Fluoride Varnishes

A Review of Their Clinical Use, Cariostatic Mechanism, Efficacy and Safety

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Fluoride-containing varnishes were developed during the late 1960s and early 1970s in an effort to improve shortcomings of existing topical fluoride vehicles, such as fluoride gels or mouthrinses, by prolonging contact of the fluoride with tooth enamel. By the 1980s, fluoride varnishes were widely used in European countries.[1] In Denmark, for example, more than 90 percent of municipal caries-preventive programs provided fluoride varnish to children up through age 18 years.[2] Along with other fluoride vehicles, the extensive use of fluoride varnishes has been associated with the decline in caries observed in many European countries.[3-7] Four reviews in the biomedical literature have addressed the laboratory and clinical evidence supporting fluoride varnish efficacy.[1,8-10] We review the state of the science of fluoride varnishes, including their efficacy, cariostatic mechanism and safety, as well as their potential use to prevent dental caries in the United States.

VARNISHES AVAILABLE IN THE UNITED STATES

The three fluoride varnishes available in the United States are Duraphat (5 percent sodium fluoride, or NaF/2.26 percent fluoride, Colgate Oral Pharmaceuticals), Duraflor (5 percent NaF/2.26 percent fluoride, Pharmascience Inc.) and Fluor Protector (1 percent difluorsilane/0.1 percent fluoride, Ivoclar-Vivadent). In 1994, Duraphat was the first fluoride varnish cleared by the U.S. Food and Drug Administration, or FDA (under class II regulations, as listed in the Code of Federal Regulations, Title 21, Parts 800 to 895). Under these regulations, the FDA has cleared these products as medical devices to be used as cavity liners and for the treatment of hypersensitive teeth. Laboratory evidence suggests that both Duraphat and Fluor Protector have properties equivalent to other dentinal tubuli sealants,[11,12] but because caries prevention is considered a drug claim, manufacturers would have to submit appropriate clinical trial evidence for review by the FDA before they could be cleared as anticaries agents.

A B S T R A C T

Background. This is a review of the clinical use, cariostatic mechanism, efficacy, safety and toxicity of fluoride varnishes.

Types of Studies Reviewed. The authors reviewed and summarized in vitro, in vivo and in situ studies; clinical trials; demonstration programs; position papers; and editorials published in English in the biomedical literature since 1966.

Results. Extensive laboratory research and clinical trials conducted in Europe and elsewhere show that fluoride varnishes are as efficacious as other caries-preventive agents. Fluoride varnishes are widely used in European caries-preventive programs. The U.S. Food and Drug Administration has cleared these products only as medical devices to be used as cavity liners and for the treatment of hypersensitive teeth. These products have not yet been cleared for marketing in the United States as caries-preventive agents.

Clinical Implications. Three fluoride varnishes are currently available in the United States. Semiannual applications are the most proven treatment regimen. Varnishes are safe and easy to apply and set in contact with intraoral moisture.

TABLE

FLUORIDE CONCENTRATIONS OF FLUORIDE VARNISHES AVAILABLE IN THE UNITED STATES.

PRODUCT NAME	MANUFACTURER	PRESENTATION	CONCENTRATION	MILLIGRAMS OF F^- IN TYPICAL VARNISH APPLICATION (0.3 - 0.5 MILLILITER)*
Duraphat	Colgate Oral Pharmaceuticals	Tube (10 mL)	5% sodium fluoride (2.26% F^-, 22.6 mg/mL F^- or 22,600 ppm† F^-)	6.8 - 11.3
Duraflor	Pharmascience Inc.	Tube (10 mL)	5% sodium fluoride (2.26% F^-, 22.6 mg/mL F^- or 22,600 ppm F^-)	6.8 - 11.3
Fluor Protector	Ivoclar-Vivadent	Single dose of 0.4 mL and ampules of 1 mL	1% difluorsilane‡ (0.1% F^-, 1.0 mg/mL F^- or 1,000 ppm F^-)	0.3 - 0.5

* Dosages in the table correspond to the amount of F^- applied in a routine varnish application, as reported in many clinical trials.[20,52,64,75]
† ppm: Parts per million.
‡ The chemical name of difluorosilane is 2,2(4),4-Trimethylhexamethylene-1,6-dicarbamate-[2-methoxy-4-(2-difluorohydroxysily)ethyl)-cyclohexane].

