the moiety to synthesis of the apatite.[11,12] Another consideration was that the data indicating that Na_2PO_3F may be only an eighth as toxic as NaF.[13] Sodium fluoride and acidulated fluoride also were evaluated because of their known usefulness as topical fluorides.[14]

Materials and Methods: In Vitro Studies

ENAMEL INSOLUBILITY.—Three different fluorides were compared for their ability to improve resistance of enamel to acid attack. Samples (500 mg) of powdered bovine enamel 30 to 80 micrometers (μm) in diameter were obtained from mandibular anterior teeth of 1-year-old calves by grinding in a silicone carbide disk. The samples were pretreated for 24 hours in 25 ml solutions of distilled water; 2% Na_2PO_3F;* 2% NaF in distilled water; and 1% NaF plus 1% KH_2PO_4 in distilled water. After pretreatment, five specimens were taken from each of the pretreatment

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* Na_2PO_3F, Ozark Mahoning Co., Tulsa, Okla.

solutions, rinsed with distilled water, and placed individually on 0.22 μm pore size Millipore filters* fitted into tissue holders. The specimens were dried for two hours at 52 C and weighed. Weight of the average specimen of enamel placed on an individual Millipore filter was 52.4 mg (weights varied from 51 to 53 mg) after pretreatment. The specimens were dried for two hours at 52 C and weighed.

Specimens were immersed in 0.4 M acetic acid-sodium acetate buffer, pH 4, for two hours, washed with 10 ml distilled water, and dried two hours at 52 C. After drying, the specimens were weighed again and weight changes were noted. In a second series, samples were pretreated for 24 hours in 25 ml solutions of distilled water; 0.4 acetate buffer, pH 3.8; 2% Na_2PO_3F in distilled water; and 1% NaF plus 1% KH_2PO_4 in distilled water. The acidic acetate buffer solution was included in this phase as a pretreatment solution to determine if improved resistance to subsequent acid solubilization was caused by previous removal of the acid soluble components of the powdered enamel. After pretreatment, samples were handled as in the first series, but were dried to a constant weight by heating for three hours at 52 C.

COMPARATIVE FLUORIDE UPTAKE.—Relative amount of fluoride uptake by enamel in different fluoride solutions was studied. Samples (500 mg) of powdered bovine enamel were added to 25 ml solutions of 1% NaF; 2% NaF; 2% Na_2PO_3F; and 1% KH_2PO_4 + 1% NaF, all in distilled water. Initial readings for fluoride ion concentration in each solution were compared to 24 hour values, and any measured loss of ions from a solution was assumed to be a measure of fluoride incorporation into enamel. The solutions were held in polypropylene rather than glass containers. Readings were performed with a specific fluoride ion electrode.† The concentration of fluoride in NaF solutions was estimated by reference to readings obtained from the same electrode with known concentrations of NaF. The concentration of fluoride in Na_2PO_3 solutions was estimated by reference to readings obtained from the same electrode with known concentrations of Na_2PO_3F.

COMPARATIVE WEIGHT LOSS OF ENAMEL.—The comparative amount of powdered enamel lost or dissolved in several different fluoride solutions was ascertained by semiquantitative means. Bovine powdered enamel was dried to constant weight by vacuum drying. Samples (1 gm) of the dried enamel were placed in 10 ml distilled aqueous solutions of 2% NaF; 1% KH_2PO_4 + 1% NaF; 2% Na_2PO_3F; and 10% Na_2PO_3F for 48 hours. The solutions then were diluted with 40 ml of distilled water and decanted over filters.‡ The residual enamel remaining on the filters then was desiccated again to constant weight and reweighed to determine the extent of enamel loss or solubilization in each of the fluoride solutions used. The experiment was performed three times and the results were averaged.

