Tri-Calcium Phosphate (TCP)
NOTE: Some uses described in this abstract collection have not been approved or cleared by the FDA. See full prescribing information for individual product indications and usage information at www.3MESPE.com.*

* Please check on correct address where IFU/prescribing info is located.
Tri-Calcium Phosphate (TCP)

In early 2009, 3M ESPE introduced two dentifrice formulations, one with 5,000 ppm fluoride (Clinpro™ 5000 Anti-Cavity Toothpaste) and one with 950 ppm fluoride (Clinpro™ Tooth Crème), that contain a calcium phosphate ingredient called TCP.

TCP, or functionalized TCP, is a unique technology involving mechanochemical ball-milling of tri-calcium phosphate with simple organic ingredients that results in a functionalized or bioactive tri-calcium phosphate. Tri-calcium phosphate was selected over other calcium phosphate systems because it appears as a transitional phase in hydroxyapatite conversion; is biocompatible and bioactive in the oral cavity; and contains sites within its structure that can be activated with, for instance, simple organic molecules. Unlike other calcium-based additives, and by meticulous design, only low levels of functionalized TCP are needed to produce strong, acid-resistant mineral nucleation without negatively affecting fluoride’s proven benefits. Additionally, tri-calcium phosphate can be custom-tailored for a variety of oral care products.

In late 2010, we introduced several patented, white fluoride varnish formulations containing TCP. In this case, TCP was custom-tailored for varnishes by milling it with a different organic ingredient. This resulted in greater mineral deposition onto dentin surfaces, providing greater antihypersensitivity potential. We are excited about how robust the TCP technology is and how it offers even broader versatility than originally thought.

We’ve assembled a collection of in vitro and in vivo studies conducted with TCP for your review. I hope you enjoy reading through the mounting collection of evidence about this truly unique, intelligent and versatile technology we call TCP.

With best regards,

Aaron Pfarrer
Scientific Affairs Manager
Preventive Products
3M ESPE
September 2011
Tri-Calcium Phosphate (TCP)

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In Vitro Remineralization of White-Spot Lesions by Fluoride Rinses With and Without Functionalized Tricalcium Phosphate ......................... 35
Tri-calcium phosphate (TCP), present in some 3M ESPE products, is an intelligent material that provides bioavailable calcium and phosphate ions to the teeth, generating significant remineralization even when used in small amounts. It functions synergistically with fluoride to enable high fluoride bioavailability at normal and “dry mouth” conditions. Our exclusive milling process protects the TCP so that the calcium does not degrade the fluoride during storage. TCP functions in neutral or slightly basic pH environments. Different organic materials can be used to tailor the TCP system to a variety of topically applied oral care preparations, such as toothpaste, oral rinses and varnishes.

This chapter summarizes several general papers and studies that demonstrate the potential clinical advantages of TCP.
Challenges of Implementing New Remineralization Technologies

A.M. Pfarrer, 3M ESPE Dental; St. Paul, MN, U.S.A. R.L. Karlinsey, Indiana Nanotech, Indianapolis, IN, U.S.A.


Synopsis: This paper provides insight into the challenges of developing new anti-caries technologies for enhancing tooth remineralization or preventing tooth decay. The authors acknowledge that fluoride remains the most widely used and thoroughly studied drug for these purposes. However, they suggest that some calcium-containing technologies, including functionalized TCP, may be incorporated into topically applied fluoride-containing preparations without negatively affecting the proven benefits of fluoride.
Enhancing Remineralization of Subsurface Enamel Lesions With Functionalized $\beta$-TCP

R.L. Karlinsey, A.C. Mackey, E.R. Walker and K.E. Frederick, Indiana Nanotech, Indianapolis, IN, U.S.A.


Synopsis: This paper discusses the development of a unique functionalized $\beta$-TCP (fTCP) using a solid-state mechanochemical process and evaluates its fluoride compatibility and remineralization efficacy. The authors conclude that fTCP intertwines synergistically with fluoride and the enamel tissue to produce superior remineralization of the subsurface lesion compared with fluoride alone.
Preparation, Characterization and *In Vitro* Efficacy of an Acid-Modified \( \beta \)-TCP Material for Dental Hard-Tissue Remineralization

R.L. Karlinsey, A.C. Mackey, E.R. Walker and K.E. Frederick, Indiana Nanotech, Indianapolis, IN, U.S.A.

**Reference:** Acta Biomater. 2010 Mar;6(3):969–78

**Aim of the Study:** To modify \( \beta \)-TCP with fumaric acid (FA) to create a promising surface and subsurface enamel mineralization system.