APPLICATION OF VARNISH

Fluoride varnishes are not intended to adhere permanently to a tooth, but to remain in close contact with enamel for several hours. Toothbrushing may be sufficient to clean the teeth before application and prophylaxis is not required.[13] During application, the clinician uses a brush, a cotton-tip applicator or a syringe-type applicator (included with the product) to apply about 0.3 to 0.5 milliliters of varnish directly onto the teeth. Dental floss can be used to ensure that the varnish reaches interproximal areas. Application time is one to four minutes, depending on the number of teeth present. Because the varnish sets in contact with intraoral moisture, thorough drying is not required before application, and wiping with a gauze or cotton rolls is adequate. To maximize contact between the varnish and the teeth, patients are instructed to avoid eating for two to four hours after the application and to avoid brushing their teeth the night of the application. The varnish remains on the tooth surface for several hours; microscopic evaluations of the enamel surface have shown that small blocks of varnish remain attached to enamel even after in vitro demineralization challenge and sonication.[14] The only disadvantage of sodium fluoride varnishes is that they cause a temporary change in tooth color.

Fluoride varnish needs to be reapplied to maintain its caries-preventive effect.[15,16] Various application schedules have been proposed and semiannual application has been tested most often.[1,9] Annual applications of Fluor Protector have shown no significant benefit.[17] Clinical trials testing four applications per year showed a wide range of caries-preventive efficacy: no differences compared with a semiannual application of Duraphat[18]; a 23 percent greater efficacy in proximal surfaces compared with that of a positive control (that is, Fluor Protector vs. a weekly supervised mouthrinse)[19]; and a 23 percent greater efficacy in proximal surfaces compared with that of a negative control.[20] In addition, intensive treatment protocols using three applications of Duraphat in one week per year (over three[21] and four years[22]) showed caries reductions of 46 to 67 percent in proximal surfaces.

LABORATORY EVIDENCE AND CARIOSTATIC MECHANISM

Calcium fluoride. The main product deposited on the enamel surface and on subsurface carious lesions after the application of topical vehicles with high fluoride content is calcium fluoride, or CaF_2.[23] Topical vehicles with low fluoride concentration tend to deposit fluorapatite, or $Ca_{10}(PO_4)_6F_2$.[23,24] While fluorapatite remains permanently bound within the crystalline structure of the enamel, most of the CaF_2 precipitates on the enamel surface, where it may be lost through exposure to alkaline solutions.[25] Numerous studies, both in vitro and in vivo, have concluded that fluoride varnishes are capable of depositing large amounts of fluoride on human enamel.[13,23,24,26-39] The amount of fluoride deposited on demineralized enamel is greater than that on sound enamel and tends to be similar in chemical structure to fluorapatite.[40]

Calcium fluoride originally was considered to be an undesirable product for topical fluoride treatment because it is readily lost to saliva,[41] but these compounds may serve as a reservoir of fluoride ions.[40,42,43] Under specific thermodynamic circumstances and in the presence of phosphate, part of this CaF_2 can be redeposited as fluorapatite (that is, during remineralization). The physical presence of the varnish would facilitate the transformation. Indeed, fluoride from the varnish may produce a redistribution of ions in the body of a carious lesion, thereby creating a favorable gradient for inward fluoride diffusion and reducing the porosity of the body of the lesion.[44] Using quantitative microradiography, Øgaard and colleagues[45] showed a 48 percent reduction in the depth of the body of naturally produced carious lesions treated with Duraphat. Varnishes also are able to deposit fluoride in artificial carious lesions formed in dentin,[46] opening the possibility for its use in preventing root caries.

Fluoride deposits. A comprehensive review of the in vitro and in vivo studies using Duraphat and Fluor Protector[9] showed consistently higher fluoride deposits produced by Fluor Protector, despite its lower fluoride concentration (Table). Additional in vitro studies of Duraphat have shown that it deposits amounts of CaF_2 equal to those of a 2 percent NaF solution (0.9 percent; 9.05 milligrams per milliliter; or 9,050 parts per million, or ppm, F^-), but over a longer period[47]; superior fluoride deposit occurs if teeth are dried before it is applied[48]; and there is no need to polish the enamel surface before applying the fluoride varnish.[49] In a recent study, Joziak and colleagues[50] claimed higher fluoride uptake in enamel treated with Duraphat than in enamel treated with Duraflor.

Numerous clinical trials conducted in the past 25 years outside the United States have examined the efficacy of fluoride varnishes in preventing dental caries.

Antibacterial effect. Only one study has tested the antibacterial effect of fluoride varnishes. In that study, Zikert and Emilson[51] found that Duraphat did not significantly affect the levels of *Streptococcus mutans* in saliva and pooled dental plaque from children receiving varnish treatment. It seems, therefore, that the main cariostatic effect of fluoride varnish probably is caused by the remineralization of early carious lesions.

