Assessing fluoride concentration uniformity and fluoride release from three varnishes

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ABSTRACT

Background. The authors investigated the fluoride content uniformity of three commercial fluoride varnishes, as well as their fluoride-release behaviors.

Methods. The authors examined 20 doses from each of two tubes of Duraphat (Colgate-Palmolive Co., New York) and Duraflor (Pharmascience Inc., Montreal), and 20 doses of individually packaged 0.25-milliliter and 0.40-mL units of CavityShield (OMNII Oral Pharmaceuticals, West Palm Beach, Fla.). Part of the dose was dissolved in chloroform, followed by fluoride extraction with distilled water. The authors painted the remaining varnish from five predetermined doses from each group onto plastic substrates for examination of fluoride release. Fluoride concentrations in the solutions were measured with a fluoride-selective ion electrode.

Results. One-way analysis of variance showed statistically significant differences between varnish groups. The fluoride content was more uniform in Duraphat and CavityShield than it was in Duraflor. The fluoride release profiles in terms of percentage of total fluoride released over time were different among different groups of varnishes and were similar among samples from the same test group. The authors found that Duraflor released consistently more fluoride in artificial saliva than did the other two varnishes.

Conclusions. Fluoride content can vary between doses dispensed from the same tube. Uniformity also varies between different varnishes and affects the retention of fluoride in the varnish.

Clinical Implications. Clinicians should be aware that the nonuniform appearance of fluoride varnish as squeezed out of the tube could indicate separation of ingredients, resulting in variation of fluoride content.

Fluoride varnishes have been the standard of practice for the professional application of topical fluoride for almost 30 years in western Europe, Scandinavia and Canada. Their effectiveness and safety are documented in more than 50 clinical trials.[1] A clinical study by Seppä and colleagues[2] suggested that Duraphat (Colgate-Palmolive Co., New York), a sodium fluoride varnish, was as effective as Nupro (Dentsply Professional, York, Pa.), an acidulated phosphate fluoride, or APF, gel, at least in preventing approximal caries. Taking into account the shorter treatment time, better taste, easier application technique and safety relative to the use of APF, these authors believed that fluoride varnish for professional applications seems justified.

Fluoride uniformity varies between different varnishes and affects the retention of fluoride in the varnish.

Four fluoride varnishes are marketed in the United States: Duraphat, Duraflor (both manufactured by Pharmascience Inc., Montreal), Fluor Protector (Ivoclar Vivadent, Amherst, N.Y.) and CavityShield (OMNII Oral Pharmaceuticals, West Palm Beach, Fla.).[3] Duraphat and Duraflor each contain 5 percent sodium fluoride (22,600 parts per million fluoride ions, or F^-) in a natural resin carrier with some alcohol included as a solvent, and are packaged in a 10-milliliter tube. CavityShield also contains 5 percent sodium fluoride in a natural resin, but is packaged in 0.25-mL and 0.40-mL doses for single use. When moistened, Duraphat, Duraflor and CavityShield set to a light yellow film. Fluor Protector contains 0.9 percent difluorosilane by weight (1,000 ppm F^-) in polyurethane-based varnish and sets to a thin transparent film. It comes in either a 0.4-mL vial for single use or a 1.0-mL ampule.

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Our experiences with Duraflor and Duraphat have shown that the varnish, as squeezed out of the tube, does not always look uniform, since dark streaking appears occasionally within the varnish. This is an indication that the ingredients within the varnish have separated. Joziak and colleagues[4] reported that they found substantially higher F^- uptake by enamel and F^- release from Duraphat than from Duraflor, even though these two varnishes are made of a similar carrier and contain the same quantity of fluoride. This phenomenon has led to the speculation that the fluoride content in the varnish may not be consistent between doses as dispensed from the tube.

The idea behind a single-unit dose such as that dispensed by CavityShield is to maintain the uniformity of the fluoride content. If sedimentation of the fluoride is obvious, clinicians can thoroughly mix the varnish with the accompanying brush before applying it to achieve this uniformity. Fluor Protector is a clear solution that exhibits no obvious sign of sedimentation.