**Methodology:** A TCP-FA material was prepared using mechanochemical ball milling. Bovine enamel samples with caries-like lesions were treated for 10 days with either distilled water, TCP or modified TCP to determine whether the modified TCP enhanced remineralization.

**Results:** TCP-FA promoted enhanced remineralization compared with distilled water and mTCP, likely due to the functionalization of \( \beta \)-TCP and FA that occurred during milling.

**Mean change in Vickers surface microhardness of subsurface enamel lesions after 10 days of cycling**

![Graph showing mean change in Vickers surface microhardness of subsurface enamel lesions after 10 days of cycling.](image)

Error bars represent the standard error of the mean. Statistically significant differences as follows: a<b<c.
Aim of the Study: To determine the feasibility of creating functionalized β-TCP (fTCP) using solid-state mechanochemical ball milling and to evaluate whether fTCP and fluoride provide better remineralization of weakened enamel than fluoride alone.

Methodology: A TCP-sodium lauryl sulfate (SLS) material was created via milling. Bovine enamel specimens with white-spot lesions were divided into five treatment groups — distilled water, 500 parts per million (ppm) fluoride, 1,100 ppm fluoride, 500 ppm fluoride plus 0.025 percent TCP<sub>98</sub>SLS<sub>2</sub> and 1,100 ppm fluoride plus 0.05 percent TCP<sub>98</sub>SLS<sub>2</sub>. Specimens cycled for 5 days between four 2-minute treatments and one four-hour acid challenge.

Results: Milling β-TCP with SLS created fTCP and protected calcium from prematurely interacting with ionic fluoride while coexisting in solution. The fTCP combined with fluoride significantly boosted remineralization efficacy compared with only fluoride.

Hypothetical mechanism demonstrating the ability of SLS in modifying β-TCP

SLS modified calcium and phosphate environments in β-TCP to produce “functionalized” calcium and “free” phosphate.
**Spectroscopic Evaluation of Native, Milled and Functionalized β-TCP Seeding Into Dental Enamel Lesions**

R.L. Karlinsey, A.C. Mackey, E.R. Walker and K.E. Frederick, Indiana Nanotech, Indianapolis, IN, U.S.A.


**Aim of the Study:** To evaluate the remineralization effects of seeding native β-TCP, milled β-TCP (mTCP) and β-TCP milled with sodium lauryl sulfate (fTCP) into weakened dental enamel.

**Methodology:** Enamel specimens from bovine molars were immersed in an acid solution (pH=5.0) at 37°C for 26 hours to produce caries-like lesions. Specimens were then subjected to a 30-minute seeding period in solutions or suspensions containing sodium lauryl sulfate (SLS), native β-TCP, mTCP or fTCP.

**Results:** The fTCP provided significant mineralization potential compared with native β-TCP and mTCP. While native β-TCP and mTCP produced no dose response, fTCP produced a dose response dependent on SLS content.

**Infrared peak orthophosphate position of lesioned enamel, native β-TCP and fTCP**

<table>
<thead>
<tr>
<th>White-Spot Enamel Lesion</th>
<th>Infrared Peak Orthophosphate (PO₄) Position (cm⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control enamel lesion</td>
<td>1031.2 (loosely bound PO₄)</td>
</tr>
<tr>
<td>(no seeding)</td>
<td></td>
</tr>
<tr>
<td>Lesion seeded</td>
<td>1031.2 (loosely bound PO₄)</td>
</tr>
<tr>
<td>with native β-TCP</td>
<td></td>
</tr>
<tr>
<td>Lesion seeded</td>
<td>1037.6* (tightly bound PO₄)</td>
</tr>
<tr>
<td>with fTCP</td>
<td></td>
</tr>
</tbody>
</table>

The fTCP provided significant mineralization potential relative to native β-TCP and mTCP.

* Statistically significant; loosely bound or tightly bound PO₄ can be associated with weaker or stronger enamel structure, respectively.
Tri-calcium phosphate (TCP), present in some 3M ESPE products, is an intelligent material for use in toothpaste that delivers a high concentration of fluoride and helps strengthen enamel. Clinpro™ 5000 Anti-Cavity Toothpaste with 5,000 ppm fluoride and Clinpro™ Tooth Créme with 950 ppm fluoride include an innovative TCP technology available exclusively from 3M ESPE. During manufacturing of the toothpaste, a protective barrier is created around the calcium, allowing it to coexist with the fluoride ions. When the toothpaste comes into contact with saliva during brushing, the barrier dissolves and allows the release of calcium, fluoride and phosphate on the tooth to help prevent tooth decay and remineralize demineralized enamel.