Proposed formulations. Besides the three fluoride varnishes available in the United States, additional formulations have been proposed, and some have undergone in vitro and in vivo testing. Most of these new formulations vary in their fluoride concentration, such as Carex (1.8 percent F^- as NaF; developed by A. Nord).[52] Bifluorid 12 (VOCO Chemi GmbH) is a varnish delivering fluoride from NaF and CaF_2 and is marketed in Europe (2.71 percent F^- as NaF and 2.92 percent F^- as CaF_2).[53] Experimental fluoride varnishes include an NaF-ethanol varnish called CDB[54] and a lower-dose NaF (1.1 percent F^-).[55] Fluoride varnishes also have been tested with chlorhexidine to determine their capacity to produce additional benefits.[56,57]

CLINICAL TRIALS

Duraphat varnish. Numerous clinical trials conducted in the past 25 years outside the United States have examined the efficacy of fluoride varnishes in preventing dental caries. All clinical trials to date have been conducted in children. Duraphat

has been the most extensively studied varnish.[20,58-65] Studies conducted between 1968 and 1985 reported caries reductions in permanent teeth ranging from 18 to 77 percent, as reviewed by de Bruyn and Arends.[9] Helfenstein and Steiner[66,67] conducted a meta-analysis of eight randomized clinical trials of Duraphat varnish that used either positive or negative controls. After ruling out the possibility of a null effect resulting from unpublished negative results, these authors fitted fixed and random statistical models. Both models estimated a 38 percent reduction in the decayed, missing or filled surfaces, or DMFS, index.

A more recent clinical trial conducted in India[64] against a negative control showed a caries reduction of 70 to 75 percent. Recently, Seppä and colleagues[55] tested a 1.1 percent F^- varnish (Duraphat) against a common 2.26 percent F^- varnish, and found equivalent benefits after a three-year follow-up. Few studies have been conducted on the efficacy of Duraphat in the primary dentition, and their results are inconclusive.[57-59] Two studies have reported no beneficial effects[58,60] and a third study reported a 44 percent reduction in caries incidence.[59] In a demonstration program involving 62 children between the ages of 12 and 24 months at high risk of developing dental caries who were treated with Duraflor, Weinstein and colleagues[68] found an 8 percent reduction between baseline and follow-up (at six months) in the number of children with decayed teeth or decalcified lesions.

Fluor Protector varnish. Other clinical studies have evaluated the efficacy of Fluor Protector varnish,[17,63,69-71] and in some clinical trials, Fluor Protector has been compared with Duraphat. In two experimental designs, Seppä and colleagues[72] and Clark and colleagues[63] found that both varnishes significantly reduced dental caries on the occlusal and buccal surfaces; however, these researchers observed that Fluor Protector had little benefit on proximal surfaces. In contrast, a recent clinical trial among 4- and 5-year-old children found that Fluor Protector had a preventive effect only on proximal surfaces of primary teeth.[73] To our knowledge, there have been no reported clinical trials using Duraflor varnish.

Tewari and associates[64] reported that after 2.5 years, the fluoride varnish resulted in a higher percentage of caries reduction than did the 2 percent sodium fluoride solution and the 1.23 percent acidulated phosphate fluoride gel.

Other topical fluorides. Some studies have compared fluoride varnishes with other topical fluoride delivery vehicles. Tewari and associates[64] compared Duraphat with a 2 percent NaF solution, a 1.23 percent acidulated phosphate fluoride, or APF, gel and a negative control. They reported that after 2.5 years, the varnish resulted in a higher percentage of caries reduction (74 percent) than did the NaF solution (28 percent) and the APF gel (37 percent). In another study comparing Duraphat varnish with APF gels in children at high risk of developing dental decay, Seppä and colleagues[65] found greater, but not statistically significant, efficacy of the varnish.

Other clinical trials have compared Duraphat varnish with a biweekly[62,74] or weekly 0.2 percent NaF rinse[75] and have compared Fluor Protector varnish with a biweekly 0.2 percent NaF rinse[71] and weekly 0.05 percent NaF rinse[19]; the results have been mixed. The clinical observation that fluoride varnishes benefit occlusal surfaces led a group of researchers to test the efficacy of Duraphat vs. dental sealants in preventing occlusal decay.[76-78] In these studies, the sealants were more effective than Duraphat.