The varnish, as squeezed out of the tube, did not always look uniform.

The purpose of this study was to investigate the uniformity of the fluoride content among doses as they were squeezed from tubes of fluoride varnishes (Duraphat and Duraflor) and single-dose packages (CavityShield). We applied some of the doses from each varnish group onto plastic substrates in the form of thin coating to characterize the effect of fluoride content on its release in artificial saliva. We did not include Fluor Protector because it exhibited no signs of sedimentation and is based on a chemistry that differs from that of the other three varnishes.

MATERIALS AND METHODS

We used two tubes of Duraphat (lot 50911, expiration date Dec. 2000; and 90231, expiration date May 2004), two tubes of Duraflor (lot 864, expiration date July 1, 2001) and 40 single-unit packages of CavityShield (20 packages of 0.25 mL and 20 packages of 0.40 mL; lot 001, expiration date April 2002) in the experiment. The work began on June 1, 2000 and was completed before July 31, 2000. We labeled the six test groups as Duraphat I, Duraphat II, Duraflor I, Duraflor II, CavityShield 0.25 mL and CavityShield 0.40 mL. We left the tubes on their sides for one week before dispensing the varnish to simulate storage conditions and the office environment. CavityShield samples were stored with their foil covering facing up. Although we could only locate one batch of Duraflor, we used two tubes to maintain a balanced number of doses. Both of the CavityShield packages contained essentially the same material, but in different volumes.

Sample preparation for fluoride uniformity test. We dispensed approximately 0.5 gram of varnish from each tube (Duraphat and Duraflor) onto a synthetic resin surface (50×75 millimeters) and mixed the varnish thoroughly with a plastic spatula. We continued this process until the tube was empty, which yielded 20 samples from each tube. We assigned numbers from 1 to 20 to each of the single-unit packages of CavityShield in both test groups. Each single-dose package was mixed thoroughly in its own well according to the manufacturer's instructions.

We placed about 0.15 to 0.20 g of varnish from each sample into a 100-mL polyethylene volumetric flask and added 5 mL of chloroform to dissolve the varnish. After the varnish was dissolved completely, we added 95 mL of distilled water to recover sodium fluoride, or NaF. The flasks were shaken vigorously for 15 seconds and left on a table to allow the water and chloroform to separate. The process was repeated two more times. The aqueous solution was then ready for fluoride determination. We expected total recovery of NaF during the first extraction because NaF does not dissolve in chloroform, and secondary and tertiary extractions yielded no appreciable amounts of fluoride.

We found the above procedure to be adequate for recovering fluoride from Duraphat varnish, but Duraflor and CavityShield samples required additional preparatory steps. In the case of Duraflor, resinous residues appeared in the water extract. Anticipating these residues to trap fluoride, we collected them by filtration, dried them, weighed them and placed them in 100-mL polyethylene volumetric flasks. We added 5 mL of ethyl alcohol to dissolve the residues, and then added 95 mL of distilled water. The solution was clear, indicating that the residues had dissolved completely and the solution was ready for us to determine the fluoride content. We determined the fluoride content of this solution and treated it as part of the total Duraflor fluoride content.

The CavityShield varnish exhibited sedimenta-

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tion of NaF particles (as the manufacturer's instructions indicated it would) and trace particles on the foil covering. We attempted to brush the particles from the foil into the mixing well before thoroughly combining the settled particles with the resin. To determine if we had incorporated the NaF particles completely, we measured the fluoride content of 10 additional packages of the 0.25-mL product and 10 packages of the 0.40-mL product. After tearing the foil cover, we placed the entire package in a 100-mL polyethylene volumetric flask. Subsequent preparation of the solution and determination of fluoride content were performed as described above. We weighed all of the packages before and after the experiment to assess the weight of varnish dissolved in chloroform.

Sample preparation for fluoride release. We took five specimens—the first, fifth, 10th, 15th and 20th—from each of the six groups to determine the amount of fluoride released. We used half of each specimen for the uniformity test, as described above, and the other half to paint a thin coating on both sides of a polyester (Mylar, DuPont, Wilmington, Del.) sheet (20×40 mm). The increase in the weight of the sheet after coating was the weight of varnish used to paint the sheet.