This chapter summarizes several studies that demonstrate the potential clinical advantages of TCP in toothpaste.
Clinpro™ 5000 Anti-Cativy — Protection Against Caries Initiation and Progression

Lesion Progression After Use of Fluoride and CaP Containing Dentifrices
M.M. Hogan, J.D. Harless, and J.S. Wefel, University of Iowa, Iowa City, IA, U.S.A.

Reference: J Dent Res 89 (Spec Iss B):3230, 2010
(www.dentalresearch.org)

Aim of the Study: To determine whether a 5,000 ppm fluoride dentifrice with TCP provides protection against caries initiation and progression.

Methodology: Demineralized human enamel samples were cycled between two 2-minute treatments, two 3-hour demineralizations, a 2-hour remineralization and overnight remineralization for 14 days. The dentifrice treatments included 5,000 ppm fluoride with TCP, 5,000 ppm fluoride, 950 ppm fluoride plus functionalized β-TCP (fTCP), 900 ppm fluoride plus casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) and 110 ppm fluoride.

Results: While the dentifrice containing CPP-ACP appeared to negate a fluoride effect and allowed a 64 percent increase in lesion area, the dentifrice containing fTCP allowed a fluoride effect, allowed only a 27 percent increase in lesion area and reduced average lesion depth by nearly 20 percent.

Overall increase in lesion depth

<table>
<thead>
<tr>
<th>Treatment</th>
<th>∆ Lesion Depth (μm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5,000 ppm F  + fTCP</td>
<td>20</td>
</tr>
<tr>
<td>5,000 ppm F</td>
<td>30</td>
</tr>
<tr>
<td>950 ppm F  + fTCP</td>
<td>40</td>
</tr>
<tr>
<td>900 ppm F  + CPP-ACP</td>
<td>50</td>
</tr>
<tr>
<td>110 ppm F</td>
<td>60</td>
</tr>
</tbody>
</table>

The dentifrice containing fTCP showed the least increase in lesion depth, while the dentifrice containing CPP-ACP showed the second-highest increase.
Cross-Sectional Microhardness Assessment of Enamel Remineralization From Calcium-Containing NaF Formulations

R.L. Karlinsey, A.C. Mackey and E.R. Walker, Indiana Nanotech, Indianapolis, IN, U.S.A.


Aim of the Study: To investigate the remineralization of white-spot enamel lesions from six fluoride-containing preparations.

Methodology: Following white-spot lesion formation, bovine enamel specimens were divided into groups and cycled between four 2-minute treatments, one 4-hour acid challenge and artificial saliva each day. Treatments included a placebo, a conventional 1,100 parts per million (ppm) fluoride dentifrice, a paste with casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) and 900 ppm fluoride, a 1,100 ppm fluoride dentifrice with ACP, a 950 ppm fluoride dentifrice with functionalized \(\beta\)-TCP (fTCP), a 5,000 ppm fluoride dentifrice with fTCP and a conventional 5,000 ppm fluoride dentifrice. After 10 days of cycling, enamel specimens were cross-sectioned and measured for penetration depth longitudinally.

Results: The placebo resulted in the deepest indentations, while the two dentifrices containing fTCP and the 1,100 ppm fluoride dentifrice containing ACP resulted in the shallowest indentations. Therefore, sodium fluoride (NaF) formulations containing calcium technologies such as fTCP show promise in remineralizing white-spot lesions.
Toothpaste

Enamel Remineralization and Fluoride Uptake From 5,000 ppm Fluoride Pastes

R.L. Karlinsey, A.C. Mackey and G.K. Stookey, Indiana Nanotech, Indianapolis, IN, U.S.A.; A.M. Pfarrer, OMNI Preventive Care, West Palm Beach, FL, U.S.A.


Aim of the Study: To determine the ability of 5,000 parts per million (ppm) sodium fluoride (NaF) pastes to remineralize demineralized enamel.

Methodology: Bovine enamel specimens were softened in an acid solution for 36 hours, then were divided between four groups: distilled water, a conventional 5,000 ppm F dentifrice, a 5,000 ppm F dentifrice with Microdent® and a 5,000 ppm F dentifrice containing TCP. Specimens cycled between four 2-minute treatments and one 4-hour acid challenge per day for 10 days, interspersed with immersion in artificial saliva.

