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Salivary Fluoride from Fluoride Dentifrices or Rinses after Use of a Calcium Pre-Rinse or Calcium Dentifrice

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Calcium · Dentifrice · Fluoride · Rinse · Saliva

Abstract
The low concentration of available calcium (Ca) in oral fluids limits the formation of Ca-mediated fluoride deposits that maintain oral fluoride (F) after a topical F treatment. The purpose of this study was to examine if a high concentration of Ca would increase salivary F when used before a F rinse or dentifrice. We found that a Ca pre-rinse (150 mmol/l Ca lactate) or Ca dentifrice (0.084 g Ca glycerolphosphate per gram dentifrice) used immediately before a 60 s 228-ppm F rinse (12 mmol/l NaF) produced a 4.6× or 3.6× increase ($p < 0.05$) respectively in the 1 h salivary F concentrations over the F rinse alone. Reducing the post-Ca F rinse to 10 s still produced a significant 2.2× increase in salivary F compared to the 60 s F rinse alone. Used with a conventional 1,100 ppm F (i.e. 1,100 μg F per gram) NaF dentifrice (Crest), the above Ca pre-rinse increased 1 h salivary F levels by 2.3× over the F dentifrice alone. However, a F rinse given before a Ca rinse produced no increase in 1 h salivary F concentrations. Although the persistence of these increases requires further study, these results suggest that a moderately high concentration of Ca given shortly before a F rinse or F dentifrice may increase the cariostatic effect of the F product.

Although the cariostatic role of enamel-bound and solution fluoride (F) has been the subject of some debate, a small increase in the concentration of F in oral fluids, such as plaque fluid and saliva, appears to have a profound effect on the de- and remineralization process [ten Cate, 1990; Margolis and Moreno, 1990; Featherstone, 2000]. This observation has focused attention on the labile or the so-called 'loosely-bound' F reservoirs [Arends and Christoffersen, 1990] that can maintain the free F concentration in plaque fluid and saliva. Although numerous studies pointed to calcium fluoride (CaF_2) or phosphate-contaminated 'calcium fluoride-like' deposits [Fejerskov et al., 1981; Rölla and Saxegaard, 1990; Arends and Christoffersen, 1990; Øgaard, 2001] as important bioavailable F reservoirs, especially on oral hard tissue, studies by Rose et al. [1996] suggest that some of the F in plaque is held as bacterial calcium-fluoride (Ca-F) complexes.

Regardless of the nature of this binding, the above studies suggest that bioavailable oral F reservoirs are in the form of Ca-F moieties. Unfortunately, during F dentifrice or rinse usage, the amount of applied F, typically

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12–48 mmol/l, is many times greater than free oral calcium (Ca), which is about 1 mmo/l in saliva and plaque fluid [Vogel et al., 1998, 2000a]. The low concentration of Ca relative to the amount of applied F implies that Ca-F deposition is limited by the rate at which Ca can be scavenged from Ca reservoirs in enamel, plaque or tissue during the short period of F application. Thus the low level of oral free Ca (and other factors) precludes more than a fraction of the applied F from being deposited as a Ca-F reservoir in oral tissue. Recently a preliminary study with a small number of non-fasted subjects demonstrated that when a 150- or a 300-mmol/l Ca rinse was allowed to first penetrate oral tissue before the use of a sodium fluoride (NaF) rinse, a very large increase in the 1 h salivary F concentration was found compared to the NaF rinse alone.

The purpose of the study reported here was to further examine the effect of Ca pre-treatment on salivary F concentration. Thus we: (1) repeated the previous study with a larger group of subjects using the 150-mmol/l Ca lactate rinse that was found to produce the greatest increase in salivary F, (2) tested this Ca pre-rinse with a conventional NaF dentifrice, and (3) investigated the delivery of Ca in the form of a Ca-containing F-free dentifrice before a F rinse. Finally, we tested a 'reverse application' in which the NaF rinse was administered before the Ca rinse.

