



# Fluoride Release and Uptake into Hydroxyapatite from Experimental Dental Varnish

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## Abstract

Fluoride releasing dental varnishes (F-varnish) typically contain 5% NaF within a resin or rosin base. The sodium fluoride concentration ([NaF]) that yields optimal fluoride enamel uptake, release, and anti-caries efficacy is unknown. Also, there is controversy on whether the release rate of fluoride into saliva is predictive of the fluoride uptake into enamel. **Objectives:** measure fluoride uptake (loosely- and tightly-bound) into hydroxyapatite (HAP) discs and fluoride release as a function of [NaF] in F-varnish. **Methods:** triplicate sets of F-varnish containing 5.0%, 2.5%, 1.25%, and 0.625% (wt/wt) NaF were prepared. 0.01-0.02g F-varnish was applied to one side of a HAP disc. Fluoride release into a continuous flow of 30mmol/L KCl at 1 mL/min was measured over 3h. The HAP discs were then cleaned and loosely-bound fluoride extracted overnight in KOH (1.0mL, 1.0mol/L). Tightly bound fluoride was extracted via serial extractions in HClO<sub>4</sub> (1.0mL, 0.5mol/L). The extraction solutions were neutralized and analyzed via fluoride ion-selective electrode. **Results:** the cumulative fluoride release profile increased hyperbolically over 3h. The total fluoride released at 3h ([F]<sub>3h</sub>) increased as a function of [NaF]. The time for 50% (t<sub>50</sub>) of the fluoride to be released was ≤ 32min for all varnishes. Loosely- and tightly-bound fluoride increased to 2.5% NaF and plateaued.

[NaF]%	[F] Tightly Bound (µg/mL)	[F] Loosely Bound (µg/mL)	[F] <sub>3h</sub> released (µgF/mg Varnish)	t <sub>50</sub> (minutes)
0.625	0.10(0.03) <sup>a</sup>	0.09(0.05) <sup>a</sup>	0.7 (0.23) <sup>f</sup>	4.40
1.25	0.15(0.02) <sup>a</sup>	0.26(0.12) <sup>a</sup>	1.87(0.86) <sup>f</sup>	31.95
2.5	0.25(0.03) <sup>a</sup>	1.20(0.03) <sup>a</sup>	2.47(0.47) <sup>f</sup>	26.10
5.0	0.19(0.05) <sup>a</sup>	1.18(0.07) <sup>a</sup>	3.82(0.84) <sup>f</sup>	19.70

Values in the table are mean(standard error).

Superscripts indicate groups that are not significantly different in each category (ANOVA, Newman-Keuls, p<0.05).

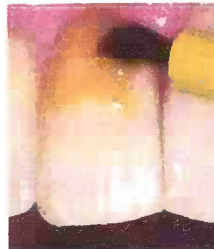
**Conclusions:** In this study, optimal [NaF] is 2.5% for saturating all the available tight and loose binding sites of the HAP disc. Fluoride release into solution is not a reliable indicator of fluoride uptake. Further studies using enamel are planned.

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## Introduction

### What do we know about F-Varnish?

- ADA recommends for caries prevention: at-risk patients
- On the basis of critical reviews of clinical literature
- US FDA does not recognize F-varnishes for caries prevention
- Research has not proven that F-varnishes can prevent caries
- Approved for cavity liners and treatment of hypersensitivity
- Numerous F-varnishes in the marketplace
- Marketed for more than 30 years
- Remains on teeth for 2 to 24 hours
- 50,000 ppm NaF (22,600 ppm F)
- 6 month efficacy



### What don't we know?

- Mechanism of action
- Optimal application frequency
- Optimal application conditions
- Optimal product composition for efficacy
- If release rate is predictive of efficacy
- Identity of the significant factors that affect efficacy
- Short term and long term effects on patients

**Purpose** to investigate the relationship between fluoride released into the surrounding solution from an F-varnish and fluoride uptake (loosely- and tightly-bound) into hydroxyapatite (HAP) discs as a function of [NaF] in F-varnish