COMPARATIVE RELEASE RATES FROM POLYURETHANE.—Comparative release rates of several types of fluorides incorporated into a polyurethane polymer were studied.[1] The polyurethane-based formulation, designated 9070, was prepared. Ten percent (w/w) Na_2PO_3F was incorporated by stirring. The mixture was spread immediately as thin films and cured at laboratory ambient conditions for half an hour. Sections 18 cm^2 in area and an average of 8 mm thick were placed in individual polypropylene beakers and covered with distilled water. Average weight of each square was 400 mg. Measurements of fluoride concentration in the water were taken after the first 8 hours, after 24 hours, and then every three days thereafter for 34 days. After each measurement, the container was rinsed briefly with 50 ml distilled water, and another 50 ml of fresh distilled water was added.

The entire procedure was repeated, except that 10% NaF (w/w) was incorporated into the polymer in place of Na_2PO_3F. The release rates of Na_2PO_3F and NaF were compared. The release rate of 10% KH_2PO_4 + NaF in the polymer then was studied briefly by the same method.

EFFECT OF 9070 WITH Na_2PO_3F ON ENAMEL SOLUBILITY.—For reasons given in the discussion section of this paper, Na_2PO_3F was selected over the other fluorides for further studies. The ability of the

* Millipore Filter, Millipore Filter Corp., Bedford, Mass.

† Orion Research Inc., Cambridge, Mass.

‡ Whatman No. 1 filters, W. & R. Balston Ltd, Eng.

fluoride-releasing material 9070 to improve the acid resistance to enamel was determined by bringing the polymer in direct contact with the enamel. Ten percent Na_2PO_3F (w/w) was incorporated in the polyurethane material by stirring, and the mixture was applied as thin films to the bottom of five polypropylene beakers, where it was allowed to cure for one hour. After curing, 100 mg samples were placed in each beaker and 15 ml of distilled water was added. After four days at room temperature, the water-enamel mixture was decanted from the beakers onto filters.* Each beaker was rinsed with 25 ml fresh distilled water and the rinse was added to the water-enamel mix on the filter paper. The filtered enamel was brought to constant weight by oven and vacuum drying. Sixty milligrams of dried enamel from each sample then was exposed to 0.4 *M* acetic acid buffered to pH 3.8 according to procedures for acid solubility studies outlined previously.

Control samples of enamel obtained from five additional beakers that were not coated with the fluoride-releasing polymer were treated in the same manner as the buffered acid. Enamel exposed to the polymer was compared with the control samples to determine the degree of resistance to acid solubilization.

STUDY OF ANTICARIOGENIC ACTIVITY OF 9070 ON RAT MOLARS.—Three groups of Sprague-Dawley rats of both sexes were used in the investigation. The rats varied from 30 to 35 days of age and weighed 65 to 78 gm. The three groups were treated separately as described.

Group 1.—The rats were anesthetized with Metofane† and placed in a restraining apparatus. The jaws were held open by retracting the cheeks and the maxillary and mandibular incisors. The maxillary molars were ground with a dental blur to blunt all occlusal surfaces. Three days after the operation, the 20 rats were returned to the restraining device, and the fluoride-releasing polyurethane was applied in a four step procedure: while the rats were anesthetized with Metofane, the cheeks were retracted and the molars were washed and air dried; 50% acetic acid was applied with a cotton pellet and a one minute etching time was allowed; the molars were washed and air dried; and the molars were coated with a single application of the sealer by means of a small cotton pellet, and air dried for two minutes.

For the 20 control rats, only the fourth step was eliminated. The teeth were etched, but no sealer coat was applied. Experimental and control rats were placed on distilled water one hour and NIDR Diet 2000‡ 24 hours after the application of the sealer.

A culture of *Streptococcus mutans* (NIDR 5715-12) then was introduced by eye dropper into the mouths of experimental and control rats. An additional sample of the culture was introduced to deionized drinking water. Feces from infected rats also were added to the water supply. The rats were given the contaminated water for three days. Only deionized water was used for the first two weeks postoperatively, then tap water that contained less than 1 ppm fluoride was given. Fluoride activity was determined by means of a fluoride ion electrode.