Materials and Methods

Subject Protocol

Rinse administration and the collection of samples were done with the informed consent of the subjects following protocols reviewed and approved by the appropriate institutional review boards. The same 12 subjects were used in all experiments; however, as noted below, in two studies, 10 and 11 subjects participated. The subjects (3 females and 9 males) were recruited from individuals working at the National Institute of Standards and Technology (Gaithersburg, Md., USA). The subjects were screened before participation to ensure good oral health, normal oral architecture, oral physiology and salivary gland function (demonstrated in a preliminary test of unstimulated saliva flow as described below). Subjects who had diabetes or who were using antihistamines were excluded from the study. All subjects lived in an area with fluoridated water and were instructed to use their normal oral hygiene procedures. The experiments were performed in the morning at least 2 h after food ingestion and ≥12 h since use of any dentifrice (or F rinse). For each subject, at least 1 week elapsed between any two rinse or dentifrice administrations. It should be noted that these administrations were not completely randomized since all four rinse administrations were performed before the four dentifrice administrations. However, within the rinse or dentifrice administrations the order of which the test materials were given was random. Because the same subject group participated in all experiments and the entire experimental period was only 10 weeks, we believe that the lack of complete randomization among all the rinse and dentifrice administrations would produce minimal statistical effects and that this factor did not materially affect the conclusions. Similarly, the analyst and subjects were only partially blinded: they were aware of which groups were being tested (rinses or dentifrices) but within these groups they were not informed of the identity of the test material or the recovered saliva sample.

Table 1. Summary of experiments. Where multiple treatments were given, they were administered in the order shown (treatment 1/treatment 2/treatment 3)

Exp.	Number	Treatment
1	10	no treatment
2	12	60 s 20 ml Ca rinse
3	12	60 s 20 ml F rinse
4	12	60 s 20 ml F rinse/60 s 20 ml Ca rinse
5	12	60 s 1.5 g F dentifrice/10 s 10 ml water rinse
6	12	60 s 20 ml Ca rinse/60 s 1.5 g F dentifrice/ 10 s 10 ml water rinse
7	12	60 s 1.5 g Ca dentifrice/10 s 10 ml F rinse
8	11	60 s 1.5 g Ca dentifrice/60 s 20 ml F rinse
9	12	60 s 20 ml Ca rinse/60 s 20 ml F rinse

Rinse/Dentifrice Administration

In the rinse experiments the subjects were requested to thoroughly rinse for the required time with the experimental or water rinses. No special brushing instructions were given for the dentifrice experiments (other than to specify the brushing time). Nine studies were done. The protocols of these experiments are summarized in table 1. The numbering used in the experiments was chosen to produce the simplest presentation of the data in the results table (table 2). In experiment (Exp.) 1, baseline (no rinse) saliva samples were collected. In Exp. 2 the subjects rinsed 1 min with 20 ml of 150 mmo/l Ca lactate (Ca lactate pentahydrate, Sigma-Aldrich, St. Louis, Mo., USA). In Exp. 3 they rinsed, in a similar manner, with 12 mmol/l (228 ppm) F as NaF (Fisher Scientific, Pittsburgh, Pa., USA). The rinse volumes in these experiments were chosen because they were similar to the volume used in other experiments with F rinses [Vogel et al., 2000b, 2001, 2002]. In Exp. 4 the subjects rinsed with the two rinses used in Exps. 2 and 3 with the Ca lactate rinse being applied immediately after the F rinse. In Exp. 9 the subjects rinsed as in Exp. 4 except that the order was reversed, i.e. the subjects rinsed first with the Ca lactate solution and then with the NaF solution. In Exp. 5 the subjects brushed for 1 min with 1.5 g of a 1,100 ppm F NaF dentifrice (Crest Regular, Procter & Gamble, Cincinnati, Ohio, USA) and then rinsed for 10 s with 10 ml of distilled water. This dentifrice mass and rinse volume were used because it is similar to the amounts used in other dentifrice/water rinse studies [Seppä et al., 1997; Zero et al., 1992a]. In Exp. 6 the subjects rinsed for 1 min with 20 ml of the above Ca lactate solution and brushed their teeth with Crest and rinsed with water as in Exp. 5. In Exp. 7 the subjects brushed for 60 s with 1.5 g of a F-free dentifrice (Fresh'n Brite, Pfizer, Morris Plains, N.J., USA) to which 0.084 g of Ca glycerolphosphate per gram dentifrice was added. The