Factors to consider. In analyzing the multiple clinical trials that have tested the efficacy of fluoride varnishes, we must consider several factors. First, some studies used a split-mouth design and concern has been raised about possible crossover of fluoride varnish onto the control teeth.[1,8] This effect would increase type I error (that is, failure to reject the null hypothesis when, in fact, there is a difference in the preventive effect of varnishes compared with control teeth). Second, some trials were unable to demonstrate caries reductions because they used positive controls (that is, another known

preventive agent). Lack of statistical differences in these studies does not mean lack of efficacy for the fluoride varnish, but instead comparable efficacy with the positive control. Third, some studies used fewer than 100 subjects or did not follow up subjects for an appropriate length of time. Fourth, some studies estimated varnish efficacy by comparing estimates of caries increments between control and test groups,[17,18,55,58-60,62-65,72,74,79] others by estimating the incidence of new carious lesions during the observation period,[19,20,21,71,75] and still others used both methods.[22,73]

A fifth factor is that trials in areas in which the community drinking water is optimally fluoridated may be less able to attain a statistical difference because varnishes need to show a preventive effect in addition to that of water fluoridation. To overcome this difficulty, one research team in Finland enrolled children with high caries experience, as defined by some upper percentile in the DMFS distribution.[18,55,65,72] It is interesting that Murray and associates[58] and Petersson[10] blamed the use of subjects from populations at high risk of developing dental caries for their inability to observe significant efficacy, because most surfaces at risk already had been affected by the disease.

Finally, some clinical trials have tested fluoride varnish efficacy in children who concurrently used fluoride toothpaste or fluoride mouthrinses or who received routine oral health examinations and dental prophylaxis. In these trials, the benefit of fluoride varnish is measured in addition to the benefit provided by the other preventive techniques.

SAFETY AND TOXICITY

Two commercially available fluoride varnishes in the United States have the highest fluoride concentration of any fluoride vehicle (22,600 ppm F^-)[80] and are intended to be delivered by dental professionals. Despite the rapid setting time of the varnish and the small dosage used, the risk exists that young children will ingest some of the product during placement. In addition, as fluoride is released from the varnishes after treatment, some fluoride will be ingested. Roberts and Longhurst[81] reported that a mean of 5.2 mg F^- (range, 0.7 to 14.5 mg F^-) was applied to 111 children (2 to 14 years of age) by 39 operators. They observed little variation in the amount of varnish applied, according to age of the child, but as the number of teeth increased, less fluoride was applied to each tooth. According to the authors, no child received acute toxic levels (that is, 1 mg F^- per kilogram of body weight).

Numerous randomized clinical trials conducted outside the United States point to the efficacy and safety of fluoride varnishes as a caries-preventive agent.

Ekstrand and associates[82] conducted analyses of plasma fluoride concentrations in four children (ages 4, 5, 12 and 14 years) after Duraphat varnish was applied. The amount of varnish applied ranged from 2.3 to 5.0 mg. Peak plasma fluoride concentrations of 3.2 to 6.3 micromolar were found within two hours of treatment, followed by a rapid two-hour decrease and a slower decrease thereafter. These levels were comparable with those found after brushing with a fluoridated toothpaste (mean ± standard deviation, 3.63 ± 0.45 µmol/L) or after ingesting a 1-mg F^- tablet (4.47 ± 0.47 µmol/L),[83] and were considerably lower than those reported for APF gels (16 to 76 µmol/L).[84] These data indicate that the risk of acute toxic reactions with the varnishes is minimal. In addition, the risk of dental fluorosis is minimal because children are not frequently exposed to fluoride varnishes, as they are to fluoride supplements.

Two cases of contact allergy to Duraphat varnish have been reported: one is a case of dermatitis in a dental assistant's hand, and the other is a case of a stomatitis in a patient.[85] These allergies were likely related to the colophony component of the varnish. The manufacturer of Fluor Protector claimed that a short-term burning sensation is a side effect if the varnish comes into contact with the gingival tissue. In product advertisements, the manufacturer of Duraphat claims that the use of varnish in patients with ulcerative gingivitis and stomatitis is contraindicated.

CONCLUSIONS

Numerous randomized clinical trials conducted outside the

United States point to the efficacy and safety of fluoride varnishes as a caries-preventive agent. The quality of supporting evidence can be considered to be level I, meaning the highest possible level of evidence, according to the system used by the U.S. Preventive Services Task Force.[86] Compared with other topical fluoride vehicles, fluoride varnishes have advantages in terms of safety and ease of application. In addition, the application of fluoride varnishes can be tailored to children who have clinical evidence of high caries attack, such as those with early childhood caries.[68]

Although clinical trial data still need to be submitted to the FDA for clearance of fluoride varnishes as caries-preventive agents, some U.S. dental professionals are using fluoride varnishes in an off-label[87] manner (an accepted practice by which fluoride varnishes could be used for caries prevention in addition to their use in treatment of hypersensitive teeth). In addition, some U.S. dental schools teach the use of fluoride varnishes to their students and provide the varnishes to patients treated in the schools' clinics.