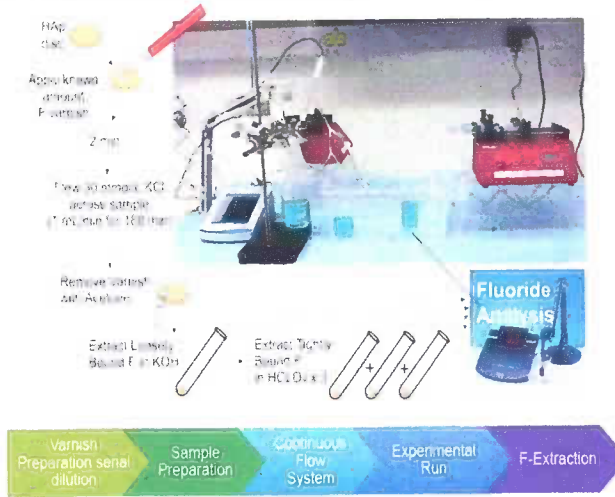
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## Hypotheses

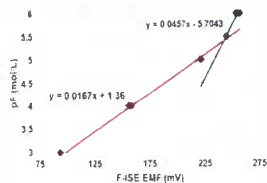
- There is a fluoride saturation point where the tooth can not take up anymore fluoride
  - Meaning: Additional fluoride will not increase anti-caries efficacy
- Fluoride release into saliva is not predictive of the fluoride uptake into the tooth
  - Meaning: Fluoride uptake by the enamel is INDEPENDENT of the fluoride release from the varnish

## Experimental Design

- F-free varnish was used to prepare 4 different [NaF] varnishes via serial dilutions: 5%, 2.5%, 1.25%, 0.625% (w/w)
- Hydroxyapatite discs (mimic tooth composition), were coated on one side with the experimental varnish
- Fluoride release into a continuous flow of 30mmol/L KCl (mimics salivary ionic strength) at 1 mL/min was measured over 3h
- The HAP discs were then cleaned with acetone.
  - Loosely bound fluoride extracted overnight in KOH (1.0mL, 1.0mol/L)
  - Tightly bound fluoride was extracted via serial extractions in HClO<sub>4</sub> (1.0mL, 0.5mol/L)
- The extraction solutions were neutralized and analyzed via fluoride ion-selective electrode

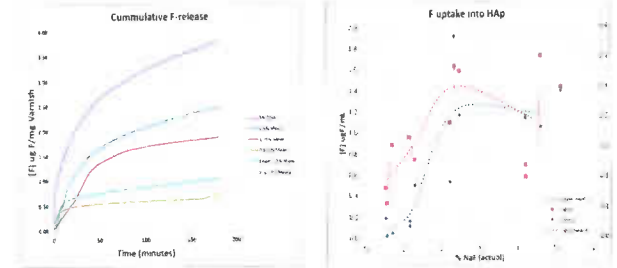


## Analysis for Fluoride



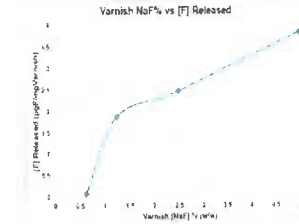
Calculate the fluoride concentration of the sample with the appropriate standard curve. NOTE: F-ISE is not as sensitive at the low [F] thus requiring the use of the non-ideal curve for pF 5.3 to pF 6.0.

## Results



The following observations can be made.

- The cumulative amount of F released into the solution increased asymptotically over time
- The total amount of F release is proportional to the NaF concentration in the varnish on the HAP substrate
- Both the loosely bound and tightly bound F uptake into the HAP disc as a function of varnish NaF concentration is non-linear
- There is an optimal NaF concentration at 2.5% that saturates HAP fluoride binding sites.



- The time where 50% of the fluoride to be released was ≤ 32 min for all experimental varnishes
- The amount fluoride released into saliva is not a reliable indicator of fluoride uptake
- Preliminary data shows that the [F]<sub>3h</sub> released from enamel discs was 1.66 (0.27) µg F/mg varnish, n=2 which is significantly different from that of the HAP discs at 2.5% NaF (p < 0.05)

## Discussion

- Tightly bound Fluoride gives long term protection by preventing dissolution
- Loosely bound fluoride gives short term protection by inducing mineralization and through antimicrobial mechanisms
- The concentration of fluoride binding sites on the HAP disc is limited.
- Saturation of fluoride binding sites gives maximal protection against demineralization (caries)
- Research indicates a 6-month efficacy for caries protection, thus the therapy should be repeated twice annually for at-risk patients
- At %'s lower than 5% NaF, a fluoride varnish can saturate the HAP disc

## Conclusions

- In this study, optimal [NaF] is 2.5% for saturating all the available tight and loose binding sites of the HAP disc
- More experiments are needed to identify compositional factors which may be significant
- Experiments using enamel instead of HAP discs are needed

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