The results of our study indicate that the solubility of sodium fluoride in natural resin is limited.

We placed each sheet of polyester with the varnish coating into a polystyrene vial to set for 24 hours. We added 20 mL of artificial saliva, and the varnish coating became completely immersed in the solution. The artificial saliva that mimics the electrolytes in typical human saliva is based on a formula by Holland.[5] We replaced the solution with fresh solutions of artificial saliva at one, three, seven, 31, 55, 124 and 213 hours after immersion. We saved the used solutions for fluoride determination. To prevent the varnish coating from peeling off, we made sure not to bend the polyester substrate during the change of solutions.

Fluoride concentration determination. We measured the fluoride concentrations with a fluoride-specific ion electrode and a digital pH/millivolt meter (model 801A, Orion Research, Cambridge, Mass.). We conducted calibrations of the apparatus with a series of fluoride reference solutions with fluoride concentrations of 0.5, 1.0, 2.0, 5.0 and 10.0 ppm (equivalent to micrograms per gram). Reference solutions for fluoride uniformity were prepared from a 100-ppm standard solution and deionized water. We prepared reference solutions for fluoride release in artificial saliva from the same 100-ppm standard solution and artificial saliva. We also prepared a third set of reference solutions with 5 percent ethyl alcohol.

We placed one milliliter of reference solution in a 7-mL polyethylene vial; an equal volume (1 mL) of total ionic strength adjustment buffer, or TISAB, solution (Orion Research) was added to the vial to quench possible confounding ions. The fluoride-specific ion electrode and digital pH/mV meter measured the fluoride concentrations in voltages. The results were used to establish reference curves, which showed the relationship between the fluoride concentration in the solutions and the voltage measured with the electrode.

The solutions prepared for fluoride uniformity measurement or the used solutions (that is, the replaced solutions) for fluoride release measurement often had concentrations much greater than the upper bound of the reference solutions. Consequently, as much as a 10-fold dilution often was needed to lower the concentration of the solutions. After dilution with the proper liquid, such as distilled water, artificial saliva or distilled water with 5 percent alcohol, we placed 1 mL of diluted solution in a 7-mL polyethylene vial along with 1 mL of TISAB solution.

We converted the voltage values obtained from the digital analyzer to fluoride concentration in parts per million using the reference curves. We further converted the values obtained to micrograms of fluoride ions per gram of initial wet weight of the varnish for the uniformity and fluoride release tests.

Data analysis. We used one-way analysis of variance, or ANOVA, and Tukey's Honestly Significant Difference, or HSD, test to analyze the mean fluoride content among the six test groups. We converted the fluoride release data for each varnish coating to cumulative release in percentage of total fluoride content.

RESULTS

ANOVA showed statistically significant differences in the mean fluoride content among the six test groups ($P < .001$). Tukey's HSD test showed two statistically significantly different groupings

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among the six test groups at $\alpha = .05$; they are designated A and B (Table 1). It is important to note that the Tukey's groupings do not suggest that varnishes in the same grouping have the same mean fluoride content, but they indicate that the ranges of means (shown in Table 1 as 95 percent confidence intervals) have a 5 percent or better chance of overlapping each other. When we used the entire package of CavityShield without mixing, we found the mean fluoride content to be statistically the same as the mean values for CavityShield shown in Table 1. This indicates that the varnish was adequately mixed.

TABLE 1

FLUORIDE CONTENT OF VARNISHES IN SIX TEST GROUPS.