Table 2. Geometric means (Geo. mean) of the salivary F concentrations (μmol/l), standard deviation factor (SDF), and 95% confidence interval (CI) 1 h after one of the treatment regimens shown

Exp. Description	1 no treatment	2 Ca rinse	3 F rinse	4 F rinse/Ca rinse	5 F dentifrice/ water rinse	6 Ca rinse/F dentifrice/water rinse	7 Ca dentifrice/ short F rinse	8 Ca dentifrice/ F rinse[a]	9 Ca rinse/ F rinse
Geo. mean	1.1	2.0^{A}	13.7^{B}	8.5^{B}	10.8^{B}	25.0^{C}	29.8^{C}	49.1^{D}	62.8^{D}
SDF	2.5	1.0	1.6	1.5	1.6	1.7	2.1	2.1	1.5
CI	0.6, 2.0	1.5, 2.6	10, 19	6.6, 10	8.0, 15	18, 35	19, 48	29, 82	48, 83

Values with the same capital letter indicate groups that do not differ statistically.

[a] One value (284 μmol/l) was an outlier [Grubbs and Beck, 1972] and was omitted. The statistical results were not changed by this omission.

subjects then rinsed for 10 s (short F rinse) with 10 ml of the same NaF rinse noted above. Exp. 8 (11 subjects) was the same as Exp. 7 except that a 60 s 20 ml NaF rinse was used. Ca glycerolphosphate was used in the Ca dentifrice experiments (Exps. 7 and 8) because of its higher solubility compared to Ca lactate. A smaller F rinse volume was used in Exp. 7 in order to be more comparable to the dentifrice experiments (Exps. 5 and 6) in which water rinsing was employed while a larger volume was used in Exp. 8 to be more comparable to the experiments with F rinses (Exps. 3 and 4). However, as described below, this choice of F rinse volume probably did not influence the results. The Ca content of the dentifrice was chosen, based on preliminary studies, to obtain a similar level of applied Ca as that which produced the maximum 1 h post-application salivary F concentration in the previous Ca rinse studies described above [Vogel et al., 2004].

Sample Collection and Analysis

One hour after F application the subjects drooled saliva from their mouth for 2 min into a pre-weighed tube. The tube was then weighed, centrifuged, and the supernatant diluted 9 parts sample with 1 part TISAB III (Thermo-Orion, Shelton, Conn., USA). The diluted saliva samples were then analyzed using the inverted electrode apparatus previously described [Vogel et al., 1990]. The saliva and dentifrice expectorated by the subjects after use of the dentifrice in Exp. 7 were collected in a plastic beaker (before the short F rinse). An aliquot of this mixture was then centrifuged and the Ca content of the supernatant determined spectrophotometrically [Vogel et al., 1983].

Statistical Procedures

A significance level of $p < 0.05$ was used in all statistical tests, which were performed using Winks statistical software (Texasoft, Cedar Hill, Tex., USA). An initial examination indicated that the salivary F data from most of the experiments were not normally distributed. Thus, in order to normalize the data [Zero et al., 1992a; Vogel et al., 2000b; Whitford et al., 2005] a logarithmic transformation of the salivary F concentrations was used prior to an analysis of variance test of the null hypothesis that there was no difference between the treatments. The Newman-Keuls multiple comparisons test was then used on the transformed data to examine the differences among the groups. For this same reason the geometric mean (Geo. mean) and standard deviation factors (SDF) are reported in place of the arithmetic mean and standard deviations [Zero et al., 1992a] in table 2. The standard deviation factor acts by multiplication and division with respect to the geometric mean. The 95% confidence interval (CI), which is reported in this same table, is also calculated from the log-transformed data. In the case of the non-F data (e.g. the mass of collected saliva, Ca analysis data), in which the data were normally distributed, the mean and standard deviation (denoted by the ± symbol) are reported. In this paper the standard deviation factor and the standard deviation are used as measures of the standard uncertainty.