An important factor involved in the acceptance of fluoride varnishes as fluoride delivery vehicles in both public health and private practice settings is the relationship between cost and their caries-preventive effect. Two Swedish studies[22,88] have conducted cost analyses of fluoride varnishes, which are of limited applicability to the United States. The current cost of varnish in the United States (about $0.65 per use for Duraflor) is comparable with that of APF gels ($0.55 per use); this small difference is likely to decrease as the cost of varnish decreases with increased use and market competition. As with any preventive strategy, the dental professional's salary contributes most to the total cost.[89] Some clinical trials have used extended-function dental assistants, dental nurses or dental hygienists to apply the varnish.[21,22,59,74,75] Cost-effectiveness ratios need to be developed for the United States.

Further research is needed to quantify the efficacy and safety of fluoride varnishes among preschool-aged children (up to age 71 months) at high risk of developing early childhood caries. Research also is needed to test the efficacy of fluoride varnish in preventing root caries and to determine the optimal fluoride concentrations. Lack of FDA clearance of fluoride varnish as a caries-preventive agent and dental professionals' limited familiarity with the technique and its efficacy may explain why fluoride varnishes have not been more widely used despite their endorsement by dental professionals.[90,91]

The caries-preventive efficacy of fluoride varnishes is equal to that of other topical fluoride vehicles in school-aged children.

The caries-preventive efficacy of fluoride varnishes is equal to that of other topical fluoride vehicles in school-aged children. They are quick and easy to apply, and are less likely than gels to be swallowed by young children. Fluoride varnishes may be a better alternative to fluoride gels to deliver topical fluoride, especially for young children. For this reason, we believe that more dental schools should include the use of fluoride varnishes in their curricula. The only disadvantage of sodium fluoride varnishes is that they cause a temporary change in tooth color, which dental professionals need to inform their patients of. On the basis of the current evidence, fluoride varnishes can be used effectively as a topical fluoride vehicle to prevent dental caries in school-aged children. ■

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1. Seppä L. Studies of fluoride varnishes in Finland. Proc Finn Dent Soc 1991;87:541-7.
2. Arnbjerg D. Use of professionally administered fluoride among Danish children. Acta Odontol Scand 1992;50:289-93.
3. von der Fehr FR. Caries prevalence in the Nordic countries. Int Dent J 1994;44:371-8.
4. Einarsdottir KG, Bratthall D. Restoring oral health: on the rise and fall of dental caries in Iceland. Eur J Oral Sci 1996;104(4, part 2):459-69.