Results: Remineralization and fluoride uptake from both the ControlRx and 5,000 ppm F with TCP dentifrice formulations were statistically superior to the conventional 5,000 ppm F dentifrice. The 5,000 ppm F dentifrice containing TCP exhibited greater rehardening than the unmodified 5,000 ppm F dentifrice with Microdent®.
Toothpaste
Tri-Calcium Phosphate (TCP)

Fluoride Availability of Professional Dentifrices
R.P. Rusin, F. Vang, P.R. Klaiber and A.M. Pfarrer, 3M ESPE Dental, St. Paul, MN, U.S.A.

Reference: J Dent Res 89 (Spec Iss B), 3226, 2010
(www.dentalresearch.org)

Aim of the Study: To compare the fluoride availability of five dentifrices, two of which contain calcium phosphate additives.

Methodology: Two dentifrices with calcium phosphate additives — a 5,000 ppm fluoride dentifrice with TCP-sodium lauryl sulfate (SLS) (CP5) and a 5,000 ppm fluoride dentifrice with calcium sodium phosphosilicate (CSP) (TR) — were compared with three dentifrices with no calcium phosphate — a 5,000 ppm fluoride dentifrice (PVP), a 5,000 ppm fluoride dentifrice, liquid gel (PB) and a conventional 5,000 ppm fluoride dentifrice (FX). Dentifrices were injected into beakers of deionized water under vigorous stirring. Five milliliters (ml) of 1,000 ppm fluoride was added to a 5-ml aliquot of slurry. Available fluoride in the beaker and fluoride concentration in the aliquot were measured before injection and at 2 and 6 minutes.

Results: At all times measured, mean available fluoride levels and percent of indicated fluoride for the TCP-SLS dentifrice and the three calcium phosphate-free dentifrices were statistically similar. TCP-SLS does not appear to inhibit fluoride availability as measured in this test, compared with dentifrices without calcium phosphate.

Fluoride availability of professional dentifrices

<table>
<thead>
<tr>
<th>Dentifrice</th>
<th>n</th>
<th>Calcium Phosphate Additive</th>
<th>Available fluoride at 2 min, ppm F/g paste (StDev)</th>
<th>Available fluoride at 6 min, ppm F/g paste (StDev)</th>
<th>Percent of indicated fluoride at 2 min, % (StDev)</th>
<th>Percent of indicated fluoride at 6 min, % (StDev)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CP5</td>
<td>5</td>
<td>TCP-SLS</td>
<td>3978 (171)*</td>
<td>4535 (171)*</td>
<td>79.6 (3.4)*</td>
<td>90.7 (3.4)*</td>
</tr>
<tr>
<td>PVP</td>
<td>5</td>
<td>none</td>
<td>4108 (307)*</td>
<td>4344 (225)*</td>
<td>82.2 (6.1)*</td>
<td>86.9 (4.5)*</td>
</tr>
<tr>
<td>PB</td>
<td>5</td>
<td>none</td>
<td>4287 (207)*</td>
<td>4496 (202)*</td>
<td>85.7 (4.1)*</td>
<td>89.9 (4.0)*</td>
</tr>
<tr>
<td>TR</td>
<td>5</td>
<td>CSP</td>
<td>1105 (102)*</td>
<td>1264 (77)*</td>
<td>22.1 (2.0)*</td>
<td>25.3 (1.5)*</td>
</tr>
<tr>
<td>FX</td>
<td>5</td>
<td>none</td>
<td>3856 (380)*</td>
<td>4222 (145)*</td>
<td>77.1 (7.6)*</td>
<td>84.4 (2.9)*</td>
</tr>
</tbody>
</table>

Mean available fluoride levels and percent of indicated fluoride for all but TR were statistically similar. Superscript letters denote groups that were not statistically different.
In Situ Remineralization of a New High-Fluoride Dentifrice

B.T. Amaechi, R. Karthikeyan, P.K. Mensinkai and K. Najibfard, University of Texas Health Science Center at San Antonio, San Antonio, TX, U.S.A.

Reference: Original research

Aim of the Study: To clinically evaluate the potential of a new high-fluoride dentifrice containing TCP to remineralize white-spot lesions and inhibit lesion formation.

Methodology: Participants wore two orthodontic appliances containing one sound enamel specimen and one carious lesion attached to mandibular molars for three 28-day phases. For each phase, participants brushed for 2 minutes twice daily with a 5,000 parts per million (ppm) fluoride dentifrice with TCP, a 5,000 ppm fluoride dentifrice, liquid gel or a fluoride-free dentifrice. After each phase, appliances were removed and specimens were analyzed.