VARNISH*	NUMBER OF DOSES	FLUORIDE CONCENTRATION RANGE (PARTS PER MILLION)	MEAN (95% CONFIDENCE INTERVAL) FLUORIDE CONCENTRATION (PARTS PER MILLION)	TUKEY'S HSD† GROUPING‡
Duraphat I	20	19,478-24,437	22,634 (22,024 to 23,244)	A
Duraphat II	20	14,116-25,074	23,866 (22,755 to 24,977)	A
Duraflor I	20	506-74,030	13,830 (6,595 to 21,065)	B
Duraflor II	20	390-47,014	20,120 (13,471 to 26,769)	A
CavityShield (0.25 milliliters)	20	16,859-23,593	20,765 (19,864 to 21,666)	A, B
CavityShield (0.40 mL)	20	13,762-19,730	18,223 (17,593 to 18,853)	A, B

* Duraphat is manufactured by Colgate-Palmolive Co., New York; Duraflor, Pharmascience Inc., Montreal; and CavityShield, OMNII Oral Pharmaceuticals, West Palm Beach, Fla.
† HSD: Honestly Significant Difference.
‡ The mean fluoride content of the groups with the same letter is not statistically significantly different at $\alpha = .05$.

Table 2 shows the fluoride concentrations of the five doses used for the fluoride release study and the percentage of fluoride released at seven, 31 and 213 hours. The figure (page 181) shows the mean percentage of total fluoride released over time for each test group. All groups exhibited rapid release within the first seven hours and slower release thereafter. Duraflor I and II released a higher percentage of fluoride than the other groups before exhibiting a slowdown between the seventh and 31st hours of release. CavityShield I and II and Duraphat I exhibited similar slowdown activity, but the percentage of fluoride released was lower than that for the other groups. Duraphat I exhibited a lower initial release than the other groups, but its slowdown rate was less rapid than that of the other groups.

DISCUSSION

The results of our analysis show that Duraphat appeared to be the most consistent in regard to fluoride uniformity (Table 1). Only the last dose from the Duraphat I tube exhibited signs of separation during dispensing, and that sample exhibited the lowest fluoride content of the group (Table 2). Both Duraflor groups exhibited a wider range of fluoride concentration than the other groups (Table 1). When dispensing the varnish from either of the Duraflor tubes, we found that the first dose was always a clear resin. After the second or third dose, however, streaks of cloudy substances appeared with the clear resin. The cloudy substance increased and the streaks of resin disappeared by about the sixth dose. The substance causing the cloudiness likely is NaF particles because the fluoride concentration increased as the clear resin decreased.

All CavityShield packages exhibited definite sedimentation of NaF particles in the mixing wells, as the manufacturer's instructions indicated they would. Tukey's HSD analysis showed that with the exception of Duraflor I, varnishes in all test groups contained similar amounts of fluoride.

Lack of fluoride uniformity. The results of our study indicate that the solubility of NaF in natural resin is limited. Most of the high fluoride concentration in these varnishes remained suspended as a solid within the resin or separated from the resin as a sediment. In our evaluation, Duraphat retained the greatest degree of uniformity, while NaF particles within Duraflor separated from the resin and settled on the side of the tube during storage. When we held the tube upside down, particles migrated toward the orifice

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TABLE 2

FLUORIDE RELEASE PROFILES OF VARNISHES IN SIX TEST GROUPS.

VARNISH*	DOSE NUMBER	FLUORIDE CONTENT (PARTS PER MILLION)	FLUORIDE RELEASED (PERCENTAGE)		
			7 Hours	31 Hours	213 Hours
Duraphat I	1	23,666	15.2	24.6	37.1
	5	24,437	10.1	17.5	28.4
	10	23,611	12.3	17.4	25.0
	15	23,076	8.1	15.3	28.6
	20	19,766	6.5	10.9	22.0
	Mean		10.5	17.2	28.2
Duraphat II	1	24,805	15.9	40.9	97.0
	5	24,367	19.0	49.1	97.1
	10	24,553	11.1	31.0	94.6
	15	25,029	15.3	43.7	97.1
	20	14,116	10.8	17.8	41.3
	Mean		14.4	36.5	85.4
Duraflor I	1	506	32.2	55.5	98.7
	5	12,557	45.1	60.9	90.6
	10	7,706	40.0	59.3	89.9
	15	11,887	63.3	74.2	86.0
	20	74,030	79.4	91.7	98.2
	Mean		50.7	66.8	91.1
Duraflor II	1	390	46.1	56.6	98.3
	5	10,593	47.0	73.9	97.2
	10	36,548	59.7	80.9	96.4
	15	6,890	63.6	69.5	75.8
	20	35,453	45.4	75.6	89.1
	Mean		51.0	69.2	88.5
CavityShield (0.25 milliliters)	1	22,970	31.1	37.0	47.9
	5	19,829	35.3	41.7	48.0
	10	21,170	40.2	53.3	64.5
	15	17,539	10.4	14.5	26.2
	20	20,167	20.6	26.6	37.7
	Mean		27.5	34.6	44.8
CavityShield (0.40 mL)	1	18,189	8.3	11.0	21.1
	5	18,170	7.2	9.7	19.3
	10	16,724	7.9	10.6	21.7
	15	19,659	46.8	52.6	56.3
	20	19,372	39.7	45.4	51.0
	Mean		22.0	25.9	33.9