5. Splieth C, Meyer G. Factors for changes of caries prevalence among adolescents in Germany. Eur J Oral Sci 1996;104(4, part 2):441-51.
6. Bratthall D, Hansel-Petersson G, Sundberg H. Reasons for the caries decline: what do the experts believe? Eur J Oral Sci 1996; 104(4, part 2):416-22.
7. Petersson GH, Bratthall D. The caries decline: a review of reviews. Eur J Oral Sci 1996;104(4, part 2):436-43.
8. Clark DC. A review of fluoride varnishes: an alternative topical fluoride treatment. Community Dent Oral Epidemiol 1982;10: 117-23.
9. de Bruyn H, Arends J. Fluoride varnishes—a review. J Biol Buccale 1987;15: 71-82.
10. Petersson LG. Fluoride mouthrinses and fluoride varnishes. Caries Res 1993;27(suppl 1):35-42.
11. McComb D, Ben-Amar A, Brown J. Sealing efficacy of therapeutic varnishes used with silver amalgam restorations. Oper Dent 1990;15:122-8.
12. Arends J, Duschner H, Ruben JL. Penetration of varnishes into demineralized root dentine in vitro. Caries Res 1997;31:201-5.
13. Seppä L. Effect of dental plaque on fluoride uptake by enamel from a sodium fluoride varnish in vivo. Caries Res 1983;17:71-5.
14. Sorvari R, Meurman JH, Alakuijala P, Frank RM. Effect of fluoride varnish and solution on enamel erosion in vitro. Caries Res 1994;28:227-32.
15. Seppä L. Fluoride content of enamel during treatment and 2 years after discontinuation of treatment with fluoride varnishes. Caries Res 1984;18:278-81.
16. Seppä L, Tuutti H, Luoma H. Post-treatment effect of fluoride varnishes in children with a high prevalence of dental caries in a community with fluoridated water. J Dent Res 1984;63:1221-2.
17. van Eck AA, Theuns HM, Groeneveld A. Effect of annual application of polyurethane lacquer containing silane-fluoride. Community Dent Oral Epidemiol 1984;12:230-2.
18. Seppä L, Tolonen T. Caries preventive effect of fluoride varnish applications performed two or four times a year. Scand J Dent Res 1990;98:102-5.
19. Axelsson P, Paulander J, Nordkvist K, Karlsson R. Effect of fluoride containing dentifrice, mouthrinsing, and varnish on approximal dental caries in a 3-year clinical trial. Community Dent Oral Epidemiol 1987; 15:177-80.
20. Modéer T, Twetman S, Bergstrand F. Three-year study of the effect of fluoride varnish (Duraphat) on proximal caries progression in teenagers. Scand J Dent Res 1984;92: 400-7.
21. Petersson LG, Arthursson L, Östberg C, Jönsson G, Gleerup A. Caries-inhibiting effects of different modes of Duraphat varnish reapplications: a 3-year radiographic study. Caries Res 1991;25:70-3.
22. Sköld L, Sundquist B, Eriksson B, Edeland C. Four-year study of caries inhibition of intensive Duraphat application in 11-15-year-old children. Community Dent Oral Epidemiol 1994;22:8-12.
23. Arends J, Schuthof J. Fluoride content in human enamel after fluoride application and washing: an in vitro study. Caries Res 1975;9:363-72.
24. Retief DH, Bradley EL, Holbrook M, Switzer P. Enamel fluoride uptake, distribution and retention from topical fluoride agents. Caries Res 1983;17:44-51.
25. Caslavska V, Moreno EC, Brudevold F. Determination of the calcium fluoride formed from in vitro exposure of human enamel to fluoride solutions. Arch Oral Biol 1975;20: 333-9.
26. Koch G, Petersson LG. Fluoride content of enamel surface treated with a varnish containing sodium fluoride. Odontol Rev 1972; 23:437-46.
27. Bang S, Kim YJ. Electron microprobe analysis of human tooth enamel coated in vivo with fluoride varnish. Helv Odontol Acta 1973;17:84-8.
28. Stamm JW. Fluoride uptake from topical sodium fluoride varnish measured by an in vivo enamel biopsy. J Can Dent Assoc 1974;40:501-5.
29. Petersson LG. In vivo fluoride uptake in human enamel following treatment with a varnish containing sodium fluoride. Odontol Rev 1975;26:253-66.
30. Edenholm H, Johnson G, Koch G, Petersson LG. Fluoride uptake and release in deciduous enamel after application of fluoride varnishes: an in vitro pilot study. Swed Dent J 1977;1:59-64.
31. Kolehmainen L, Anttila A, Keinonen J. Fluoride content of surface enamel treated with fluoride-containing varnishes and an amine fluoride solution as measured with a sensitive physical method. Proc Finn Dent Soc 1978;74:109-12.
32. Retief DH, Sorvas PG, Bradley EL, Taylor RE, Walker AR. In vitro fluoride uptake, distribution and retention by human enamel after 1- and 24-hour application of various topical fluoride agents. J Dent Res 1980;59:573-82.
33. Retief DH, Harris BE, Bradley EL. In vitro enamel fluoride uptake from topical fluoride agents. Dent Mater 1985;1:93-7.