Results: Both 5,000 ppm fluoride dentifrices inhibited softening of sound enamel and remineralized white-spot lesions; the fluoride-free dentifrice did neither. The TCP dentifrice produced the smallest lesion sizes; therefore, fluoride plus TCP may provide anti-caries benefits greater than fluoride alone.
Aim of the Study: To evaluate the in vitro occlusion of dentin tubules from fluoride- and fluoride-free hypersensitivity dentifrices, including two prototype sodium fluoride (NaF) dentifrices containing a functionalized TCP (fTCP) technology, using a remineralization/demineralization model.

Methodology: Bovine dentin specimens were demineralized and divided into six treatment groups: distilled water; a conventional 1,100 ppm fluoride dentifrice, 1,100 parts per million (ppm) fluoride; a dentifrice prototype, 1,100 ppm fluoride with functionalized TCP (fTCP); a dentifrice prototype, 5,000 ppm fluoride with fTCP; a calcium sodium phosphosilicate dentifrice; and a paste with CPP-ACP and 900 ppm fluoride. Groups were remineralized for 7 days and demineralized for 3 days.

Results: The two dentifrices containing the fTCP technology showed complete tubule occlusion with mineral layer formation, calcium sodium phosphosilicate dentifrice and paste with CPP-ACP and 900 ppm fluoride showed considerable occlusion and distilled water and conventional 1,100 ppm fluoride dentifrice showed virtually no occlusion.
In Vitro Assessments of Experimental NaF Dentifrices Containing a Prospective Calcium Phosphate Technology


Aim of the Study: To determine the fluoride dose response of experimental NaF dentifrices containing TCP and evaluate relative enamel and dentin abrasivity.

Methodology: Softened bovine enamel specimens were divided into treatment groups and treated for 10 days using a standardized pH cycling model. Following cycling, specimens were analyzed and subjected to 10 more days of pH cycling. Specimens were analyzed again, then placed in a 2-hour acid challenge, followed by an additional 16-hour acid challenge. The model allows not only an evaluation of remineralization potential but also an evaluation of the quality of mineral formed during remineralization by measuring its resistance to demineralization. Abrasivity of the dentifrice formulations was also evaluated using standardized testing with both dentin and enamel substrates.

Results: All dentifrice formulations exhibited acceptable enamel and dentin abrasivity although the dentifrice formulations with TCP and the formulation with CPP-ACP exhibited slightly lower dentin abrasivity than the 5,000 ppm fluoride dentifrice, liquid gel.

Surface microhardness values at each measurement point are summarized below. Following remineralization and acid challenges, the dentifrice containing 5,000 ppm F and TCP exhibited the greatest anticaries potential.
In Vitro Remineralization of White-Spot Enamel Lesions From NaF Dentifrices With and Without Calcium

R.L. Karlinsey, A.C. Mackey and G.K. Stookey, Indiana Nanotech, Indianapolis, Indiana, U.S.A.; A.M. Pfarrer, OMNI Preventive Care, West Palm Beach, FL, U.S.A.


Aim of the Study: To report on the remineralization of white-spot enamel lesions from five treatment groups.

Methodology: Bovine enamel specimens were softened in an acid solution, then were divided between five treatment groups: deionized water, a paste with casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) and 900 ppm fluoride, a 1,450 ppm fluoride dentifrice with calcium phosphate nano particles and protein, a 1,000 ppm fluoride unmodified dentifrice and a 1,000 ppm fluoride modified dentifrice with functionalized β-TCP (fTCP). Specimens cycled between four 2-minute treatments and one 4-hour acid challenge per day for 10 days, interspersed with immersion in artificial saliva.

Results: The 1,000 ppm fluoride dentifrice with fTCP showed mean Vickers hardness recoveries and fluoride uptakes higher than those of the paste with CPP-ACP and 900 ppm fluoride and the unmodified 1,000 ppm fluoride dentifrice and statistically similar to those of the 1,450 ppm fluoride dentifrice with calcium phosphate nano particles and protein. Incorporating fTCP into a 1,000 ppm fluoride dentifrice may boost anti-caries performance.
Aim of the Study: To use a well-established pH-cycling caries-simulation model to assess whether 5,000 parts per million (ppm) sodium fluoride (F) dentifrices with and without a functionalized β-TCP (fTCP) additive inhibit demineralization and/or promote remineralization.

Methodology: Bovine enamel samples cycled between two 1-minute treatments, a 6-hour acid challenge, and a 17-hour remineralization per day for 9 days. The dentifrice treatments included a 5,000 ppm fluoride dentifrice with TCP, a 5,000 ppm fluoride dentifrice, a positive control 1,100 ppm fluoride dentifrice and a 100 ppm fluoride negative control (diluted from a conventional 1,100 ppm fluoride dentifrice).