Results

The salivary flow rates in the 1 h post-treatment saliva samples were not statistically different: the average value of all the studies was (0.98 ± 0.53) g/min. The 1 h post-treatment salivary F concentrations in Exps. 1–9 are presented in table 2. The Ca rinse alone (in Exp. 2) produced a small but significant increase in F, compared to the baseline samples (Exp. 1). When Ca was given before a F rinse or dentifrice (Exps. 6–9), it produced significant increases in the 1 h post-salivary F concentration compared to the corresponding methods of delivering NaF alone (Exps. 3 and 5). The maximum increase, 4.6× and 3.8× respectively, was found when Ca was administered as a rinse or Ca-containing dentifrice with a 1-min F rinse (Exps. 8 and 9). The Ca rinse/F dentifrice (Exp. 6) and Ca dentifrice/10 s F rinse (Exp. 7) produced lower 1 h salivary F concentrations but they were still 2.3× and 2.2× greater than the corresponding method of delivering NaF without Ca (Exps. 3 and 5). The Ca content of the expectorate after use of the Ca dentifrice in Exp. 7 was 94 ± 14 mmol/l, which was somewhat lower than the target value of 150 m*M* for a Ca rinse. Administering Ca subsequent to a F rinse (Exp. 4) appeared to decrease the

1 h salivary F concentrations relative to the NaF rinse alone (Exp. 3). The decrease, however, was not significant.

Discussion

The baseline salivary F concentrations (table 2) were similar [Vogel et al., 2002] or slightly lower than reported in similar experiments [Vogel et al., 2000b, 1992, 2001]. The 1 h post-NaF rinse salivary F concentrations (Exp. 3) are also similar to the values found in these previous experiments. The 1 h post-NaF dentifrice values, which are not significantly different from the NaF rinse values, are somewhat higher than those found in other studies [Seppä et al., 1997; Zero et al., 1992a] in which a similar dentifrice and similar post-dentifrice water rinse protocol were used.

As noted in the Introduction, the low concentration of free Ca in oral fluid relative to the amount of applied F limits Ca-F deposition from a F dentifrice or F rinse. Several methods have been employed to supply additional Ca with F during these types of therapy. However, such procedures can be complicated by the rapid precipitation of CaF_2 particles that do not appear to adhere to tooth surfaces [Chow et al., 1992]. Chow and co-workers have pioneered a number of approaches to control CaF_2 formation during simultaneous application of Ca and F, most particularly an extensively tested method in which Na_2SiF_6 is mixed with Ca chloride immediately before use [Chow et al., 1992, 2000, 2002; Vogel et al., 1992, 2001]. In this study we have adopted a somewhat simpler approach: the penetration of the pores of oral tissue and plaque by high levels of Ca to create a high driving force for the formation of bioavailable Ca-F moieties when the F treatment is subsequently applied. Although the disadvantages of such a two-step procedure are apparent, the increase in 1 h salivary F concentration in the Ca pre-rinse/F rinse study in Exp. 9 (table 2) was nearly 4.6 × compared to a conventional NaF rinse. It should be noted, however, that this increase was only about half that found in a preliminary study [Vogel et al., 2004], perhaps due to the use of a subject panel who were allowed to eat up to 1 h before rinse administration in the previous study. Although the location of the oral Ca-F deposits produced by this procedure is not established, several authors have suggested that, due to its large surface area, oral soft tissue is the major source of F available for release into saliva [Zero et al., 1992b; Jacobson et al., 1992].

Evidence that the increase in 1 h salivary F is due to the reaction of F with elevated free Ca in the oral tissue, induced by the Ca pre-rinse, can be seen by noting that no increase in salivary F occurs when the order of administration is reversed in Exp. 4 (F before Ca). In fact in Exp. 4 there is a trend toward lower salivary F levels which might be due to the diffusion of the applied F from the tissue or plaque F into the fluid phase of the Ca rinse – an effect, as described below, which is well known with respect to dentifrices.