* Duraphat is manufactured by Colgate-Palmolive Co., New York; Duraflor, Pharmascience Inc., Montreal; and CavityShield, OMNII Oral Pharmaceuticals, West Palm Beach, Fla.

and resulted in a varnish richer with fluoride particles in subsequent doses.

Clinically, it is important for practitioners to discard any clear varnish freshly squeezed out of the tube because it contains only a fraction of the intended fluoride content. The operator should hold the tube upside down for a few seconds before dispensing another dose. This should yield greater fluoride in the varnish but will not guarantee uniformity.

To ensure a uniform mixture, the clinician may opt to use a rotary device, such as a tube shaker, which results in continuous mixing of the varnish inside the tubes, or seek advice from the manufacturer. In the case of CavityShield, we achieved uniformity by mixing the varnish in the individual wells.

Fluoride varnishes were developed to prolong the contact time between fluoride and enamel. However, the fluoride in the varnish still is released into the oral environment. Specimens from the same test groups usually exhibited similar release profiles, which means that the amount of fluoride did not dictate the mechanism of release. The fluoride release data show that the percentage of fluoride released into the artificial saliva varied according to the type of varnish, which indicates that the resin carriers and additives used by the manufacturers have a significant effect on fluoride release.

Elevated fluoride levels. Twetman and colleagues[6] found that one hour after fluoride varnish application, a significant elevation of fluoride levels in whole saliva occurred with Bifluorid 12 (VOCO, GmbH, Cuxhaven, Germany) (6 percent F^-) and Duraphat (2.26 percent F^-), but the elevation was insignificant with Fluor Protector (0.1 percent F^-). The authors found similar patterns of fluoride activity in the parotid and submandibular-sublingual secretions. The elevated fluoride levels in saliva lasted six hours for all of the varnishes tested. The results suggest a correlation between the fluoride content in the varnish and fluoride levels detected in saliva after application. This finding is consistent with our data regarding fluoride release in artificial saliva.

Preventing caries. The current concept of the caries-preventive mechanism of fluoride

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varnish is based on the formation of globular calcium fluoride on the enamel surface, which serves as a reservoir and releases fluoride ions in response to pH changes in the mouth. Since pure calcium fluoride crystal is cubical rather than spherical, these globular deposits also have been described as calcium fluoridelike.

The reason for prolonged retention of calcium fluoride on the enamel surface is the protective coating of pellicle proteins and secondary phosphate. At lower pH levels, such as during a caries attack, the pellicle coating is lost and an increased dissolution rate of calcium fluoride occurs. The fluoride ions released in this way may adsorb onto the enamel surface and inhibit dissolution of hydroxyapatite or increase the rate of remineralization.[7] Therefore, the quantity and duration of fluoride released into the mouth from the varnish may not be critical for long-term caries inhibition. Nonetheless, the fluoride retained in the varnish is the quantity that would become available for adsorption by the enamel.

For example, of all the varnishes currently on the market, Fluor Protector contains the least amount of fluoride and exhibits insignificant fluoride elevation in whole saliva,[6] but deposits markedly more fluoride on enamel than do the other varnishes.[8] The low pH value of Fluor Protector has been credited for its greater affinity for enamel uptake. Duraflor, on the other hand, exhibited a high degree of fluoride release in our study, which means less fluoride is available for adsorption by the enamel. This phenomenon might explain the results of a study by Joziak and colleagues,[4] who reported low fluoride uptake by enamel from Duraflor.