Results: The dentifrice containing fTCP did not interfere with fluoride, performed at least as well as the clinically proven 5,000 ppm fluoride dentifrice and appeared to exhibit the greatest protection against lesion progression.

The negative control showed the most relative mineral loss while the dentifrice with 5,000 ppm fluoride plus fTCP showed the least relative mineral loss.
Aim of the Study: To evaluate the demineralization and remineralization effects on enamel lesions after treatment with dentifrices containing fluoride and calcium phosphate (CaP) using a pH-cycling model *in vitro*.

Methodology: Teeth were demineralized, sectioned and divided into six treatment groups: a conventional 1,100 ppm fluoride dentifrice diluted to a 110 parts per million (ppm) fluoride control (CCPD), a paste with CPP-ACP and 900 ppm fluoride (MIPP), a 950 ppm fluoride dentifrice (CPTC), conventional 1,100 ppm fluoride dentifrice (CCPP), a 5,000 ppm fluoride dentifrice with TCP (CP5K) and a conventional 5,000 ppm fluoride dentifrice (PREV). Teeth sections cycled for 14 days between 2-minute treatments, 3-hour demineralization and artificial saliva, then were measured for lesion area and depth.

Results: After cycling, the low-fluoride group showed the most lesion progression, while the 5,000 ppm fluoride dentifrice with TCP and the conventional 5,000 ppm fluoride dentifrice showed the least progression and were not significantly different from each other.

The low-fluoride group (CCPD) showed the most lesion progression and the two 5,000 ppm fluoride groups (PREV, CP5K) showed the least.
Remineralization Potential of 5,000 ppm Fluoride Dentifrices Evaluated in a pH Cycling Model

R.L. Karlinsey, A.C. Mackey and E.R. Walker, Indiana Nanotech, Indianapolis, IN, U.S.A.; B.T. Amaechi, R. Karthikeyan and K. Najibfard, University of Texas Health Science Center at San Antonio, TX, U.S.A.; A.M. Pfarrer, 3M ESPE Dental, St. Paul, MN, U.S.A.


Aim of the Study: To determine the anti-caries potential of two dentifrices, one with fast dispersion for improved enamel fluoride uptake and one containing an innovative TCP system for enhanced remineralization, in an in vitro pH cycling model.

Methodology: Following white-spot lesion formation, enamel specimens were divided into three treatment groups: a fluoride-free dentifrice, a 5,000 ppm fluoride dentifrice, liquid gel and a 5,000 ppm fluoride dentifrice with TCP. The groups cycled between four 1-minute treatment periods and one 4-hour acid challenge per day for 10 days, interspersed with immersion in artificial saliva.

Results: For all analyses, the dentifrice containing fTCP imparted superior remineralization at both the enamel surface and within the subsurface lesion and may provide more significant anti-caries benefits than fluoride-only and fluoride-free dentifrices.

Proving the remineralization did not happen only at the surface but happened subsurface too
Surfactant-Modified β-TCP: Structure, Properties and *In Vitro* Remineralization of Subsurface Enamel Lesions

R.L. Karlinsey, A.C. Mackey, E.R. Walker and K.E. Frederick, Indiana Nanotech, Indianapolis, IN, U.S.A.


**Aim of the Study:** To evaluate the efficacy of TCP-sodium lauryl sulfate (SLS) plus 5,000 parts per million (ppm) fluoride relative to 5,000 ppm fluoride alone in remineralizing weakened enamel emulating early caries formation.

**Methodology:** Bovine enamel specimens cycled between two 2-minute treatments in either distilled water, 5,000 ppm fluoride solution or 5,000 fluoride solution plus 800 ppm TCP-SLS, one 4-hour acid challenge and two more 2-minute treatments per day for 5 days, interspersed with immersion in artificial saliva.

**Results:** TCP-SLS plus 5,000 ppm fluoride significantly boosted remineralization of subsurface enamel lesions, with microhardness values increasing up to 30 percent greater than fluoride alone.

**Optical images of subsurface lesion and sound enamel cross-sections after 5 days of pH cycling**

Optical images showing the subsurface lesion and sound enamel cross-sections after 5 days of cycling when treated with (A) distilled water (negative control); (B) 5,000 ppm fluoride (positive control); and (C) 5,000 ppm fluoride plus 800 ppm TCP-SLS. The bulk of the lesion area is indicated by the white bars and arrow.
In Vitro Remineralization of Human and Bovine White-Spot Enamel Lesions by NaF Dentifrices: A Pilot Study

R.L. Karlinsey, A.C. Mackey, T.J. Walker, K.E. Frederick, D.D. Blanken, S.M. Flaig and E.R. Walker Indiana Nanotech, Indianapolis, IN, USA.