When the Ca was delivered as a dentifrice before the 1-min NaF rinse (table 2, Exp. 8), the 1 h salivary F appears to be somewhat reduced compared to that obtained with the 150-mmol/l Ca rinse/F rinse in Exp. 9. This trend may have been due to the 37% lower concentration of Ca found in the saliva/dentifrice expectorate compared to the 150-mmol/l Ca rinse. However, a second study (7 subjects) using a high concentration Ca glycerolphosphate dentifrice (0.3 g/g) that produced a Ca concentration in the expectorate of 175 ± 40 mmol/l, increased F levels by only 20%. This suggests that, perhaps due to the formation of Ca compounds or complexes from the sodium lauryl sulfate (SLS) component of the Ca-containing dentifrice, the 1 h salivary F concentration is insensitive to moderate changes in the Ca content of the dentifrice.

Surprisingly, decreasing the post-Ca dentifrice F rinse time to only 10 s (Exp. 7) only decreased the 1 h salivary F concentration by about 39%. The use of a smaller volume (10 vs. 20 ml) for the NaF rinse in this experiment probably had a minimal effect on the observed F concentration since only a fraction of the applied F is orally deposited from the rinse during application and 10 ml should be enough to ensure complete oral coverage.

In accordance with studies on commercial rinses and dentifrices, the 1 h salivary F concentrations were reduced for the NaF dentifrice (Exp. 3) [Zero et al., 1988, 1992a] relative to the NaF rinse (Exp. 5). However, in the current study the difference was not significant. Several factors decrease the delivery of F from a dentifrice relative to a rinse, most importantly, water rinsing, which is customarily done after dentifrice application, has been shown to drastically reduce salivary F [Duckworth et al., 1991; Seppä et al., 1997; Sjögren and Birkhed, 1994]. Although the 1 h salivary F concentrations from the NaF rinse and dentifrice were similar (table 2), the Ca pre-rinse produced a much higher salivary F concentration when used before the F rinse (Exp. 9) than when used before the F dentifrice (Exp. 6). Given the very high concentration of salivary F found when the Ca pre-rinse or

Ca dentifrice was used before a F rinse (Exps. 8 and 9), this suggests that the post-F dentifrice water rinse had a highly deleterious effect on high levels on Ca-F moieties. Such an effect is not unanticipated given the high driving force for Ca-F dissolution under these circumstances. The formation of Ca complexes or compounds by component of the F dentifrice, for example SLS, may also be a factor in removing some of the Ca held in the tissue after the Ca rinse.

The Ca pre-rinse alone (Exp. 2) produced a small but statistically significant increase in the 1 h salivary F concentrations (table 2) relative to baseline levels (Exp. 1). Such results, and the very high levels of F found in Exps. 8 and 9, suggest that high concentrations of Ca in a pre-treatment could induce the formation of large amounts of bioavailable F reservoirs from rinses or dentifrices with a reduced F concentration. It is noteworthy in this regard that a 114-ppm Na_2SiF_6 type F rinse with an enhanced level of added Ca produced more remineralization in an intraoral model than a conventional 228-ppm F rinse [Chow et al., 2002]. Although a sequential rinse procedure has not been tested in this regard, the concentrated Ca pre-rinse has the potential advantage of reducing oral fluid phosphate through precipitation of Ca-PO_4 minerals. Phosphate, which is very high in oral fluid [Vogel et al., 1998, 2000a], appears to induce the formation of non-bioavailable (insoluble) Ca-F-PO_4 phases when high levels of Ca are used to enhance F deposition from F rinses more dilute than 114 ppm [Chow et al., 2002].