34. Bruun C, Givskov H, Stoltze K. In vivo uptake and retention of fluoride in human surface enamel after application of a fluoride-containing lacquer (Fluor-Protector). Caries Res 1980;14:103-9.
35. Koch G, Petersson L, Gleerup A, Löwstedt E. Kinetics of fluorine in deciduous enamel after application of fluoride-containing varnish (Duraphat): I. Update, distribution and release. Swed Dent J 1982;6: 39-44.
36. Seppä L, Luoma H, Hausen H. Fluoride content in enamel after repeated applications of fluoride varnishes in a community with fluoridated water. Caries Res 1982;16:7-11.
37. Dijkman AG, de Boer P, Arends J. In vivo investigation of the fluoride content in and on human enamel after topical applications. Caries Res 1983;17:392-402.
38. Grobler SR, Øgaard B, Rølla G. Fluoride uptake and retention by sound enamel after in vivo Duraphat application. J Dent Assoc S Afr 1983;38:55-8.
39. Seppä L. Effects of a sodium fluoride solution and a varnish with different fluoride concentrations on enamel remineralization in vitro. Scand J Dent Res 1988;96:304-9.
40. Ögaard B, Rölla G, Helgeland K. Fluoride retention in sound and demineralized enamel in vivo after treatment with a fluoride varnish (Duraphat). Scand J Dent Res 1984; 92:190-7.
41. Brudevold F, McCann HG, Nilsson R, Richardson B, Cocklica V. The chemistry of caries inhibition problems and challenges in topical treatments. J Dent Res 1967;46:37-45.
42. Ögaard B, Rölla G, Helgeland K. Alkali soluble and alkali insoluble fluoride retention in demineralized enamel in vivo. Scand J Dent Res 1983;91:200-4.
43. Koulourides T. Summary of session II: fluoride and the caries process. J Dent Res 1990;69(spec issue):558.
44. Holmen L, Ögaard B, Rölla G, Thylstrup A. A polarized light and scanning electron microscope study of the effect of Duraphat treatment on in vivo caries. Scand J Dent Res 1986;94:521-9.
45. Øgaard B, Duschner H, Ruben J, Arends J. Microradiography and confocal laser scanning microscopy applied to enamel lesions formed in vivo with and without fluoride varnish treatment. Eur J Oral Sci 1996;104: 378-83.
46. Tveit AB, Tötdal B, Klinge B, Nilvéus R, Selvig KA. Fluoride uptake by dentin surfaces following topical application of TiF_4, NaF and fluoride varnishes in vivo. Caries Res 1985; 19:240-7.
47. Bruun C, Givskov H. Formation of CaF_2 on sound enamel and in caries-like enamel lesions after different forms of fluoride applications in vitro. Caries Res 1991;25:96-100.
48. Koch G, Hakeberg M, Petersson LG. Fluoride uptake on dry versus water-saliva wetted human enamel surfaces in vitro after topical application of a varnish (Duraphat) containing fluoride. Swed Dent J 1988;12: 221-5.
49. Hellwig E, Klimek J, Schmidt HFM, Egerer R. Fluoride uptake in plaque-covered enamel after treatment with the fluoride lacquer Duraphat. J Dent Res 1985;64:1080-3.
50. Joziak MT, Schemehorn BR, Tavss EA, Fisher SW, Gambogi RJ. Comparison of enamel fluoride uptake and release from fluoride varnishes (abstract 1684). J Dent Res 1998;77(spec issue B):842.
51. Zickert I, Emilson CG. Effect of a fluoride-containing varnish on Streptococcus mutans in plaque and saliva. Scand J Dent Res 1982;90:423-8.
52. 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.
53. Attin T, Hartman O, Hilgers R-D, Hellwig E. Fluoride retention of incipient enamel lesions after treatment with a calcium fluoride varnish in vivo. Arch Oral Biol 1995;40:169-74.
54. Acuna V, von Beetzen M, Caracatsanis M, Sundström F. In vitro fluoride uptake by enamel and dentin: a comparative study of two varnishes. Acta Odontol Scand 1990;48:89-92.
55. Seppä L, Pöllänen L, Hausen H. Caries-preventive effect of fluoride varnish with different fluoride concentration. Caries Res 1994;28:64-7.
56. Sorvari R, Spets-Happonen S, Luoma H. Efficacy of chlorhexidine solution with fluoride varnishing in preventing enamel softening by *Streptococcus mutans* in an artificial mouth. Scand J Dent Res 1994;102:206-9.
57. Petersson LG, Magnusson K, Andersson H, Deierborg G, Twetman S. Effect of semiannual applications of a chlorhexidine/fluoride varnish mixture on approximal caries incidence in schoolchildren: a three-year radiographic study. Eur J Oral Sci 1998;106:623-7.
58. Murray JJ, Winter GB, Hurst CP. Duraphat fluoride varnish: a 2-year clinical trial in 5-year-old children. Br Dent J 1977; 143:11-7.
59. Holm AK. Effect of a fluoride varnish (Duraphat) in preschool children. Community