This project was supported by an award (R43DE020998) from the National Institutes of Health’s Office of the Director and National Institute of Dental and Craniofacial Research.


Aim of the Study: To evaluate the in vitro remineralization effects of four dentifrice systems using microhardness and fluoride uptake analyses.

Methodology: In vitro testing for the potential remineralization of the white-spot lesions in bovine and human enamel was performed using a 10-day pH cycling model. The study involved the following NaF silica-based dentifrices: 1) placebo (0 ppm F), 2) 500 ppm F, 3) 1,150 ppm F and 4) 500 ppm F plus functionalized tri-calcium phosphate (fTCP). Each day consisted of 4 two-minute treatments, one four-hour acid challenge (pH = 5.0) and immersion in artificial saliva (pH = 7.0) between these events. After cycling, specimens were analyzed for surface microhardness (SMH), enamel fluoride uptake (EFU) and cross-sectional microhardness (CSM). Statistical analyses revealed significant differences (ANOVA, least significant difference (LSD), p<0.05) among the four groups, with the placebo and 500 ppm F dentifrices providing significantly less remineralization relative to the 1,150 ppm F and 500 ppm F plus fTCP dentifrices.
Results: Notably, while cross-sectional microhardness (CSM) measurements for both enamel types generated similar profiles for the four groups, surface microhardness (SMH) and enamel fluoride uptake (EFU) revealed human enamel was more sensitive to the 500 ppm F dentifrice groups compared to bovine enamel. This apparent sensitivity may be due to the inherent structural differences between the two substrates.
Varnish

Tri-calcium phosphate (TCP), present in some 3M ESPE products, is an intelligent material for use in varnish that delivers protection to the teeth and helps relieve sensitivity. The newest formulations of Vanish™ 5% Sodium Fluoride White Varnish and Clinpro™ White Varnish include an innovative TCP technology available exclusively from 3M ESPE that helps deliver calcium, fluoride and phosphate — all key ingredients for building strong teeth.

This chapter summarizes two studies that demonstrate the potential clinical advantages of TCP in varnish.
New Varnish Releases Fluoride, Calcium and Phosphorous *In Vitro*


**Reference:** J Dent Res 89 (Spec Iss B), 1215, 2010 (www.dentalresearch.org)

**Aim of the Study:** To determine how much calcium, fluoride and phosphorous are released from a white varnish containing a functionalized TCP (fTCP) compared with a 5% sodium fluoride (NaF) white varnish with TCP.

**Methodology:** Varnishes were applied to frosted glass slides and immersed into separate 25 milliliters of distilled water at 37°C. Calcium, fluoride and phosphorous concentrations were measured at 1, 4, 8 and 24 hours.

**Results:** The white varnish with TCP released calcium, fluoride and phosphorous, while the 5% sodium fluoride white varnish with TCP released only fluoride. The fTCP in the next-generation varnish did not inhibit the amount of fluoride released and enabled the release of calcium and phosphorous from the varnish *in vitro*.

**Cumulative release (mg/cm²) varnish with TCP, 5% NaF white varnish with TCP and a control slide after 24 hours**

<table>
<thead>
<tr>
<th>Material</th>
<th>n</th>
<th>[Ca] @ 24 hr Mean, StDev</th>
<th>[P] @ 24 hr Mean, StDev</th>
<th>[F-] @ 24 hr Mean, StDev</th>
</tr>
</thead>
<tbody>
<tr>
<td>Varnish with TCP</td>
<td>5</td>
<td>0.8072, 0.15666&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.8215, 0.2472&lt;sup&gt;e&lt;/sup&gt;</td>
<td>40.2, 4.1&lt;sup&gt;e&lt;/sup&gt;</td>
</tr>
<tr>
<td>5% NaF Varnish with TCP</td>
<td>5</td>
<td>0.1331, 0.0360&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.0646, 0.0224&lt;sup&gt;d&lt;/sup&gt;</td>
<td>36.8, 1.8&lt;sup&gt;e&lt;/sup&gt;</td>
</tr>
<tr>
<td>Control</td>
<td>5</td>
<td>0.0000, 0&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.0562, 0.0186&lt;sup&gt;d&lt;/sup&gt;</td>
<td>0.3, 0.1&lt;sup&gt;f&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

Varnish with TCP released calcium, fluoride and phosphorous, the 5% sodium fluoride white varnish with TCP released only fluoride and the control slide had no release. Identical subscript letters indicate released concentrations that are statically not different.
Aim of the Study: To compare the remineralization and acid resistance effects provided by a 5% sodium fluoride (NaF) white varnish with TCP, a fluoride-free placebo, an experimental varnish with TCP and no treatment.