There are a number of limitations on the use of the sequential Ca-before-F procedure described here. Firstly, the Ca application should be done immediately before the F rinse or dentifrice. Secondly, low levels of Ca appear to be relatively ineffective [Vogel et al., 2004]. Thus, Whitford et al. [2005] found that a 20-mmol/l Ca pre-rinse in a 50-mmol/l acetate buffer (equivalent to 15 mmol/l of free Ca) had no effect on salivary F concentrations in samples collected 1 h after brushing with a F dentifrice. Whitford's results may also partly reflect the reduction in salivary F levels noted above when the F source is a commercial dentifrice rather than an aqueous rinse. Thirdly, there appears to be also a limitation on the maximum Ca that can be used since Ca carryover into the subsequently applied F agent can lead to loss of F by precipitation of CaF_2 in the applied phase [Vogel et al., 2004]. Finally, there is the possibility of increased calculus formation when high concentrations of Ca are frequently applied. However, Ca lactate, which was used in the F rinse studies, has been shown to actually reduce calculus in clinical studies [Schaeken and van der Hoeven, 1990, 1993]. With regard to Ca glycerolphosphate, which was used in the Ca dentifrice studies, this compound has been used in high concentrations in sodium monofluorophosphate dentifrices for many years. There are no published reports of this dentifrice formulation producing an increase in calculus formation.

The clinical implications of this study are unclear, especially since the persistence of the high post-treatment 1 h salivary F levels shown in table 2 has not been investigated. Furthermore, the F concentrations in phases that are more relevant to caries, such as tooth mineral, plaque, and especially plaque fluid, remain to be fully examined. However, promising preliminary plaque fluid data has recently been presented using a Ca pre-rinse/F rinse [Vogel et al., 2005]. In any case, the results presented here suggest that administration of a moderately high concentration of Ca immediately before application of topical fluorides may increase the cariostatic effect. There are of course disadvantages in a two-step procedure but it is noteworthy that the Ca-containing dentifrice used with a short (10 s) F rinse (table 2) produced a 2.2 × increase in salivary F compared to a 60 s F rinse and a 2.8 × increase with respect to the use of a F dentifrice. Such a procedure is entirely comparable to the post-F dentifrice water rinsing which most of the public currently perform.

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References

Arends J, Christoffersen J: Nature and role of loosely bound fluoride in dental caries. J Dent Res 1990;69(Spec Iss):601–605.

Chow LC, Takagi S, Carey CM, Sieck BA: Remineralization effect of a two-solution fluoride mouth rinse – an in situ study. J Dent Res 2000;79:991–995.

Chow LC, Takagi S, Frukhtbeyn S, Sieck BA, Parry EE, Liao NS, Schumacher GE, Markovic M: Remineralization effect of a low-concentration fluoride rinse in an intraoral model. Caries Res 2002;36:136–141.

Chow LC, Takagi S, Shih S: Effect of a two-solution fluoride mouthrinse on remineralization of enamel lesions in vitro. J Dent Res 1992;71: 443–447.

Duckworth RM, Knoop DTM, Stephen KW: Effect of mouthrinsing after toothbrushing with a fluoride dentifrice on human salivary fluoride levels. Caries Res 1991;25:287–291.

Featherstone JD: The science and practice of caries prevention. J Am Dent Assoc 2000;131:887–899.

Fejerskov O, Thylstrup A, Larsen MJ: Rational use of fluorides in caries prevention. A concept based on possible cariostatic mechanisms. Acta Odontol Scand 1981;39:241–249.

Grubbs FE, Beck G: Extension of sample sizes and percentage points for significance test of outlying observations. Technometrics 1972;14: 847–854.

Jacobson APM, Stephen KW, Strang R: Fluoride uptake and clearance from the buccal mucosa following mouthrinsing. Caries Res 1992;26: 56–58.

Margolis HC, Moreno EC: Physicochemical perspectives on the cariostatic mechanisms of systemic and topical fluorides. J Dent Res 1990; 69 (Spec Iss):606–613.

Øgaard B: CaF_2 formation: cariostatic properties and factors of enhancing the effect. Caries Res 2001;35(suppl 1):40–44.

Rölla G, Saxegaard E: Critical evaluation of the composition and use of topical fluorides with emphasis on the role of calcium fluoride in caries inhibition. J Dent Res 1990;69(Spec Iss):780–785.

Rose RK, Shellis RP, Lee AR: The role of cation bridging in microbial fluoride binding. Caries Res 1996;30:458–464.