Newbrun[9] reported an increased cariostatic effect that occurred as fluoride content in dentifrices increased from 250 to 2,000 ppm. Studies of topical fluoride gels have shown that the number of globules and sizes of calcium fluoride globules deposited on enamel surfaces depend on the pH, the concentration of the fluoride solutions and the exposure time.[7] However, a dose-response relationship seems to be absent in the caries-preventive mechanism of fluoride varnishes.

Seppä and colleagues[10] did not find significant differences in the ability of two Duraphat varnishes (2.3 percent and 1.1 percent F^-) to prevent demineralization in 274 children aged 12 to 14 years after three annual applications. Haugejorden and Nord[11] reported similar observations when they compared the efficacy of Carex (1.8 percent F^-) (developed by A. Nord) with that of Duraphat (2.26 percent F^-) on the posterior approximal surfaces of 350 children aged 10 to 12 years after six semiannual applications. Clinical studies comparing Fluor Protector with Duraphat have either favored Duraphat[12-14] or showed no significant differences in caries reduction.[15] The efficacy of Duraflor was demonstrated in a clinical trial[16] in which teeth receiving a single application of Duraflor were found to exhibit 50 percent less demineralization than the control teeth without varnish or those with placebo varnish.

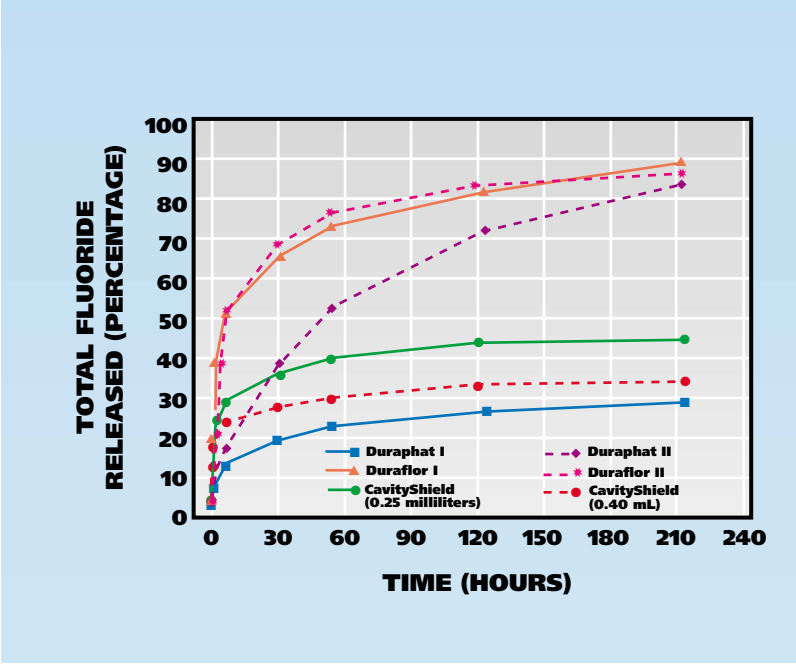

Figure. Mean fluoride release profiles for the six test groups. Duraphat is manufactured by Colgate-Palmolive Co., New York; Durafluor, Pharmascience Inc., Montreal; and CavityShield, OMNII Oral Pharmaceuticals, West Palm Beach, Fla.

Featherstone and Zero[17] commented that increasing fluoride indiscriminately would not necessarily produce better clinical results in regard to preventing caries. It appears that, in most cases, the amount of fluoride incorporated into the varnishes might have exceeded the threshold needed to develop sufficient calcium fluoride on the enamel surface. However, the lack of fluoride uniformity and the high quantity of fluoride released into the mouth might reduce the retention of calcium fluoride to levels below that threshold.