The experimental rats were moved to cages occupied by control rats at weekly intervals, and vice versa. With this rotation system, variations in environment (humidity, temperature, and ventilation) from cage to cage were reduced.

Group 2.—Twenty experimental rats and 20 control rats were used in group 2. Both experimental and control rats were treated as in group 1, except that the maxillary molars were not rounded with the dental bur.

Group 3.—Experimental and control rats were treated as in group 1, except that the teeth were not ground and the rats were not inoculated with the bacterium. Only five experimental rats and five control rats were used in this phase.

EVALUATION PROCEDURE.—All rats were killed with an overdose of chloroform 46 days after introduction of Diet 2000. The upper and lower jaws were removed, and the molars were washed with a stiff brush and placed in a solenoid cleansing device. Remaining debris was removed with a fine explorer, and the teeth were fixed in a solution of 80 parts absolute alcohol and 20 parts 10% neutral aqueous formalin. The

* Whatman No. 1 filters, W. & R. Balston Ltd, Eng.
† Pitman-Moore Co., Indianapolis, Ind.
‡ Nutritional Biochemicals Co., Cleveland, Ohio.

presence of lesions was determined intially by gross examination under a dissecting microscope; the molars then were sectioned in half and stained by a procedure suggested by Van Reen and Cotton, as outlined originally by Konig.[15] The examiner was not told whether the jaws examined belonged to experimental or control rats.

Results: In Vitro Studies

REDUCTION OF ENAMEL SOLUBILITY WITH FLUORIDES.—After pretreatment of bovine enamel with NaF, acidulated NaF, and Na_2PO_3F solutions, reduction in acid solubility was compared to that of controls (Tables 1, 2). Acidulated NaF was slightly superior to NaF without acid phosphate and to Na_2PO_3F in enhancing resistance of enamel to acid attack.

COMPARATIVE FLUORIDE UPTAKE.—Amount of fluoride ion incorporation by bovine enamel was greatest when the enamel was exposed to acidulated NaF (Table 3). The rate of uptake of fluorides from both Na_2PO_3F and nonacidulated NaF solutions was comparable if the rate is based on the relative concentrations of fluoride ions in the two solutions.

WEIGHT LOSS OF ENAMEL IN FLUORIDE SOLUTIONS.—Weight loss of bovine enamel exposed to NaF or acidulated NaF was far greater than that of enamel exposed to Na_2PO_3F (Fig 1). Loss of weight of enamel in Na_2PO_3F was statistically insignificant.

TABLE 1
REDUCTION OF ENAMEL SOLUBILITY WITH FLUORIDES IN SPECIMENS DRIED FOR TWO HOURS AT 52 C

Pretreatment Solution	Solution pH	Loss of Weight After Two Hours in pH 4 Acid Solution* (mg)
Distilled water	6.6	36.6
2% Na_2PO_3F	7.6	17.0
2% NaF	6.6	15.0
1% NaF plus 1% KH_2PO_4	5.3	12.7

* Sample weight, 262 mg.

TABLE 2
REDUCTION OF ENAMEL SOLUBILITY WITH FLUORIDES IN SPECIMENS DRIED TO CONSTANT WEIGHT

Pretreatment Solution	Weight Loss After Immersion in Acetate Buffer (%)
Distilled water	17.8
0.47% acetate buffer, pH 3.8	16.8
2% Na_2PO_3F	2.4
1% H_2PO_4, plus 1% NaF	1.6

TABLE 3
FLUORIDE ION UPTAKE OF ENAMEL OVER FLUORIDE-RELEASING POLYURETHANE

Solution	Amount of Fluoride Uptake in 24 Hours (ppm)
1% NaF	1,000
2% NaF	1,600
2% Na_2PO_3F	500
1% NaF plus 1% KH_2PO_4	2,000

COMPARATIVE RELEASE RATES FROM POLYURETHANE.—Release of fluoride ions from Na_2PO_3F in cured polyurethane was much more rapid during the first 72 hours than from NaF in cured polyurethane. During this interval the water contained 22 ppm fluoride ions from Na_2PO_3F in the system, after which there was a rapid decline in the amount of fluoride that went into solution (Fig 2). In contrast, only 7 ppm fluoride was found in solution from NaF system in the initial 72 hours, and there was a more gradual decline in the amount of fluoride subsequently released from the cured polymer. Over the next 37 days, 48 ppm fluoride was found in solution from the NaF system.