Schaeken MJM, van der Hoeven JS: Influence of calcium lactate rinses on calculus formation in adults. Caries Res 1990;24:376–378.

Schaeken MJM, van der Hoeven JS: Control of calculus formation by a dentifrice containing calcium lactate. Caries Res 1993;27:277–279.

Seppä L, Salmenkivi S, Hausen H: Salivary fluoride concentration in adults after different fluoride procedures. Acta Odontol Scand 1997; 55:84–87.

Sjögren K, Birkhed D: Effect of various post-brushing activities on salivary fluoride concentration after toothbrushing with a sodium fluoride dentifrice. Caries Res 1994;28:127–131.

Ten Cate JM: In vitro studies on the effects of fluoride on de- and remineralization. J Dent Res 1990;69(Spec Iss):614–619.

Vogel GL, Carey CM, Chow LC, Ekstrand J: Fluoride analysis in nanoliter- and microliter-size fluid samples. J Dent Res 1990;69(Spec Iss): 522–528.

Vogel GL, Chow LC, Brown WE: A microanalytical procedure for the determination of calcium, phosphate and fluoride in enamel biopsies. Caries Res 1983;17:23–31.

Vogel GL, Chow LC, Schumacher GE, Takagi S: Salivary-F after NaF rinsing greatly increased by concentrated calcium pre-rinse. J Dent Res 2004;83(Spec Iss A):IADR CD-ROM Abstr No 1332.

Vogel GL, Mao Y, Carey CM, Chow LC, Takagi S: In vivo fluoride concentrations measured for two hours after a NaF or a novel two-solution rinse. J Dent Res 1992;71:448–452.

Vogel GL, Shim D, Schumacher GE, Takagi S: Plaque fluid and Salivary fluoride one hour after a Ca pre-rinse/NaF rinse. Caries Res 2005; 39:316 abstr 85.

Vogel GL, Zhang Z, Carey CM, Ly A, Chow LC, Proskin HM: Composition of plaque and saliva following a sucrose challenge and use of a α-tricalcium-phosphate-containing chewing gum. J Dent Res 1998;77:518–524.

Vogel GL, Zhang Z, Carey CM, Ly A, Chow LC, Proskin HM: Composition of plaque and saliva following use of an α-tricalcium phosphate-containing chewing gum and a subsequent sucrose challenge. J Dent Res 2000a;79:58–62.

Vogel GL, Mao Y, Chow LC, Proskin HM: Fluoride in plaque fluid, plaque, and saliva measured for two hours after a NaF or NaMFP rinse. Caries Res 2000b;34:404–411.

Vogel GL, Zhang Z, Chow LC, Schumacher GE: Effect of a water rinse on 'labile' fluoride and other ions in plaque and saliva before and after conventional and experimental fluoride rinses. Caries Res 2001;35:116–124.

Vogel GL, Zhang Z, Chow LC, Schumacher GE: Changes in lactate and other ions in plaque and saliva after a fluoride rinse and subsequent sucrose administration. Caries Res 2002;36:44–52.

Whitford GM, Buzalaf MAR, Bijella MFB, Waller JL: Plaque fluoride concentrations in a community without water fluoridation: effects of calcium and use of a fluoride or placebo dentifrice. Caries Res 2005:39:100–107.

Zero DT, Fu J, Espeland MA, Featherstone JDB: Comparison of fluoride concentrations in unstimulated whole saliva following the use of a fluoride dentifrice and a fluoride rinse. J Dent Res 1988;67:1257–1262.

Zero DT, Raubertas RF, Fu J, Pedersen AM, Hayes AL, Featherstone JDB: Fluoride concentrations in plaque, whole saliva, and ductal saliva after application of home-use topical fluorides. J Dent Res 1992a;71:1768–1775.

Zero DT, Raubertas RF, Pedersen AM, Fu J, Hayes AL, Featherstone JDB: Studies of fluoride retention by oral soft tissues after the application of home-use topical fluorides. J Dent Res 1992b;71:1546–1552.