On the other hand, one might conclude that because Duraphat and CavityShield retained most of their fluoride during the first 31 hours

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in artificial saliva, they should provide greater sources of fluoride for calcium fluoride formation (Table 2). However, such a conclusion could be justified only if the fluoride retained in the varnish diffused toward the enamel and reacted with the enamel to form calcium fluoride. Ultimately, it is the quality of loosely bound calcium fluoride and the quantity of this fluoride in terms of its dissolution rate that prevent caries. Therefore, future studies should investigate the formation of calcium fluoride resulting from the application of fluoride varnish in a simulated or real oral environment.

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CONCLUSION

Both Duraphat and Duraflor varnishes contained the amount of fluoride specified on their packages. However, the concentration of fluoride varied among the doses as dispensed from the tubes. Duraphat appeared to be the most consistent in regard to fluoride uniformity, while Duraflor exhibited a greater degree of variation between doses. Single-dose CavityShield exhibited variation in fluoride concentration to the same degree as did Duraphat. In addition, the fluoride release profiles from the varnishes into artificial saliva differed among the three varnishes studied. ■

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1. Beltrán-Aguilar ED, Goldstein JW, Lockwood SA. Fluoride varnishes: a review of their clinical use, cariostatic mechanism, efficacy and safety. JADA 2000;131:589-96.
2. Seppä L, Leppanen T, Hausen H. Fluoride varnish versus acidulated phosphate fluoride gel: a 3-year clinical trial. Caries Res 1995; 29:327-30.
3. Vaikuntam J. Fluoride varnishes: should we be using them? Pediatr Dent 2000;22:513-6.
4. Joziak MT, Schemechorn BR, Tavas EA, Fisher SW, Gambogi RJ. Comparison of enamel fluoride uptake and release from fluoride varnishes (abstract 1684). J Dent Res 1998;77:842.
5. Holland RI. Use of potentiodynamic polarization technique for corrosion testing of dental alloys. Scand J Dent Res 1991;99(1):75-85.
6. Twetman S, Skold-Larsson K, Modeer T. Fluoride concentration in whole saliva and separate gland secretions after topical treatment with three different fluoride varnishes. Acta Odontol Scand 1999;57:263-6.
7. Øgard B, Seppä L, Rölla G. Professional topical fluoride applications: clinical efficacy and mechanism of action. Adv Dent Res 1994; 8(2):190-201.
8. Seppä L. Studies of fluoride varnishes in Finland. Proc Finn Dent Soc 1991;87:541-7.
9. Newbrun E. Current regulations and recommendations concerning water fluoridation, fluoride replacements and topical fluoride agents. J Dent Res 1992;71:1255-65.
10. Seppä L, Pöllänen L, Hausen H. Caries-preventive effect of fluoride varnish with different fluoride concentrations. Caries Res 1994; 28(1):64-7.
11. Haugejorden O, Nord A. Caries incidence after topical application of varnishes containing different concentrations of sodium fluoride: 3-year results. Scand J Dent Res 1991;99:295-300.
12. Seppä L, Tuutti H, Luoma H. Three-year report on caries prevention using fluoride varnishes for caries risk children in a community with fluoridated water. Scand J Dent Res 1982;90(2):89-94.
13. Seppä L, Pöllänen L. Caries preventive effect of two fluoride varnishes and a fluoride mouth rinse. Caries Res 1987;21:375-9.
14. Clark DC, Stamm JW, Tessier C, Robert G. The final results of the Sherbrooke-Lac Megantic fluoride varnish study. J Can Dent Assoc 1987;53:919-22.
15. Kolehmainen L. Evaluation of a fluoride-containing varnish in children with low caries incidence. Scand J Dent Res 1981;89:228-34.
16. Todd MA, Stately RN, Kanellis MJ, Donly KJ, Wefel JS. Effect of a fluoride varnish on demineralization adjacent to orthodontic brackets. Am J Orthod Dentofacial Orthop 1999;116(2):159-67.
17. Featherstone JDB, Zero DT. Laboratory and human studies to elucidate the mechanism of action of fluoride containing dentifrices. In: Embery G, Rölla G, eds. Clinical and biological aspects of dentifrices. Oxford, England: Oxford University Press; 1992:41-5.

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