Rate of discharge of fluoride in acidulated NaF from the cured polymer was 11 ppm at the end of 72 hours. Further readings were not made because of problems that involved deleterious changes in the

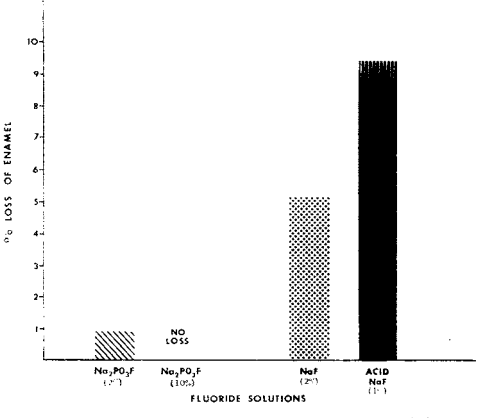

FIG 1.—Loss of weight of enamel in different fluoride solutions.

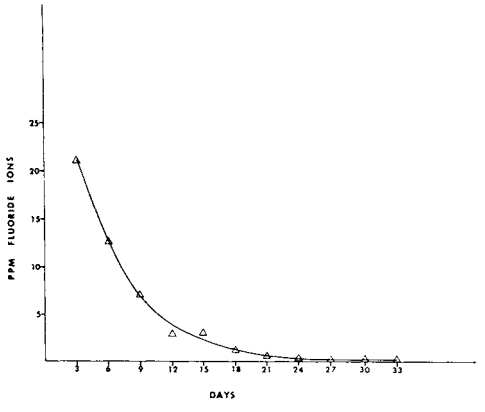

FIG 2.—Release rate of fluoride from Na_2PO_3F in cured polyurethane system.

polymer when acidulated NaF was incorporated in the formulation.

EFFECT OF POLYURETHANE WITH Na_2PO_3F ON ENAMEL SOLUBILITY.—In control samples of enamel there was an average weight loss of 81.8 mg after exposure to acetic acid. Weight loss in acid was only 51.3 mg when the enamel previously was in contact with the polymer containing Na_2PO_3F; this amounted to a 37% reduction in acid solubility over controls.

In Vivo Studies

ANTICARIOGENICITY OF POLYURETHANE WITH Na_2PO_3F.—Fewer carious lesions were observed in the developmental grooves of rat molars coated with the polymer that contained Na_2PO_3F than in uncoated controls (Table 4). In group 1, 8 lesions were noted in teeth coated with the polyurethane material, as opposed to 25 lesions for uncoated or control teeth. This amounted to a 68% reduction in incidence of caries. In group 2, where the maxillary molars were not bevelled down with a bur, there were 36 lesions in the molars treated with the polymer, as opposed to 56 in the molars of the control rats. In group 3, where the rats did not receive an inoculation of streptococci, one lesion was found in the coated teeth and no caries were found in the control rats.

Initially, the polyurethane material covered much of the occlusal surface, filled the developmental grooves (Figs 3, 4), and occupied the space between the molars. After 48 hours much of the coating was gone. At the time of killing no evidence of the coating remained. All lesions, including actual cavitations, were small. In no instance was there a pronounced loss of enamel. In groups 1 and 2 the incidence of caries was greater in the mandibular teeth than in the maxillary teeth (Table 4) and more common in first and second molars than in third molars.

Discussion

Evidence for the potential superiority of a long-term topical fluoride over conventional short-term (4 to 12 minute) applications has been produced by several workers.[3,5] These investigators have demonstrated that most of the fluoride deposited on the teeth after a four minute application of commonly available acidulated fluorides may be washed off after 24 hours. If the deposited fluoride is isolated from the oral environment for 6 to 16 hours, much of it is converted to insoluble fluorapatite.