Methodology: Bovine incisor enamel samples with lesions were tested for baseline surface microhardness. They received one of the four varnish treatments, then were immersed in saliva, rinsed and characterized by microhardness. Next, samples underwent a 24-hour acid challenge, then were rinsed and characterized again by microhardness.

Results: Lesions treated with the 5% sodium fluoride white varnish with TCP and varnish with TCP exhibited a greater surface microhardness gain and better resistance to acid than the placebo and no treatment. Varnish with TCP delivered the best results.

Varnish with TCP and the 5% NaF varnish with TCP showed greater surface microhardness gain and better resistance to acid than the fluoride-free placebo or no treatment.
Rinse

The chemistry of functionalized tri-calcium phosphate (TCP) can be tailored to a specific modality, such as mouthrinse, to provide short- or long-term mineral delivery and fluoride compatibility.

This chapter summarizes studies that demonstrate the potential clinical advantages of TCP in rinse.
Remineralization of Eroded Enamel by a NaF Rinse Containing a Novel Calcium Phosphate Agent in an *In Situ* Model: A Pilot Study

B.T. Amaechi, R. Karthikeyan, P.K. Mensinkai and K. Najibfard, University of Texas Health Science Center at San Antonio, San Antonio, TX, U.S.A.; A.C. Mackey, R.L. Karlinsey, Indiana Nanotech, Indianapolis, IN, U.S.A.


**Aim of the Study:** To evaluate the remineralization potential of 225 parts per million fluoride (NaF) rinses with and without functionalized β-TCP on eroded enamel in a double-blind crossover *in situ* model.

**Methodology:** Bracket-mounted enamel blocks were bonded to a mandibular molar in 20 participants who were then assigned to one of three treatments lasting 28 days: no rinse (saliva only) and 225 ppm fluoride rinse with and without TCP. The treatments were administered twice a day following one-minute brushing with a fluoride-free paste. Each cohort repeated this 28-day process using the remaining two treatments, with each phase separated by week-long washout periods with a fluoride-free dentifrice. Enamel blocks were then analyzed using transverse microradiography.

**Results:** All three treatments led to remineralization; however, the fluoride plus TCP rinse led to significantly more remineralization relative to saliva and the fluoride-only rinse.

**Photograph of the *in situ* appliance**
**In Vitro** Remineralization of White-Spot Lesions by Fluoride Rinses With and Without Functionalized Tricalcium Phosphate


This study was supported by a National Institute of Dental and Craniofacial Research grant DE01876-01.

**Reference:** Caries Res 44(Abstr 23):180, 2010

**Aim of the Study:** To determine the feasibility of combining a functionalized TCP system with a 0.05 percent NaF aqueous rinse formulation as a means of enhancing remineralization of early caries lesions *in vitro*.

**Methodology:** Following white-spot formation, bovine enamel specimens were grouped into three treatments (water, 225 ppm fluoride or 225 ppm fluoride plus TCP), were evaluated in a six-day pH cycling regimen and were analyzed for surface and cross-sectional microhardness. Additionally, separate enamel specimens containing white-spot lesions were analyzed for enamel fluoride uptake after a single 30-minute exposure.

**Results:** The 225 ppm fluoride plus TCP provided significantly greater surface and subsurface remineralization, as well as enamel fluoride uptake, relative to the water and fluoride-only rinses.

**Change in surface microhardness [$\Delta$ VHN], change in lesion size [$\Delta$ Z (vol. %•µm)] and fluoride uptake into demineralized enamel [EFU (µm F/cm^3)]**

<table>
<thead>
<tr>
<th>Group</th>
<th>$\Delta$ VHN ± SEM</th>
<th>$\Delta$ Z (vol.%•µm) ± SEM</th>
<th>EFU (µm F/cm^3) ± SEM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Distilled Water</td>
<td>-1.2 ± 0.9a</td>
<td>11,595 ± 480b</td>
<td>44.9 ± 4.4a</td>
</tr>
<tr>
<td>225 ppm F</td>
<td>21.4 ± 1.3b</td>
<td>6,933 ± 509a</td>
<td>1,056.5 ± 58.0b</td>
</tr>
<tr>
<td>225 ppm F + TCP</td>
<td>32.8 ± 2.8c</td>
<td>5,637 ± 530b</td>
<td>1,324.8 ± 81.6c</td>
</tr>
</tbody>
</table>

Stats were performed using one-way ANOVA, SNK, p<0.05 and a<b<c.
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