Dent Oral Epidemiol 1979;7:241-5.
60. Grodzka K, Augustyniak L, Budny J, et al. Caries increment in primary teeth after application of Duraphat fluoride varnish. Community Dent Oral Epidemiol 1982;10: 55-9.
61. Holm GB, Holst K, Mejàre I. The caries-preventive effect of a fluoride varnish in the fissures of the first permanent molar. Acta Odontol Scand 1984;42:193-7.
62. Seppä L, Pöllänen L. Caries preventive effect of two fluoride varnishes and a fluoride mouthrinse. Caries Res 1987;21:375-9.
63. Clark DC, Stamm JW, Tessier C, Robert G. The final results of the Sherbrooke-Lac Mégantic fluoride varnish study. J Can Dent Assoc 1987;53:919-22.
64. Tewari A, Chawla HS, Utreja A. Comparative evaluation of the role of NaF, APF & Duraphat topical fluoride applications in the prevention of dental caries—a 2.1/2 years study. J Indian Soc Pedod Prev Dent 1990;8:28-35.
65. Seppä L, Leppänen T, Hausen H. Fluoride varnish versus acidulated phosphate fluoride gel: a 3-year clinical trial. Caries Res 1995;29:327-30.
66. Helfenstein U, Steiner M. Fluoride varnishes (Duraphat): a meta-analysis. Community Dent Oral Epidemiol 1994;22:1-5.
67. Helfenstein U, Steiner M. A note concerning the caries preventive effect of Duraphat. Community Dent Oral Epidemiol 1994;22:6-7.
68. Weinstein P, Domoto P, Koday M, Leroux B. Results of a promising open trial to prevent baby bottle tooth decay: a fluoride varnish study. ASDC J Dent Child 1994;61: 338-41.
69. Kolehmainen L, Kerosuo E. The clinical effect of application of a urethane lacquer containing silane fluoride: a one-year study. Proc Finn Dent Soc 1979;75:69-71.
70. Kolehmainen L. Evaluation of a fluoride-containing varnish in children with low caries incidence. Scand J Dent Res 1981;89: 228-34.
71. Bruun C, Bille J, Hansen KT, Kann J, Qvist V, Thylstrup A. Three-year caries increments after fluoride rinses or topical applications with a fluoride varnish. Community Dent Oral Epidemiol 1985;13:299-303.
72. 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.
73. Petersson LG, Twetman S, Pakhomov GN. The efficiency of semiannual silane fluoride varnish applications: a two-year clinical study in preschool children. J Public Health Dent 1998;58:57-60.
74. Kirkegaard E, Petersen G, Poulsen S, Holm SA, Heidmann J. Caries-preventive effect of Duraphat varnish applications versus fluoride mouthrinses: 5-year data. Caries Res 1986;20:548-55.
75. Koch G, Petersson LG, Rydén H. Effect of fluoride varnish (Duraphat) treatment every six months compared with weekly mouthrinses with 0.2 per cent NaF solution on dental caries: a two-year clinical study. Swed Dent J 1979;3:39-44.
76. Bravo M, Llodra JC, Baca P, Osorio E. Effectiveness of visible light fissure sealant (Delton) versus fluoride varnish (Duraphat): 24-month clinical trial. Community Dent Oral Epidemiol 1996;24:42-6.
77. Bravo M, Baca P, Llodra JC, Osorio E. A 24-month study comparing sealant and fluoride varnish in caries reduction on different permanent first molar surfaces. J Public Health Dent 1997;57:184-6.
78. Bravo M, García-Anllo I, Baca P, Llodra JC. A 48-month survival analysis comparing sealant (Delton) with fluoride varnish (Duraphat) in 6- to 8-year-old children. Community Dent Oral Epidemiol 1997;25:247-50.
79. Koch G, Petersson LG. Caries preventive effect of a fluoride-containing varnish (Duraphat) after 1 year's study. Community Dent Oral Epidemiol 1975;3:262-6.
80. Burt BA, Eklund SA. Dentistry, dental practice, and the community. 5th ed. Philadelphia: Saunders; 1999:320.
81. Roberts JF, Longhurst P. A clinical estimation of the fluoride used during application of a fluoride varnish. Br Dent J 1987;162: 463-6.
82. Ekstrand J, Koch G, Petersson LG. Plasma fluoride concentration and urinary fluoride excretion in children following application of the fluoride-containing varnish Duraphat. Caries Res 1980;14:185-9.
83. Ekstrand J, Koch G, Petersson LG. Plasma fluoride concentration in pre-school children after ingestion of fluoride tablets and toothpaste. Caries Res 1983;17:379-84.
84. Ekstrand J, Koch G, Lindgren LE, Petersson LG. Pharmacokinetics of fluoride gels in children and adults. Caries Res 1981;15:213-20.
85. Isaksson M, Bruze M, Björkner B, Niklasson B. Contact allergy to Duraphat. Scand J Dent Res 1993;101:49-51.
86. U.S. Preventive Services Task Force. Guide to clinical preventive services. 2nd ed. Baltimore: Williams & Wilkins; 1996:XXXIX-lV.
87. Fiset L, Grembowski D. Adoption of innovative caries-control services in dental practice: a survey of Washington state dentists. JADA 1997;128:337-45.
88. Petersson LG, Westerberg I. Intensive fluoride varnish program in Swedish adolescents: economic assessment of a 7-year follow-up study on proximal caries incidence. Caries Res 1994;28:59-63.
89. Vehmanen R. An economic evaluation of two caries preventive methods (dissertation). Turku, Finland: University of Turku; 1993.
90. Mandel I. Fluoride varnishes—a welcome addition. J Public Health Dent 1994;54(2):67.
91. Bawden JW. Fluoride varnish: a useful new tool for public health dentistry. J Public Health Dent 1999;58:266-9.