The present investigation, together with previous data, indicates that a polyurethane-based polymer that contains fluoride is a promising material for use as a long-term topical fluoride. It bonds well to enamel in

TABLE 4
TABULATION OF CARIOUS LESIONS

Group No.	No. of Rats	Treatment	Inoculation Strain	No. of Lesions: Maxillary Molars	No. of Lesions: Mandibular Molars
1	20	Maxillary Molars, ground, coated	NIDR 6715-12	3	5
1	20	Maxillary Molars, ground, uncoated	NIDR 6715-12	7	18
2	20	Coated	NIDR 6715-12	12	24
2	20	Uncoated	NIDR 6715-12	24	32
3	5	Coated	None	0	1
3	5	Uncoated	None	0	0

Note: All animals were on NIDR Diet 2000 for 46 days.

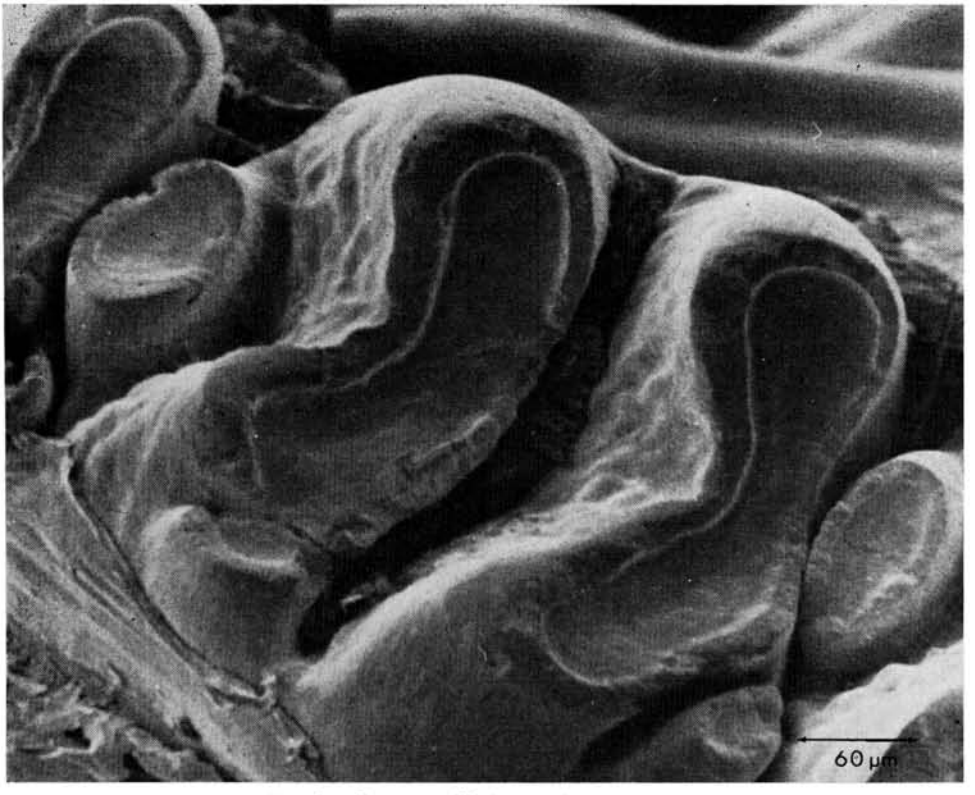

FIG 3.—Rat mandibular molar, uncoated.

the presence of water,[1,16] particularly after pre-etching with citric acid. The polyurethane-based material also releases fluoride rapidly for the first 72 hours after cure (Fig 2), and it improves resistance to acid etching. A 37% reduction in acid solubility was obtained in this investigation. Evidence that the fluoride-releasing polyurethane is a workable long-term topical fluoride for reducing caries is supported by animal data (Table 4). Reduction in carious lesions ranged from 36 to 68% after a single application to rat molars, depending on the procedures used. The polymer is virtually harmless and nonirritating, whether taken orally or placed in contact with the pulp.[17,18]

The usefulness of fluoride-releasing polyurethanes as a topical fluoride in human teeth has been reported in a companion study using X-ray probe analysis.[19] In the X-ray probe analysis, between 1,200 and 4,400 ppm fluoride were found on extracted teeth 30 to 45 days after in vivo application of the polyurethane. This is significant because only about 1,000 ppm apparently is required for protection of enamel against tooth decay.[20] The microprobe data that shows the maintenance of high concentrations of fluoride in vivo in enamel is in direct contrast with previous reports of zero retention of fluoride after one day in vitro,[5] and about 200 to 500 ppm fluoride after seven days in vivo with conventional topical fluoride systems.[3,21]

The compound Na_2PO_3F was selected over NaF or acidulated NaF for incorporation in the polyurethane polymer for several reasons. It has a more rapid release rate at early intervals after application (Fig 2). This is important because it is desirable for a material to release as much fluoride as possible to the enamel before the polymer is abraded off. The greater release rate may be because Na_2PO_3F is much more soluble in water than NaF. Other workers obtained similar results with dentifrices that contained both fluorides. Na_2PO_3F had 58% solubility and NaF had only 7 to 8% solubility when the dentifrice was exposed

FIG 4.—Rat mandibular molar coated with polyurethane that contains fluoride.

to small amounts of water.[22] Another advantage of Na_3PO_2F is that it has little tendency to solubilize enamel. It was found that NaF, as well as acidulated fluoride, solubilizes enamel (at least powdered enamel) very rapidly (Fig 1). The tendency of some fluorides to break down enamel when in high concentrations may be one of the explanations for the deleterious effects of highly fluorinated water on the teeth of children. One possible reason for the solubilizing effects of NaF and the desolubilizing effects of Na_2PO_3F is suggested by Ericsson's observation that more Ca and P are liberated from enamel with NaF than from enamel with Na_2PO_3F.[23]

A greater incorporation of fluoride into enamel was observed in acidulated NaF solutions than with the other fluorides. Acidulated fluoride also was slightly superior to the other fluorides in enhancing the resistance of powdered enamel to acid attack. However, these advantages appear to be negated by our observations that acidulated fluoride (and even neutral NaF) solubilized or removed large amounts of enamel (Fig 1) and had a relatively slow release rate from cured polyurethane. Acidulated NaF seemed to be potentially deleterious to the desired physical properties of the polyurethane polymer.

Conclusions

A polyurethane material that contained fluoride was studied as a possible system for longterm topical fluoride application. It was necessary initially to determine the most suitable fluoride compound for incorporation into the polyurethane formulation. Therefore, a number of evaluation tests were run on widely investigated fluoride systems. Stannous fluoride was not considered because of its known instability and because preliminary tests indicated that it dissolved too slowly in aqueous solutions. Extensive testing was limited to NaF, acidulated NaF, and Na_2PO_3F.

A greater uptake of fluoride into powdered enamel was observed in acidulated NaF solutions than with the other fluorides.

Acidulated NaF also was slightly superior to the other fluorides in enhancing the resistance of enamel to acid etch. However, Na_2PO_3F was selected because it has a more rapid release rate of its fluoride ion from the cured polyurethane polymer in water and because tendency to desolubilize enamel was less than that of the other fluorides tested.

The cured fluoride-releasing polyurethane was effective in reducing the acid solubility of enamel in vitro. In the in vivo study, it was effective in reducing the incidence of carious lesions in molar teeth of albino rats that were subjected to a diet high in sugar, and inoculated with a cariogenic bacterium. It was concluded, on the basis of this investigation and concurrent X-ray probe studies, that the fluoride-releasing polyurethane might be used as a topical fluoride for coating all surfaces of teeth, including pits, fissures, and interproximal surfaces.

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